WorldApiExpo
International Apitherapy and Apiculture Exhibition
20 - 29 May 2021 | Digicon Online Platform

1ST JOINT INTERNATIONAL APITHERAPY CONGRESS

1st JOINT INTERNATIONAL APITHERAPY CONGRESS PROCEEDINGS BOOK

ONLINE, 20-26 MAY 2021

ISBN: 978-605-4123-57-5

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1st JOINT INTERNATIONAL APITHERAPY CONGRESS PROCEEDINGS BOOK

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Editors,

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Published: 03.09.2021

ISBN: 978-605-4123-57-5

EDITORS' NOTE

The 1st Joint International Apitherapy Congress was organized online successfully in Turkish, English and Spanish languages. We are very happy that various health science-related fields attended the congress. By this event, the distinguished and respected scientists came together to exchange ideas, develop and implement new research and joint projects in apitherapy.

There were 150 speakers from 30 different countries. We would like to thank all participants and supporters. Hope to see you at our next congress.

Best wishes,

Asst. Prof. Ali Timuçin Atayoğlu (Turkey), International Federation of Apitherapy
Dr. Andres Castillo Montenegro (Ecuador), Latin-American Federation of Apitherapy
Dr. Stefan Stangaciu (Romania), International Federation of Apitherapy
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SCIENTIFIC PROGRAM

Day 1 - 20.05.2021

10:00-11:15*	**World Bee's Day Celebration and WorldApiExpo Opening Ceremony** Mr. Beşir Kemal Şahin, *Ekspotürk, Chairman of the Board* Asst. Prof. Ali Timuçin Atayoğlu, *President of the International Federation of Apitherapy (IFA)* Dr. Stefan Stangaciu *Secretary General of the International Federation of Apitherapy,* Dr. Andres Castillo Montenegro, *President of the Latinamerican Federation of Apitherapy (FELAPI)* Mr. James Townsend Fearnley, *Director of the International Propolis Research Group (IPRG)* Dr. Cristina Mateescu, *President of Scientific Commission on Apitherapy in Apimondia* Asst. Prof. Mahmut Tokaç, *Director of Traditonal & Complementary Medicine Ethical Committee in Istanbul Medipol University* Mr. Özen Altıparmak, *Chairman of the Board of Altıparmak Gıda, the main sponsor of the Congress* Dr. Yalçın Sezer, *Chairman of the Board of the Agricultural Honey Producers Society* Mr. Ziya Şahin, *Chairman of the Board of Turkish Beekeepers Association* Mrs. Ayşe Ayşin Işıkgece, *Deputy Minister of Agriculture and Forestry, Republic of Turkiye* Prof. Sabahattin Aydın, *Deputy Minister of Health, Republic of Turkiye*
11:20-11:40*	**Memorial Ceremony for Prof. Muhsin Doğaroğlu** Asst. Prof. Ali Timuçin Atayoğlu, *President of the International Apitherapy Federation (IFA)* Agr. Eng. Mustafa Kösoğlu, *Director of Beekeeping Department, Agean Agricultural Research Institute* Dr. Bahri Işık, *Consultant in the Directorate of Agriculture and Forestry of Beykoz District* Prof. Banu Yücel, *Dean of Agriculture Faculty of Ege University* Dr. Mehmet Zafer Kalaycı, *Director of Traditional, Complementary and Functional Medicine Department of Health Ministry, Republic of Turkiye*
11:45-13:30*	**"If There are Honeybees There is Life" Painting Competition Award Ceremony** **Moderator:** Celal Toprak, *President of Food Safety Platform* Assoc. Prof. Meral Kekeçoğlu, Director of *Beekeeping Research, Development and Application Center of Düzce University* MSc. Eng. Aslı Elif Tanuğur Samancı, B*ee'O Propolis Founding Partner* Prof. Nigâr Demircan Çakar, *Rector of Düzce University*
07:30-08:00**	**FELAPI Session Opening Ceremony** Asst. Prof. Ali Timuçin Atayoğlu, *President of the International Federation of Apitherapy (IFA)* Dr. Stefan Stangaciu, *Secretary General of International Federation of Apitherapy (IFA)* N.D. José Cabrera, *Vice-President of the Latinamerican Federation of Apitherapy (FELAPI)* Dr. Andres Castillo Montenegro, *President of the Latinamerican Federation of Apitherapy (FELAPI)*
08:00-08:45**	**Panel 1** **Presentation,** Dra. Maria Eugenia Sierra (Colombia) **The History of Apitherapy in Cuba,** Dr. Moises Asis (USA) **Questions,** Dr. Andrés Castillo (Ecuador)
08:45-09:30**	**Panel 2** **Presentation,** N.D. José Cabrera (Ecuador) **The History of Apitherapy in Brazil,** Jhonatan José Filisberto (Brasil) **Questions,** Dr. Andrés Castillo (Ecuador)
09:30-10:15**	**Panel 3** **Presentation,** Dra. Maria Eugenia Sierra (Colombia) **Apitherapy, the Rediscovery of a Natural Therapy that Heals without Damaging,** Trinidad Terrazas Gastélum (México) **Questions,** Dr. Andrés Castillo (Ecuador)
10:30-11:15**	**Panel 4** **Presentation,** N.D. José Cabrera (Ecuador) **Apitherapy and Live Food,** M.D. Jose Vásquez (Brasil) **Questions,** Dr. Andrés Castillo (Ecuador)

11:15-12:00**	**Panel 5** **Presentation,** Dra. Maria Eugenia Sierra (Colombia) **The Apitherapy of the future,** Dr. David García (Colombia) **Questions,** Dr. Andrés Castillo (Ecuador)
13:15-14:00**	**Panel 6** **Presentation,** N.D. José Cabrera (Ecuador) **Curative Crisis in Apitherapy,** Lcda. Emma Vásquez Fuentes (México) **Questions,** Dr. Andrés Castillo (Ecuador)
14:00-14:45**	**Panel 7** **Presentation,** Dra. Maria Eugenia Sierra (Colombia) **The therapeutic diversity of apitherapy and bee derivatives in Brazil,** Dr. Leonardo Sarmento (Brasil) **Questions,** Dr. Andrés Castillo (Ecuador)
Day 2 - 21.05.2021	
10:00-10:45*	**Special Session** **Moderator:** Asst. Prof. Ali Timuçin Atayoğlu (Turkey), Dr. Andres Castillo Montenegro (Ecuador), Dr. Cristina Mateescu (Romania) and Prof. Li Wan-yao (China) **Prof. Fang Zhu,** Founder President of the Apicultural Science Association of China
11:00-11:45*	**Apitherapy in the World: Part 1** **Moderator:** Dr. Stefan Stangaciu (Romania) **Apitherapy in Romania: Present Situation and Perspectives,** Dr. Stefan Stangaciu (Romania) **Apitherapy in Bosnia and Herzegovina,** Prof. Midhad Jasic (Bosnia and Herzegovina) **Apitherapy in Hungary,** Dr. János Körmendy-Rácz (Hungary)
12:00-12:45*	**Apitherapy in the World: Part 2** **Moderator:** Asst. Prof. Ali Timuçin Atayoğlu (Turkey) and Dr. Cristina Mateescu (Romania) **Apitherapy in China,** Prof. Li Wan-yao (China) **Apitherapy in Slovenia,** Dr. Andreja Kandolf Borovšak (Slovenia) **Apitherapy in Ecuador,** Dr. Andres Castillo Montenegro (Ecuador)
14:00-14:45*	**Apitherapy in the World: Part 3** **Moderator:** Mr. James Townsend Fearnley (United Kingdom) **The Honeybee and the Human Heart,** Mr. James Townsend Fearnley (United Kingdom) **Apitherapy in India,** Mr. Pushpendra Singh Bhandari (India) **Apitherapy in USA**, Dr. Chris Adam Kleronomos (USA)
15:00-15:45*	**Apitherapy in the World: Part 4** **Moderator:** Dr. János Körmendy-Rácz (Hungary) **Apitherapy in Iran,** Mr. Javad Asgharpour (Iran) **Apitherapy in Morocco,** Prof. Badiaa Lyoussi (Morocco) **Resistance of The Waste Products of The Wax Moth Larva and COVID-19,** Mr. Mykola Heveliuk and Assoc. Prof. Tetiana H. Chukhrai (Ukraine)
16:00-16:45*	**Medicinal Bee-Plants & Medicinal Beekeeping** **Moderator:** Prof. Kadriye Sorkun (Turkey) and Asst. Prof. Devrim Oskay (Turkey) **Sustainability in Bee Products Production**, Agr. Eng. Mustafa Kösoğlu (Turkey) **Principles of Medicinal Beekeeping,** Dr. Stefan Stangaciu (Romania) **Medicinal Bee Plants,** Prof. Kadriye Sorkun (Turkey)
17:00-17:45*	**Ethics and Legislation in Apitherapy** **Moderator:** Prof. Hanefi Özbek (Turkey) **Status of Bee Products: Approved or Not?,** Dr. Cristina Mateescu (Romania) **Regulations on Apitherapy Products,** Ph. Fikriye Handan Öztunca (Turkey) **Ethical and Legal Issues in Apitherapy,** Asst. Prof. Mahmut Tokaç (Turkey)
07:30-08:00**	**Connection, WorldApiExpo**

	Mission of FELAPI, N.D. José Cabrera (Ecuador) **Objectives for FELAPI,** Dr. Andrés Castillo (Ecuador)
08:00-08:45**	**Panel 1** **Presentation,** Dra. Maria Eugenia Sierra (Colombia) **The world of Injectable Apitoxin,** Dr. Roberto Grand (Argentina) **Questions,** Dr. Andrés Castillo (Ecuador)
08:45-09:30**	**Panel 2** **Presentation,** N.D. José Cabrera (Ecuador) **Pollen and Honey as part of the treatment in diseases of the nervous system,** MVZ. Tisbe Lidia Dominguez (México) **Questions,** Dr. Andrés Castillo (Ecuador)
09:30-10:15**	**Panel 3** **Presentation,** Dra. Maria Eugenia Sierra (Colombia) **Immunosuppressive patients and apitoxynotherapy,** Bio. Agro. Hugo Romano Galicia (México) **Questions,** Dr. Andrés Castillo (Ecuador)
10:30-11:15**	**Panel 4** **Presentation,** N.D. José Cabrera (Ecuador) **Red Propolis: History, biological activities of its main phenolic compounds and Apitherapy,** M.Sc. Edivaldo Ferreira Pacheco (Brasil) **Questions,** Dr. Andrés Castillo (Ecuador)
11:15-12:00**	**Panel 5** **Presentation,** Dra. Maria Eugenia Sierra (Colombia) **The Actuation of Propolis Against the Coronavirus,** Dr. Mikhael Márques (Brasil) **Questions,** Dr. Andrés Castillo (Ecuador)
13:15-14:00**	**Panel 6** **Presentation,** N.D. José Cabrera (Ecuador) **Treatment of Amyotrophic Lateral Sclerosis (ALS) with Apitherapy and Natural Medicine,** Lic. Enf. Angélica Delgado (México) **Questions,** Dr. Andrés Castillo (Ecuador)
14:00-14:45**	**Panel 7** **Presentation,** Dra. Maria Eugenia Sierra (Colombia) **Breathing exercise with propolis,** Sandra Mercado (Ecuador) **Questions,** Dr. Andrés Castillo (Ecuador)
Day 3 - 22.05.2021	
09:00-09:45*	**Special Session on Propolis (Balparmak)** **Moderator:** Prof. Sibel Silici (Turkey) **The Source of Propolis: A Critical Point for its Health Benefits,** Dr. Etil Güzelmeriç (Turkey) **Determination of Bioactive Components of Commercial Propolis Samples Sold in the Market,** Prof. Osman Sağdıç (Turkey)
10:00-10:45*	**Propolis in Apitherapy** **Moderator:** Prof. Vassya Bankova (Bulgaria) **A Comparison of Commercial Propolis Extracts in Terms of Analysis Results,** Prof. Sevgi Kolaylı (Turkey) **Quantitative Evaluation of Marker Components of Several Propolis Samples Obtained from Black Sea Region (Turkey),** Dr. Etil Güzelmeriç (Turkey) **What Should Be the Ideal Rate for Ethanolic Propolis Extraction?,** Yakup Kara, MSc (Turkey)
11:00-11:45*	**Honey in Apitherapy** **Moderator:** Prof. Mehmet Emin Duru (Turkey) **Characteristics of Honey for Apitherapy,** Prof. Mehmet Emin Duru (Turkey) **Impact of Pasteurization Process on Hydroxymethylfurfural (HMF) Amount and Diastase Activity of Honey,** Agr. Eng. Gökhan Akdeniz (Turkey)

	Ivy Honey with Physicochemical and Bioactive Properties, Lec. Gülşah Okumuş Yükünç (Turkey)
12:00-12:45*	**Bee Venom in Apitherapy** **Moderator:** Asst. Prof. Ali Timuçin Atayoğlu (Turkey) **Effects of Bee Venom and Anatolian Propolis on Human Breast and Over Cancer Cells,** Dr. Feyzi Doğru (Turkey) **The Factors Effecting Therapeutic Value of Honeybee Venom,** Assoc. Prof. Meral Kekeçoğlu (Turkey) **Qualities of the Bee Venom in Apitherapy,** Assoc. Prof. Rahşan İvgin Tunca (Turkey)
14:00-14:45*	**Royal Jelly in Apitherapy** **Moderator:** Prof. Nuray Şahinler (Turkey) **Composition of Royal Jelly and Uses in Human Health,** Prof. Nuray Şahinler (Turkey) **Nutritional element, bioactivity and amino acid analysis of lyophilized royal jelly,** Prof. Sibel Silici (Turkey) **Effect of Different Feeding Methods on Quality and Biochemical Characteristics of Royal Jelly,** İlknur Coşkun, MSc (Turkey)
15:00-15:45*	**Apilarnil in Apitherapy** **Moderator:** Prof. Banu Yücel (Turkey) **Apilarnil (drone larvae) - Harvesting, Utilization, Clinical cases,** Alina Varadi and Dr. Mirela Strant (Romania) **Apilarnil – An integrative Component for post Cancer Treatment,** Dr. Thomas Gloger (Germany) **A Natural Androgen Source: Apilarnil (Drone Larvae),** Lec. Gülsüm Merve Boyracı (Turkey)
16:00-16:45*	**Pollen & Bee Bread in Apitherapy** **Moderator:** Prof. Kadriye Sorgun (Turkey) and Prof. Mehmet Rüştü Karaman (Turkey) **Anatolian Bee Bread: Probiotic and Antioxidant Properties,** MSc. Eng. Aslı Elif Tanuğur Samancı (Turkey) **Color Separation, Physicochemical and Functional Properties of Bee Pollens Collected in Turkey,** Tuğçe Daştan, MSc (Turkey) **The Process of Pollen Transformation into the Bee Bread: Microbiology of Bee Bread,** Lec. Atiye Değirmenci (Turkey)
17:00-17:45*	**Api-air in Apitherapy** **Moderator:** Dr. Stefan Stangaciu (Romania) **Beehive Air Therapy "Healing with Bees",** Beate McKenzie (UK) and Jürgen Schmiedgen (Germany) **Beehive Air Therapy: From Identifying Chemical Compounds to Evidence-Based Clinical Practice,** Tiago Guardia de Souza e Silva, PhD (Brasil) **Experiences of the Hungarian Bee-hive air applications,** Dr. János Körmendy-Rácz (Hungary)
07:30-08:00**	**Connection,** WorldApiExpo **Upcoming FELAPI Events,** N.D. José Cabrera (Ecuador) **Highlights of FELAPI,** Dr. Andrés Castillo (Ecuador)
08:00-08:45**	**Panel 1** **Presentation,** Dra. Maria Eugenia Sierra (Colombia) **Heavenly Pharmacy: Therapeutic Actions of Hive Products,** SaLcdo. Enrique Manuel Rivera (México) **Questions,** Dr. Andrés Castillo (Ecuador)
08:45-09:30**	**Panel 2** **Presentation,** N.D. José Cabrera (Ecuador) **Bee venom in the Treatment of Chronic Ailments,** José S. Brandt (Brasil) **Questions,** Dr. Andrés Castillo (Ecuador)
09:30-10:15**	**Panel 3** **Presentation,** Dra. Maria Eugenia Sierra (Colombia) **Determination of The Antibiotic In Vitro Propolis Ethanolic Extract on *Staphylococcus Aureus* and *Escherichia Coli* This in Bovine Puerperal Metritis,** Dr. Luis Galarza (Ecuador) **Questions,** Dr. Andrés Castillo (Ecuador)
10:30-11:15**	**Panel 4** **Presentation,** N.D. José Cabrera (Ecuador) **Scientific Apitherapy and Traditional Chinese Medicine in Clinical Veterinary Medicine: Integrative Approach to Complex Pathologies. Clinical Cases.,** Dra. María López Pazos (Chile) **Questions,** Dr. Andrés Castillo (Ecuador)

11:15-12:00**	**Panel 5** **Presentation,** Dra. Maria Eugenia Sierra (Colombia) **Apitherapy And Intestinal Permeability and Its Relationship with Autoimmune Diseases,** Pamela Rubí Cruz Mendiola (México) **Questions,** Dr. Andrés Castillo (Ecuador)
13:15-14:00**	**Panel 6** **Presentation,** N.D. José Cabrera (Ecuador) **Use of Apitoxin As an Adjunct in Treatment of Anti-Inflammatory and Immunological Therapy,** Josiane Rossi Engelmann (Brasil) **Questions,** Dr. Andrés Castillo (Ecuador)
14:40-14:45**	**Panel 7** **Presentation,** Dra. Maria Eugenia Sierra (Colombia) **Use of Prevention and Treatment Techniques for Hypersensitivity and Allergy to Bee Poison,** N.D. Bryan Navarrete (Ecuador) **Questions,** Dr. Andrés Castillo (Ecuador)
14:45-15:30**	**Panel 8** **Presentation,** N.D. José Cabrera (Ecuador) **Use of apitoxin with platelet-rich plasma in patients diagnosed with arthritis and osteoarthritis,** N.D. David Yaulema (Ecuador) **Questions,** Dr. Andrés Castillo (Ecuador)
Day 4 - 23.05.2021	
10:00-10:45*	**Safety & Quality of Apitherapy Products** **Moderator:** Etienne Bruneau (Belgium) and Otilia Bobis, PhD (Romania) **Authenticity, Bioactivity and Safety of Bee Products,** Assoc. Prof. Aslı Özkök (Turkey) **Food Safety in Apitherapy Products,** Prof. Nevzat Artık (Turkey) **Authenticity of Propolis Products from The World Market,** Prof. Esra Çapanoğlu Güven (Turkey) **The Effect of Autoclave Sterilization on Microbial Decontamination and Bioactive Properties of Bee Pollen,** Lec. Atiye Değirmenci (Turkey)
11:00-11:45*	**Bio-pharmacology of Apitherapy Products: Part 1** **Moderator:** Prof. Badiaa Lyoussi (Morocco) **Physicochemical and biological functionalities of bee products,** Prof. Badiaa Lyoussi (Morocco) **Chemical Compositions, Cytotoxic, Antioxidant and Antiviral Effects of Propolis Samples from Different Geographical Regions of Anatolia,** Prof. Banu Yücel (Turkey) **Scientific Studies of APHIS Laboratory on Romanian Bee Products in High Visibility Journals,** Otilia Bobis, PhD (Romania)
12:00-12:45*	**Bio-pharmacology of Apitherapy Products: Part 2** **Moderator:** Prof. Ertuğrul Kaya (Turkey) **The Concept of Antioxidant Pro-oxidant in Honeybee Products,** Prof. Abdurrahim Koçyiğit (Turkey) **Antimicrobial properties and bio-pharmacological effects of apitherapy products,** Dr. Nisa Sipahi (Turkey)
14:00-14:45*	**Prevention & treatment of complications in Apitherapy** **Moderator:** Prof. Hasan Hüseyin Oruç (Turkey) **Treatment of anaphylactic shocks,** Dr. Kaan Yusufoğlu (Turkey) **Adverse Effects of Honeybee Products,** Prof. Hasan Hüseyin Oruç (Turkey) **Grayanotoxin (GTX) Determination in Honeybee Venom and the Risks of Using it in Apitherapy,** Assoc. Prof. Meral Kekeçoğlu (Turkey)
15:00-15:45*	**In-Vivo Trials in Apitherapy** **Moderator:** Asst. Prof. Mustafa Ünal (Turkey) **Preclinical Studies in Apitherapy**, Asst. Prof. Mustafa Ünal (Turkey) **The Effect of Olive Oil-Based Propolis on Biochemical Parameters in Healthy Volunteers:** A Clinical Study, Prof. Sibel Silici (Turkey) **Effect of Short and Long-Term Use of Commercial Propolis Extracts on Liver Enzymes in Rats,** Olgay Kaan Tekin, PhD (Turkey)

	Effects of Apitherapy on Th1 Th2 Balance in Rats with Type II Collagen-induced Arthritis, Dr. Yingfang Zhou (China)
16:00-16:45*	**Apitherapy in Veterinary Medicine** **Moderator:** Prof. Levent Aydın (Turkey) and Assoc. Prof. Mustafa Necati Muz (Turkey) **Importance of Bee Health in Apitherapy From Veterinary Perspective,** Prof. Levent Aydın (Turkey) **Using Facilities of Propolis in Cattle Breeding: Preventing Neonatal Diarrhea and Promoting Growth of Calves**, Prof. Banu Yücel (Turkey) **Complex Pathologies in Animals. Approach to Integrative Veterinary Medicine, with emphasis on Scientific Apitherapy and Traditional Chinese Medicine,** Dra. María Alejandra López Pazos (Chile)
17:00-17:45*	**Special Session Propolis Extraction (Balparmak)** **Propylene glycol (propolis extraction solvent) danger in pregnant and their babies,** Prof. Sibel Silici (Turkey)
07:50-08:00**	**Connection,** WorldApiExpo
08:00-08:45**	**Panel 1** **Presentation,** Dra. Maria Eugenia Sierra (Colombia) **Bioactive compounds of the Brazilian propolis and its mechanisms of action in cell,** Prof. Niraldo Paulino (Brasil) **Questions,** Dr. Andrés Castillo (Ecuador)
08:45-09:30**	**Panel 2** **Presentation,** N.D. José Cabrera (Ecuador) **Bee venom, Pain memory and Tissue degeneration: Basic clinical correlation,** Dr. Andrés Jagua Gualdron (Colombia) **Questions,** Dr. Andrés Castillo (Ecuador)
09:45-10:30**	**Panel 3** **Presentation,** Dra. Maria Eugenia Sierra (Colombia) **From the Hive to the Office: Use of Propolis in Dentistry,** Dr. Rafael Felitti (Uruguay) **Questions,** Dr. Andrés Castillo (Ecuador)
10:30-11:15**	**Panel 4** **Presentation,** N.D. José Cabrera (Ecuador) **Impact of Nutritional Genomics and Apitherapy on Healthy and Pathological Aging,** Dr. Roger Fernandez (Bolivia) **Questions,** Dr. Andrés Castillo (Ecuador)
11:15-12:00**	**Panel 5** **Presentation,** Dra. Maria Eugenia Sierra (Colombia) **Injectable Apitoxin in Oncology,** Dr. MVZ. Jorge Lucomsky (Argentina) **Questions,** Dr. Andrés Castillo (Ecuador)
13:15-14:00**	**Panel 6** **Presentation,** N.D. José Cabrera (Ecuador) **Diabetes: Non-infectious Pandemic of the modern era: Approach and treatment with apitoxin,** Dra. Laura Inés Chiaramello (Uruguay) **Questions,** Dr. Andrés Castillo (Ecuador)
14:00-14:45**	**Panel 7** **Presentation,** Dra. Maria Eugenia Sierra (Colombia) **Optimal Use and Applications of Apitherapy Protocols Based on Statistical and Ethical Evidence (ABEE),** Dr. Andrés Castillo Montenegro (Ecuador) **Questions,** Dr. Andrés Castillo (Ecuador)
14:45-15:30**	**Panel 8** **Presentation,** N.D. José Cabrera (Ecuador) **Dissemination of Microparticles of Propolis and Essential Oils for the Treatment and Prevention of Respiratory Infections,** Dra. Luciana Ghersi Gálvez (Perú) **Questions,** Dr. Andrés Castillo (Ecuador)
15:45-16:30**	**Panel 9**

	Presentation, Dra. Maria Eugenia Sierra (Colombia) **A Decade of Research on Mexican propolis,** Dr. Tonatiuh Cruz (México) **Questions,** Dr. Andrés Castillo (Ecuador)
16:30-17:15**	**Panel 10** **Presentation,** N.D. José Cabrera (Ecuador) **Apitherapy applied in Aesthetics (aesthetic api): Skin and Acne,** Dra. Maria Eugenia Sierra (Colombia) **Questions,** Dr. Andrés Castillo (Ecuador)

Day 5 - 24.05.2021

09:00-09:45*	**Special Session (Bee'O Propolis)** **Detection of adulteration and off-label expressions in commercial propolis extracts. What should be the legal regulations on this problem?** Prof. Sevgi Kolaylı (Turkey) and MSc. Eng. Aslı Elif Tanuğur Samancı (Turkey)
10:00-10:45*	**Immunology, Infectious diseases, COVID-19 and Apitherapy: Part 1** **Moderator:** Prof. Bayram Kıran (Turkey) **Immunomodulation Effect of Nutrition with Bee Products,** Prof. Bayram Kıran (Turkey) **Importance of Beehive products in the Prevention and Treatment of COVID-19,** Dr. Stefan Stangaciu (Romania), Asst. Prof. Ali Timuçin Atayoğlu (Turkey)
11:00-11:45*	**Immunology, Infectious diseases, COVID-19 and Apitherapy: Part 2** **Moderator:** Asst.Prof. Ali Timucin Atayoglu (Turkey) **The Importance of Propolis in COVID-19 Treatment,** Prof. Sevgi Kolaylı (Turkey) **EPP-AF Propolis Reduced the Time of Hospitalization of COVID-19 Patients - Pilot, Randomized and Controlled Clinical Trial,** Andresa Berretta, PhD (Brazil) **COVID-19 and Anatolian Propolis: A Case Report,** Asst. Prof. Duygu Zorlu (Turkey)
12:00-12:45*	**Immunology, Infectious diseases, COVID-19 and Apitherapy: Part 3** **Moderator:** Prof. Orhan Deger and Assoc. Prof. Aydın Aydınlı (Turkey) **Propolis in COVID-19 Infection,** Prof. Sibel Silici (Turkey) **Apitherapy against COVID-19 Infections,** Prof. İbrahim Demirtaş (Turkey) **COVID-19 and Propolis,** Dr. Cristina Aosan (Romania)
14:00-14:45*	**Cancer and Apitherapy: Part 1** **Moderator:** Assoc. Prof. Özgür Tanrıverdi (Turkey) **Propolis in Cancer: Scientific Evidences,** Prof. Erdem Yeşilada (Turkey) **Propolis in Breast Cancer,** Dr. Allison Pınar Eronat (Turkey) **Clinical Report of Propolis in the Treatment of Lung Cancer,** Prof. Jiang Deyong (China)
15:00-15:45*	**Cancer and Apitherapy: Part 2** **Moderator:** Prof. Şevki Arslan (Turkey) **Bee Venom and Melittin in Possible Cancer Treatment,** Prof. Şevki Arslan (Turkey) **Antitumoral Effect of Anatolian Honeybee Venom on Glial Tumor Cell,** Assoc. Prof. Meral Kekeçoğlu (Turkey) **Use of Beehive Products to Prevent and/or Treat Basal Cell Carcinoma,** Dr. Bridget Goodwin (Australia)
16:00-16:45*	**Epigenetic and Apitherapy** **Moderator:** Assoc. Prof. Gülsen Meral (Turkey) **Relationship between Telomere Length and Beekeepers,** Assoc. Prof. Thirumulu Ponnuraj Kannan (Malaysia) **Apiterapeutical properties of major proteins of royal jelly in light of epigenetics,** Dr. Jozef Šimúth and Dr. Katarína Bíliková (Slovakia)
17:00-17:45*	**Special Session on Apiphytotherapy (Balparmak)** **A Multiple Task Health Collaboration of Naturals: Apitherapy+Phytotherapy,** Prof. Erdem Yeşilada (Turkey)
07:30-08:00**	**Connection,** WorldApiExpo **FELAPI Next events,** N.D. José Cabrera (Ecuador) **FELAPI Outstanding,** Dr. Andrés Castillo (Ecuador)
08:00-08:45**	**Panel 1** **Presentation,** Dra. Maria Eugenia Sierra (Colombia)

	Sustainable Production Units, the ideal home for bees, MSc. Marilyn Herrera (Ecuador) **Questions,** Dr. Andrés Castillo (Ecuador)
08:45-09:30**	**Panel 2** **Presentation,** N.D. José Cabrera (Ecuador) **Sustainable Pollen Production in Colombia and Verification of its Attributes as a Nutritional Supplement,** Marta Cecilia Quicazán (Colombia) **Questions,** Dr. Andrés Castillo (Ecuador)
09:30-10:15**	**Panel 3** **Presentation,** Dra. Maria Eugenia Sierra (Colombia) **Quality control in products made with Apitoxin,** N.D. José Cabrera (Ecuador) **Questions,** Dr. Andrés Castillo (Ecuador)
10:30-11:15**	**Panel 4** **Presentation,** N.D. José Cabrera (Ecuador) **Reflections, News and Recommendations in Therapy with Products from the Beehive,** Prof. Enrique Eduardo Patiño (México) **Questions,** Dr. Andrés Castillo (Ecuador)
11:15-12:00**	**Panel 5** **Presentation,** Dra. Maria Eugenia Sierra (Colombia) **Conservation of Native Stingless Bees in Mexico and its Relationship with Modern Therapy,** M.Sc. Bióloga Margarita Medina (México) **Questions,** Dr. Andrés Castillo (Ecuador)
13:15-14:00**	**Panel 6** **Presentation,** N.D. José Cabrera (Ecuador) **Treatment with Meliponiterapia and Natural medicine in Pressure ulcers,** Dr. Gustavo Medina (México) **Questions,** Dr. Andrés Castillo (Ecuador)
14:00-14:45**	**Panel 7** **Presentation,** Dra. Maria Eugenia Sierra (Colombia) **Medicinal uses and vision of the products of Melipona bees in Mexico,** PHD. Genoveva Ocampo (México) **Questions,** Dr. Andrés Castillo (Ecuador)
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09:00-09:45*	**Nutrition and Apitherapy** **Moderator:** Prof. Ercan Dülgeroğlu (Turkey) **Importance of Bee Product in Nutrition,** Prof. Midhad Jasic (Bosnia and Herzegovina) **Principles of Api-Nutrition,** Alina Varadi and Dr. Mirela Strant (Romania) **Fermented Honeybee Products in Apitherapy,** Prof. Ercan Dülgeroğlu (Turkey)
10:00-10:45*	**Apitherapy in Clinical Practice: Part 1** **Moderator:** Prof. Ahmet Yaser Müslümanoğlu (Turkey) **Applications of Apitherapy in Urology,** Dr. Dursun Ünal (Turkey) **Application hints for the use of bee venom summarizing some case studies; Treatment for ligament and sinew injuries,** Dr. Thomas Gloger (Germany) **Clinical study of propolis in the treatment of diabetes and its complications,** Prof. Jiang Deyong (China)
11:00-11:45*	**Apitherapy in Clinical Practice: Part 2** **Moderator:** Assoc. Prof. Onur Öztürk (Turkey) **Healing Activity of Honey on Topical Application on Wounds,** Prof. Ahmed Hegazi (Egypt) **Why Should Be Used Apitherapy In the Treatments,** Asst. Prof. Betül Battaloğlu İnanç (Turkey) **Palliative Care and Apitherapy,** Asst. Prof. Sibel Doğan (Turkey)
12:00-12:45*	**Apitherapy in Clinical Practice: Part 3** **Moderator:** Asst. Prof. Mustafa Ünal (Turkey) and Prof. Volodymyr Postoenko (Ukraine) **Role of Apitherapy in Rehabilitation of the patients with Obesity and Diabetes type 2,** Mr. Andrii Dinets (Ukraine)

	The importance of Api-phytotherapy in the Surgical approach of open Arthritis - case report, implications and perspectives, Dr. Andrei Zbuchea (Romania) **Apitherapy in Preventive Medicine,** Asst. Prof. Ali Timuçin Atayoğlu (Turkey)

14:00-14:45*	**Skin Health and Dermo-Cosmetics in Apitherapy** **Moderator:** Dr. Bridget Goodwin (Australia) **Use of bee products for a healthy skin,** Dr. Sona Dubna (Czech Republic) **Skin Health and Dermo-Cosmetics in Apitherapy: Exploring Possibilities for Expanded Use of Bee Products in Skin Rejuvenation Treatments and Formulations**, Dr. Bridget Goodwin (Australia) **Honeybee Silk: A Valuable Biomaterial**, Assoc. Prof. Oktay Yıldız (Turkey)	**Special Session (Bee'O Propolis)** **Bee products for ealthy living and Anatolian Propolis with Scientific Studies,** Prof. Ayper Somer (Turkey) and Msc. Eng. Aslı Elif Tanuğur Samancı (Turkey)

15:00-15:45*	**Pediatry and Apitherapy** **Moderator:** Prof. Mamdouh Abdulrhman (Egypt) **Honey Nebulization against Respiratory diseases in Children,** Prof. Mamdouh Abdulrhman (Egypt) **The child's reaction to bee stings: Kindergarten responsibility (or educator's responsibility),** Pdg. Nina Ilič (Slovenia) **Bee products for children**, Dr. Mirela Strant (Romania)

16:00-16:45*	**Apitherapy in Oral Medicine** **Moderator:** Dr. Munir Ravalia (United Kingdom) **Propolis In Oral Health,** Dr. Munir Ravalia (United Kingdom) **Uses and applications of Beehive products in Dentistry,** Dr. Rafael Felitti Campomar (Uruguay) **The propolis influence on the Dental plaque accumulation and on Dental plaque and SARS-CoV-2 interrelation,** Dr. Anna-Kurek Gorezka (Poland)

17:00-17:45*	**Apitherapy Tourism** **Moderator:** Dr. Stefan Stangaciu (Romania) **Api-tourism and Api-Wellbeing in Slovenia,** Mrs. Tanja Arih Korosec (Slovenia) **Apitherapy Tourism, a new form of health-related Tourism,** Dr. Stefan Stangaciu (Romania)

Day 7 - 26.05.2021

09:00-09:45*	**Api-Der Presentations Opening (Turkish)** Dr. Ali Timuçin Atayoğlu (Turkey), *Uluslararası Apiterapi Federasyonu Başkanı, İstanbul Medipol Üniversitesi* Mr. Zekeriyya Erdurmuş (Turkey), *T.C. Tarım ve Orman Bakanlığı, Hayvancılık Genel Müdürü* Mr. Ziya Şahin (Turkey), *Türkiye Arı Yetiştiricileri Merkez Birliği Yönetim Kurulu Başkanı* Mr. Yalçın Sezer (Turkey), *Tarımsal Bal Üreticileri Merkez Birliği Yönetim Kurulu Başkanı*

10:00-10:45*	**Api-Der Presentations Panel 1 (Turkish)** **Moderator:** Agr. Eng. Gülten Bulut (Turkey) **Arı Ürünleri Üretimi ve Apiterapideki Önemi, Dünyadaki Arıcılık Konusunda Dünyadaki Gelişmeler,** Agr. Eng. Gülten Bulut (Turkey) **Yeni Dünya Sisteminde Sektörlerin E-ticaret ve Dijital Pazarlama Stratejileri**, Mr. Olgu Şengül (Turkey)

11:00-11:45*	**Api-Der Presentations Panel 2 (Turkish)** **Moderator:** Agr. Eng. Gülten Bulut (Turkey) **Amerika'da Arıcılık Çalışmaları,** Prof. Osman Kaftanoğlu (Turkey) **Bal Arısı Zararlısı Varroa Destructor Mücadelesinde Arı Ürünlerinde Arı Dostu Alternatif Yaklaşımlar**, Dr. Annely Brandt (Germany)

12:00-12:45*	**Api-Der Presentations Panel 3 (Turkish)** **Moderator:** Agr. Eng. Gülten Bulut (Turkey) **Zirai Mücadelede Kullanılan Pestisitler, Kısıtlamalar ve Çevre Dostu Ürünlerin Kullanımı Konusunda Bakanlığımızın Yaklaşımları,** Dr. Yunus Bayram (Turkey) **Bitki Hastalık ve Zararlılarıyla Mücadelede Biyolojik Mücadele Yöntemleri,** Assoc. Prof. Lerzan Erkılıç (Turkey) **Böcekler ve Ekoloji, İklim Değişikliğinin Böcekler Üzerine Olası Etkileri,** Prof. Cem Özkan (Turkey)

14:00-14:45*	**Api-Der Presentations Panel 4 (Turkish)** **Moderator:** Agr. Eng. Gülten Bulut (Turkey) **Türkiye'de Organik Arıcılık Uygulamaları Mevzuat, Kontrol ve Denetimler**, Dr. Mehmet Hasdemir (Turkey) **Organik Arıcılığın Yapılabilirliği, Üretimde Yaşanan Sorunlar,** Eng. Vahap Eryılmaz (Turkey)
15:00-15:45*	**Api-Der Presentations Panel 5 (Turkish)** **Moderator:** Agr. Eng. Gülten Bulut (Turkey) **Ayçiçeği Üretiminde Kullanılan Bal Arılarının Tohum Kalitesine Etkisi ve Arılı Kovanların Kiralanması,** Agr. Eng. Burhan Dağdaş (Turkey) **Bodur Elma Bahçelerinde Polinasyon Amaçlı Kiralanan Arı Kolonilerinin Elma Verimi ve Kalitesine Etkileri,** Eng. Hasan Dural (Turkey) **Polen Üretimi ve Pazarlanmasında Dünyaya Açılan Kapı**, Mr. Murat Akdi (Turkey)
16:00-16:45*	**Special Session (ApiMaye)** **Apiterapi Uygulamaları İçin Arı Ürünlerinin Üretiminde İyi Tarım Uygulamalarının Kullanılması**, Dir. Muzaffer Yıldırım (Turkey) and Dir. Emre Yıldırım (Turkey)
17:00-17:45*	**Special Session on Sustainable Beekeeping (Balparmak)** **Training Programme to Ensure Sustainable Beekeeping Activities in Turkey**, Dr. Emel Damarlı (Turkey)

*GMT+03:00, İstanbul
**UTC-5:00, Latin America

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Oral Presentation

People raise bees, and bees support and nourish human health

Prof. Fang Zhou

Honorary President of the Congress
Apicultural Science Association, China

Abstract

Thank you for organizing this professional and international conference so that our apitherapy colleagues may have the opportunity to communicate with each other. Thanks to Dr. Ali Timucin, the President of the Turkish Apitherapy Association, and everyone who worked at that conference. Please allow me to share with you the concept of "People raise bees, and bees support and nourish human health". This is just a way back to nature: experiencing beekeeping activities, sharing the spirit of bees, using natural bee-products to maintain health and enhance vitality. For thousands of years, people have been caring honeybees and collecting natural bee products with a mutual benefit, which enabled the harmonious relationship between humans and honeybees. “Beekeeping” is not only a moderate exercise for the human body, but it is also good for the human psychology. If we care to the ecology of bees, we can obtain natural, clean, pure and active bee products. "People raise bees, and bees support and nourish human health" is a way to return to nature to achieve the harmony of nature, man and bee, which is in line with the Chinese philosophy that emphasizes "the harmony between man and nature" and tells that “man is an imitation of nature". Islam also guides people to the direction of bee products such as honey. "Apitherapy" combines ancient and modern practices. Apitherapy health care is using bee products for both preventing and curing diseases, and also for maintaining health. I sincerely hope that the apitherapy health care will flourish. And, I wish a successful conference. Thank you very much!

Keywords: Apitherapy, Beekeeping, Human Health, China

Oral Presentation

Records of the Value of Bee Products in Chinese Pharmacopoeia and Literature

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Abstract

Bees were created millions of years ago, and they have been on earth thousands of years earlier than humans. Bee products have been recognized as a food and medicine since ancient times. Apitherapy health care is using bees and bee products to provide medical care, health care, nursing and rehabilitation for human beings so as to nourish life, strengthen vitality and promote longevity. Since ancient times, apitherapy plays a very important part in Chinese health preservation culture, and the records about using bees and bee products to treat diseases are significant. “Chinese Materia Medica” and “Chinese Pharmacopoeia” edited by Ministry of Health of the People's Republic of China and Administration of Traditional Chinese Medicine recorded not only the medical and health effects of honey, royal jelly, propolis, beeswax, and other bee products, but also pharmacological results. It improved the apitherapy system and these are outstanding achievements of Chinese apitherapy professionals. Prof. Fang Zhou is recognized as the founder of modern apitherapy in China.

Keywords: Apitherapy, Bees, Pharmacopoeia, Materia Medica, Prof. Fang Zhou

Oral Presentation

The History of Apitherapy in Cuba

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Abstract

Cuba is a beautiful Caribbean archipelago native for stingless bees *Melipona beechei* until 1764 when first colonies of *Apis mellifera* were introduced from Florida after British cession of Havana City in a trade-in for the North American peninsula. In recent decades, the nation has achieved a significant production of honey and beeswax, as well as a widespread use in veterinary and human medicines of beehive products, mainly propolis, pollen, honey, and apitoxin. Apitherapy is initiated in Cuba after a book is published in 1979, El propóleo, un valioso producto apícola ("Propolis, a valuable bee product"), and the establishment of propolis laboratories for animal and human use of api-preparations in all provinces along the country, the popular use of propolis and other products, the celebration of national and international symposia on Apitherapy since 1988, and the inclusion of Apitherapy in medical and veterinary courses on Traditional Chinese Medicine, Complementary and Alternative Medicines, and in therapeutic practice. Main uses of bee products are the treatment of parasitosis, ulcers, wound healing, burns, viral and bacterial infections, but Apitherapy has remained back -as it happens in all other countries under influence of world health organisation- in the promising treatment and prevention of Wuhan coronavirus or COVID19.

Keywords: Cuba, History, Apitherapy

Oral Presentation

The History of Apitherapy in Brazil

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Abstract

From indigenous tribes to medical clinics. From unknown names to recognized names. From self-dictations to graduates. From bee lovers to beekeepers. Apitherapy in Brazil has been gaining space every year. Today doctors support, therapists are influenced, researchers give way to their curiosity and interest by giving scientific evidence to the already old acquaintance, and lovers of life and nature encourage integrative and natural treatments. Apitherapy in a young but rich nation, inspiring lives and motivating love and healing to people.

Keywords: History, Apitherapy, Brazil

Oral Presentation

Apitherapy; the Rediscovery of a Natural Therapy that Heals without Damaging

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Abstract

Apitherapy is complementary medicine that promotes the use of bee products, such as honey, pollen, bee bread, royal jelly, propolis, apitoxin or bee venom, honeycomb wax, drone larvae and whole bees for nutrition and even the air of the hive for the improvement of health and quality of life, prevention and treatment of diseases and cosmetics. Apitherapy includes among its many procedures, apitoxin-therapy or bee venom therapy, and apipuncture, which is acupuncture using bee stings, or injectable bee venom. It is not known when the elements of hives began to be used as medicinal treatments, but these products were already used in Egyptian culture. For example, propolis was used to embalm mummies and bee venom was used by Cleopatra as a treatment for pain. When the ancient Egyptians went on their expeditions, they preserved the meat in barrels filled with honey. In the Koran, a Muslim holy book completed in the year 632, it says that, from the abdomen of bees, a liquid of different kinds comes out, which contains a remedy for men. Apitherapy101 for everyone. Moses Assisi. Characters in history, such as Alexander the Great, used bee venom for rheumatism. Its healing properties are even mentioned in religious texts such as the Bible or the Koran. Formerly, only honey, pollen and propolis were the elements that were used from hives as medicinal therapies. However, Phillip Terc, considered the father of apitherapy, in 1888 began to use bee venom. The doctor used his venom to treat people with rheumatic diseases, thus initiating the apitherapy method that is currently used. A very natural alternative. Apitherapy is an alternative therapy based on elements from beehives to prevent and cure various diseases. Elements such as: honey, pollen, royal jelly, bee bread, wax, propolis, bee venom, drone larvae, bee venom, whole bees, hive air are used.

Keywords: Apitherapy, Rediscovery, History

Oral Presentation

Apitherapy and Live Food

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Abstract

The nutritional and healing properties of products made by bees have been presented by scientists on all continents, with emphasis on nutrition and degranulation of toxins. It is very common for Apitherapy patients to feel, after years or months, the return of some pain or symptoms. However, this is easily observed in patients who do not practice a "VIVA" frugal, vegetarian diet, as indicated by Dr. Stangaciu and all the medical experts who spoke at the Third International Congress of Apitherapy, Romania. With high purifying, repairing, enzymatic and nourishing power, bee products (honey, pollen, propolis, royal jelly, apitoxin and bumblebee larvae) help to clean and degranulate the toxins lodged in the arteries, in the intercellular and intracellular spaces clogged by over the years. These toxins, bad cholesterol, acrylamide and uric acid damage the cardiovascular system, acting drastically on the cellular nutrition of the glands, organs and tissues, causing the lack of oxygen and food, motivating the death of the cell or genetic mutation, as stated by Dr Internet video shinya: tissue death, organ necrosis. We can be sure that with the restorative capacity, cleaning and nourishing the system, the Apitherapy added to the VIVA diet, we will have a safe longevity, full of vitality and free from the devastating toxins of health.

Keywords: Hypersensitivity, Allergy, Bee poison

Oral Presentation

The Apitherapy of the Future

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Abstract

This conference seeks to leave a vision of the apitherapy of the future based on the new post-covid world context so that apitherapy has an impact on public health and the preponderance it deserves within medical systems. It is necessary to identify the problems that apitherapy currently has low public recognition, polarized discourses, absence of a cohesive collective vision, lack of a chain of transmission of knowledge. The practice of apitherapy cannot remain at the most basic levels of evidence, because these are more susceptible to bias and have a lower inference of causality. The opinion of an expert is valid, the case series is valid but that is the lowest quality evidence that exists within the degrees of evidence. For this reason, in order to be heard by public opinion and medical institutions, it is important to raise the bar and start doing basic and clinical research, clinical studies, meta-analyzes, and publishing in indexed journals. It is there where apitherapy begins to be legitimized. Not all those who are part of the apitherapy chain must do research at this level, this is the responsibility of a part of that chain, doctors, health professionals, researchers and it is they who must transfer the information. that knowledge (according to the functions, competences and scope) to the other actors of that chain, which ends in the end user, who is the consumer, through the apitherapists and beekeepers.

Keywords: Apitherapy, Health, Research, Treatment

Oral Presentation

Curative Crisis in Apitherapy

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Abstract

In Apitherapy, particularly in treatments with bee venom, a reaction may occur that has nothing to do with an allergic reaction or anaphylactic shock. Apitherapists should know how to distinguish. Some patients, during this process get worse. This is what we call a "healing crisis." The healing crisis is part of the healing process, it is a non-aggressive, non-pathological process, which is intended to create a positive impact on the well-being of the patient. Therefore, you have to let it evolve. As Apitherapists, it is important to inform our patients about this healing process. The time that the curative crisis lasts varies from patient to patient, but is generally 24 to 72 hours, in patients with chronic degenerative diseases it could last longer. The healing crisis is a painstaking effort by each of the body's organs to remove waste products and ease the path to regeneration. It is an acute reaction of the organism on the disease. Its tendency is towards recovery and is, therefore, in accordance with natural principles. During the healing crisis the old and damaged tissues are replaced by new and healthy tissues. This crisis occurs according to Hering's law of healing which postulates the following: The healing process goes from the internal to the external, with the skin often being the last stage of elimination of the disease. Symptoms gradually disappear from top to bottom. This can be experienced better in cases of low back pain, when it disappears from that area and pain in the knees or ankles appears. The discomfort goes through different organs, starting with the internal organs "yin" and ending in the viscera "yang". All symptoms disappear in the reverse order of their appearance. The general symptoms of the healing crisis are: Low-grade fever or temperature higher than 38 degrees, Muscle and joint pain, headache, diarrhea or sweating, Urine with a strong color and odor, expulsion of phlegm and mucus, erythema, inflammation and itching. All of the above is a stage of elimination of toxins prior to the restoration of organs and health. It must be taken into account that during the healing crisis a type of aggravation of the symptoms or disease (s) of the patient could occur. The healing crisis is often confused with a worsening of the disease, it must be clear that a healing crisis is very similar to the critical states of the disease, since the symptoms of the disease that afflicts the patient will be re-experienced, but there are a very important difference: elimination. In the healing crisis the elimination is perfect. Defecation is natural. All the organs of elimination fulfill their function in a normal way. On the contrary, in the critical states of the disease, the elimination processes are stopped or unsatisfactory, which further complicates the pathological state of the patient. In the healing crisis the elimination processes are accelerated due to the abundance of vital energy recovered. All secretions and other forms of waste accumulated in the body dissolve and flow freely, thus establishing a process of general cleansing and purification. To heal the disease, the patient needs to go through the healing crisis, in the treatment with bee venom or Apitoxin it occurs between the first and fourth sessions, so we must prepare our patients. The healing crisis makes the patient relive the illnesses or ills that he has been experiencing throughout his life, even if he does not remember them, since the organism does not forget and goes through the accumulated ills in the opposite direction. There are many clinical experiences that show that reliving the ailments of the past helps to achieve total healing. Faced with a healing crisis, the

treatment with bee venom should not be aborted, thinking that it is a setback or worsening of the disease. On the contrary, you have to take control of it: Recommendations: Avoid consuming pork, shellfish and canned meat. Natural water intake greater than 2.5 liters. Administer detoxification diet. Use natural antibiotic (propolis extract). Cold compresses. The above recommendations will help to successfully cope with the healing crisis and see the disease overcome in a period of 12 to 16 weeks. Therefore, we must conclude that the healing crisis is part of the healing process, we must teach our patients to understand it so that they process it and allow themselves to experience it, since it is the way to transform their disease into health.

Keywords: Apitherapy, Healing crisis, Response, Treatment

Oral Presentation

The Therapeutic Diversity of Apitherapy and Bee Derivatives in Brazil

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Abstract

In the whole world exists more than 20,000 species of bees and Apis mellifera, is only one of them. In Brazil it is estimated that there are more than 2,500 species of native stingless bees, one of the greatest diversities on the planet. We can check the pharmaceutical potential with wings (The pharmaceutical bees with wings - N. Iorich), that we have in our hands and remain unexplored and unknown and little studied. As an apitherapist, I try to exploit these regenerative and healing properties of honey and bee products to the fullest in my patients. As a Beekeeper I have been developing edible and cosmetic products, aimed at application in Apitherapy (Compound honeys with propolis, pollen, royal jelly, herbal medicines, nuts, mead, mouth sprays, ointments, creams, lotions, soaps, shampoos, conditioners, moisturizing oils, etc.)

Keywords: Apitherapy, Alternatives, Derivates, Brazil

Oral Presentation

Apitherapy in Romania: Present Situation and Perspectives

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Abstract

Apitherapy has a long tradition in Romania, starting with the use of honey and bee stings by our ancestors that lived here 2,000 years ago. Before our revolution in 1989, when we changed the political and social system, we have had particularly good exchanges in the apitherapy field with former socialist countries like China and Russia. This enabled us not only to check new ideas from these countries, but also to put them in practice. In Romania we have also since 1926 a national journal of beekeeping which literally published hundreds of articles related directly or indirectly to apitherapy. We have already over 500 medical doctors certified in Apitherapy, Phytotherapy and Aromatherapy and many apitherapy oriented therapists and beekeepers. We also have created in 2007 the Romanian Apitherapy Society which continues the great tradition of research, education, and clinical practice of our previous generation of apitherapists which included many great names, for us, like Dr. Alexandru Partheniu, Dr. Mircea Ialomițeanu, Dr. Constantin Popovici, Dr. Mircea Popescu, Dr. Traian Gîdoiu, Dr. Neacșu Constantin which worked in various specialties of medicine. In Romania have been organized many various apitherapy events like courses, symposia, and congresses with international participation. In 2012 in Germany, we have proposed the creation of the International Federation of Apitherapy having as main goal to create an international bridge between scientists, apitherapists and beekeepers from all over the world. The perspectives of apitherapy development are very good, due to the late excellent technological communication advancements (Google, Facebook, PUBMED, etc.). We will continue to help the International Federation of Apitherapy (IFA) to develop apitherapy in all countries, including by organizing several Courses/Workshops/Round tables, several times each year, with recognized national and international experts in apitherapy. Only with such more frequent international events can the scientific findings and the relevant information on bee products and apitherapy really be put in practice and thus help millions of human beings that are still suffering of thousands of various diseases, all over the world.

Keywords: Apitherapy, Romania, Beekeepers

Oral Presentation

Apitherapy in Bosnia and Herzegovina

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Abstract

In recent decades, the use of bee products in Bosnia and Herzegovina (B&H) has transformed. A significant number of mixtures based on bee products, previously belonged to folk medicine, are part of the official pharmacy and medicine these days. The beneficial effects of honey, royal jelly, pollen, wax and propolis, and more recently bee venom and api-air have been recognized. Although evidence-based medical research is scarce, there are more and more bee-based preparations in B&H pharmacies. In B&H, there are numerous preparations of apitherapeutic products. There are 5 to 7 thousand beekeepers, and a larger number of them (10 to 20%) prepare apitherapeutic products in accordance with folk medicine. Two main honeybee products are propolis and pollen, and 1 to 2% of beekeepers prepare and royal jelly also. The products are not standardized, and their sale is mostly done on the doorstep. Most apitherapeutic products in pharmacies are based on propolis and royal jelly. Two B&H pharmaceutical companies pack royal jelly-based mixtures. In recent years, api-air has been expanding, and there are between 20 and 30 Api chambers. They started to be applied 4 to 5 years ago and their number is constantly increasing. There are still a small number of commercial pharmaceutical preparations that can be found in pharmacies and increasing the use of apitherapeutic preparations can be a good basis for reducing chemistry in healthcare. A significant segment in the application of apitherapy products is certainly the establishment of product standardization, which in BiH is still at a very low level due to the lack of BiH standards or legislation covering this area. In recent years, through the Congress on Beekeeping and Bee Products with International Participation, which will be the sixth in a row this year, the importance and significance of standardization and application of apitherapy products in BiH is slowly rising.

Keywords: Apitherapy, Bosnia and Herzegovina, Bee products

Oral Presentation

Apitherapy in Hungary

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Abstract

Hungary - like the other countries - has a long tradition of naturopathy. We have had some very active medical professionals who have helped heal many people. Semmelweis is one of the best known. In apitherapy, we have Bodog F. Beck. He became apostolic apitherapy in the USA, New York City, in Manhattan. His two books: "Bee Venom Therapy" and "Honey and Health", are still relevant today. His biography is summarized in seven languages in the book "Dr Beck Félix Bódog élete" - "The life of Dr Bodog F. Beck". The current regulation on apitherapy has been in effect since 1997. The apitherapists are naturopaths. The ordinance contains training centers, exams, exercise authorizations, room and insurance obligations. Naturopaths and doctors, but also nurses, are part of the training system. One collects educational points every five years. Hungarian legislation makes research and education a duty of the state. The Hungarian Apitherapy Society has taken over some of these tasks, whose legal status is "in the public interest". Nevertheless, some of Society's educational programs are accredited. Approximately 5,600 alternative practitioners were examined, who, thanks to their qualifications, were also able to carry out apitherapeutic treatments in phytotherapy and aromatherapy. Most people use phytotherapy. The number of people who also use apitherapy is lower. Every alternative practitioner, like doctors, takes the Hippocratic oath. Those who use apitherapy are responsible people. This is also proven by the fact that no fatal misconduct has occurred in Hungary in the past 34 years during the known regulatory period due to apitherapy treatment.

Keywords: Hungary, Apitherapy, Current situation, Legal rules, Beck.

Oral Presentation

Apitherapy in China

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Abstract

In China, we have an advantage of having observation with a large number of clinical cases. We have done researches to standardize bee acupuncture therapy, using different methods. In addition to this point, we have also observed the effects of bee stings on diseases, such as rheumatoid arthritis and spondylitis. Some research done to observe some of its immune response, and response of some cells in joint cavity. Although bee acupuncture is widely used, it is painful after all. The pain after bee acupuncture makes it difficult for patients to accept it. Our Phd and master students have done a series of systematic research on some adverse and unwanted reactions of bee stings, mainly to observe the clinical reactions of some patients, for example, the pain after bee needles. We have done research on fever, itching, swelling and redness. For example, its frequency, degree, and time of occurrence have all been observed in series. We have worked on some standards, so that bee-acupuncture can be practiced more safely and effectively.

Keywords: Apitherapy, China, Standards, Research

Oral Presentation

Apitherapy in Slovenia

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Abstract

Beekeeping has a rich tradition and is very important in Slovenia. The Carniolan bee (Apis mellifera carnica, Pollmann 1879) is a protected bee subspecies in Slovenia. Beekeeper Anton Janša (1734–1773) was first teacher of beekeeping on the world. His birth date May 20 is proclaimed as World Bee Day. Honey and wax were produced and traded in Slovenia as early as the 12th century. At the end of the 19th century, the field of apitherapy was most marked by dr. Filip Terč. He was of Czech descent and moved to Maribor with his family in 1875. As early as 1879, he began trying to treat rheumatic diseases with apitoxin. He performed this type of treatment on about 700 patients, thus gaining the title of a pioneer of modern apitherapy in the history of medicine and beekeeping. At the Congress of Apitherapy in March 2006 in Passau, March 30, the birthday of Dr. Filip Terč, for the International Day of Apitherapy was announced. The Slovenian Beekeeper's Association is one of the best organized national beekeeper's associations. In cooperation with Apitherapy section of Beekeeping Association of Maribor named by dr. Filip Terč runs a training program for apitherapists. One of the peculiarities of Slovenians beekeeping is a bee house. A bee house is a building in which we put beehives under a common roof. Often, we can find a bed in bee houses, intended for the beekeeper. Many have used the favorable microclimate of the bee house for the implementation of apitherapy as apiair therapy. Recently a standard of national professional qualification as Apitherapist was prepared and in the future a modern Apicenter that will combine apitherapy, wellness and wellbeing is planning to be build.

Keywords: Slovenia, Apiair therapy, Filip Terč

Oral Presentation

Comparison and Clinical Utility of Apitoxin Sensitivity Tests Used in The Treatment of The Most Common Diseases and Its Predictive Value in Relation to The Results Obtained in The Medium Term

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Abstract

The controlled medical process called Apitherapy is based on the use of all the products of the hive, among them apitoxin stands out for its special qualities and is one of the fundamental pillars to obtain the best results. The proper management of apitoxin is the greatest challenge when we make decisions in the clinical management of patients and when executing the procedure to treat the most common groups of diseases. Around the world, numerous application techniques have been developed, which I have classified in relation to the most logical and natural common denominator, indirect, when the therapist has full control over the application, and direct when the therapist has no control over the application. app. Within each group a variety of techniques are opened, classified according to their ability to act as an inducing stimulus to achieve a response reflected in the therapeutic results within acceptable averages and always within the margins of individual response and safety. Knowing the prevalence of its use provides us with significant information on the most effective, efficient and safe techniques when using Apitoxin.

Keywords: Apitherapy, sensitivity test, protocols, procedures, ABEE, statistics

1. Introduction

Apitherapy is the tool that has the greatest therapeutic potential and the wide capacity to adapt to any medical treatment system, it provides support in all stages of the pathology. This is because it has several modulating functions at the cellular level, extracellular matrix, tissues, organs and structural and energy systems, thus achieving harmony in the immune barrier.

Among the products of the hive, bee venom enters the bloodstream by nature and is considered invasive, so it will be the most careful and its responsible use requires standardized protocols and procedures to minimize risks and adverse effects, thus achieving acceptable results. in the shortest possible time.

The sensitivity test is the first step to be taken for the bee venom induction process, always trying to be the least invasive. The use of a minimum dose protocol induces the patient to achieve therapeutic results with the least exposure, thus achieving two effects:

1. Inherent response and adaptation to bee venom (short term)
2. Inherent organic response and adaptation of the individual, the same that will ensure well-being in the medium and long term.

Identifying the sensitivity test and determining the type of sensitivity and the percentage of tolerance is essential to establish the minimum dose protocol and therefore a safe process within the therapeutic field.

The sensitivity test constitutes the fundamental pillar for each process of application of bee venom and in the scientific evidence it even provides predictive values of the organic state and response of the individual instantly and in the future.

These studies and presentations will establish the main guidelines on the bee venom sensitivity test, as well as its current alternatives, interpretation and even diagnostic approach.
Place and Time: QualityMed Private Apitherapy Center from August 2019 to March 2020
Objectives: Determine the differences between Apitoxin sensitivity tests in relation to the most common pathologies. Determine the clinical scope of the Apitoxin susceptibility test. Determine the predictive scope of the Apitoxin susceptibility test.

2. Materials and Methods

It was considered 120 patients diagnosed with four of the most prevalent pathologies, who had not had contact with bee venom in the last 4 years.
Degenerative diseases: Osteoarthritis 30 cases
Immune diseases: Rheumatoid Arthritis 30 cases
Episodic neurological diseases: Migraine 30 cases
Cardiovascular diseases: Arterial Hypertension 30 cases
To form the study group, 3 groups were made up of 10 patients of each type of disease. Each group was subjected to different sensitivity tests in each session and then entered the controlled medical treatment plan with Apitherapy using a minimum dose protocol, where it was also considered:
Carry out the sensitivity test with three methodologies, one different for each study group:

1. The first one using immediate puncture at 90 degrees with live bee sting in DU 14,
2. The second using <10 IU of 6x apitoxin equivalent to <0.001 mg / ml subcutaneously with needle number 30 in DU 14
3. The third using apitoxin oral solution 0.01 mg / ml sublingual for 3 minutes.

The response caused by the sensitivity test was tabulated into two types, taking into consideration the classification of the sensitivity test measurement of the manual of protocols and procedures in apitherapy:

1. Low sensitivity if it corresponds to type A B C parameters
2. High sensitivity if it corresponds to type D and E parameters
3. Other parameters linked to types F G H I and O will be excluded.

Carry out controlled medical treatment with Apitherapy in all patients using a minimum dose protocol and repeating the sensitivity test in each session:

1. Group 1: Minimum dose protocol using live bee apitoxin
2. Group 2: Minimum dose protocol using injectable apitoxin
3. Group 3: Minimum dose protocol using oral apitoxin and live bee

Execute an average of 7 sessions and at the end perform the individual qualification of results regarding the relief of their symptoms, based on qualitative and quantitative confirmation methods of each case, grouping them into three types of response on a scale of 1 to 9:

1. Low, if the grade achieved is between 1 and 3 b.
2. Medium, if the grade achieved is between 4 and 6 c.
3. High, if the grade achieved is between 7 and 9

3. Results

The first study group determines a better acceptance of the stimulus with low sensitivity in a ratio of 9 to 1 and a result at a medium level in patients with arterial hypertension. In the case of arthritis, the ratio is 7 to 3 with results in the medium level.
The second study group determines a better acceptance of the stimulus with low sensitivity in relation to 9 to 1 and a result at a high level in patients with osteoarthritis.
The third study group determines an absolute acceptance of the stimulus with low sensitivity in relation to 10 to 0 and a result at a high level in patients with migraine.

GROUP 1: Better acceptance of the stimulus with low sensitivity (9 to 1) and a MEDIUM result in arterial hypertension. In arthritis the ratio is 7 to 3 with results at the MEDIUM level.
GROUP 2: Better acceptance of the stimulus with low sensitivity (9 to 1) and a HIGH result in osteoarthritis.
GROUP 3: Absolute acceptance to the stimulus with total sensitivity (10 to 0) and a HIGH result in migraine.

4. Conclusions

The sensitivity test opens the immune portal of each patient and determines an optimized clinical response when obtaining results with the minimum dose protocol in apitherapy. In the case of migraines, the sensitivity test with oral apitoxin and its therapeutic combination with live bee apitoxin offer the best evolution and prognosis.
In the case of Arterial Hypertension and Arthritis, the sensitivity test with live bee apitoxin and its therapeutic combination with live bee apitoxin offer the best evolution and prognosis. In the case of Osteoarthritis, the sensitivity test with injectable apitoxin and its therapeutic combination with injectable apitoxin offer the best evolution and prognosis. Choosing the most appropriate sensitivity test provides us with predictive values in the evolution of certain pathologies. The sensitivity test and the minimum dose protocol are considered as keys to therapeutic success

5. Recommendations

Repeat studies related to a larger number of patients • Repeat the sensitivity test and its reading in each session. Cardiovascular diseases such as hypertension opt for sensitivity test and protocols linked to live bee apitoxin. Immunological diseases such as arthritis, opt for susceptibility testing and protocols related to live bee apitoxin. Degenerative diseases such as osteoarthritis, opt for a sensitivity test and protocols related to injectable apitoxin. Episodic neurological diseases such as migraine, opt for sensitivity test and protocols related to oral apitoxin and live bee.

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Oral Presentation

The Honeybee and the Human Heart

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Abstract

Rudolf Steiner in his nine lectures on bees in 1913 spoke of the honeybee as an organism of unique importance to the health of the human beings. “Whoever looks at a beehive should actually say with an exalted mind; making this detour by way of the beehive the entire cosmos can find its way into human beings and help to make them sound in mind and body” In the same lectures he warned us that within a hundred years the honeybee population would be struggling for survival because of intense commercialisation. In 2013 just one hundred years after Steiner issued that warning, 60% of the honeybee population in the US died. Hippocrates the founder of modern medicine told us that “the art of medicine consists of three elements: the patient the disease and the doctor”. Rudolf Steiner 2420 years after Hippocrates told us that “A real medicine can only exist when it penetrates into a knowledge which embraces the human being in respect of body, soul and spirit “Propolis which I have studied for 30 years is remarkable in that it provides the honeybee with a immune defence mechanism collected and composed from the immune defence mechanism (the resins) from trees and plants within its own local ecosystem. Scientific study of propolis over the last hundred years has demonstrated the multiple function of propolis as a medicine as anti-bacterial, anti-inflammatory, anti-fungal, anti-oxidant... the list goes on. But really propolis is not ANTI anything it is PRO (before) Polis (the city) it is the defender of the city of the honeybee. The unique and close relationship between the honeybee and the human being now supported by scientific study illustrates how propolis also supports the human immune system,not by being fighting or destroying bacteria or viruses but by disabling, disconnecting, and balancing. ”by way of the beehive the whole cosmos can find its way into human beings” If we have no sense of purpose or meaning in life our immune system collapses. If we have no loving supportive relationships our immune system collapses and if we are physically injured our immune system goes down. Our immune system is indeed built of body, soul and spirit. The true medicine of the future must look beyond the synthetic, single molecule - magic bullet medicine and recognise the unique threefold and living element of the evolving new medicine. James Fearnley has published several books and has contributed to over 30 scientific papers on the remarkable properties of propolis. He is building a BEEARC in North Yorkshire in the UK. At the BeeArc researchers will study and develop Apiceuticals and at the same time explore the way which the honeybee can inspire us in all three realms of our existence the social, the economic and the spiritual.

Keywords: Propolis, Honeybee, Three-dimensional Medicine, The human heart. Social, Economic, Spiritual

Oral Presentation

Apitherapy in India

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Abstract

Bee products in India have been used since ancient times for nutritional and therapeutical uses. In India, traditional medical sciences like Ayurveda, Unani, Siddha used honey (considered it an elixir of immortality) and bees wax extensively. There are different honeys based on various types of wild Indian honeybees, as mentioned since ages in Ayurveda and used accordingly. Honeys were classified as per the bee species and all had different medicinal properties. Fresh and aged honeys showed different effects on the body. Some clinical cases with the bee products as per Ayurveda, show positive results and give hope for using these products also for chronic cases in the future. Finally, we need to combine the knowledge from the ancient medical sciences like Ayurveda, Unani with modern Apitherapy protocols for serving mankind.

Keywords: Ayurveda, Apitherapy, Wild honeybees

Oral Presentation

Apitherapy in Morocco

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Abstract

Ancient civilizations used bee products for management of pathologies. Modern apitherapy is a comprehensive concept of health! Apitherapy is intended for healthy patients: prevention is better than cure. This is the major advantage of the daily food use of bee products quality. Pollen, honey and royal jelly are not composed of isolated active ingredients but are formed by organic components with a synergistic biological activity. Their preventive role is proven in human medicine. Apitherapy has a long tradition in Morocco with the use of honey, propolis. Honey is one of the oldest food of humanity. Honey has long been used in traditional practice in Morocco to treat infections, for management of wounds and burns, Varicose ulcers, Eschars, diarrhea, eye diseases, old age, immunity problems, stress, stomach problems, respiratory problems. Propolis is largely used as an antibiotic and immunity problems. Pollen has been used for losses of appetite (anorexia), minor depressive states (neurasthenia). In dermatological sphere, cardiovascular sphere (Arteriosclerosis, high blood pressure) and digestive sphere (Functional constipations, enterocolitis and diverse colitis.). Royal jelly used as immunostimulant, menopause trouble treatment. Bee venom from live bees became popular in recent years due to the need of many patients who find little or no benefit from traditional drugs in dealing with their conditions. Its major use is for: rheumatic conditions multiple sclerosis, psoriasis, relief pain. In Morocco, we have been organized many various apitherapy events like courses, symposia, and congresses with international participation with main goal to create an international bridge between scientists, apitherapists and beekeepers from regions of Morocco. Only with such more frequent international events can the scientific findings and the relevant information on bee products and apitherapy really be put in practice and thus help millions of human beings that are still suffering of thousands of various diseases, all over the world. Apitherapy is not an approved official treatment in Morocco. It is mainly practiced by some beekeepers and some medical doctors. Local scientific work related to Apitherapy using locally produced beehive products is an essential evidence to support claims of nutritive and curative efficacy of these products. Scientific research in the field gives hope for clinical trials in Morocco. This requires multidisciplinary consortium in the field of apitherapy with future participation in improving health of people as an option where it is effective while other traditional approaches fail or at least are ineffective or pose negative side effects to suffering patients.

Keywords: Apitherapy, Bee products, Morocco

Oral Presentation

Resistance of the Waste Products of the Wax Moth Larva and COVID-19

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Abstract

Only the larva which is 1 – 5 cm long has a medicinal value! The healing effect of the larva of the small wax moth and the large wax moth is identical! It is possible to distinguish the larva of the small wax moth from the larva of the large wax moth only in the lab. 8 days - ovicell, 30 days - larva, then 9 days - propupa. Tracking the development of moth is difficult - with frequent examinations of the frames, the wholeness of the colony is interfered, uncontrolled growing of the larva leads to the loss of medicinal raw materials. Overgrown larvae are used for masks and creams. Immediately put the homogeneous mass of larvae in the freezer at -18 degrees, otherwise it will turn black. Waste products of the wax moth larva. The first studies of the metabolic waste products were carried out at the Bogomolets National Medical University in Kyiv, with the guidance of Professor Masyutina. Advice - store a native waste product of the wax moth larva at room temperature, in a dry, dark place, covering the jar with gauze. Groups of small larvae at room temperature will eat up the remaining wax, once again improving the quality of the raw material. Expiry date - 1 year, then make a spiritus extract. Expiry date - up to 7 years domiciliary. Ladder scheme. It is used for a gradual entry into a therapeutic dose in order to relieve the vessels from excessive stress when body clearance. It is relevant for children, with a tendency to allergies, with unstable blood pressure, for the elderly and weakened people. Adults: 5 drops each morning and evening - 3 days. 10 drops each morning and evening - 3 days, 15 drops each morning and evening - 3 days, 20 drops each morning and evening - 3 days…. Further, the dose depends on the weight. Children - 1 capsule = 1 year of life: 1 cap in the morning and in the evening - 3 days, 2 drops in the morning and in the evening - 3 days. 3 drops in the morning and evening - 3 days in a tablespoon of water 15 - 20 minutes before meals. An accelerated scheme is possible - 1 day instead of 3. A drop from a pipette has a greater specific gravity by 1/3 than a drop from a euro dispenser. 20 drops from a pipette = 30 drops from a euro dispenser.

Keywords: Wax Moth, Larva, COVID-19

Oral Presentation

Sustainability in Bee Products' Production

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Abstract

Turkey stands out with different climatic conditions, rich floral and genetic resources. It is an important beekeeping country, which is third in colony presence and second in honey production in the world ranking. Mainly honey, pollen, royal jelly, bee bread, propolis, bee venom and recently apilarnil are products that have gained importance in Apitherapy. When the benefits of these products, which are used for honeybees in their own life processes, were seen in human health, the demand for these products increased and the development of apitherapy products has speeded up. The climate change has been affecting especially bees as in all living organisms in recent years. The sustainability of the honeybee colony has become important as a result of mistakes in colony management, pressure of diseases and pests, adversities in changing environmental conditions and the climate changes. Current and future possible problems of the Turkish Beekeeping should be determined. At this point, an answer to the question of what we can do should be searched and future strategies should be developed.

Keywords: Bee products, Colony, Sustainability, Honeybee

Oral Presentation

Principles of Medicinal Beekeeping

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Abstract

Depending on the final goals and local conditions there are many forms of beekeeping. In Asia we can see honey hunters that climb very tall Tualang trees to get honey and bee bread from the wild colonies of Apis dorsata. In California we have every spring thousands of bee colonies that are used to intensively pollinate almonds trees that are sprayed with various insecticides. This is what we can call “industrial” beekeeping. Beekeepers that pay a high attention to the cleanliness of the environment and of their own beehives are practicing what we call “ecological” or “bio” beekeeping. If the final goal is to get beehive products to be used to prevent and treat human and animal diseases, we speak about “medicinal” beekeeping. The main characteristic of medicinal beekeeping is the presence, in high amounts, of specific pharmacologically active substances that originates from specific medicinal bee plants. The classical beekeeping is usually related to multifloral based bee products. Medicinal beekeeping is focused on mono-floral origin of bee products. If a patient has for example a rheumatic, an immune system disease or Covid-19, pine honey (rich in polyphenols and minerals), or other forms of honeydew honey, will be better than a multifloral honey. When the main goal is to get honey to be used in surgery (against many forms of wounds, burns and boils), for intravenous administration or in the production of eye drops, besides the conditions of cleanliness and richness in active compounds, medicinal honey should be free of potentially pathogene bacteria like Clostridium botulinum and must be checked, before its use, by specialists in microbiology. Medicinal beekeeping allows the creation of beehive products for millions of patients located worldwide. Any person, no matter where they live, have had, has, or will have a disease, so the practice of medicinal beekeeping should be studied and applied by all beekeepers from all over the world, to finally create a win-win situation that reaches the patients too.

Keywords: Mono-Floral Based Bee Products, Cleanliness, Medicine-Oriented Beekeeping.

Oral Presentation

Status of Bee Products: Approved or Not?

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Abstract

Looking for a healthy and natural lifestyle, both consumers and producers are more and more interested in bee products from primary production to food supplements and/or medicines, medical devices or cosmetics. That is why an attentive review on the legal status of the bee products (honey, bee pollen, bee bread, propolis, royal jelly, bee larvae, bee venom etc.) on the international market is an important issue in both valuing the beekeeping production and protecting the consumers' health. If defined as food, bee products make no exception and should comply primarily with the requirements of Codex Alimentarius – the „Food Code" adopted by the Codex Alimentarius Commission, which is the central part of the Joint FAO/WHO Food Standards Program meant to protect consumer health and promote fair practices in food trade. In the European Union, food (food supplements or functional food included) is regulated by EU Regulation (EC) 2002/178, the „General Food Law" which aims to protect human health and consumer's interest in relation to food. Other regulations are related to the nutritional and health claims made on for food - EC 1924/2006, EC Regulation 1169/2011 and EU Novel Food Regulation 2015/2283 are particularly important as regards the safety, health effects on consumers etc.) Almost the same regulations for food are to be found for FDAs in various other parts of the world. However, there are still many obstacles for bee products as, according to the evaluations of the experts many of them cannot be labelled but with a nutritional declaration, health claims not being authorized. As for traditional medicines, the registration procedure should consider the products with a long tradition of safe use" including "substances of animal origin (honey, royal jelly, propolis etc.). In Europe, a possible extension of the scope of EC Directive 2004/24 to is expected. Even if this extension is not accepted, a legal framework of their use is to be considered.

Keywords: Bee Products, Food Supplements, Medicines, Traditional Medicines

Oral Presentation

Regulations of Apitherapy Products

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Abstract

In our draft legislation study, our priority is supplying of quality, efficacy and safety of the products used in apitherapy. “Traditional and Complementary Medical Practices Regulation” published on 27th of October in 2014 in Turkey. In parallel with the increase in the number of apitherapy specialists, the interest in this field is increasing day by day. Apitherapy is very popular nowadays and products are available on the market as only cosmetic and supplementary foods with no claim or indication. We started our work on monographs with a group that we formed with academicians who are experts in their fields. We looked for answers to some questions to shed light on our work. Some of these questions are “What are the medicinal products used in apitherapy? What should be the requirements in terms of production site and good manufacturing practices for bee products? How should standardization be achieved? What is the necessity of determining specific criteria for product groups? Whether the indication or purpose of use will be declared in the products.” Initially, eight product groups were determined for bee products to be used in apitherapy for monographs are about to be prepared. With the initial working group and meetings held online during the pandemic process, monographs of honey, propolis, royal jelly, bee venom, bee pollen and bee bread (perga), apilarnil and beeswax were created. In these monographs some specifications are determined. We have a cooperation with the Ministry of Agriculture and Forestry for this job. With this legislative work that we have started, we are aiming to ensure that bee products are available in the market as supplementary food and cosmetic products, as well as medicinal products used in apitherapy, by determining the framework of use of the products.

Keywords: Apitherapy, Turkey, Legislation, Monograph

Oral Presentation

Ethical and Legal Issues in Apitherapy

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Abstract

Although Apitherapy and other Traditional and Complementary Medicine (T&CM) practices continue to exist with the history of humanity, they have been ignored in medical circles for a certain period of time, but have recently started to come to the fore in the world for the last 50 years and in our country for about 10 years. However, ethical and legal issues related to these practices have also started to be on our agenda. Whether T&CM practices are in compliance with Medical Ethics and what kind of responsibilities they impose on their practitioners are the main problems. In this study, ethical issues and legal responsibilities in T&CM applications in general and Apitherapy applications in particular are examined. In addition, the legal situation regarding T&CM and Apitherapy in Turkey will be explained.

Keywords: Apitherapy, T&CM, Traditional Medicine, Medical Ethics

Oral Presentation

The World of Injectable Apitoxin

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Abstract

Clinical experience will be developed in treatments with Apitoxin and other hive products (Honey, and Propolis) in various joint, bone and muscle pathologies, chronic diseases (Arthrosis, Arthritis) and others such as Disc Hernias, Auto Immune Diseases (Lupus, Multiple Sclerosis) etc. performed in outpatient consultations with evolution tracking, complementary therapies and rehabilitation treatments in patients of different ages. Immediate results and over time aimed at giving a better quality of life and their integration into their usual activities. Therapeutic schemes, dosage, form of administration, frequency and duration thereof.

Keywords: Bee Venom, Injectable, Lupus, Immunological Diseases, Integrative

Oral Presentation

Pollen and Honey as Part of The Treatment in Diseases of The Nervous System

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Abstract

The cells of the nervous system require specific nutriments to their formation, development and operation. The pollen and the honey have the nutriments necessary for the human nervous system. Most studies on nutrition and cognitive function have been carried out in animals, whit industrial supplements and diets of fruits and vegetables, then this area of function cognitive, pollen and honey are little explored. The porpoise of complement with pollen and honey is offer practical options to patients with neurotransmitters deficiency, cognitive impairment and, neurodegenerative diseases, because the incidence of these diseases is becoming a public health problem. In clinic practice the patients with supplement pollen—honey progress in them health, for example in case whit deficiency of neurotransmitters has been observed decrease in aggressiveness, walking wandering and panic episodes.

Keywords: Pollen, Honey, Nervous System, Apitherapy, Diseases

Oral Presentation

Immunosuppressive Patients and Apitoxicotherapy

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Abstract

This article is intended to find the utmost importance of a consultant in the face of the possibilities of risk measures by an apitherapist, in the face of the knowledge to assess it against any risk of fully invasive treatment. That is why, it should be an unappealable rule to take vital signs before, during and at the end of an apitoxicotherapy treatment, in case the apitherapist himself has considered the inoculations in the consultant as a first-defense line treatment. Always at any risk, it is vital to let the consultant know about the risks, but also the benefits that the consultant will get, whether in the short, medium and long term. In the last year, the analysis of the changes that consultants start treatment with apitoxicotherapy has been carried out, since they have been seen in situations where it puts them, with changes of mind, derived from the stress caused by the knowledge and see bees for the first time in the specific treatment with apitoxicotherapy. Such mood swings go hand in hand with taking vital signs, as they are; temperature, blood pressure, blood glucose level, oxygen saturation. In addition to knowing about its weight, size and giving a treatment steadily assertive, a treatment according to its weight and ideal size, and not offering pharmacopoeia api, more than what organism requires.

Keywords: Immunosuppressive, Pharmacopoeia Api, Apitoxicotherapy

Oral Presentation

Red Propolis: History, Biological Activities of Its Main Phenolic Compounds and Apitherapy

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Abstract

The presentation of the Red Propolis theme at this Congress will go through a brief account of the history of the discovery of red propolis in northeastern Brazil, reinforcing the idea that the production of propolis in any geographical region of the world, where there is respect and love for bees, propolis can be produced with excellent quality for the health of human beings, plants and animals. Northeast red propolis belongs to Group 13 of Brazilian propolis studied so far, and its botanical origin is Dalbergia ecastophyllum (L.) Taub., Popularly called Rabo de Bugio, Cipó do Macaco, Marmeleiro da Praia, Verônica Branca, etc. Many studies have been done on the biological and pharmacological activities of Red Propolis, its phenolic compounds, especially flavonoids. The main isoflavone found in group 13 propolis is Formononetine, which has an anti-inflammatory, antioxidant and neuroprotective action. Following it is present in the red propolis Isoliquiritigenina, Liquiritigenina, Pinocembrina, Pinobanksina, Luteolina, Rutina, Pinobanksin-3-acetate, Biochanina A, Quercetina, Daidzeina and Dalbergina. In this context, research using red propolis has been used since its botanical discovery (2005) to be able to conduct effective apitherapies. Without wishing to exhaust the subject related to research, some topics of greater relevance were selected in studies related to the biological and pharmacological activities of Red Propolis, such as antitumor, analgesic, anti-inflammatory, anti-HIV, antifungal, antiprotozoal, prostate hypertrophy, injury medullary, protective hepatic, antimicrobial, healing, hypotensive, anticariogenic and much more.

Keywords: Propolis, Phenolic, Apitherapy

Oral Presentation

The Actuation of Propolis Against the Coronavirus

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Abstract

Propolis is a resinous extract produced by bees that mix resins or parts of plants with beeswax and other substances. Its composition varies according to the geographic location, botanical origin, climatic factors and species of bee. It has been used since antiquity as an antiseptic, antimicrobial, anti-inflammatory, anti-ulcer, antioxidant, anti-angiogenic and wound healing agent, activities attributed to phenolic compounds, including flavones, flavonols, flavanones, dihydroflavonols, caffeic acid phenethyl ester (CAPE), cinnamic acids and their esters. There are more than 300 compounds found in different propolis. Due to its promising functional properties, there is currently a growing interest in the commercialization of propolis. It still has potential against viral targets and immunoregulatory properties. A randomized controlled clinical trial with standardized green propolis in hospitalized adult patients with COVID-19 showed great benefits and there are several metabolic pathways that elucidate it.

Keywords: Coronavirus, COVID-19, Propolis, Brazil, Phenolic, Immunoregulation

Oral Presentation

Treatment of Amyotrophic Lateral Sclerosis (ALS) with Apitherapy and Natural Medicine

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Abstract

The importance of this presentation lies in satisfying the population's need for a natural treatment that allows patients to no longer ingest a large amount of allopathic medications that are already part of the daily life of people with Amyotrophic Lateral Sclerosis (ALS), since they have to take several tablets a day to combat their symptoms, heal without damaging and improve the quality of life of the patients, as well as stop the progressive progression of the disease. ALS is an autoimmune disease that specifically attacks motor neurons, causing progressive weakness, muscle atrophy and progressive loss of muscle strength leading to loss of movement and in severe cases the inability to breathe as well as disability. ALS does not affect sensory neurons or cognition, the diagnosis is confirmed by the observation of sclerotic plaques in the axons of the motor neurons, in turn it is exclusion, it is carried out when ruling out any other disease with similar manifestations. Through the use of Apitherapy, it seeks to stop the degenerative progression of the disease and mitigate the impact it produces on quality of life, allows neuronal survival, control of inflammation and reduction of beta amyloid, induces neurogenesis, controls stress oxidative. Phytotherapy allows patients to provide large amounts of antioxidants, strengthens their immune system, avoid and fight infections and provides antidepressant effects, reduces insomnia and chronic fatigue. Biological medicine provides molecules that represent a real direct donor source of energy for cellular functions, stimulating neuronal survival.

Keywords: ELA, Sclerosis, Apitherapy, Natural Medicine, ALS, Autoimmune

Oral Presentation

Respiratory exercise with Propolis spray: Uses and benefits to improve Health.

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Sandra Mercado - Biomagnetismo, Guayaquil, Ecuador

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Abstract

The day we are born we inhale and the day we die we exhale what we do in that intermission depends on us; and if it is with Propolis spray much better. What we have learned in a pandemic, something of Vital importance is to understand that we inhale oxygen through our nostrils and exhale carbon dioxide, this means that the masks prevent the correct oxygenation for our cells, by inhaling carbon dioxide, which is a toxic waste and The prolonged use of the masks will slowly but irremediably damage our cells, since respiration is at the cellular level and in the gas exchange that exists at the level of the pulmonary alveoli we are little by little damaging our organism. "Propolis is not a treatment to cure covid-19, it is a prevention treatment to raise our defenses" Dr. Tonatiuh Cruz. In the year 2020 in the middle of the pandemic, it was where the Respiratory Exercise helped hundreds of people who came to our office requiring help not only from Biomagnetism therapy but also to help them breathe better. Propolis, one of the best natural antibiotics, is also anti-inflammatory, antiviral, antiseptic, and all of us who are in natural medicine or in health prevention know its extraordinary benefits since the time of our grandmothers and in archaeological investigations we also observe that it has been used since ever. Something that caught my attention was the content of pinocembrin and caffeine esters, which in my opinion is what helps in the gas exchange that occurs in the pulmonary alveoli, this of course is under investigation. He uses an electronic equipment called Quantum Magnetic Resonance Examination and the Propolis spray that he used which is from La Melífera Laboratories. We present the examinations of each patient, the first and the last to be performed, where I make a comparison of the effect produced with the respiratory exercise.

Keywords: Respiratory Exercise, Propolis, Pinocembrine, Coffeeate Esters, Increase Defenses, Covid-19.

Oral Presentation

A Comparison of Commercial Propolis Extracts in Terms of Analysis Results

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Abstract

Propolis is consumed in different extract forms as supplementary food. Standardization of raw propolis is difficult because the composition of raw propolis depends on many factors such as flora of the area, harvesting season, collection style, and bee strain. However, propolis extracts could be standardized. In this study, different commercial propolis extracts were purchased from markets and their quality parameters were compared with each other. The pH, total phenolic substance, total flavonoid, and total antioxidant capacity values of 15 different commercial samples, including aqueous, ethanolic, water-based and vegetable oil, were compared. Accordingly, the total polyphenol values of ethanolic, aqueous and glycol extracts differ. The pH values were ranged from 4,0 to 10 in the samples. It was determined that the highest total polyphenol values in ethanolic and glycolic samples, and the water and olive oil samples had the lowest values. Although the polyphenol value of the water-based propolis sample was very low, it was observed that the total antioxidant capacity was very high. This example shows that antioxidant activities were found correlated with their total polyphenolic contents. Our results suggest that these parameters may play an important role in the preparation, consumption, and standardization of propolis extracts. However, the most important criteria to be sought in commercially purchased propolis are the use of solvents that will not harm human health and that products with high polyphenol content are more valuable.

Keywords: Propolis, Antioxidant capacity, Polyphenol, Solvents.

Oral Presentation

Quantitative Evaluation of Marker Components of Several Propolis Samples Obtained from Black Sea Region (Turkey)

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Abstract

Propolis having a tremendous *popularity* is a resinous bee product. To produce propolis, honeybees (*Apis mellifera* L.) collect resins found in the plant leaves, buds and stems or plant exudates and then mix them with their saliva and wax. Thus, propolis chemical composition is highly related with the plant species found around the beehive. Several studies have been conducted to reveal its antioxidant, antimicrobial, anti-inflammatory, immunomodulatory activities. However, this should be highlighted that chemical component analysis is supreme importance for interpreting the pharmacological activity of propolis samples having different botanical origin. Therefore, this study aimed to develop and validate an efficient, reliable, and precise high-performance liquid chromatography (HPLC) method for quantification of marker components for propolis samples collected from Black Sea Region (Turkey). In this study, a new HPLC method was developed to simultaneously quantify key markers (caffeic acid, quercetin, 3-methyl quercetin (3-MQ), apigenin, kaempferol, chrysin, pinocembrin, galangin and caffeic acid phenethyl ester (CAPE)) in 47 propolis samples (P1-47) obtained from different localities in Black Sea Region in Turkey. Chromatographical separation was achieved on C_{18} column (150 mm × 3.9 i.d. and a particle size of 5 µm) using two mobile phase systems which were ultrapure water acidified with 0.1% *o*-phosphoric acid (Phase A) and acetonitrile (Phase B) at a flow rate of 1 mL/min. The investigated compounds were monitored from 260 nm to 340 nm. Determination and identification of the investigated peaks in the samples were performed by comparing the retention times (t_R) and the DAD spectrums with that of the standards. The method was then validated according to the International Conference on Harmonization (ICH) requirements, which include specificity, linearity, limit of detection (LOD), limit of quantification (LOQ), precision and accuracy parameters. Consequently, the highest caffeic acid, quercetin, 3-MQ, apigenin, kaempferol, chrysin, pinocembrin, galangin and CAPE contents were quantified as 15.66 mg/g, 3.63 mg/g, 9.31 mg/g, 5.92 mg/g, 7.87 mg/g, 50.90 mg/g, 81.06 mg/g, 78.74 mg/g and 28.54 mg/g, respectively by a validated HPLC method.

Keywords: Propolis, HPLC, Validation, Chemical Composition, Black Sea Region (Turkey)

This study was supported by The Scientific and Technological Research Council of Turkey (TÜBİTAK), Project No: 118S645.

Oral Presentation

What should be the ideal rate for Ethanolic Propolis Extraction?

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Abstract

Propolis, a resinous substance produced by bees to protect their hives from external factors, has recently come to an important place for human health. It has proven to be a remarkable product by overcoming various health problems thanks to its ingredients such as phenolic substances, sterols, minerals, and amino acids. In addition to these, propolis is a natural product that should not be consumed raw and should be extracted with appropriate solvents. It is seen that various solvents and different methods are used in propolis extraction. It is known that 70% Ethanol is commonly used for medical use and solvent systems with higher alcohol content are used for chemical analysis. However, researchers have also tried different extraction methods with organic and inorganic solvents. It is necessary to determine the solvent-propolis ratio used in extraction well in order to protect human health and to provide the highest benefit. The main purpose of all these comes from the principle of minimum cost and maximum efficiency. In this context, the solvent-propolis ratio with the highest efficiency was tried to be determined by using 70% ethanol solvent system in our study. By keeping the solvent volume constant, extracts with different proportions in the range of 1:1/2-1:1/10 were prepared, and the total phenolic content was analyzed per ml of extract. It is observed that the total phenolic content obtained per ml of extract decreases with the increase in the amount of propolis in the extracts prepared. Based on this, it can be thought that the point where the solvent system reaches saturation may be the ideal ratio for solvent-propolis extraction. In our study, the yields of extracts in the ratios of 1:1/2, 1:1/3, 1:1/4, 1:1/5 and 1:1/10 were found as 43%, 47%, 49%, 62% and 67% respectively. Decreasing the solvent-propolis ratio may increase the yield of phenolic content that can be taken from propolis, but in this case, the solvent consumption will increase. For this reason, it is seen that the use of 1:1/5 and 1:1/10 ratios, where more than 50% yield is started, may be the most suitable solvent-propolis ratio for maximum efficiency and minimum cost.

Keywords: propolis, extraction, solvent-propolis ratio, TP

1. Introduction

Preventive or curative treatment methods made with bee products (honey, pollen, propolis, royal jelly, bee venom, and bee bread) are called apitherapy (Şahin and Kemal, 2019). Honeybees collect the sticky substances and resinous leaks found in the buds and leaves of the plants using their hind legs and upper jaws and soften them by moistening them with the enzymes in their mouths. Propolis, which is in the form of pellets, is collected in pollen baskets on the hind legs and transported to the hive (Akçay et al., 2020; Bankova et al., 2019). Honeybees use propolis for many purposes such as adjusting the internal temperature (~34°C) and humidity (40-65%) of the hive, repairing cracks and damaged areas, narrowing the entrance holes, preventing the growth of various microorganisms (virus, bacteria, etc.) and disinfecting the hive. For honeybees, Pine resins (Pinus spp), Birch (Betula spp), Poplar and its species

(Popolus spp), Horse chestnut (Aesculus Hippocastonum), Willow (Salix spp), Redwood (Alnus spp), Fir (Abies spp), Plum (Prunus spp), Oak (Quercus spp), Ash (Froxinus Excelsior) secretions, lipophilic substances in leaves and buds are important sources of propolis (Kolayli and Keskin, 2020). When bees cannot collect propolis from the environment, they collect substances containing various dyes, asphalt, and mineral oils to be used as propolis.
Propolis has a distinctive pungent aromatic odor and can be found in varying colors such as brown, green, yellow, and red depending on the season it is collected and the botanical source. While propolis has a soft, flexible, and sticky structure in heat, it has a hard and brittle structure in cold. In many studies, it has been stated that the chemical content of propolis collected from different geographical regions varies depending on the region, vegetation, climatic conditions, and bee race. It has been identified that there are more than 300 chemical components belonging to flavonoids, terpenes and phenolics in propolis. Raw propolis generally consists of 50% resin, 30% wax, 10% essential oils, 5% pollen and 5% other organic ingredients (Galeotti, 2018; Kolayli and Keskin, 2020).
Propolis is a bee product whose extract should be prepared and consumed. However, the lack of clear information about the active ingredient content of the extracts prepared causes suspicion and concern for the user. Although there are various studies on this subject, a complete standardization on propolis has not been made yet (Keskin, 2018). As a result of the literature reviews, it is seen that different methods are used for the propolis extraction process (Table 1).

Table 1. Solvent-propolis ratios and methods used in the preparation of propolis extracts in the literature

Researcher	Solvent-propolis ratio	Method
Tosi et al. (1996)	%30	%60 EtOH, glycerol, propylene glycol etc.
Trusheva et al. (2007)	1:1/50	%70 EtOH (ultrasonic and microwave)
Keskin (2018)	1:1/10	%96 EtOH, 7 days
Karlıdağ and Genç (2019)	1:1/10	%98 EtOH, 24 hours
Jug et al. (2014)	1:1/5	%80 EtOH, 24 hours
Xu et al. (2006)	1:1/25	%80 EtOH, 3 hours
Biscaia et al. (2009)	1:1/4	%70 EtOH, 7 days
Mokhtar et al. (2019)	1:1/10	%70 EtOH, 7 days
Khacha-Ananda et al. (2013)	1:1/20	%70 EtOH, 3 days in the dark

2. Materials and Methods

Propolis samples obtained from beekeepers affiliated to the Turkish Beekeepers Association were ground in a blender after being frozen. It was stored at -20 degrees until analysis time. Samples prepared at the ratios of 1:1/2, 1:1/3, 1:1/4, 1:1/5 and 1:1/10 were extracted at 200 rpm for 24 hours at room temperature. 70% EtOH/water was used as solvent. Filtering was done with filter paper to remove solid particles. Then, total phenolic content analysis was performed from this extract.

2.1. Total phenolic content analysis

Total amount of phenolic substance was measured by Folin Ciocalteu method (Singleton and Rossi.1965). This method gives the response to all phenolics including phenolic acids, flavonoids, anthocyanins, and tannins etc. in the solution. The results were expressed as mg gallic acid equivalent (GAE) / ml by using the intensity of the blue color at 760 nm readings.

3. Results

In our study, the TP value of the extract (94,325 mg GAE/ml extract) at a 1:1 solvent-propolis ratio was accepted as 100% and an evaluation was made. It is observed that the yield of total

phenolic content obtained per ml of extract decreases with the increase in the amount of propolis in the extracts prepared (Table 2). Decreasing the solvent-propolis ratio may increase the yield of phenolic content that can be taken from propolis, but in this case, the solvent consumption will increase.

Table 2. TP values and % yield of extracts with different solvent-propolis ratios

Solvent-propolis ratio	TP mg GAE/ g sample	% Yield
1:1/2	67,443	%43
1:1/3	46,219	%47
1:1/4	35,136	%49
1:1/5	30,561	%62
1:1/10	15,753	%67

4. Discussion

By determining the optimum solvent-propolis ratio as well as the optimum solvent selection, the benefit to be obtained can be maximized. Researchers and producers prepare propolis extracts in different proportions and with different methods (Tablo 1) (Karlıdağ and Genç, 2019; Xu et al., 2006; Trusheva et al., 2007; Biscaia et al., 2009; Khacha-Ananda et al., 2013). However, the highest efficiency can be obtained with information about how much solvent-propolis should be used. Using Ethanol, which is the best solvent for propolis, and obtaining the highest efficiency is the main goal for researchers and producers. In our study, we aimed to determine the ideal solvent-propolis ratio by considering this issue.

5. Conclusion

It is seen that the use of 1:1/5 and 1:1/10 ratios, where more than 50% yield is started, may be the most suitable solvent-propolis ratio for maximum efficiency and minimum cost.

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Oral Presentation

Impact of Pasteurization Process on Hydroxymethylfurfural (HMF) Amount and Diastase Activity of Honey

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Abstract

Turkish Food Codex describes honey as a natural product that honeybee gathers plants' nectar, secretion of plants' living parts or secretion of plant-sucking insects which live on plants' living parts and then, makes change on them by putting them to distinctive substances, decreases content of water and ripens it by storing in honeycomb and which can crystalize by its nature, in The Notification of Honey (Notification No.: 2020/7). Four processes generally as filtration, homogenization, pasteurization and resting on air come into prominence in an integrated honey processing and packing facility. Filtration is made in order to remove factors which trigger the crystallization of honey as the foreign matters arising from honey harvest in honey and undesirable matters at invisible micron level are detracted. Honey's chemical and physical features differ in season, vegetation cover and climate. Honey is homogenized in a homogenization tank in order that it can be standardized to represent the party. Furthermore, pasteurization process is made in order that development of osmophilic ferments resistant to sugar can be prevented, and honey's viscosity and crystallization are decreased. Remnants of melted wax can be in honey with the impact of temperature despite that honey is filtered, and air bubble can occur due to the circulation in this process. Therefore, honey is taken into the tank of resting on air after it is processed. In this research; the impact of pasteurization process on hydroxymethylfurfural amount and diastase activity of six-party honey sample was examined. Approximate HMF values of samples which were received from homogenization and pasteurization units were respectively determined as 5,70±0,72 mg/kg and 6,76±0,69 mg/kg, and the difference between them was found significant statistically (p=0,014). Approximate diastase numbers of samples which were received from homogenization and pasteurization units were respectively determined as 12,82±1,32 and 11,42±1,38, and the difference between them was not found significant statistically (p=0,068). After the pasteurization process, it was determined that honey's HMF (40 mg/kg at most) and diastase numbers (8 at least) are in the limits which are stated on Notification of Honey by Turkish Food Codex.

Keywords: Honey, HMF, Diastase Activity, Pasteurization, Homogenization

Oral Presentation

Ivy Honey with Physicochemical and Bioactive Properties

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Abstract

Ivy honey is a special monofloral honey gathered by honeybees from the nectar and pollen of the ivy (*Hedera helix* L.). Ivy honey, which has been discovered in recent years, is an interesting honey with its characteristic taste and smell properties and therapeutic effects. In this study, physicochemical properties, phenolic compounds and biological activities (antioxidant and antimicrobial) of ivy honey obtained from Kırıkkale in Turkey were investigated. pH, moisture, color, electrical conductivity and optical rotation values of the honey sample were determined for physicochemical parameters. The composition of the phenolic compounds were analyzed by HPLC-UV (gallic acid, protocatechuic acid, *p*-hydroxybenzoic acid, catechin, caffeic acid, vanillic acid, syringic acid, epicatechin, *p*-coumaric acid, ferulic acid, rutin, daidzein, luteolin and *t*-cinnamic acid). Total phenolic contents and ferric reducing antioxidant power (FRAP) were performed as antioxidant determinants. The values obtained show that ivy honey is a precious honey with monofloral flower honey quality and high antioxidant and antimicrobial properties.

Keywords: Ivy Honey, Physicochemical Properties, Phenolic Compounds, Antioxidant Activity, Antimicrobial Activity

1. Introduction

Honey is a bee product collected by *Apis mellifera* bees from nectar of flowers or secretions of living parts of plants and chemically modified with specific organic substances, e.g. salivary secretions and enzymes (Ávila et al. 2019, Commission 2001). Honey is not only a natural sweetener with high sugar content (fructose 25-45 % and glucose 20-40 %), but also a functional food with biological properties such as antioxidant, antimicrobial, antiviral, anti-inflammatory, antimutagenic, wound and sunburn healing effects (Abderrahim et al. 2019, Baghel et al. 2009, Benhanifia et al. 2011, Kucuk et al. 2007, Shahzad and Cohrs 2012, Simonetti et al. 2020, Sipahi et al. 2017, Osés et al. 2020, Watanabe et al. 2014). These various health-promoting effects depend on its nutritional content and bioactive substances including organic acids, amino acids, enzymes, proteins, minerals, vitamins and especially, phenolic compounds (Alvarez-Suarez et al. 2014, Mračević et al. 2020).

It has been reported that biological activities of honey in parallel with chemical composition and are greatly influenced by its botanical and geographical origin, climate and weather conditions, as well as processing and storage conditions (Seraglio et al. 2021). The botanical origin of honeys is one of its main quality parameters. For this reason, the chemical composition and therapeutic properties of types of honey from different regions have been investigated since past few decades (Can et al. 2015, do Nascimento et al. 2018, Dżugan et al. 2020, Kanbur et al. 2021, Kavanagh et al. 2019, Mračević et al. 2020).

Ivy honey is a special monofloral honey gathered by honeybees from the nectar and pollen of the ivy (*Hedera helix* L.). Ivy honey, which has been discovered in recent years, is an interesting honey with its characteristic taste and smell properties and therapeutic effects. Usually, ivy has nectar-rich, small, yellow-green and umbrella-like flowers. Ivy is a significant source of food and honey for honeybees, by reason of being obtainable from the end of summer to the end of autumn for honeybees and providing of high amount of nectar and pollen for winter stores. The taste of the ivy honey in the first months after harvest is strong and unpleasant. During the ripening process, ivy honey acquires its characteristic features such as strong taste and smell of ivy, delicate texture and light color. Due to the high glucose content of ivy honey, it crystallizes shortly after being collected from the hive and forms solid white combs, and therefore it becomes difficult to remove ivy honey from bee combs (Makowicz et al. 2018). There are very few studies on the physicochemical and bioactive properties of ivy honey in the literature. The main aim of this study was to carry on a preliminary investigation to shed light on the main characteristic properties of ivy honey. For this purpose, physicochemical properties, and biological effects (antioxidant and antimicrobial activity), and phenolic compounds of ivy honey (*Hedera helix* L.), which is mainly responsible for these activities, were investigated in this study.

Figure 1. Ivy (*Hedera helix* L.)

Figure 2. Ivy honey

2. Materials and Methods

2.1. Honey sample

The ivy honey was collected from a single experienced beekeeper from Kırklareli in Turkey in the 2018-2019 harvest season. The tests were performed within the two months following collection. Honey sample was stored under room conditions in a controlled manner until analysis.

2.2. Physicochemical properties

Some physicochemical characteristics of the honey were in agreement with European Union (Bogdanov et al. 1997). The color value of the honey was determined using a Hunter spectrometer (CR-400, Minolta, Osaka, Japan). Moisture and water-soluble dry matter (º brix) were measured using a refractometer (Atago, Tokyo, Japan) according to the International Honey Commission (IHC) (2009). pH value of honey sample was measured with a digital pH meter in 10% (w/v) solution at 21 °C (WTW, Microprocessor pH meter, Germany), electrical conductivity with a conductometer (Hanna Instrument, HI 2030-02, Romania), and optical activity or rotation with a polarimeter (Beta PPP7, England). All analyses were carried out in triplicate.

2.3. Analysis of phenolic compounds by HPLC

Fourteen standards (gallic acid, protocatechuic acid, *p*-hydroxybenzoic acid, catechin, caffeic acid, vanillic acid, syringic acid, epicatechin, *p*-coumaric acid, ferulic acid, rutin, daidzein, luteolin and *t*-cinnamic acid) of phenolic compounds were analyzed using HPLC (Elite LaChrom Hitachi, Japan), in a UV–Vis detector. The sample was injected into the HPLC system with a reverse phase C18 column (150mm x 4.6 mm, 5 mm; Fortis). Acetonitrile, water and acetic acid were used for the mobile phase by applying the programed gradient. The mobile phase consisted of (A) 2 % acetic acid in water and (B) acetonitrile: water (70:30). The samples and standarts injection volume were 25 mL, column temperature at 30 °C and flow rate at 1.5 mL/min. The programed solvent used began with a linear gradient held at 95 % A for 3 min, decreasing to 80 % A at 10 min, 60 % A at 20 min, 20 % A at 30 min and finally 95 % A at 50 min (Can et al. 2015). For quantitative determining, each phenolic component calibration curves were between 0.998 and 1.000.

2.4. Determination of total phenolic content (TPC)

Total phenolic content of the methanolic honey extract was determined with Folin-Ciocalteu reagent according to the method of Slinkard and Singleton (1977) by using gallic acid as a standard. Briefly, 680 mL distilled water, 20 mL methanolic honey extract and 400 mL of 0.2 N Folin–Ciocalteu reagent were mixed in a test tube and vortexed. Following a 3-min incubation, 400 mL of Na_2CO_3 (7.5 %) was added and the mixture was incubated for 2 h at room temperature. After incubation, the absorbance was measured at 760 nm in a spectrophotometer (Thermo Scientific EvolutionTM 201, UV-VIS Spectrophotometer, USA). The concentration of total phenolic compounds was expressed as milligram of gallic acid equivalents (GAE) per 100 g honey samples, by using a standard graph. All measurements were performed in triplicate.

2.5. Determination ferric reducing antioxidant power (FRAP)

The antioxidant capacity of the methanolic honey extract was determined according to a modified version of ferric reducing antioxidant power (FRAP) assay of Benzie and Strain (1996). Briefly, FRAP reagent was prepared by mixing 25 mL of 300 mM acetate buffer, pH

3.6, with 2.5 mL of 10 mM TPTZ solution in 40 mM HCl and 2.5 mL of 20 mM $FeCl_3.6H_2O$ solution. Then, 3 mL freshly prepared FRAP reagent and 100 mL of the extract were mixed and incubated for 4 min at 37°C, and the absorbance was read at 595 nm against a reagent blank containing distilled water. $FeSO_4.7H_2O$ was used as the standard solution and the antioxidant capacities of the extract were calculated as µmol $FeSO_4.7H_2O$ equivalent of 100 g sample by using the calibration graph.

2.6. Determination of antimicrobial activity

All test microorganisms were obtained from ATCC and RSKK were reconstituted from its lyophilized form according to the manufacturer's protocol, were as follows: *Escherichia coli* ATCC (25922), *Yersinia pseudotuberculosis* ATCC (911), *Klepsiella pneumonia* ATCC (18883), *Pseudomonas aeruginosa* ATCC (27853), *Staphylococcus aureus* ATCC (25923), *Enterococcus faecalis* ATCC (29212), *Bacillus cereus* (702 Roma), *Bacillus subtilis* ATCC (6633), *Lactobacillus casei* (RSKK 591), *Mycobacterium smegmatis* ATCC (607), *Candida Albicans* ATCC (60193), *Candida tropicalis* ATCC (13803), *Saccharomyces cerevisiae* (RSKK 251).

Antimicrobial activity of the extract was determined using the disc diffusion method. Bacterial suspension turbidity 0.5 McFarland and fungal suspension turbidity 2.0 McFarland standards were prepared. The concentration of bacterial suspensions was thus adjusted to 10^7 cells/mL, and that of fungal suspension to 108 cells. Sterile swabs were immersed in the test organism. Excess fluid was removed, and the inoculated was applied to the entire surface of the plate in at least three directions. Discs were applied to the plate within 15 min of inoculation. Solutions 1/5 mL in size were impregnated on 6-mm diameter sterile blank discs (Oxoid) (20 mL per disc). Inhibition zones were measured using digital calipers after incubation for 24 and 48 h at 37° C (for bacteria). The results were expressed in terms of the diameter of the zones; 56 mm, inactive; 7–9 mm, very low activity; 9–11 mm, low activity; 12–14 mm, average activity and >15 mm, high activity. Ampicillin, streptomycin and fluconazole were used positive controls, and all determinations were made in triplicate.

3. Results

3.1. Physicochemical parameters

The physicochemical properties of the ivy honey were shown in Table 1.

Table 1. Physicochemical parameters of the ivy honey

Physical Parameters		**Ivy Honey**
pH		4.14 ± 0.01
Moisture (%)		18 ± 0.05
Brix (%)		82 ± 0.05
Conductivity (mS/cm)		0.27 ± 0.01
Optic rotation		-1.802 ± 0.02
Colour	**L**	29.00 ± 2.50
	a	38.05 ± 0.32
	b	49.63 ± 3.10

3.2. Identification and quantificaiton of phenolic compounds

Phenolic compounds are the main components responsible for the bioactive properties of honey, especially its antioxidant, antimicrobial and anti-inflammatory properties (Alvarez-Suarez et al. 2014, Hadagali and Chua 2014, Puupponen-Pimiä et al. 2001). Fourteen phenolic compounds investigated at HPLC-UV in the phenolic profile of the ivy honey (Table 2).

Table 2. Phenolic compounds content (µg/mL) in the ivy honey sample

Compounds	Ivy honey
Gallic acid	n.d.
Protocatechuic acid	1.22
p-OH benzoic acid	0.91
Catechin	1.58
Vanillic acid	0.27
Caffeic acid	0.44
Syringic acid	n.d.
Epicatechin	n.d.
p-coumaric acid	0.22
Ferulic acid	0.10
Rutin	n.d.
Daidzein	n.d.
t-cinnamic acid	n.d.
Luteolin	0.47

*n.d: not.

3.3. Total phenolic content (TPC)

The total phenolic content (TPC) of the ivy honey was determined as 35 mg of gallic acid equivalent (GAE)/100 g honey (Table 3).

Table 3. Total phenolic content and antioxidant activity of the ivy honey

Antioxidant parameters	Ivy honey
TPC (mg GAE/100 g honey)	35±0.00
FRAP (µmol $FeSO_4.7H_2O$/100 g honey)	176±5.00

3.4. Ferric reducing/antioxidant power assay (FRAP)

The antioxidant activity of the ivy honey determined with FRAP assay was found as 176±5.00 µmol $FeSO_4.7H_2O$/100 g honey (Table 3).

3.5. Antimicrobial activity

The antimicrobial activities of the ivy honey against eleven bacteria and three fungi strains were examined, and the results were calculated by measuring the resulting inhibition zones (Table 4).

Table 4. Antimicrobial activity of the ivy honey (1/2 diluted) against the microorganisms

No	Ec.	Yp.	Kp.	Pa.	Sa.	Ef.	Bc.	Bs.	Ms.	Ca.	Ct.	Sc.	Sm.	Lc.
IH1	-	10	12	6	12	-	6	-	-	-	-	-	-	-
IH2	6	6	10	6	12	-	8	-	-	-	-	-	-	10
IH3	-	12	14	6	12	-	10	-	-	-	-	-	-	6
Amp.	10	10	10	18	35	10	15	15					NT	NT
Strep.									35					
Flu.										25	25	25		

Ec: *E. coli*, Yp: *Y. pseudotuberculosis*, Kp: *K. pneumonia*, Pa: *P. aeruginosa*, Sa: *S. aureus*, Ef: *E. faecalis*, Sm: *S. mutans*, Bc: *B. cereus*, Bs: *B. subtilis*, Lc: *L. casei*, Ms: *M. smegmatis*, Ca: *C. albicans*, Ct: *C. tropicalis*, Sc: *S. cerevisiae*, Amp.:Ampicillin, Str.: Streptomycin, Flu.: Fluconazole, (-): not dedected

4. Discussion

4.1. Physicochemical parameters

The pH of honey influences its texture, stability and shelf life depending on the growth of microorganisms. Because of the content of the various amino acids, especially proline, and organic acids, the pH value of honey has generally acidic character. (Boussaid et al. 2018, Habib et al. 2014, Terrab et al. 2002). pH value of the honey was determined as 4.14 ± 0.01. The pH value was acceptable and comparable with the results reported by Kavanagh et al. (2019) have been reported that the pH values of Irish honey samples ranged from pH 3.24 to pH 4. 4.83 and the pH values of Ivy honeys were 3.79 and 3.91.

The moisture content (%) of the honey was found as 18, which are within the allowed parameters (⩽20%) according to Turkish (TSE) and European (CEU) standards. The moisture content of honey is an important indicator of maturity degree depending on the harvesting time and it can vary from season to season and from year to year (Acquarone et al. 2007). Honeys harvested before full maturation have a high moisture content, leading to honey fermentation by some osmophilic yeasts that can develop in honeys with high moisture content. On the other hand, due to the maturation of honey, its moisture content decreases, and no microorganism activity is observed (Bogdanov et al. 2005, Kolayli et al. 2017).

The honey's electrical conductivity value was found as 0.27 mS/cm and it was below the maximum limit of 0.8 mS.cm−1 set by the Codex Alimentarius. Recently, this parameter was evaluated in the international standards in substitution for ash content (Codex Alimentarius 2001). The electrical conductivity of honey is closely related to the mineral substances, various ions, organic acids, proteins and amino acids it contains. It is a useful criterion to evaluate the botanical origin of honey and therefore it is frequently used for routine honey control, Moreover, it has been reported that the electrical conductivity is a differentiation parameter for honeydew honeys that have higher conductivity than blossom honeys (Acquarone et al. 2007, Bogdanov et al. 2004, Chefrour et al. 2009). In the study on Irish honey samples by Kavanagh et al. 2019, the Ivy honey samples' moisture content (%) 23.70 and 24.80 and electrical conductivity values 236.63 and 260.70 µS/cm.

Optical activity is the ability of a chiral molecule to rotate the plane of plane-polarized light measured using a polarimeter. Each of honey samples shows specific and different optical activity depending on the types and concentrations of sugars it contains. While blossom honeys generally have negative optical rotation (or levo-rotatory) values, honeydew honeys have positive (or dextro-rotatory) rotation values. This property has been used for discriminating of honeydew honeys and adulterated honeys (Belay et al. 2013, Cavrar et al. 2013, Dinkov et al. 2004). The optical rotation angle of the ivy honey was negative and -1.08.

The ivy honey's color values were determined as Hunter L* a* b* shown in Table 1. The color values for honeys were expressed as L* for darkness/lightness (0 black, 100 white), a* (-a greenness, +a redness), and b* (-b blueness, +b yellowness) (Anupama et al. 2003). The L value of the honey was 29, with lower L value indicating a darker honey color. Compared with Turkey blossom honey samples, the values varied from 2.64 to 8.04 and b values ranged from 11.50 to 23.56, ivy honey has much higher a and b values (Tornuk et al. 2013). Ivy honey was differed greatly from other blossom honeys in terms of color values. The reason can be that the compounds such as chlorophyll, carotene and xanthophyll in pollen of ivy (*Hedera helix*) give yellow-red to the ivy honey (Tezcan et al. 2011). The colour of honey is a useful parameter for the characterization of the product and depends on various factors such as botanical origin, mineral composition, pollen content, geographical and climatic conditions, storage and processing conditions (da Silva et al. 2016, Visquert et al. 2013). In addition, depending on the storage and processing temperatures of raw honey, the formation of various brown pigments

by Maillard reactions involving non-enzymatic chemical changes of sugars and free amino acids causes raw honey to darken (Brudzynski and Miotto 2011, Starowicz and Zieliński 2019).

4.2. Identification and quantificaiton of phenolic compounds

For the ivy honey, phenolic compounds of protocatechuic acid, *p*-OH benzoic acid, catechin, vanillic acid, caffeic acid, *p*-coumaric acid, ferulic acid and luteolin were identified at various levels. Among these phenolic substances, catechin (1.58 µg/mL) and protocatechuic acid (1.22 µg/mL) were found in the highest concentration, respectively.

Sixty-two honey samples collected from different regions of Turkey involved different amounts of phenolic compounds including protocatechuic acid, *p*-OH benzoic acid, catechin, vanillic acid, caffeic acid, syringic acid, epicatechin, *p*-coumaric acid, ferulic acid, rutin, quercetin, apigenin, kaempferol and isorhamnetin. However, chlorogenic acid, myricetin and fisetin were not detected in any honeys (Can et al. 2015). Gallic acid was determined as the most abundant phenolic compound in Brazilian honeys; also protocatechuic, cinnamic and p-coumaric acids and quercetin and myricetin were detected in significantly smaller amounts (do Nascimentoa et al. 2018). Nevertheless, gallic and cinnamic acids were not determined in the ivy honey. Similar to the phenolic contents of the ivy honey, gallic and syringic acids were not detected in Polish honey samples, but differently *p*-coumaric and vanillic acids, which were not detected in their samples, were found in small amount in our honey sample (Kaškonienė et al. 2009). The studies have reported that the phenolic composition may change depending on the floral and geographical origin of honey (Ávila et al. 2019, Serem and Bester 2012).

4.3. Total phenolic content (TPC)

The TPC of twenty-three different monofloral honey samples, obtained from different geographical regions of Turkey, were varied between 34.37 and 470.70 mg GAE/100 g honey (Gul and Pehlivan 2018). Aker and Nisbet (2020) reported a range of TPC from 106.04 to 166.46 mg GAE/100 g in 65 honey samples from different regions of Turkey, and found a difference in TPC depending on the botanical origin of the honey. The TPC of the monofloral Algeria honeys ranged from 14.5 mg GAE/100 g to 94.69 mg GAE/100 g. Similar a range of values have been reported in the literature.

4.4. Ferric reducing/antioxidant power assay (FRAP)

Antioxidant activities of Turkish honey samples varied of a wide range between 0.59 and 4.30 µmol $FeSO_4.7H_2O$/g (Can et al. 2015). In the study on Malaysian honey samples, their antioxidant activities ranged from 87.47 to 576.91 µM Fe (II)/100 g (Moniruzzaman et al. 2013). Polish buckwheat honey samples were observed variable antioxidant activity between 195 and 680 µmol Trolox equivalent (TE)/100 g (Dżugan et al. 2020). Antioxidant activity of the ivy honey showed a value similar to the antioxidant activity reported in the literature, and it varies especially due to the differences in the botanical and geographic origin of honey (Nayik and Nanda 2016).

4.5. Antimicrobial activity

Diluted ivy honey samples exhibited different degrees of inhibition effects against *Y. pseudotuberculosis*, *K. pneumonia*, *P. aeruginosa*, *S. aureus*, *B. cereus* and *L. casei*. The activity against pathological bacteria as *E. faecalis* and *E. coli* with fungi was not observed. The highest inhibition was determined against Y. pseudotuberculosis, K. pneumonia and S. aureus. The factors such as high level of sugars, low value of pH, high osmolarity, antibacterial peptides and H2O2 which is an oxidation reaction product of glucose by glucose oxidase play a crucial role in the antimicrobial properties of honey (Szweda 2017). In addition, it has been

reported that phytochemicals, especially phenolic compounds, are important antibacterial ingredients of honey. Because of antimicrobial potential of honey, it has been used for treatment of various wounds and burns (Manyi-Loh et al. 2011, Samarghandian et al. 2017).

5. Conclusion

Ivy is a significant source of food and honey for honeybees, by reason of being obtainable from the end of summer to the end of autumn for honey bees and providing of high amount of nectar and pollen for winter stores. For this reason, it is of great importance to increase the studies on the production and properties of ivy honey. This study is the first to determine of physicochemical and bioactive properties of ivy honey in Turkey. For this purpose, physicochemical parameters (pH, humidity, color, electrical conductivity and optical rotation values), phenolic compound profile, antioxidant and antimicrobial activities of ivy honey were examined. The data obtained showed that ivy honey was a high quality of monofloral flower honey with high antioxidant and antimicrobial properties. However, this study is a preliminary study and for determination of the characteristic and bioactive properties of ivy honey from Turkey, further studies must be on a large number of samples from different regions.

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Oral Presentation

Effects of Bee Venom and Anatolian Propolis on Human Breast and Over Cancer Cells

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Abstract

Cancer is a disease characterized by uncontrolled cell proliferation and uncontrolled apoptosis. This condition is related to the oxidative stress that the cell is subjected to. Propolis stands out especially with its antioxidant effects. Bee venom, on the other hand, has effects preventing cell proliferation on cancer cells. Bee venom and propolis have the potential to affect cancer cells in ovarian and breast cancer, which are gynecological cancers. There are many adverse effects related to the chemotherapeutics used in the treatment of these cancers. İn addition, post-treatment recurrence and chemotherapeutic resistance are among the problems encountered. The propolis solution used in the study was obtained from 96% ethanol extract and contains 28mg / ml polyphenolic substance. Bee venom is a crystalline, water-soluble substance, used crude in the experiment, and about half consists of a protein called melittin. A2780 ovarian cancer and MCF-7 breast cancer cell lines were used in the study. Bee venom and propolis were applied to all cell lines at 1- 5- 25- 50 and 100 µg / ml concentrations for 24 hours. Cell viability was determined by the 3- (4,5-dimethylthiazol-2-yl) -diphenyl tetrazolium bromide (MTT) method. According to the MTT results, the inhibitory logarithmic concentration 50 (LogIC50) value was calculated. The propolis used contains 28mg / ml polyphenolic substance. Bee venom contains 46.33% melittin. In the study, it was determined that A2780 and MCF-7 human cancer cells significantly decreased cell viability at all applied concentrations (1- 5- 25- 50 and 100 µg / ml) of bee venom and propolis for 24 hours compared to the control groups. ($p<0.05$) This study; As a result, it shows that bee venom and poplar type Anatolian propolis used have strong cytotoxic and antitumor properties against human breast cancer and ovarian cancer cell lines. Animal studies to be made may be a reference to human studies on this subject.

Keywords: Propolis, Bee venom, Ovarian cancer, Breast cancer

Oral Presentation

The Factors Effecting the Therapeutic Value of Honeybee Venom

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Abstract

Honeybee venom is produced by the venom gland that located in the abdominal cavity of Apis mellifera (L.) for colony defense. This toxin is injected directly under the skin to the enemies of honeybees through their sting. Due to its specific composition, it has been using in both the health and cosmetics sectors. The amount of active ingredient in its content determines the quality and apitherapeutic value of honeybee venom. For this reason, in order to determine the quality of the honeybee venom, the amount of Melittin, Apamin and Phospholipase A2 in its content are determined by HPLC-UV analysis. Many critical points regarding the production of quality bee venom suitable for apitherapy in terms of content, have not been clearly standardized yet. In this study, it was aimed to examine the effect of different harvesting methods and season on honeybee venom content (melittin, apamin, and phospholipase A2) and its therapeutic value and form a basis for future studies. For this purpose, HPLC-UV analysis of samples collected from inside and outside the hive by electroshock method during the active season in Turkey-Düzce province was compared. In terms of the harvesting method, no statistical difference was determined in the apamin, melittin, and phospholipase A2 values of honeybee venom samples collected from inside and outside the hive. In addition, it has been determined that there is no statistically significant difference between the bee venoms collected in different months and at different times in terms of the criteria investigated. With this preliminary study, the effects of harvesting time, device location and seasonal factors on honeybee venom content, which are among the curious issues in the production of honeybee venom suitable for apitherapy, have been determined. In the light of the data obtained from this preliminary study, with more comprehensive and long-term studies, questions about seasonal variation, location, breed, feeding and harvest time will be answered and standards regarding production factors will be established.

Keywords: Honeybee venom, Apitherapy, Production, HPLC-UV

Oral Presentation

Qualities of the Bee Venom in Apitherapy

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Abstract

Bee products such as bee venom used in apitherapy applications because of its feature has a critical role while some of them are important for human nutrition. Live bees are mostly used in bee venom application as an apitherapy method. One of the recently available product is bottled bee venom. Honeybees produce their venom in their venom gland and store it in the venom sac. The venom production reaches its maximum level in two to three weeks old worker bees. 0.1 milligrams of dry venom is obtained in one sting action. Standardized devices use electroshock method for bee venom collection process. For protection of bee venom, freeze-drying is reported to be most effective method. The venom dries fast at room temperature and solidifies with air contact as its color turns to whitish. Bee venom is consisted of peptides, polypeptides, enzymes, biogenic amines, lipids, sugars, amino acids and water. The characteristics of bee venom used in apitherapy and the effect of its content on various diseases are briefly discussed.

Keywords: *Apis mellifera* L; Bee Venom; Apitherapy; Enzyme; Biogenic Amines

Oral Presentation

Composition of Royal Jelly and Uses in Human Health

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Abstract

Royal jelly; It is a secretion substance secreted from the hypopharyngeal and post cerebral glands of 5-15 days worker bees, and is in the form of a cream-colored gel, which is the special food source of queens. In this article, the chemical structure and effects of royal jelly on human beings health has been stated. It contains plenty of protein, which has a complex structure. Apart from these, water contains organic acids, steroids, minerals, sugars in its structure. The compounds in its structure vary depending on the season, the location and production conditions. The chemical structure of royal jelly consists of 60-70% water, 9-18% protein, 7-18% sugar, 0.8-3% minerals, 3-8% lipids and vitamins, free amino acids and other components. As with all bee products, the components in the structure of it show different effects when it enters the human body. By the antioxidant activity of proteins in the structure of it is used in the treatment of many diseases such as asthma, depression, cancer, hypertension that occur as a result of oxidative stress in the human body. Another miraculous effect of royal jelly has been observed on male sperm quality and female menopause period. Apitherapy is among the literature that royal jelly shows neuromodulatory activity. In an experimental Alzheimer's disease model, royal jelly consumption has been observed to significantly improve spatial memory in mice. It has taken its place among functional foods today. It has been proven by many studies that royal jelly can have positive results in supporting the immune system for human beings, diseases that occur as a result of aging, joint and rheumatic diseases, reproductive and urinary tract infections. Royal jelly is a miraculous product and its area of use is not only in the medical, but also in the food and cosmetics sectors. Studies on the importance of royal jelly and royal jelly should be expanded, considering both its contribution to the country's economy and its contribution to human health.

Keywords: Bee, Royal Jelly, Apitherapy

1. Royal Jelly

Royal jelly; It is a secretion substance secreted from the hypopharyngeal and post cerebral glands of 5-15 days worker bees, and is in the form of a cream-colored gel, which is the special food source of queens. Royal jelly has a pungent and sour taste. Royal jelly is especially used as a nutrient for queen bees. A bee with superior functional and morphological character than other hive members is formed as a result of this feeding of the queen bees that are fed with royal jelly throughout their life. For this reason, royal jelly is called 'royal jelly (RJ)' in English (Şahinler, 2000; Payel et. Al, 2011; Özkök, 2020).

The importance of royal jelly, which was noticed 1600 years ago, is a bee product with a sharp scent in the consistency of gelatin, which is secreted from the mandibular and hypopharyngeal glands of young worker bees of 5-15 days, plays an important role in the growth of the queen and throughout its life, and is used for feeding 1-3-day-old larvae (Akyol, 2015).

In terms of physical properties, royal jelly is a bee product with a fluid, yoghurt consistency, viscous, cream colored, pungent odor and sour taste. Royal jelly is partially soluble in water and its density is 1.1 g / ml. Although its viscosity varies according to the environmental conditions, it is a product with a pH between 3.4-4.5 (Lecker et al., 1981; Uçar, 2018).

The color of this bee product, which is yellow in color, varies depending on the storage conditions. The cake has an odor and the taste has a sour taste. Density varies according to water content, time, room temperature. Its structure gradually becomes more viscous in the refrigerator at room temperature and 5 ° C (Arslan and Bayraktar, 1988). These changes in viscosity actually occur by the reduction of amino acids and nitrogen in its structure and by the increase of nitrogenous compounds that are insoluble in water. It contains plenty of protein from royal jelly, which has a complex structure. Apart from these, water contains organic acids, steroids, minerals and sugars in its structure. The compounds in its structure vary depending on the season, the location and production conditions (Kösoğlu et al. 2013).

The chemical structure of royal jelly consists of 60-70% water, 9-18% protein, 7-18% sugar, 0.8-3% minerals, 3-8% lipids and vitamins (B-complex vitamins, vitamin C, and vitamin E), free amino acids and other components (Sabatini et al. 2009). The vitamins in its structure have been researched and the ratios of these vitamins are 2-3 µg / g Vitamin H, 3-5 µg / g Vitamin C, 1.3-2 µg / g Vitamin B1, 7.5-10 µg / g Vitamin B2, 2-8 µg / g Vitamin B6 has been reported (Benfenati et al., 1986).

Proteins constitute the majority of the dry weight of royal jelly. Proteins in its structure are classified in two groups as water-soluble and insoluble proteins. An average of 73-74% of nitrogenous compounds in royal jelly are proteins. Of these, four of the six major proteins are glycoproteins. The remaining nitrogenous compounds have been reported to contain 2.3% amino acids and 0.16% peptides in their structure. Looking at the components of royal jelly, the existing proteins contain all the essential amino acids for humans. In a study, it was reported that there are 29 antioxidant peptides in the structure of royal jelly, short chain peptides with amino acid numbers between 2-4 have higher antioxidant effect and have a protective effect against lipid peroxidation (Krell, 1996; Guo et al., 2007).

Approximately 185 organic compounds were determined in the structure of royal jelly. The most important of these compounds is the Royalactin protein, which is in the protein group. Apis protein, which is also in its structure, has been reported to contain the protein that stimulates the proliferation of human monocytes (Aslan, 2019). -hydroxy-2-decenoic acid (HAD) (Sugiyama et al., 2012) Except for this bioactive compound, hormones such as acetylcholine, adenosine monophosphate (AMP) N1 oxide, polyphenols and testosterone, adenosine, progesterone, prolactin, and estradiol have been added. It is among other beneficial bioactive ingredients proven to be contained in milk. Additionally, royal jelly is the only known natural source of acetylcholine, one of the transmitter substances (Ramadan and Al-Ghamdi; 2012).

Lipids in the structure of royal jelly are substances that consist of free fatty acids and add most of their biological properties to royal jelly. Fatty acids consist of mono and dihydroxy-acids with 8-10 carbons and dicarboxylic acids in the chain. It is 10-hydroxy-2-decenoic acid (HAD), on the other hand, it forms the majority of fatty acids. This compound has been reported to make up about 70% of the lipids present in royal jelly and more than 50% of the free fatty acids. Apart from 10-HDA, 10-hydroxydecanoic acid (HDAA) consists of 17% of free fatty acids and other fatty acids are mostly 9-hydroxy-2-decenoic acid, 8-hydroxy octanoic acid, 3-hydroxydecanoic acid, 3 10-dihydroxydecanoic (Li et al., 2013; Ferioli et al., 2014).

The content of ash in the mineral substances used in royal jelly constitutes approximately 2-5% of the dry weight of royal jelly. The potassium, phosphorus, sulfur, calcium sulfur, phosphorus, iron content of royal jelly, which has a very rich structure in terms of mineral substances, higher.

Potassium 2462--3120 mg / kg, phosphorus amount 1940--2350 mg / kg, sulfur 1420--1154 mg / kg, calcium 145--113 mg / kg, magnesium amount 264--312 mg / kg and sodium 106--142 mg / kg It has been reported. In addition, it contains elements such as tin, nickel, antimony, bismuth and valvrome in its structure. Zn, Fe, Cu, Al and Mn elements are also among the elements that are involved in biomedical activities, which are abundant in the structure of royal jelly. Each element and mineral in the structure of royal jelly has a role in the body. Potassium mineral, which is among the minerals, balances blood pressure, reduces the risk of stroke, regulates the fluid balance in the body, regulates the electrical activity of the heart and the work of the muscles (Stocker et al., 2005; Garcia-Amoedo et al., 2007; Blakanska et al. , 2017; Kamyab et al., 2020).

It is included in extreme compounds in the structure of royal jelly. However, studies on volatile compounds are few. Because these compounds are easily affected by many factors such as environmental conditions, harvest time, storage conditions. Although not much research can be done, according to those reported; It consists of acetone, 2-nonano, benzaldehyde, 2-butanone, 2-pentanone and hexanals, which are called carbonyl compounds. Octanoic acid, which is 7% of the volatile fraction, also contains a compound that can show protective activity against varroa mite, which is an important disease for bees. Ferulic acid, which is one of the polyphenolic compounds with high antioxidant activity in its structure, is the only phenolic acid found and it has been reported that it constitutes more than 68% of the total amount of polyphenols in royal jelly. In lower proportions, flavanones, flavones, and flavanols were found in royal jelly (Isidorov et al., 2009; Lopez et al., 2014; Miguel et al., 2017).

In this epidemic period, which affects the whole world, healthy nutrition has become more important for us to increase body resistance. Royal jelly is also among the foods that are important for our health. The pharmacological activity of royal jelly with its antioxidant, disinfectant effect, antitumor, immunomodulator, antimicrobial, antihypercholesterolemic, anti-inflammatory effect and wound healing, hypoglycemic (antidiabetic) effects was supported by studies conducted on experimental animals (Ramadan and Al-Ghamdi, 2012; and et al., 2016).

2. Royal jelly and Human health

2.1. Antioxidant activity: oxidative stress

As with all bee products, the components in the structure of royal jelly show different effects when it enters the human body. For example, proteins in the structure of royal jelly have antioxidant activity. With this effect, royal jelly is used in the treatment of many diseases such as asthma, depression, cancer hypertension that occur as a result of oxidative stress in the human body (Akyol, 2015). Nonalcoholic fatty liver disease (NAFLD) is closely related to oxidative stress occurring in hepatic cells when looking at patagonists. In the study performed on ovariectomized (OVX) rats, the effects of royal jelly on NAFLD were examined by giving 150, 300 and 450 mg / kg doses. As a result of the study, royal jelly was reported to improve anxiety level and serum lipid profile, as well as alleviate hepatic steatosis and liver damage in rats given royal jelly. In the study, it was stated that royal jelly contains compounds with antioxidant activity that will enable to control oxidative stress exerting hepatoprotective activity in ovariectomized mice (You et al., 2020).

In studies conducted on mice, the activity of royal jelly against DNA damage and its effectiveness on oxidative stress was investigated, and it was observed that it had a preventive effect on oxidative stress as a result of the research. In another study, a study was conducted on its endocrinological efficacy, and it was concluded that royal jelly has an antiaging effect (Viuda-Martos et al., 2008 Cornara et al, 217).

2.2. Proliferative, Antitumoral activity

Among cancer, which is one of the most common diseases of our age, there are results showing that royal jelly has the property of preventing metastasis on tumor cells (Vucevic et al., 2007). It has effects on cell regeneration, cell production and metabolism in the body, giving strength and vitality to organisms, decreasing cholesterol, total lipid-phospholipid level in the blood, regulating blood pressure, regulating blood pressure, and reducing fatigue (Aydın & Tekeoğlu, 2018) .Zhang et al. Stated that it has an inhibitory effect on tumor growth in fibrosarcoma tissues, royal jelly has an inhibitory effect on tumor growth, and this effect is particularly dependent on cytokine regulation. RJ (Royal jelly) has anti-cancer effects especially with prolonged consumption, its immunomodulatory activity is an additional utility, but also provides good potential for new chemotherapeutics (Zhang et al, 2017).

Trans-10-hydroxy-2-decenoic acid (10-HDA) compound, which is the most unique biological component in its structure and has high biological activity, has been reported to have estrogenic and differential effects, antitumor, antibiotic, immunomodulatory effects, and differential activities. As a result of studies, there are findings that royal jelly supplements for six months improve mental health, glucose intolerance and erythropoiesis in some people (Eshraghi, and Seifollahi, 2003; Sugiyama et al., 2012; Stratev et al., 2015, Morita et al., 2012).

2.3. Activity on reproduction and development

One of the miraculous effects of royal jelly is on sperm quality. According to the results of the studies conducted to improve human health naturally, it has been proven that royal jelly has an important effect on the number and motility of sperm, and even gives positive results in its use in infertility treatment. In women, it has been noted that the use of royal jelly in the early development of menopause caused by female hormones and some diseases caused by menopause (such as osteoporosis, dyslipidemia) has been reported to have a positive response to diseases. In a study conducted, the changes that occurred in the cardiovascular and bone structures of royal jelly in postmenopausal women were controlled. Significant changes in lipid levels were noted in women given 150 mg of royal jelly for 3 months, and they stated that it could be an alternative option to improve dyslipidemia caused by menopause (Lambrinoudaki et al., 2016).

It is known that royal jelly has been used to prevent infertility for years. It has been proven by studies conducted today that royal jelly has a positive effect on reproductive development. Sperm quality was examined using royal jelly on goats, and when the results of the examination were examined, it was emphasized that royal jelly increased the sperm quality, in addition, it decreased the rate of defective acrosomes, but did not make a significant change in DNA fragmentation (Alcay et al, 2017). In a study conducted to examine the DNA content in testicular tissue, it was found that royal jelly could be used as a preservative, but the toxic effects of cyclosporine A used alone decreased depending on the dose and time (Gawish et al 2016). In a different study, different amounts of royal jelly were added to the sperms by freezing them. It has been emphasized that royal jelly can increase sperm quality and sperm viability in an invitro environment (Shahzad et al, 2016). In a study conducted on male mice, it was aimed to determine the effect of royal jelly on some spermatological properties. As a result of the experiment, it has been determined that royal jelly has a positive effect on sperm quality by increasing spermatozoa density and spermatozoa motility and decreasing the rate of abnormal spermatozoa (Karaçal et al, 2006).

2.4. Antiaging activity

Kaku et al. In their study, they investigated the effect of royal jelly on bone quality by focusing on the posttranslational modifications of type I collagen. As a result, they reported that the

reduction of collagen crosslinks (pyridinoline and deoxypyridinoline), which represents an aspect of bone quality, was significantly attenuated. They emphasized that they demonstrated that royal jelly can improve bone quality by modulating the posttranslational modification of type I collagen. Another study reported that royal jelly is a valuable nutrient in the calcium storage of bones and prevention of osteoporosis (Hidaka et al., 2006).

10-HDA, the main active ingredient of royal jelly, is effective in increasing the synthesis of ovulation hormones, maintaining the continuity of the follicle pool and hormonal cycle.A research has been carried out on the effectiveness of 10-HDA in royal jelly against aging on the skin caused by ultraviolet rays. As a result of the study, it was stated that the production of procollagen type I and TGF-21 in human skin with UVB rays treated with 10-HDA increased, but the MMP-1 level did not change, but royal jelly could potentially protect the skin against UVB-induced photo-aging by increasing collagen production (Park et. al., 2011 Pasupuleti et al., 2017).

2.5. Neuroprotective Activity

Apitherapy is among the literature that royal jelly shows neuromodulator activity. In an experimental Alzheimer's disease model, royal jelly consumption has been observed to significantly improve spatial memory in mice. Again, in this experiment, royal jelly has been proven to reduce neurodegeneration and particularly curative effects against amyloid-beta toxicity (Zamani et al., 2012; Wang et al., 2016).

Studies have reported that royal jelly will be a promising food for Parkinson's patients. In the study conducted on experimental animals, it was observed that its improved motor behavioral changes in animals with Parkinson's disease. In the results of the research, it has been reported that the protective effects of these compounds probably play a role in free radicals, proinflammatory cytokines and mitochondrial proteins, cell death. Immunochemistry and cell viability analyzes revealed a higher survival rate of dopaminergic neurons treated with these compounds both in vivo and in vitro. Based on the results of the research, it was reported that royal jelly could potentially be a safe adjuvant treatment for Parkinson's disease (Taherianfard et al., 2017; Ali & Kunugi, 2020).

Being confined in a certain area and being exposed to cold causes corticosteroids to be released in our body. As a result, our antioxidant defense system in the central nervous system can be adversely affected. In a study conducted to observe this situation, the levels of corticosteroids in the brain and cerebellum and the status of our antioxidant defense system were investigated on rats. They also reported that royal jelly reduces lipid peroxidation in the brain cerebellum striatum and hippocampus, strengthens the glutathione defense system in the cerebral cortex and striatum, and decreases the corticosterone level by strengthening the brain antioxidant system. As a result, they suggested that royal jelly can be used anti-stress and neuroprotective under tress conditions (Teixeira et. Al., 2017).

In another study, royal jelly-induced potential changes of neutrophic factors, receptors, and neural cell markers were investigated to observe neuroprotective effects on mRNA expressions and neurogenesis variations. As a result of the research, thanks to royal jelly, mRNA expressions derived from the Glial cell line increased neurotrophic factor (a strong neurotrophic factor), neurofilament H (a specific marker for neural axons in the hippocampus) (Hashimoto, 2005). Aslan et al. Experimentally caused spinal cord injury in their study on rabbits and gave royal jelly to the rabbits 24 hours later. As a result of the study, it was revealed that royal jelly given after 24 hours increased the number of cells leading to cell death, apoptosis, decreased lipid peroxidation, and strengthened the antioxidant defense system (Aslan et al, 2012). Menopause adversely affects the nervous system in women. In order to reduce the negative effect of menopause on the nervous system, 400 mg / kg of royal jelly was given to rabbits fed

in vivo with a high cholesterol diet. As a result of the study, it was reported that it showed beneficial neurological effects against post-menopausal neurological disorders (Yoon et al, 2018). In a study conducted in rats, royal jelly was given depending on their weight, and the spatial memory and brain neurotransmitter concentration increased, dopamine and serotonin were used in certain parts of the brain together with their metabolites. It has been demonstrated (Pyrzanowska et al., 2014).

2.6. Wound Healing

Royal jelly positively affects the healing process of wounds in humans. According to research, in an in vivo study, the proliferative and migration effects of royal jelly on epidermal keratinocytes (HaCaT) were investigated. The study reported that royal jelly proteins (MRJP2, MRJP3 and / or MRJP7) would exhibit potential wound healing bioactivity as well as improve wound closure through MRJP-induced cellular proliferation and migration (Park et al., 2011)
In a study on foot ulcers and the use of royal jelly on foot ulcers, a study was conducted on patients with foot ulcers in the Khorshid Hospital in Isfa-han, Iran. In the results of the study, they reported that there were no adverse effects on the patients, and that royal jelly helped to dilate blood vessels to increase vasodilation around the affected wound and blood flow. They also suggested that royal jelly can be used in the prevention of infections due to its antimicrobial activities in patients with foot ulcers (Siayash et al, 2015).

3. Results

The proteins, minerals and vitamins in the structure of royal jelly have many positive effects on human health. Royal jelly is a bee that protects the body chemistry with its many biological activities and medicinal functions, shows positive effects on the nervous system, ensures the continuity of the functions of organs such as kidney and liver, protects from diseases with its antimicrobial activities, meets the energy needs of the organism, and provides growth and development by showing a positive effect on growth hormones. product. It is a product that is increasingly used with its positive effects on the cardiovascular system, anti-cancer effect, and immune system enhancing effect. Today, it is seen that the methods used in the treatment of diseases are insufficient to eliminate health problems, and some methods used have serious side effects. For this reason, the use of natural products in the field of apitherapy has become widespread by supporting their activities such as antimicrobial-antitumoral-antiaganine.
Royal jelly has taken its place among functional foods today. It has been proven by many studies that royal jelly can have positive results in supporting the immune system for human beings, diseases that occur as a result of aging, joint and rheumatic diseases, reproductive and urinary tract infections. Royal jelly is a miraculous product and its area of use is not only in the medical sector, but also in the food sector, in the cosmetics sector. Studies on the importance of royal jelly and royal jelly should be expanded, considering both its contribution to the country's economy and its contribution to human health.

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Oral Presentation

Nutrient, Bioactivity and Amino Acid Analysis of Lyophilized Royal Jelly

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Abstract

Royal jelly is a white-yellowish viscous bee product with a sour taste, secreted from the hypopharyngeal and mandibular glands of young worker bees. In this study, nutrient (moisture, ash, protein, carbohydrate, lipid, energy), bioactivity (antioxidant activity) and amino acid content of lyophilized royal jelly samples were determined. Accordingly, the moisture, ash protein, carbohydrate, lipid and energy values of royal jelly were 14.26, 2.96, 40.13, 41.86, 0.79 g /100 g and 335 kcal/100 g, respectively. The 10 HDA content of the samples was 5.62 g /100 g, and the antioxidant activity was 23.68 mgTE/100 g. As a result of the amino acid analysis of royal jelly samples, alanine, glycine, valine, leucine, isoleucine, thereonine, serine, proline, arginine, aspartic acid, methionine, glutamic acid, phenylalanine, lysine, histidine and tyrosine were determined. While the amino acid content varied between 10.54-42.36 mg/g, the most amino acids were aspartic acid, glutamic acid and proline. It is important to establish quality standards in royal jelly and it is thought that such studies will contribute to setting standards

Keywords: Liyophilized Royal Jelly, Amino Acid, Nutritional Elements, 10 HDA, Antioksidant Activity

1. Introduction

Royal jelly is a creamy, whitish, pungent and sour-bitter nutrient product that is secreted by the lower jaw and throat glands on the head of worker bees that are 5-15 days old, used for feeding young larval juveniles and queen bees. Young worker bees aged 5 to 15 days; They meet the nutritional needs of the larvae by feeding the worker bee, queen bee and drone larvae from the 1st larval stage to the 3rd larval stage with royal jelly. While the worker and drone larvae on the 4th day are fed by other worker bees (3 to 6 days of age) with the brood food they produce by eating honey and pollen, the queen bee larvae continue to be fed with royal jelly. Studies have shown that royal jelly has antibacterial, anti-inflammatory, vasodilator, hypotensive, antioxidant antidiabetic, antihypercholesterolemic and antitumoral activity. These activities have been attributed to the proteins and peptides, phenolic compounds and fatty acids found in royal jelly (Viuda-Martos et al.)

Royal jelly is a unique food that is given in the honeybee colony from the egg to the maturity period of the queen bee, and only during the egg period of the other castes. Although both develop from a fertilized egg, the morphological and physiological differences between the worker bee and the queen bee are the result of royal jelly feeding. This unique feature has attracted the attention of researchers and as a result of the studies, royal jelly has become widely used in healthy foods and cosmetics today. Royal jelly is generally a bee product containing water (60-70%), crude protein (12-15%), carbohydrates (10-16%), lipids (3-7%) and trace amounts of vitamins and minerals (Lercker et al., 1981, Chen and Chen 1995; Crane 1990). Since the protein components and free fatty acid concentration in its structure can change during the storage of the product, it significantly affects the quality. Researchers furosin (Emanuele et al., 2002; Messia et al. 2005), superoxide dismutase (Chaozhong and Youlu, 1999), glucose

oxidase (Cuiwen and Fuxin, 1990), 10-hydroxydec-2-enoic acid (Jean-Francosis et al., 2003) suggested some quality and freshness indices such as 57 kDA protein (Masaki et al., 2001) in royal jelly analysis.
In this study, the nutritional elements (moisture, ash, protein, carbohydrate, energy), bioactivity (antioxidant) and amino acid content of royal jelly samples produced in apiculture were determined.

2. Materials and Methods

2.1. Samples
Samples of lyophilized royal jelly were obtained from Nutral Therapy Co. (Erciyes Teknopark).

2.2. Nutrient analysis and antioxidant activity
The moisture (AOAC 934.01), ash (AOAC 900.02), protein (AOAC 960.52), carbohydrate (Atwater; Miller and Watt, 1973), fat (D.05G8) and gluten (AOAC 991.19) content value of liyophilized royal jelly samples were determined according to AOAC methods. The 1,1-diphenyl-2-picrylhydrazyl DPPH assay was used to determine the antioxidant capacity of lyophilized royal jelly samples (Fan et al., 2014).

2.3. Amino acid analysis of lyophilized royal jelly samples
The 26 individual amino acid standards, including histidine (His), serine (Ser), arginine (Arg), glycine (Gly), aspartic acid (Asp), glutamic acid (Glu), threonine (Thr), alanine (Ala), hydroxylysine (Hylys), proline (Pro), cysteine (Cys), lysine (Lys), tyrosine (Tyr), methionine (Met), valine (Val), isoleucine (Ile), leucine (Leu), phenylalanine (Phe), taurine (Tau), g-aminobutyric (GABA), aminoisobutyric acid (AABA), ornithine (Orn), glutamine (Gln), asparagines (Asn), hydroxyproline (Hypro) and tryptophan (Trp), were purchased from Sigma. They were dissolved in deionized water individually at the desired concentration as the stock standard solutions. Working standard solution including all amino acids was prepared by mixing stock standard solutions, and the final concentration was 5 pmoles/mL of all amino acids except cystine, which had a concentration of 2.5 pmoles/mL (Liming et al. 2009)

2.4. Sample preparation
RJ (1 g) was dissolved with 25 mL of 90% ethanol, dispersed for 1 min with the help of the sonicator and homogenized with the Polytron for 2 min. The homogeneous solution was centrifuged for 5 min at 5000 rpm and the supernatant decanted. Then, the sediment was extracted twice more with 25 mL of 90% ethanol. The extracted solutions were combined and dried with a rotary vacuum evaporator at 40 8C, redissolved and filled up to 50 mL with deionized water. The extracts were filtered through a 0.22 mm syringe filter (Millipore, MA, USA) prior to injecting into the UPLC system (Liming et al. 2009).
0.5 g RJ was accurately weighed and transferred into a Pyrex screw-cap tube, 3 mL of deionized water and 3 mL of 12 M HCl were added and then homogenized for 1 min with the help of the Polytron. A moderate stream of purified nitrogen was blown into the liquid to remove the air in the test tube, and then the tightly sealed tube was kept upright in an oven at 110 8C for 24 h. After removing the tube from the oven and cooling to room temperature, the acid hydrolysate was filtered through a common filter paper and neutralized to pH 4.8–5.2 using 6 M NaOH, redissolved and filled up to 50 mL with deionized water. And then, 2.0 mL extracts were pipetted and made up to 10.0 mL in a volumetric flask with deionized water. The extracts were filtered through a 0.22 mm syringe filter (Millipore, MA, USA) before injection.

2.5. UPLC conditions

All analyses were performed on a Waters Acquity UPLC system, including a binary solvent manager, a sample manager fitted with a 2 mL loop, and a Tunable UV (TUV) detector, The standards or samples were separated using a gradient mobile phase consisting of 5% AccQTag Ultra Eluent A (A) and AccQTag Ultra Eluent B (B). The gradient condition was: 0–0.54 min, 0.1% B; 0.54– 5.74 min, 0.1–9.1% B; 5.74–7.74 min, 9.1–21.2% B; and finally, reconditioning the column with 0.1% B isocratic for 0.86 min after washing column with 59.6% B for 0.90 min. The flow rate was set at 0.70mL/min and the injection volumes for all samples and standards were 1.0mL. The column temperature was set at 55 8C. The peaks were detected at 260 nm (Liming et al. 2009). The stock solution of mixed standards containing 26 amino acids was prepared and diluted to appropriate concentrations for the establishment of calibration curves. Each concentration of the mixed standard solution was injected in triplicate, and then the calibration curves were constructed by plotting the peak areas versus the concentrations of each amino acid. The stock solution containing 26 amino acids was diluted with deionized water to appropriate concentrations, and an aliquot of the diluted solutions was injected into UPLC for analysis.

2.6. Recovery and precision

The recovery was performed by adding a known amount of individual amino acid standards into a certain amount (1.0 g for FAAs and 0.5 g for TAAs) of RJ. Three replicates were performed for the test. The quantity of each amino acid was subsequently obtained from the corresponding calibration curve.

3. Results

The moisture, ash, protein, carbohydrate and 10-HDA content of lyophilized royal jelly samples are given in Table 1. Royal jelly is used as fresh and lyophilized. Moisture, lipid, 10-HDA, protein and ash content (g / 100g) of fresh and lyophilized royal jelly, respectively (60-70%; <5), (3-8; 8-19), (> 1.4-> 3.5), (9-18; 27-41), (0.8-3.0; 2-5) (Sabatini et al. 2009). Kauser and More (2019) analyzed thesis and lyophilized royal jelly produced in India. While the moisture, ash, lipid, total protein, carbohydrate and 10 HDA contents of fresh royal jelly were determined as 60%, 1.22, 2.49, 11.99, 12.30 and 3.22, respectively, in lyophilized royal jelly, 3.8, 2.59, 11.57, 33.57, 1.28 and 2.31 were determined.

Table 1. Nutrient elements, 10 HDA content and antioxidant activity of lyophilized royal jelly samples

Nutritional parameters	Content	Parameter	Content
Moisture	14.26±2.3 g/100g	*10-HDA*	5.62±0.9 g/100g
Ash	2.96±0.6 g/100g	*Antioksidant activity*	23.68±4.2 mgTE/100g
Protein	40.13±3.2 g/100g	*Energy*	335±12.6 kcal/100g
Carbohydrate	41.86±2.4g/100g		
Lipid	0.79±0.1g/100g		

As a result of the analysis, 16 amino acids were detected in lyophilized royal jelly; alanine, glycine, valine, leucine, isoleucine, threonine, serine, proline, arginine, aspartic acid, methionine, glutamic acid, phenyl alanine, lysine, histidine, and tyrosine. The most abundant of these amino acids are aspartic acid, glutamic acid and proline. While the average amino acid amount in royal jelly samples is 21.39 mg / g, the most abundant amino acid aspartic acid is methionine the least present.

Table 2. Amino acid content of lyophilized royal jelly samples

Amino acid	Content (mg/g)	Amino acid	Content (mg/g)
L-alanin (Ala)	10.91±1.2	*L-Arginine (Arg)*	12.52±2.4
Glycine (Gly)	17.36±0.9	*L-Aspartic acid (Asp)*	42.36±4.2
L-Valine (Val)	19.29±2.4	*L-Methionine (Met)*	10.54±0.8
L-Leucine (Leu)	25.79±3.2	*L-Glutamic acid (Glu)*	36.70±3.2
L-Isoleucine (Ile)	17.20±2.1	*L-Phenylalaniene (Phe)*	16.51±2.3
L-Threonine (Thr)	18.35±1.8	*L-Lysine (Lys)*	24.99±3.1
L-Serine (Ser)	26.55±1.7	*L-Histidine (His)*	13.90±1.8
L-Proline (Pro)	32.93±3.4	*L-Tirosine (Tyr)*	16.30±1.6

4. Discussion

Amino acids, which are the building blocks of proteins in our body, are necessary for vital processes such as protein production, hormone and neurotransmitter synthesis. In addition, 20 different amino acids are needed in the human body, only 9 of these amino acids are essential (histidine, isoleucine, leucine, methionine, phenylalanine, threonine, tryptophan and valine). They must be taken with foods from outside, that is, they cannot be synthesized in the body. Of these amino acids, phenylalanine is the precursor to neurotransmitters such as tyrosine, dopamine, epinephrine and neuropinephrine, which act as conduits in the nervous system. Valine helps to stimulate muscle growth and regeneration and is associated with energy production. Threonine is an essential part of structural proteins such as collagen and elastin, which are important components of skin and connective tissue. It has a role in fat metabolism and immune function. Methionine, which plays a role in metabolism and detoxification, is necessary for tissue formation and absorption of zinc and selenium minerals. Leucine is effective in regulating blood sugar, wound healing and stimulating growth hormone production. Isoleucine, which plays a role in muscle metabolism, is effective in immune function, hemoglobin production and energy regulation. Lysine is needed in the production of immune function collagen and elastin. Histidine is required for histamine production and the myelin sheath surrounding nerve cells. The deficiency of these amino acids in the human body can affect the whole body, especially the nervous, reproductive, immune and digestive systems. For this reason, the level and ratio of amino acids are very important for a healthy life.

Liming et al. (2009) detected 24 amino acids in royal jelly samples obtained from 10 different apiaries in China. Among these, methionine and AABA were either not detected or almost non-existent. They found the average FAA content of 9.21 mg/g. While proline was the most abundant amino acid at a concentration of 5.19 mg/g, the others were gln, lysine and glutamic acid. In other previous studies, proline and lysine have been reported as the most abundant amino acids in royal jelly (Takenaka 1987, Emanuele et al. 2003). Liming et al has a total amino acid content of 111.27, aspartic acid is the most abundant amino acid (21.04). reported this as glu (12.29) and lys (10.05) and leu (9.53). The differences in the amino acid content of royal jelly may have resulted from the differences in royal jelly samples and the analysis methods. Boselli et al. (2003) As a result of GC-MS analysis of royal jelly samples produced in Italy, the total amino acid content was determined an average of 7.3 mg/g, while the major free aminocides were proline, lysine, glutamate, beta-alanine, phenylalanine, aspartate and serine.

5. Conclusion

Lyophilized royal jelly is an easier product than royal jelly in terms of use, dosing, preservation and storage. It should be used as a supplementary food in terms of nutritional elements and amino acid content.

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Oral Presentation

Effect of Different Feeding Methods on Quality and Biochemical Characteristics of Royal Jelly

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Abstract

Royal jelly (RJ) is a valuable bee product with many functional properties, produced by worker bees to feed the queen, secreted from the hypopharyngeal glands. RJ has a complex structure and contains proteins, amino acids, carbohydrates, lipids, sterols, fatty acids, minerals and vitamins. The biochemical characteristics of RJ can be affected by the season, colony population, larval age, harvest time and feeding methods. In this study, the effect of different feeding methods on the biochemical properties of RJ was investigated. RJ production was carried out continuously with different feeding methods for 5 months. Syrup, syrup+pollen, honey+pollen, apilarnil+syrup were evaluated for different feeding methods. RJ production could only be made until the end of August, and the RJ obtained in the last period is very low. Samples collected to determine the effect of different production period and method, on the quality and biochemical properties of RJ. Total Protein Amount, Amino acid content, Water content, Acidity, pH, Color, Total lipid content, Fatty Acid Profile, 10-HDA, Sugar Profile, Starch/Pollen Ratio, Pollen Analysis, C13/C12 Ratio, Total Phenolics, flavonoids and Sterols were examined. Statistical evaluations were made, and results were evaluated. As a result of two-way analysis of variance (ANOVA) in repeated measurements, RJ production varied according to time ($P<0.05$); on the other hand, it was determined that there was no difference between feeding methods. Therefore, it appears that there is no feedingXtime interaction. There is no significant statistically difference between feeding groups and royal jelly parameters. But it's observed that feeding methods by time has a significant effect on protein, fat, sugar profile, total flavonoid and some amino acid ($P<0.05$) values. Interaction is thought to result from differences in nectar flow between months. It has been observed that amino acid and flavonoid contents according to the months increased depending on the richness of the plant sources, which is important for royal jelly production. For the production of high-quality RJ rich in protein, amino acid and flavonoid properties, RJ production must be done with apilarnil support. So, it can be evaluated as apitherapeutic in apitherapy, which has gained in recent years in our country.

Keywords: Royal Jelly, Feeding Methods, Quality Parameters, Functional Parameters.

This study financially supported by Directorate General of Agricultural Researches and Policies (TAGEM).

Oral Presentation

Apilarnil (Drone Larvae) - Harvesting, Utilization, Clinical Cases.

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Abstract

Apilarnil is triturated 7-day-drone larvae and the nutritive content of drone cells obtained through a special method, patented by Nicolae V. Ilieșiu, a romanian beekeeper. Apilarnil has a complex composition, being extremely rich in strong nutritive and biologically active substances, easy to assimilate. Contains a large amount of nutritive, growth and restructuring substances within a small volume, including proteins and free amino acids, minerals (calcium, magnesium, phosphorus, iron, manganese, copper, zinc, sodium, potassium) and vitamins (A, B1, B2, B6, PP, choline, …). Due to its complex composition and to the presence of substances that have hormonal role, Apilarnil is extremely useful for sexual dynamics disorders, for regulating gonad function, both men and women. Apilarnil is energizing, vitalizing, regenerating, increases physical and psychical endurance, improves metabolism. It can be used in a wide range of disorders: for stimulating children and pubescents' growth, in denutrition, metabolism deficit, problems of physical development, physical and psychic phenomena linked to old age, chronic liver diseases, various neuropsychological disorders, dermatological diseases, etc. Another aspect that should be mentioned is that, according to the studies carried out, Apilarnil consumption, even in large doses, has no mutagenic risk, no teratogen effect and no risk of chronic toxicity. At last, harvesting, storage and transport conditions are extremely important influencing the quality of the product and implicitly the therapeutic results.

Keywords: Apilarnil, Drone Larvae, Apitherapy

Oral Presentation

Apilarnil: An integrative Component for Post-cancer Treatment

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Abstract

Drone larvae or Apilarnil is the male counterpart to Royal Jelly. Its composition is unique, although Apilarnil is always associated with high protein diet. This is not the case. Moreover, there is a wide variety of building blocks available. On top there are hormones and a lot of antioxidants. The third important topic is that it has immunomodulatory properties. This easy accessibility of vital building blocks helps the liver and does not stress the whole system so much. The contained hormones revitalise the system and enable strength and will. The content of antioxidants is even higher than in royal jelly. The last part is the stimulation of the immune system. This means on the long run that the body enables himself to gain the upper hand. These three mentioned modes are important systemic properties of Apilarnil. This makes Apilarnil an ideal diet or cure for all people or patients who are weakened by illnesses, circumstances, or toxic treatment like chemotherapy. It is important to build up a therapeutic scheme, equals a logic approach with systematic anamnesis. Other bee products might be included. This is synergistic. In this case Apilarnil is a wonderful tool for healing and recovery.

Keywords: Apilarnil, Diet, Cancer Treatment, Bee Products

Oral Presentation

A Natural Androgen Source: Apilarnil (Drone Larvae)

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Abstract

Apilarnil is a bee product produced from drones larvae in the 3-7 days brood stage. It is viscous and yellowish-grey colour with a characteristic egg odor. Many factors such as larvae age, production stage, colony region is effective on the biochemical composition of drones, however apilarnil contains 65-75% water, 7-10% protein, 6-12% carbohydrate and 3.5-8% lipid, 0.7-2% ash. It is also called “Complete food” thanks to its essential amino acids. Apilarnil, which has been used in traditional medicine for many years, is consumed by people with the effect of being a natural food for the purpose of supporting medical treatment. It has been demonstrated by studies that it has many biological activities on account of its high nutritional components. Apilarnil, which is especially rich in testosterone, prolactin, progesterone and estradiol hormones, has traditionally been used to increase vitality, treat infertility and sexual problems in men and women. In this study, the studies on the androgenic effect of apilarnil in the literature have been compiled to evaluate whether apilarnil is a natural alternative source against chemical drugs used in androgen deficiency syndrome.

Keywords: Apilarnil, Drone Larvae, Androgenic Effect

Oral Presentation

Anatolian Bee Bread: Probiotic and Antioxidant Properties

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Abstract

Bee bread is a natural bee product produced by bees by combining pollen with special enzymes and placing it in the hive cells. It consists of carbohydrates, fats, proteins, fatty acids, vitamins and minerals that are essential for human health. Bee bread's nutritional value and natural probiotic bacteria content is high. Probiotics are living microorganisms that provide a health benefit when used in sufficient quantities. Different bacterial strains have different probiotic potential and present specific immunological effects. In this study, moisture, total phenolic, total flavonoid, total antioxidant capacity and probiotic properties of 20 different bee bread samples collected from 5 different regions of Anatolia were investigated. The mean total phenolic, total flavonoid and total antioxidant capacity results of bee bread samples were found as 10.3 ± 3.62 mg GAE / g, 3.5 ± 2.15 mg KE / g and 21.7 ± 9.96 mg TE / g, respectively. Bee bread samples contain an average of 3.0 x 109 cfu probiotic bacteria per gram, and 34 different probiotic bacteria species were detected in the samples. Bacillus subtilis, Lactobacillus acidophilus, Lactobacillus plantarum and Lactobacillus ruminatum are the most common types of probiotic bacteria found in Anatolian bee bread. In addition, different probiotic bacteria such as Lactobacillus reuteri, Lactococcus spp., Lactobacillus delbrueckii and Lactobacillus kefir were found in bee bread samples taken from different regions of Anatolia. According to the analysis results, it has been observed that the bee bread samples collected from different regions of Anatolia have high antioxidant activity and are rich in probiotic content. While probiotic products sold in the market contain one or two strains of bacteria, Anatolian bee bread, a natural product, contains at least 6 different probiotic bacteria strains.

Keywords: Bee bread, Perga, Probiotic, Antioxidant capacity, Total phenolic matter

Oral Presentation

Color Separation, Physicochemical and Functional Properties of Bee Pollens Collected in Turkey

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Abstract

Pollen is an essential nutrient for development and reproduction of honeybees. Bee pollen, on the other hand, is a natural bee product collected from the beehive and used as a food supplement. Different scientific studies are carried out to determine the health effects of bee products in the world. In this study, the botanical origin of 41 bee pollen samples collected from Turkey was determined and their effect on physicochemical and functional properties was examined. Samples were separated according to colors and classified according to botanical origin by palynological analysis. Total protein, fat content and fiber content were analyzed by kjeldahl, weibull-Stoldt and enzymatic-gravimetric method respectively. Mineral and amino acid contents were determined using ICP-MS and GC-MS. Total phenolic contents, antioxidant activities and flavonoid contents were analyzed by Folin Ciocalteu, using DPPH and by HPLC-PDA respectively. 66 plant taxa belonging to 38 plant families were identified; predominantly Cistus, Taraxacum, Trifolium, Brassica, Papaver and Crataegus. Protein contents of the samples were between 12.7% and 28.6%. Onobrychis sp., Papaver rhoeas and Trifolium pratense were high in protein. It was determined that the protein value of red-brown pollens was higher than other colors. The fat content of the samples were varied 2.1% and 14.8%. Total phenolic contents were between 7.0 and 32.0 mg GAE/g. Antioxidant activity and total flavonoid contents were found between 31,4%-97,0% and 3.4-9.7 mg/g respectively. Some flavonoid components including kaempferol, naringenin, myricetin and catechin were detected in higher amounts. Potassium, calcium, magnesium, iron, copper, zinc were detected high levels. The highest mineral concentrations were detected in the willow, hawthorn and clover bee pollen, respectively. Lysine, glutamic acid, aspartic acid and proline amino acids were found highly. As a result, it has been proven that bee pollen is an important source of protein and minerals, and its physicochemical and functional properties vary according to plant species.

Keywords: Bee Pollen, Physicochemical Analysis, Functional Properties, Polyphenols

Oral Presentation

The Process of Pollen transformation into the Bee bread: Microbiology of Bee bread

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Abstract

The fermented product produced by bees in the honeycomb cells with pollen, honey and effect of various enzymes in their digestive systems is called bee bread (perga). Pollen is a product that bees collect from plants to meet their needs and form lumps on their hind legs. Bee bread is more stable food for feeding of bees due to the low pH (3.8-4.3) and the presence of antimicrobial compounds. In addition to being the least known bee product, bee bread has found relatively small area in the literature compared to other bee products. In recent years, researchers have focused on the composition and apitherapeutic properties and stated that this is a functional food. In this review, the possible fermentation mechanisms mentioned in the literature microorganism groups effective in this process are summarized in the process of pollen transformation into bee bread. In addition, the effect of fermentation on the digestibility of those products has been reviewed.

Keywords: Pollen, Bee Bread, Fermentation

Oral Presentation

Beehive Air Therapy "Healing with Bees"

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Abstract

The first mentioning of beehive air therapy was in 1920 when a Russian beekeeper noticed the positive effects of beehive air. It's components mainly consist of bee propolis and beeswax and also honey aromas. However, today beehive air is the least known and studied product from the beehive and it is hard to find relevant clinical studies despite there being many patented beehive air devices commercially available. Beehive air treatments are classed as wellness not therapy. The reason behind this is that up until recently there was no medical device available on the market. There is very little to no scientific or academic literature available on beehive air therapy. Jürgen Schmiedgen, who is a certified BIO (DE-ÖKO-006) and apitherapy beekeeper, has developed new beehive air device. The journey started in 2013 when he heard about the successes of beehive air therapy and bought a few devices from Hans Much, the owner of "Apiair". He quickly realized that the beehive air device was not without fault. He has been studying the detectable, positive effects of beehive air. The new beehive air device combines the know-how of reliable business partners with Jürgen Schmiedgen's professional background and in-depth knowledge of bees. It is medically certified and patented for Europe. The result is a system that harnesses the unique effect of beehive air on humans and animals while ensuring the welfare of bees. Our first Apitherapy Centre for beehive air therapy was established in 2016 in Thermalbad-Wiesenbad. In 2018, Prof. Dr. Karl Speer did a scientific study to identify the components in the beehive air with the aim to get beehive air therapy acknowledged as an alternative healing method and the acceptance by health insurances. Requirements for the patient treatment, apiary and beekeeping will be presented as well as Beehive air therapy as a concept with a new medical device. The application of beehive air therapy is recommended for respiratory conditions like hay fever, infection-susceptibility, asthma, bronchitis, COPD (chronic obstructive pulmonary disease), headaches, migraines, sinusitis, allergies, depression, insomnia.

Keywords: Beehive Air Therapy, Medical Product, Beehive Air Components, Respiratory Conditions, Apitherapy

Oral Presentation

Beehive Air Therapy: From Identifying Chemical Compounds to Evidence-Based Clinical Practice

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Abstract

The inhalation of the air of beehives of Apis mellifera species has been used therapeutically for several years, and it has been recognized as a potential technique for treating respiratory diseases, strengthening the immune system, reducing stress, and improving general well-being. However, in inspire of successful cases across many countries around the world, the scientific proof of the efficacy of inhaling the air of beehives is still lacking, indicating the need for research on the topic. This presentation aims to review the status of research on characterizing chemical compounds of beehives' air and highlight the importance of clinical studies as a route to validating beehive air therapy in modern medicine. A series of studies on chemical composition of beehive's air have already identified more than 50 volatile compounds prevenient from the products of the beehive (e.g., honey, beeswax, propolis, etc.), and indicated that the pharmacological properties of the beehive's air compounds are closely related to their anti-inflammatory, anti-asthmatic, and antimicrobial actions. Although the analyses of the chemical composition of the beehive's air support the validity of the beehive air therapy for the treatment of respiratory disorders, scientific evidence from clinical studies is still scarce. As the popularity of this natural therapy grows, it also calls the attention of public health authorities, which are starting to require scientific demonstration of safety and effectiveness before accepting the beehive air inhalation as a valid therapy. Therefore, the need for clinical studies on beehive air inhalation is emerging as an essential step to make this therapy recognized not only by its fans, but also by the medical community and health authorities.

Keywords: Beehive Air Therapy, Clinical Studies, Scientific Validation

Oral Presentation

Experiences of the Hungarian Bee-hive Air Applications

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Abstract

Hungarian legislation makes research and education a duty of the state. The Hungarian Apitherapy Society has taken over some of these tasks, like education for beekeepers and naturopaths. The association has run five beehive and beehive air therapy courses in Hungary and one abroad in the past six years. Those interested came from beekeepers and naturopaths. As a result, we can record that sophisticated and application-oriented houses have been built. Special therapies related to the beehive have been used since the end of the 19th century. Beehive therapy uses several physical effects of the beehive at the same time: music, warmth, vibrations, energetic force field and the smell of bees and hives. The therapy was first introduced in Ukraine, Russia and the successor states of the Soviet Union. Essentially, the patient rests on a bed that is formed at the top of the beehives. Beehive air therapy uses the effects of the volatile molecules, humidity and warmth in the beehive air. The patient inhales the air through a personal mask. Bee houses have now been built in almost all parts of Hungary. Both the “bed” and the medically approved BeeCura beehive air system is used. The use of beehives and bee air therapy can only be found in Slavic language literature and some western studies. Nevertheless, experiences in Hungary - with a small number of them - are supported: results can be expected for heart disease, lung problems, allergies, stress and migraines. The anti-migraines effect is exciting when a sustained impact of more than six months has been observed. The observational study, which also meets the expectations of the Ethics Council, could provide evidence-based results in the future.

Keywords: Hungary, apitherapy, beehive air, beehive therapy.

Oral Presentation

Heavenly Pharmacy: Therapeutic Actions of Hive Products

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Abstract

For thousands of years, the therapeutic use of beehive products has been known; mainly honey, propolis and wax. The Egyptians used them to heal wounds, and treat the gastro-intestinal, kidney and eye diseases; and the Greeks used them for detoxication, expectorant, and even rejuvenating properties. These products were used in Egyptian culture. For example, propolis was used to embalm mummies and bee venom was used by Cleopatra as a treatment for pain. Its healing properties are even mentioned in religious texts such as the Bible or the Koran.

Keywords: Apitherapy, Koran, Hive Products, History

Oral Presentation

Bee Venom in the Treatment of Chronic Diseases

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Abstract

Apitoxin and its properties. Principles of action of bee venom. Indications for bee venom. Application. Safety. Conclusion.

Keywords: Bee Venom, Chronic Diseases

Oral Presentation

Determination of The Antibiotic In Vitro Propolis Ethanolic Extract on *Staphylococcus Aureus* and *Escherichia Coli* This in Bovine Puerperal Metritis

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Abstract

This research work entitles ‘’Determination of The Antibiotic In Vitro Propolis Ethanolic Extract on Staphylococcus Aureus and Escherichia Coli This in Bovine Puerperal Metritis’’, was held in the city of Cuenca, Azuay Province, Republic of Ecuador, whose research execution was in the period between November 2012 and April 2013. This study was aimed to evaluate the in vitro antimicrobial activity of ethanol extracts of Propolis (EEP) as a natural alternative to combat Staphylococcus aureus and Escherichia coli (bacteria isolated in the laboratory under cultivation in sheep blood agar) present in the clinical metritis of dairy cows in the Victoria’s Portete. This action was compared with the sensitivity caused by an antibiotic that offered greater commercial antimicrobial agar plate than Amoxicillin and Clavulanic Acid. They were produced for this ethanolic extracts of Propolis to 10% and 30% Propolis were collected from apiaries in the area and processed in the University of Cuenca. Was used for susceptibility testing of bacteria concentration adjusted to 0.5 McFarland scale and employing Muller Hinton agar. 3 sensitivity discs were used for measuring the effect of Amoxicillin and Clavulanic Acid, EEP sensitivity discs of 10% and 30%, and as a control, ethyl alcohol 96º measures of inhibitory halos generated Propolis treatments whit Amoxicillin and Clavulanic Acid, on Staphylococcus aureus and give no zone of inhibition on Escherichia coli, whereas sensitivity discs ethyl alcohol of 96ºgive no zone of inhibition. The inhibitory action of the halos of the two concentrates are similar Propolis have lower dispersion than the antibiotic employed. This means that the concentrates of Propolis give stable results.

Keywords: Propolis, Staphylococcus aureus, Escherichia coli, metritis, veterinary, antibiotic

Oral Presentation

Scientific Apitherapy and Traditional Chinese Medicine in Clinical Veterinary Medicine: Integrative Approach to Complex Pathologies with Clinical Cases.

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Abstract

The development of Integrative Treatment Protocols Based on traditional Chinese medicine and biomedical results on the use of bee products, using the properties of each beehive product and their synergy, I developed different Treatment Protocols for different pathologies in animals. The protocols combine many different therapeutic tools (Apitherapy, Traditional Chinese Medicine, Phytotherapy, Nutritional Support, Physiotherapy, Modern Allopathic Medicine), to treat and support many animal species. However, Apitherapy has been decisive in the therapeutic results of these clinical cases. Twenty years of work in Integrative Clinical Veterinary Medicine show that beehive products are fundamental elements in the excellent results offered by CENTROVETERA - Apitherapy Veterinary Medical Center. To obtain the best results, we must pay attention to the quality of the bee products and the specific protocol for the needs of each patient. To achieve the first, in the practical and private work of CENTROVETERA, we include the supply of the "best" hive products for "api-phyto-medical formulations" for animals, to walk from pathology to health. The presentation graphically shows examples of Integrative Treatments, including beehive products in different animal patients and applied in different ways. To simplify presentation, the patients were ordered by medical specialties, such as Dermatology and Integument; Surgery (large wounds, skin and general dermatological diseases); Neurological / neuromuscular diseases, degenerative diseases, autoimmune diseases, reproduction, etc.

Keywords: Apitherapy, Apitherapy In Veterinary Medicine, Bee Products for Apitherapy, Apipuncture, Clinical Integrative Veterinary Medicine

Oral Presentation

Apitherapy and Intestinal Permeability and Its Relationship with Autoimmune Diseases

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Abstract

It is well known that the intestine is the home of our immune system, so a permeated or leaky intestine will directly influence our health, we are all at some point of fragility, therefore how can our simple diet be the trigger for diseases such as diabetes, hypertension, arthritis, lupus, sclerosis, among other diseases of autoimmune origin, and how can bee products added to the daily diet generate a change in our quality of life? Can an autoimmune disease diagnosis be stopped or even reversed by approaching the condition from intestinal permeability? Knowing the real origin of autoimmunity will have a significant impact on the well-being and speedy recovery of a patient, and consequently on the good results of the Apitherapist. It is therefore necessary to make the patient aware from the first apitherapy session, about the self-control of their disease without the need to resort to drugs or treatments that would condemn their quality of life forever. This approach also results in a significant decrease in the number of bees used in patients with autoimmune diseases.

Keywords: Apitherapy, Large Intestine, Autoimmunity, Immunological

Oral Presentation

Use of Apitoxin as an Adjunct in Treatment of Anti-Inflammatory and Immunological Therapy

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Abstract

The therapeutic properties of apitoxin with the aim of treatment with anti-inflammatory, neuroprotective, anti-tumor, antiviral and analgesic characteristics, resulting in stimulation of melittin in the immunomodulation of cellular response.

Keywords: Apitherapy, Autoimmune Diseases, Anti-inflammatory

Oral Presentation

Use of Prevention and Treatment Techniques for Hypersensitivity and Allergy to Bee Poison

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Abstract

Learn techniques that allow you to act prudently when applying apitoxin to the patient, in addition to preparing it before with detox techniques, healthy eating, flavors of Traditional Chinese medicine and a therapeutic plan that allows your body to adapt to apitoxin being safe and effective. Avoid having to go through anaphylactic shock, and learn methods that help balance your immune system, thus improving your general body structure, mental, emotional and psychological characteristics.

Keywords: Hypersensitivity, Allergy, Bee poison

Oral Presentation

Use of Apitoxin with Platelet-Rich Plasma in Patients Diagnosed with Arthritis and Osteoarthritis

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Abstract

Knowing the regenerative properties of injectable apitoxin, it has been mixed with Platelet Rich Plasma optimizing the repair factors of the blood, achieving joint restoration quickly and effectively. This is useful in joints with arthritis and osteoarthritis of the knee, ankle, shoulder and spine, among others. The PRP seeks to improve the natural conditions of the joint, remembering that damaged joint tissues have poor blood circulation and poor synovial fluid nutrition due to its poor mobility caused by arthritis or osteoarthritis. It is possible to repair this joint by avoiding what is damaging it, such as being overweight, smoking, incorrect ergonomics among others, improving the diet and performing exercises according to the compromised joint; the percentage of apitoxin and PRP delivery will depend on the degree of joint damage considering the apitherapy protocols; and the level of acceptance of apitoxin, do not forget other types of use of apitoxin such as sublingual, topical or by electrophoresis; and the consumption of the other biological products of the hive.

Keywords: Apitherapy, Apitoxin, Platelet rich plasma, Arthritis, Osteoarthritis, Biological Therapies, Restore

Oral Presentation

Authenticity, Bioactivity and Safety of Bee Products

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Abstract

Honeybees evolved with flowering plants nearly 50 million years ago. While they provide pollination of plants, they collect nectar, resinous, pollen etc. from plants and turn them to the bee products for their life. On the other hand, human beings discovered bee products 15 thousand years ago and used them for their own sake. Bee products are divided into two groups. First one is; honeybees collect from plants and partially add from their bodies. These are honey, pollen, bee bread, and propolis. Second one is; honeybees secrete them from their bodies or directly from the bee body. These are royal jelly, beeswax, bee venom, and apilarnil. These products show antioxidant, antibacterial, antifungal, antiviral, antitumoral etc. beneficial bioactivities in humans and so todays they are very popular for the consumers. These products are also used in medical treatment methods and this kind of treatment method is called "Apitherapy". Apitherapy is used by the doctors from all over the world in the prevention and treatment of the diseases in the last 50-60 years. In our studies of honey, pollen and propolis, we have found that these products have very high antioxidant values and vary according to the plant species they contain. We also determined that in our microorganism studies propolis was effective against Salmonella enteritidis, Listeria monocytogenes, Peptostreptococcus anaerobius, Peptostreptococcus micros, Lactobacillus acidophilus, Actinomyces naeslundii, Prevotella oralis, Prevotella melaninogenica, Porphyromonas gingivalis, Fusobacterium nucleatum, and Veillonella parvula bacteria. On the other hand, we found that thyme honey, a monofloral honey species, is effective against Staphylococcus aereus, Enterococcus faecalis, Klebsiella pneumoniae, Acinetobacter baumannii and Pseudomonas aeruginosa bacteria. These excellent products will become a new source of hope and health for the increasingly polluted and artificial world. Therefore, the production, authenticity, safety, and consumption of these products will be thanks to the standards prepared by the authorized institutions under reliable conditions.

Keywords: Apitherapy, Authenticity, Bee Products, Honeybees, Safety

Oral Presentation

Food Safety in Apitherapy Products

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Abstract

Food safety; it is defined as complying with the necessary rules and taking precautions in the production, processing, storage, transportation and distribution stages of food in order to ensure safe food production, and includes the concepts of safe, beneficial and healthy food. Risks arising from food are evaluated separately in the processing, transportation, storage, purchasing, preservation, preparation, cooking stages of food from production to consumption and are grouped as physical, chemical, and biological risks. Food safety in our country is a system carried out according to a risk-based inspection procedure. The official authority responsible for food safety is the Ministry of Agriculture and Forestry. The "General Directorate of Food and Control" carries out the studies on Food Safety and Food Codex. Microbiological, chemical and physical hazards used in the production, processing and preparation of food can make food unsafe. Since these dangers exist at every stage from the production to consumption of food, contamination of food becomes inevitable when necessary precautions are not taken (2). Bee products are an extremely important food group that are considered therapeutically as well in terms of food safety due to their use in both food and apitherapy fields. Beekeeping; it is an activity that is defined as the production of products such as honey, royal jelly, propolis, bee venom, pollen and beeswax by using the bee and all necessary resources.

Keywords: Apitherapy, Food safety, Bee products

Oral Presentation

Authenticity of Propolis Products from The World Market

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Abstract

The resinous bee product collected by bees from the leaves and buds of trees such as poplar, eucalyptus, alder, pine and chestnut are called propolis. The flavonoids and phenolic acids present in large amounts in propolis play an essential role in its biological activity. The affluence of propolis in terms of these components makes it a powerful antioxidant source. In this study, 50 Anatolian raw propolis samples were investigated based on their wax, total phenolic content, total flavonoid content, and total antioxidant capacities. Besides, 157 propolis products collected from 20 different country were examined based on dry matter, total phenolic, flavonoid content, and total antioxidant capacities. Moreover, phenolic profiles of the 29 propolis product samples with antioxidant capacity higher than 100 mg TE/ml were investigated via LC-MS/MS. The results indicated that the dry matter content of the samples ranged between 0.1% and 98.3%. Their total phenolic content was between 0.0-108.1 mg GAE/g and total flavonoid contents were between 0.0- 174.5 mg KE/g. According to the antioxidant capacity (CUPRAC) analysis, the sample's total antioxidant capacity was found to be between 0.0 and 555.0 mg TE/g. Phenolic compounds from propolis were not detected in the phenolic profile of 20 samples and it was determined that antioxidant capacity was increased by adding different substances. Antioxidant capacity and phenolic profile analysis results of only 6 samples are consistent with the amount of propolis indicated on the label. According to results, there is a big difference in the total phenolic contents and antioxidant capacities between samples. Besides, in 96% of the samples examined, there were differences between the stated amount of propolis on the label as well as the actual dry matter and the antioxidant capacity. Propolis is regarded as a natural healing source by many people. Thus, consumers should not be misinformed about the content of products and a standard for propolis including extraction methods must be established to regulate the content of products and take unfair competition under control on the market.

Keywords: Anatolian Propolis, Authenticity, Antioxidant, Phenolic

Oral Presentation

The Effect of Autoclave Sterilization on Microbial Decontamination and Bioactive Properties of Bee Pollen

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Abstract

The bee pollen today has begun to recognize as an important product by consumers and food industry as the result of investigations of its nutritional and therapeutic properties. However, three main parts of pollen wall, pollen coat, exine, and intine form a quite resistant structure to prevent the intracellular compounds from digestive degradation. Fermentation, which is considered to be an effective method of breaking down the exine layer of bee pollen, facilitates the release of compounds from the pollen matrix and contributes to an increase in the fraction absorbed during digestion. The fermented product produced by bees in the honeycomb cells with pollen, honey and effect of various enzymes in their digestive systems is called bee bread. This product has prompted researchers to adapt the fermentation in the hive to lab conditions. Research interest has been raised about spontaneous fermentation and/or fermentation with added bacteria of pollen. In this study, the effect of autoclave sterilization (121 °C, 15 min) on microbial decontamination and bioactive properties of bee pollen was investigated. TPCs were found as 8.95 mg GAE/g DW for non-processed pollen, 29.32 mg GAE/g DW for autoclaved pollen. TPCs were 19.67, 32.09, 11.55 mg GAE/g DW for pollen substrates with pollen:water ratios 1:1, 1:2, and 3:1 after autoclave sterilization, respectively. The FRAP values have been shown statistically significant increase for all samples after sterilization. Non-processed pollen, autoclaved pollen, pollen substrates with pollen:water ratios 1:1, 1:2, and 3:1 after autoclave sterilization showed free radical scavenging activity on DPPH with SC50 7.66, 3.32, 3.27, 3.12, and 4.90 mg/mL DW, respectively. The number of LAB in non-processed pollen on MRS is $13.4x10^4$ CFU/g. Total mesophilic aerobic count in PCA is found as $21.7 x10^4$ CFU/g. Yeast-molds in MEA is $6.1 x10^5$ CFU/g. Growth of microorganisms after autoclave sterilization was not detected.

Keywords: Bee pollen, Sterilization, Fermentation, Phenolic, Antioxidant

1. Introduction

Bee pollen is a product that bees collect from plants to meet their needs and form lumps on their hind legs. It is known as one of the oldest nutritional supplements in and contains almost all nutritive components for a diet (Bakour et al., 2019). The pollen has a protective wall composed of two layers: intine and exine. Because the layers of the pollen wall are highly resistant to degradation, this complex structure can restrict the digestibility of this product. There were differences in the degree of digestion of various types of pollen, with the different degree of digestibility for carbohydrates and proteins. Pollen grains with more and larger pores may be easier to digest since digestive enzymes can easily penetrate into the cell content (Aylanc et al. 2021). Various studies have reported that cell wall-disruption can improve nutrient digestibility of bee pollen (Dong et al. 2015, Uțoiu et al. 2018, Wu et al. 2019).

There is increasing interest for using bee pollen as the substrate to obtain novel probiotic pollen-based foods. Research interest has been arised about spontaneous fermentation and/or

fermentation with added bacteria of pollen. Commercial/classic bacterial media for LABs is De Man, Rogosa ve Sharpe (MRS), plain or modified Rogosa, tomato juice, lactobacillus carrying medium. Bee pollen may be used as optimum cultivation/growth medium for probiotics/lactic starters. Lactic acid fermentation can also lead to the destruction of cell walls and increase the nutritional value of the pollen (Kaskoniene et al. 2020). It has been reported that raw and spontaneously fermented bee pollen was more exposed to uncontrolled growth of yeasts, molds, and other bacterial groups (Di Cagno et al. 2019). Therefore, different pretreatments should be improved to sanitize and adapt bee pollen prior to inoculation and induction of fermentation processes. It is thought that autoclaving may effectively improve the digestibility and bioavailability of intracellular bioactive compounds by cracking pollen wall and provide microbiological safety. Raw bee pollen and pollen substrates with different pollen:water ratios 1:1, 1:2, and 3:1 were autoclaved at 121 °C for 15 minutes. The effect of heat-pressure treatments was evaluated on total phenolic content, antioxidant activity and microbiological decontamination of bee pollen.

2. Materials and Methods

Bee pollen samples were collected in the spring of 2018 from hives located in Gumushane-Torul, Turkey. Samples were stored at +4 °C until they were analysed.

Substrates with different pollen:water ratios of 1:1, 1:2, 3:1 were prepared. Bee pollen without water and pollen substrates with different pollen:water ratios were autoclaved at 121 °C (103.42 kPa), 15 minutes. 2 g of non-processed pollen and autoclaved pollen substrates with/without water were extracted with 15 mL methanol (95%, v/v) at 37 °C, 100 rpm for 72 hours by maceration.

The Folin–Ciocalteu method has been performed to measure total phenolic content of the samples as described by Slinkard and Singleton (1977). The results were expressed as mg GAE per g of dry weight.

Antioxidant activity of samples was evaluated by ferric reducing antioxidant power (FRAP) (Benzie and Strain, 1999) and 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging activity (Brand-William et al. 1995) assays. FRAP reagent was prepared mixing 25 mL of 300 mM acetate buffer (pH 3.6), 2.5 mL of 10 mM TPTZ dissolved in 40 mM HCl, and 2.5 mL of 20 mM $FeCl_3.6H_2O$. A 100 µL of the sample was mixed with 3 mL of freshly prepared FRAP reagent, this mixture was incubated at 37 ºC. The absorbance was measured at 595 nm against reagent blank containing distilled water at the end of the 4 min of incubation time. The FRAP values being calculated as µmol Trolox per g of dry weight. DPPH assay was based on the discoloration of DPPH free radical. The purple colour of DPPH decays in the presence of antioxidants. The change of absorbance is monitored against reagent and sample blank at 517 nm.

Total mesophilic aerobic bacteria, yeast and moulds, lactic acid bacteria before and after autoclave sterilization were enumerated. Serial dilutions of samples were plated on Plate Count Agar for total mesophilic aerobic bacteria (35 °C, 72 hours), Malt Extract Agar for yeast and moulds (25 °C, 5 days), MRS Agar for lactic acid bacteria (35 °C, 72 hours) (Speck, 1976).

The results were expressed as mean values and standard deviations (mean ± SD) for three replicates. Data were tested using SPSS version 20.0 software (SPSS Inc., Chicago, IL, USA). p values <0.05 were accepted as the statistically significant.

3. Results

The number of LAB in non-processed pollen on MRS is 13.4×10^4, total mesophilic aerobic bacteria count in PCA 21.7×10^4, yeast-molds 6.1×10^5 colony forming unit per g of bee pollen. Growth of microorganisms after autoclave sterilization was not detected.

TPC was found as 8.95±0.23 mg GAE per g of dry matter for non-processed pollen. TPCs after autoclave sterilization were shown in Table 1.

Table 1. TPCs of pollen substrates

Sample name	TPC (mg GAE/g DM)
Raw pollen	8.95±0.23[e]
After sterilization	
Pollen	29.32±1.02[b]
Pollen:water 1:1	19.67±0.71[c]
Pollen:water 1:2	32.09±1.52[a]
Pollen:water 3:1	11.55±0.33[d]

[a-e] Different letters represent statistically significant differences (P<0.05).

The variation of FRAP values after sterilization is shown in Table 2. FRAP values increase almost two-fold for pollen without water and pollen:water ratio of 1:1. A lower variation was observed for pollen:water ratio of 3:1 pollen substrate, while in pollen:water ratio of 1:2, threefold increase was found.

Table 2. FRAP values of pollen substrates

Sample name	FRAP (µmol Trolox/g DM)
Raw pollen	12.41±0.51[e]
After sterilization	
Pollen	22.78±2.96c
Pollen:water 1:1	26.04±0.21[b]
Pollen:water 1:2	38.66±0.99a
Pollen:water 3:1	17.08±1.81[d]

[a-d] Different letters represent statistically significant differences (P<0.05).

A general and significant increase in the 50% radical-scavenging activity (SC_{50}) was found in processed bee pollen substrates (Table 3). No statistical differences were found between SC^{50} values of pollen substrates with the ratio of 1:1, 1:2 and pollen without water after sterilization.

Table 3. SC_{50} values of pollen substrates

Sample name	SC_{50} (mg/mL)
Raw pollen	7.66±0.13[c]
After sterilization	
Pollen	3.32±0.08[a]
Pollen:water 1:1	3.27±0.19[a]
Pollen:water 1:2	3.12±0.17[a]
Pollen:water 3:1	4.90±0.13[b]

a-c Different letters represent statistically significant differences (P<0.05).

4. Discussion

Total phenolic content increases significantly for all samples. Pollen:water ratio of 1:2 had the highest TPC. Similar increase was found by Zuluaga et al. (2015) for bee pollen without water addition. Total phenolic content increase from 13.34 to 16.34, 20.35, and 18.00 mg GAE per g of bee pollen for 5, 10 and 15 minutes autoclaving, respectively. It is stated that the reduction in values of total phenolic compounds and antioxidant capacity at 15 min of treatment could have happened because the heat treatment achieve the breakdown of pollen wall, and the time of exposure to heat lasts enough that the bioactive compounds are sufficiently available and to

be decreased by effect of high temperature. Another study for heat/pressure treatment of bee pollen reported that 80 kPa/115 °C for 10 minutes is optimal for improving the availability of nutrients for fermentation. This study stated subsequent release of cytoplasmic content from the pollen grain regardless of the heat treatment duration and water:pollen ratio (Mora-Adames et al. 2021).

The increase in antioxidant activity of pollen substrates may also be associated with the formation of new compounds with new antioxidant properties. Since the polyphenols at an intermediate oxidation state may exhibit higher radical scavenging activity than non-oxidized ones (Nicoli et al. 1999), heat treatment may also improve the oxidation of phenolic compounds. It was known that the Maillard reaction occurs slowly at 35 °C and increases temperatures over 55 °C (Lee et al. 2017). Maillard reaction products can significantly retard food oxidation. The antioxidative activity of Maillard reaction products is due to different antioxidant mechanisms, including chelation of metal ions, radical chains breaking, breakdown of hydrogen peroxide, and scavenging of reactive oxygen species (Nooshkam et al. 2019; Nooshkam and Madadlou, 2016).

5. Conclusion

Stable, safe, and standardized pollen-based products have greatest economic potential. Bee pollen as a novel substrate will go beyond food segment by improving bioavailability and and proper microbiological risk assessment. It is clear that we need to know much more about the technological processes to improve digestibility and microbiological safety of bee pollen which is favorable for human nutrition and healthcare. The results obtained in the present work suggest that heat/pressure treatment may be performed to achieve the higher digestibility and microbiological decontamination of bee pollen. This research will provide a starting point for bee pollen decontamination in controlled fermentation process of pollen substrates.

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Oral Presentation

Physico-Chemical and Biological Functionalities of Bee Products

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Abstract

Bee products are inexhaustible sources of bioactive molecules. There are extensively used in folk medicine for the prevention and self-treatment of several diseases and has become actually the objective of many scientific investigations. Different biological and pharmacological effects of honey, pollen, propolis, royal jelly and bee bread have been referred to their antioxidant, antibacterial, antitumoral, anti-inflammatory agents, antihyperglycemic effect and renal disease protection. Oxidative stress is believed to be responsible for the occurrence of several pathologies. Scientific reports from our laboratory have shown that bee products have a wide chemical composition and multi-functional properties. In this context, and in order to understand the relationship between biomolecules from beehive products and their functional potential, we will investigate the antioxidant properties of Moroccan bee products, their capacities for preventing lipid peroxidation and scavenging free radicals was generally correlated with their phytochemical screening. In vivo, propolis and honey preparations were able to attenuate diabetic hepato-renal damage, probably through antioxidant and detoxification properties. The protective role of some honeybee products against reactive oxygen species-induced damage and nephrotoxicity in diabetic rats, gives hope that some of these products will have similar protective action in humans. In the rat diabetic nephropathy model, honey, propolis and pollen also showed significant effect on glucose homeostasis and improving kidney function. The possible mechanism of action is discussed. A compilation on therapeutic properties of honeybee products in experimental animal models and human health will be presented. It might be concluded that bee products are a potential target, to be used in the management of chronic kidney diseases, proteinuria, diabetes, cancer and inflammation. Overall, chemical characteristics of bee products may allow the extracts to be used as bioactive ingredients in the food industry, but they also present potential for the pharmaceutical or nutraceutical sectors for the prevention and/or treatment of health disorders.

Keywords: Propolis, Bee pollen, Honey, Royal jelly, Phenolic compounds

Oral Presentation

Chemical Compositions, Cytotoxic, Antioxidant and Antiviral Effects of Propolis Samples from Different Geographical Regions of Anatolia

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Abstract

Propolis is a natural bee product with many biological activities and it has been used in the many industrial areas such as pharmaceutical, food, cosmetics and others. In this study; we aimed to evaluate the chemical content, antioxidant, antiviral activities, cytotoxicity, and the iNOS of propolis samples collected from 39 different regions of Anatolia. Phenolic, flavonoid and triterpene profile were determined by LC-HRMS method. The main phenolic compounds were identified as flavonoids including diosmetin, rhamnocitrin, isosakuranetin, naringenin, chrysin, 3-O-methyl-quercetin, and acacetin, the main phenolic acid was found as caffeic acid. The major triterpene compounds were also detected as oleanoic acid and hederagenin. The volatile oil composition of these 39 propolis were also examined in this study by HS-SPME technique and analyzed by GC-MS method. α-Pinene, β-pinene and limonene were found as the main compounds in most of the samples. Cytotoxic activities against MDA-MB-231, PC-3, A549, HeLa, and a non-tumor cell line HEK293 were performed by MTT method. The iNOS was also determined using lipopolysaccharide (LPS) induced RAW 264.7 macrophage cells. Propolis samples exhibited significant cytotoxic and nitric oxide inhibition activities with significant range of IC50 values. Antioxidant capacity was investigated by DPPH method. Most of the propolis extracts exhibited more than 80% DPPH scavenging activities, almost similar or higher than the positive controls. Antiviral activities of the samples were measured as virucidal activity. All propolis samples promised for the significant inhibition of avian coronavirus that was studied for the first time in propolis of Turkey. In the light of the data obtained, it is expected that more detailed studies will be carried out in each region according to the seasons and different localities that will provide some critical information on the preparation of the local Anatolian propolis product for different applications such as medicine, cosmetics, and food industry. In this respect, it is predicted that the potential of Anatolian propolis has been proven with this study and will lead the development of locally registered geo-branded products in the future and will provide significant support to local producers.

Keywords: Propolis, Cytotoxicity, Antioxidant, Antiviral, iNOS, Avian Coronavirus

Oral Presentation

Scientific Studies of APHIS Laboratory on Romanian Bee Products in High Visibility Journals

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Abstract

Bee products are complex natural products, made by the bees, representing rich sources of both nutrients and bioactive compounds. As bee products are divided into two groups (own secretion of the worker bees and products that require raw material from outside the hive that are mixed with own secretion of the bees), the nutritional value, characteristics and economic benefits depend greatly on their origin and production methods. Honey, bee pollen, bee bread, propolis, royal jelly, Apilarnil, queen larvae or bee larvae, are “alive” products, demonstrated by their analysis. Antioxidant, antimicrobial and antitumor properties were proved in different studies of our department, studies published in high ranked journals, having hundred citations until now. Honey is a complex matrix, which possesses antioxidant and antimicrobial properties due to peroxide activity and bioactive compounds from the class of polyphenols. The darker the honey, the higher the antioxidant and antibacterial potential is. Propolis is considered a powerful natural antibiotic, with excellent results as antibacterial and antitumor agent due to its unique combination of resins in the chemical composition. Bee pollen and beebread beside its excellent nutritional value, possesses antitumor properties, demonstrated by our research team and published recently. Royal jelly is used by the worker bees to feed the queen which have a lifetime ten times higher than a worker bee. The composition and bioactivity of this valuable product was investigated, and results were also published in important scientific journals. The publication of all studies from APHIS Laboratory will be highlighted, the visibility and international recognition for our team being also presented.

Keywords: APHIS Laboratory, Bee Products, Chemical Composition, Bioactivity, High Rank Journals

Oral Presentation

The Concept of Anti-oxidant Pro-oxidant in Honeybee Products

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Abstract

Honeybees (*Apis mellifera*) are "Golden insects" that produce honeybee products. The main honeybee products are honey, propolis, pollen, bee venom, royal jelly, bee bread, and beeswax, and their use for medical purposes is called apitherapy. Apitherapy has been widely used in traditional medicine since ancient times. In addition to the use of honey as a nutrient, these products are used for medical purposes as an antioxidant, anti-inflammatory, antimicrobial, anticancer, anticoagulant, antiseptic, and wound healing. Although bee products contain many different molecules, bioactive substances are antioxidant molecules in phenolic structure. However, antioxidant molecules, especially in the phenolic structure found in bee products, may have a pro-oxidant in biological systems depending on their doses and may cause generate reactive oxygen species (ROS). Bee products can be used as an antiproliferative agent in cancer therapy by taking advantage of their pro-oxidant effects. With this presentation, the concept of antioxidant and pro-oxidant effects of bee products, which are extensively used in apitherapy will be discussed in the light of literatures.

Keywords: Apis Mellifera, Apitherapy, Antioxidants, Reactive Oxygen Species

Oral Presentation

Antimicrobial Properties and Bio-Pharmacological Effects of Apitherapy Products

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Abstract

Apitherapy is the medical use of bee and bee products. It is known that apitherapy was used in Ancient Egyptian Medicine 6000 years ago, and bee and bee products were used for therapeutic purposes in Ancient Greece and Rome. In the past years, only honey was known to be used as a nourishing and reinforcing food. But today, apitherapy products and scientific research with these products have shown a variety. These products are honey, propolis, pollen, beebread, royal jelly, bee venom and wax, which are the products of honeybee Apis mellifera L. for protective or therapeutic purposes against diseases. Apitherapy products containing high levels of polyphenolic compounds are considered to be effective on various diseases in the body and beneficial for health. The effectiveness of honey, propolis and bee venom on many gram-positive and gram-negative bacteria has been demonstrated. It is also known that they have an antimicrobial effect on resistant bacteria, some viruses and fungi. Moreover, all apitherapy products have many pharmacological effects depending on the type, type of use and dose of the product. Immune boost, antimicrobial, anticancer and anti-inflammatory effects of these products are demonstrated in many preclinical and clinical studies. Products shows its beneficial effects for health via their bioactive molecules. Due to its pharmacological effects, it is understood that the development of apitherapy products is important for Public Health and that appropriate clinical research needs to be increased. Concentrated and standardized apitherapy products may be useful in eliminate microbial biofilms and antimicrobial treatment. Also, they can make a high contribution to the treatment of other diseases. This review describes the pharmacological properties and antimicrobial effects of apitherapy products.

Keywords: Apitherapy, Antimicrobial, Propolis, Bee Venom, Pharmacological Effects

Oral Presentation

Treatment of Anaphylactic Shocks in Apitherapy

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Abstract

Anaphylaxis is a severe allergic reaction to venom, food, or medication. Most cases are caused by a bee sting or eating foods that are known to cause allergies, such as peanuts or tree nuts. Anaphylaxis causes a series of symptoms, including a rash, low pulse, and shock, which is known as anaphylactic shock. Generally, apitherapy is well-tolerated by people. It may cause skin lesions and generally not need any treatment. But some cases could may happen serious clinical conditions. Treatment of anaphylaxes is standard for all cases. It may be evaluated separately for all cases. If there are symptoms of shock we must start treatment immediately. Epinephrine (adrenaline) is first line therapy for anaphylactic shock. It may reduce your body's allergic response. In adults, administer a 0.3 mg intramuscular dose using a premeasured or prefilled syringe, or an autoinjector, in the mid-outer thigh (through clothing if necessary). Oxygen therapy is important especially for the conditions which goes with uvula edema. Intravenous (IV) antihistamines and cortisone to reduce inflammation of your air passages and improve breathing. A beta-agonist (such as albuterol) is used to relieve breathing symptoms.

Keywords: Anaphylactic Shock, Allergy, Epinephrine, Bee sting

Oral Presentation

Adverse Effects of Honeybee Products

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Abstract

The purpose of this presentation is to provide a brief overview of the adverse effects of the bee products. Honeybee products are directly or from natural sources produced by honeybees such as honey, propolis, pollen, royal jelly, bee venom and bee wax. People often derive benefits from nature and apply these products as dietary supplements or therapeutics against various diseases. Until recently little has been known of their effects on animals. Uses of honeybee products are constantly increase for industry of food, cosmetic, and apitherapy. Honeybee products have different pharmacological and toxicological effects depend on the product and components. Adverse effects of bee products are limited for types of bee products and consumers' ages. Honeybee products depend on susceptibility of consumers, types of bee products, constituents of bee products and dose of bee products can cause some allergic reactions such as dermatitis including swelling, redness, burning, peeling of skin, oedema of different sides of body, and anaphylaxis. Therefore, we should have good enough information related to useful and harmful effects of honeybee products; educated and certificated doctor, dentist and veterinaries should applicate in practice when use of honeybee products for apitherapy, food and other aims is extremely important. Patients with allergy to bee products should avoid the source of allergens. Patients at high risk should undertake protective measures for adverse effects of bee products.

Keywords: Apitherapy, Honeybee Products, Adverse Effects

Oral Presentation

Preclinical Studies in Apitherapy

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Abstract

The interest in apitherapy has increased in recent years. Honey, royal jelly, pollen, propolis, bee bread (perga), bee venom and male bee larvae (apilarnil) are used. Studies with modern methodology are required for the general acceptance of apitherapy in modern medical circles. Preclinical studies generally include test tube in vitro (cells and tissues) and in vivo (animal) studies. The aim is to produce information about the effectiveness, safety and toxicity of the substance in question. Substances that have successfully passed the preclinical stages can then proceed to phase studies, that is, they may meet humans. In apitherapy and other traditional methods, this process has not been followed. In this respect, for traditional methods preclinical studies have become an attempt to prove that they are effective. Apitherapy products are not consisting of a single molecule, but in blends with many active substances. This makes the work difficult. Virtual reality and mathematical modeling can help.

Keywords: Apitherapy, preclinical studies, virtual reality, mathematical modeling

Preclinical studies are conducted to determine efficacy, toxicity and safety. With PD (Pharmacodynamics - what the drug does to the body) and PK (Pharmacokinetics - what the body does to the drug) studies a safe starting dose is estimated.
Modern medical methodology has set clear standards for research in the field of health and requires health practices to be made with evidence set forth in these standards. However, the treatment traditions that have lived throughout history have developed and settled outside these criteria. Although it is widely used today under names such as complementary, alternative and traditional medicine, it is not possible to say that it is accepted without frowning in general medical circles (Frass et al.2012). They play a more active role in some countries with weak health systems (Gupta et al.2014). Confusion regarding the definition has not been resolved, either. Complementary, alternative or integrative: Which of the medical terms apitherapy would be described with? National Center for Complementary and Alternative Medicine (NCCAM) describes complementary-alternative medicine as 'different medical and health systems, practices and products that are different from conventional medicine, applied by people who have had different training in integrative medicine.' It is possible to use conventional and traditional medicine together with proven efficacy and reliability. So the effectiveness and safety of apitherapy must be proven. The first step towards this goal is preclinical studies. Hive products have already been known and consumed as healing throughout history. Today, it is classified under the concept of "functional food", which is a more modern term. Functional foods are foods used to promote and maintain health. As the chemical structure of foods and their functions in the bio system is understood, this term is expanded and accepted. Except for bee venom, all bee products can be used as both nutrients and therapeutic agents. Although apitherapy applications are within the context of traditional medicine, it opens up a space for itself in modern medicine with numerous pre-clinical and clinical studies conducted with modern methodology. Increase in international publishing activities give a good idea on this

issue (Figure 1).

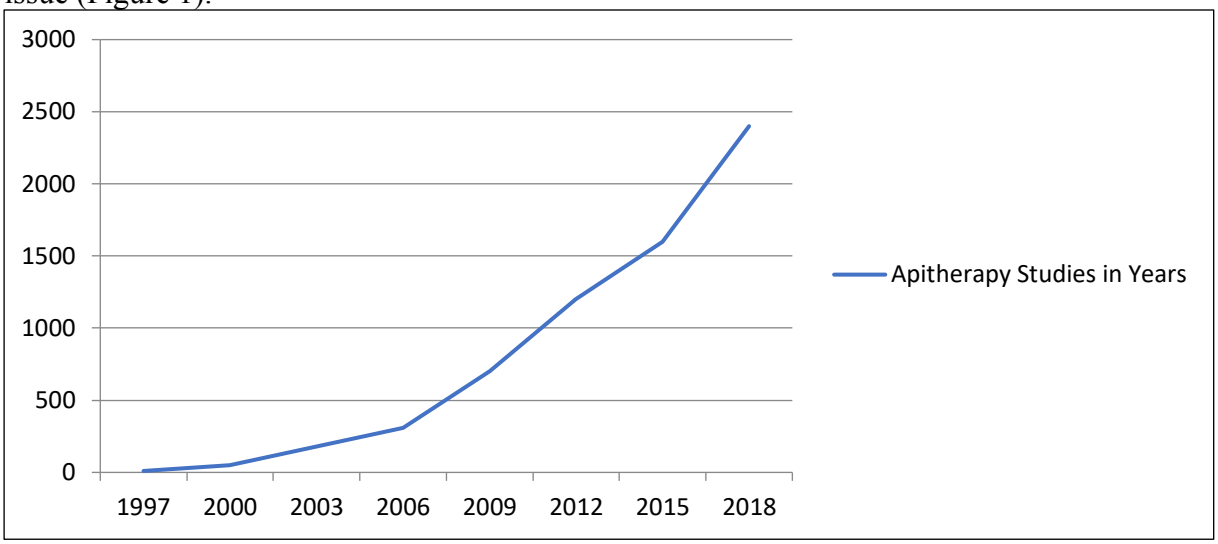

Figure 1. International Apitherapy Studies in Years

When it comes to pre-clinical studies, test tube (in vitro) and animal studies (in vivo) come into mind. One should keep in mind that preclinical studies are not on high grounds in so called evidence-based pyramid (figure 2).

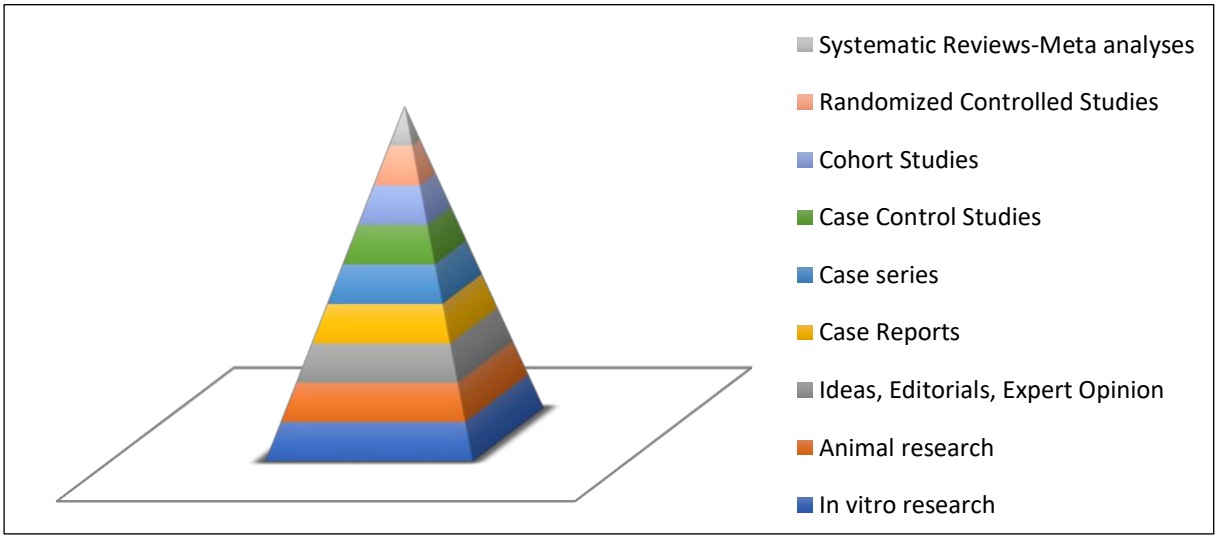

Figure 2. Evidence Pyramid (For toxicology, food safety etc)

That is not to say that they are unimportant but rather it is a long way of putting in clinical practice. Not all successful in vitro or animal studies translate in clinical use with the same results. It is often the case that they fail in phase studies and never make it to human use. Even after passing all the phases, in clinical use some unfavorable results and side effects may arise. That's mean throwing away good deal of money, work and resources. Therefore, preclinical studies should be planned well. Better still, in the age of artificial intelligence all experiments can be run in an artificial world of simulated environment before actual experiments. Considering the complex nature of apitherapy products this is important because taking all variations into consideration is very difficult.

Standardized physiological or pathological cell lines are used in laboratory studies (eg. HepG2 cell line in liver cancer studies). Various animals with certain characteristics are used in vivo studies. Finding an animal species matching human characteristics is always a challenge. The

fact that preclinical studies can be carried out by many disciplines, beside clinical medicine, has contributed immensely to the increase in number of studies (Kanbur et al. 2009, El-Hanoun et al 2014). Many Scientists in different fields have helped to understand the ingredients of bee products and this process have increased interest towards apitherapy products in the medical world.

Another purpose of preclinical studies is to reveal drug interactions. People with chronic or serious illnesses frequently use a traditional product along with their drugs (Tulunay et al. 2015). Apitherapy products are often in that traditional product list for various reasons. If this interaction is understood clearly, it will further contribute to the treatment positively. Again, artificial intelligence can be of a great help here. Possible co-use of apitherapy products in combination with modern medicine should be explored seriously and this decision should not be left to desperate patients and unscrupulous vendors. Drug - apitherapy products interactions can be studied in virtual environments mediated by artificial intelligence. Modeling studies in virtual reality environment can simulate a product completely in virtual environment and give an idea about possible results. Terms such as 'in silico' or 'single phase study' are used for these studies and they are gathering momentum. Perhaps in the near future we will use the terms in vitro, in vivo and 'in silico' together. For a long time, mathematical models are used by economists and meteorologists to predict business and weather forecasts and now, usability of similar modeling for the medical world are considered. The effectiveness of such models has been demonstrated in some diseases (Soler et al. 2006, Kozlowska et al. 2019). Complex compounds such as apitherapy products may be difficult to evaluate clinically but such applications may help.

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Oral Presentation

The Effect of Olive Oil-Based Propolis on Biochemical Parameters in Healthy Volunteers: A Clinical Study

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Abstract

In this single-center, randomized study in healthy male volunteers under fasting conditions, it was aimed to determine the effect of olive oil-based propolis on biochemical parameters after administration of two different doses. For this purpose, the volunteers were given a phenolic-restricted diet for two weeks before the study, and then the anthropometric measurements and biochemical tests of the volunteers were completed. Volunteers who met the study criteria were included in the study. Blood and urine samples were taken from the volunteers on days 0, 15 and 30. In the study, olive oil-based propolis (OEP) consumption was compared to determine the effect of olive oil and the difference between doses. When the urine and CBC tests of the volunteers participating in the study (22 male volunteers) were examined, there was no statistically significant difference ($p>0.05$), while the difference between the groups was found to be significant in terms of biochemical tests, triglyceride, HDL, cholesterol and calcium levels, and GGT and LDH enzyme activities ($p<0.05$). The triglyceride level of blood lipids was 121.66 mg/dL in the olive oil group (control), while it decreased to 114.25 mg/dL in the group consuming 2.5 ml OEP and 77.80 mg/dL in the group consuming 5 ml OEP. HDL cholesterol level was 40.95 mg/dL in the group consuming only olive oil, 47.85 mg/dL in the group consuming 2.5 ml OEP, and 49.48 mg/dL in the group consuming 5 ml OEP. As a result, the higher blood lipid lowering effect was observed in volunteers consuming 5 mL of OEP compared to the other groups suggests that this effect may have been caused by propolis.

Keywords: Clinical Study, Olive Oil Extract, Propolis, Volunteers

1. Introduction

Apitherapy, which has been in existence since the beginning of humanity and whose importance has emerged with increasing studies in recent years, draws attention with the prevention of many diseases and support for treatment. Natural products such as honey, pollen, perga, propolis, royal jelly and apilarnil are friendly to all cells in the body and have high antioxidant capacity. In the structure of these products, which honeybees process by collecting nectar and pollen from plants; There are many compounds such as protein, carbohydrates, vitamins, coenzymes, polyphenols, aroma compounds, phytosterols, terpene and terpenoids, aliphatic compounds, fatty acids. Since plants have unlimited capacity to produce aromatic and aliphatic compounds, there are plenty of polyphenolic substances in the structure of honey, pollen, propolis and other bee products produced with raw materials collected from plants by honeybees (Silici, 2020)

Functional foods; beyond meeting the basic nutritional needs of the body, they are food or food components that are effective in preventing diseases and leading a healthier life by providing additional benefits on human physiology and metabolic functions (Mehenktaş ve Beyaz, 2004).

Among these products, propolis has an important place. Many plants protect their leaves, flowers, fruits and buds from cold and microorganism attack by producing a resinous compound with strong antimicrobial, waterproof and heat-insulating properties. This resinous substance, which is usually secreted from the colletary tissue of plants, is collected by honeybees (*Apis mellifera* L.) with the help of their jaws (mandible), mixed with wax and saliva, turned into pellets and transported to the hive in the pollen basket (corbicula). In this state, the chemical structure of the resin differs, so it is called propolis. Considering its function in nature, the resin produced by the plant is necessary for the protection of the plant bud from microorganisms and for the continuation of the generation, while propolis is essential for the protection and survival of the honey bee1. Honeybees collect resin and produce propolis in order to maintain homeostasis, to prevent uncontrolled air flow in the hive, to reduce microbial growth, to waterproof the hive walls, to strengthen the structural stability in primitive hives, to narrow/close the entrances and holes that will make the hive vulnerable, and to prevent stinking of dead creatures in the hive (Burdock, 1998).

The color of propolis varies from green, red, yellow, and brown depending on the plant source, collection time and storage period, and generally in its natural structure 50% resin and herbal balm, 30% beeswax, 10% essential and aromatic oils, 10% pollen and There are other organic substances3. The chemical compounds in the structure of propolis (hundreds of different compounds including flavonoids, terpenes, phenolic compounds and their esters, sugars, hydrocarbons and mineral elements) were also identified with the development of separation and purification techniques. In regions with continental climates such as Europe, Asia and North America, the bud secretions of different tree species are the source of propolis. Samples originating from these regions have similar chemical composition, with phenolics, flavonoid aglycones, aromatic acids and their esters being the main compounds. It was identified 5-phenyl trans, trans-2,4 pentadienoic acid and 5-phenyl-trans-3-pentenoic acid in propolis (poplar) obtained from New Zealand (Markham et al. 1996). On the other hand, long-chain fatty alcohols (dodecanol, tetradecanol, tetradecenol, hexadecanol) and caffeic acid esters were identified as the main components in a poplar propolis of Egyptian origin (Hegazi et al. 2001). While the flavonoid aglycones, phenolic acids and esters detected in Polish propolis indicate poplar type propolis, the buds of birch (*Betula pendula* Roth.), alder (*Alnus glutinosa* L.), pine (*Pinus sylvestris* L.) and willow trees are also shown as sources of propolis (Popova et al. 2017). Phenolic acids in poplar type propolis are mainly represented by benzoic and cinnamic acid/derivatives. The most common benzoic acid derivatives are; While p-hydroxybenzoic acid, p-methoxybenzoic acid and gallic acid are the most common cinnamic acid derivatives, caffeic acid, ferulic acid, p-coumaric acid, isopheric acid and 3,4 dimethoxycinnamic acid are shown. Phenol alcohols include benzyl and cinnamyl alcohol, aromatic esters include benzoic acid benzyl ester, cinnamic and caffeic acid ether ester and benzoic acid phenylmethyl ester, ketophenols include acetophenone and methylactophenone, phenolic aldehydes include vanillin and isovaniline, benzoic, cinnamic acid. and coniferyl aldehyde are expressed among the commonly found components (Bankova et al. 2000; 2005; Greenaway et al. 1991). In another study, 38 flavonoids were detected in propolis, and it was reported that the flavonoids found in propolis are glycosidic aglycones found in plants (Dobrowolski et al. 1991). Honeybees secrete beta-glucosidase enzyme, which hydrolyzes flavonoid glycosides into aglycons and sugars. When defining poplar-type propolis, in addition to phenolic acid and flavonoids, monoterpenes such as geraniol, nerol and borneol, which are approximately 0.5%, sesquiterpenes such as beta-eudesmol, alpha-acetoxy beraulenol, beta-bisabolol, cariophilene, guaiol, guaien, beta-selinene and farnesol, sesquiterpenes and glutinols. terpenes are also included (Kardar and Siedel, 2015). Propolis has many biological and pharmacological activities such as immunomodulator, antitumor, anti-inflammatory, antioxidant, antibacterial, antiviral, antifungal and antiparasitic

(Kanbur et al. 2015; Çetin et al. 2010; Özkul et al. 2005; Eroğlu et al. 2005; Koç et al. 2008). Most of the research on propolis is in vitro or on experimental animals. The number of clinical studies is very small. Therefore, in this study, it was aimed to determine the effects of two different doses of olive oil-based propolis on post-application biochemical parameters in healthy male volunteers.

2. Materials and Methods

2.1. Volunteers

Men of Caucasian race, those between the ages of 18-55, those who were interpreted as physically and mentally healthy by standard laboratory tests, those who do not smoke or smoke less than 5 times a day, BMI (including both values) between 18.5 -30 kg/m2, written Those who gave informed voluntary consent were included in the study. BMI of each individual; Calculated in kg/m2 using the equation of body weight (kg)/height (m^2). Screening in the selection of volunteers for study; The standard clinical trial included medical history, a complete clinical examination, measurement of height, weight, body temperature, standard ECG, blood pressure measurement, and heart rate counting after 5 minutes of supine position. Pre-study screening and post-study clinical examination and hematologic; Hemoglobin, hematocrit, leukocyte, erythrocyte and thrombocyte (whole blood) count, electrolyte; Sodium, potassium, calcium, chloride, Substrates; creatinine, total protein, total bilirubin, blood sugar, BUN, uric acid, Enzymes; AST, ALT, GGT, ALP, urine test; Laboratory parameters such as pH, leukocyte, nitrite, protein, glucose, ketone, urobilinogen, bilirubin, specific gravity, microscopic examination of blood and sediment were checked. Those taking antioxidant or fish oil supplementation, consuming more than 3 servings of fruit and vegetables daily, regularly consuming red grape juice or red wine for the 3 months before the study, those with diabetes, hypertension, heart disease or endocrine disorder, abnormal blood chemistry profile, fasting at screening LDL Cholesterol concentration >3.37 mmol/L (>130 mg/dL) or fasting triacylglycerol concentration >3.39 mmol/L (>300 mg/dL), those receiving hypolipidemic treatment, those receiving anticoagulant or thyroxine treatment, and those allergic to bee products were excluded from the study.

2.2. Propolis

In the study, olive oil-based propolis containing 25% pure poplar type propolis produced under HACCP conditions and containing 558.03 □g/ml CAPE was used by Nutral Therapy Ltd. Sti (Erciyes Technopark, Kayseri).

2.3. Clinical studies

The study was conducted in Erciyes University Faculty of Medicine, Hakan Çetinsaya Good Clinical Practice Center (IKUM), in healthy male volunteers, under fasting conditions, single-centre, double-blind, randomized, with the application of olive oil and different propolis doses. Ethics Committee Approval for the study was received from Erciyes University Clinical Research Ethics Committee (dated 25.12.2019 and decision no 2019/868) and the Ministry of Health (dated 02.01.2020 and numbered 77979112). The center where the research is carried out is a center that has the opportunity to intervene in cases of doctors, nurses and emergencies. Heart rate, blood pressure, and temperature were measured in volunteers before and during dosing. Blood samples were drawn from volunteers for determination of blood enzyme levels 15 days before dosing and on the morning immediately before dosing. Volunteers remained on the clinical ward for at least 11 hours before receiving propolis for the study and up to 8 hours after taking the drug. 8 ml of blood was drawn at certain points in the 1 hour before and during

the 8 hours after propolis ingestion and once in the 24th hour. Blood was collected in lithium heparin tubes.
The volunteers were divided into three groups, each randomly distributed, and they continued to take 2.5 ml olive oil (control) 2.5 ml and 5 ml olive oil-based propolis every day in the first stage, as a single dose morning fasting conditions, and for one month after the acute application. Although it was planned to start the clinical study with 40 healthy volunteers, 22 volunteers were included in the study and the volunteers were considered to have completed the study at different times due to the covid 19 pandemic.

2.4. Biochemical analyzes
Measurement of biochemical parameters in serum was carried out in Erciyes University Gevher Nesibe Hospital Central Biochemistry Laboratory.

2.5. Statistical analysis
SPSS 16.0 (Statistical Package for the Social Sciences) Software package program was used for all data obtained as a result of the research. Arithmetic Mean($\bar{x}$) for descriptive statistics, because it is desired to find out whether there is a difference between the groups by comparing the data with each other; standard error ($S\bar{x}$) is used; the data of the variables were determined with the Shapiro-Wilk normality test, and the data of the parametric and within-group dependent variables were determined by the Repeated-measures ANOVA test; Data belonging to parametric and independent variables were analyzed with one-way ANOVA test. While using Post-hoc Tukey test for data showing homogeneity of variance in one-way ANOVA test; Games-Howell Post-Hoc test was applied to the data without homogeneity of variance. While the data belonging to the dependent variables within the group determined to be nonparametric were analyzed with the Friedman test; Data belonging to nonparametric independent variables were analyzed with the Kruskal-Wallis H test. The significance level for all statistical tests was determined as $\alpha = 0.05$.

3. Results
In the statistical comparison made to determine the effect of olive oil and the difference between doses in the research, it was found that the triglyceride value from blood fats decreased more than the group consuming only olive oil in the groups consuming both 2.5 ml and 5 ml olive oil-based propolis at the end of the 15t^{h} day, while the group consuming 5 ml OEP (oil extract of propolis) had 2.5 ml OEP. It was determined that the consuming group decreased more than the triglyceride values ($p<0.05$). Among the analyzed values, GGT enzyme activity was highest in the olive oil group, while it decreased in the group consuming 2.5 ml OEP, while the highest decrease was observed in the group consuming 5 ml OEP (Table 1). Differences between other values were not statistically significant ($p>0.05$). Again, these values are within normal reference values.

Table 1. Comparison of the groups consuming olive oil and olive oil-based propolis on the 15th day of the experiment

Parameter	Olive oil	OEPI	OEPII	P
Urine				
pH	5.78±0.21	5.77±0.14	5.80 ±.37	0.678
Erythrocyte	0.71±0.042	0.33±0.016	0.40±0.04	0.984
Hematological parameters				
WBC	6.86±0.66	7.07±0.39	6.72±0.54	0.447
Hemoglobin (HBG)	16.45±0.33	16.13±0.34	16.68±0.66	0.995
Platelet (PLT)	271±26.11	278±32.47	238.2±12.13	0.433
Erythrocyte (RBC)	5.27±0.05	5.52±0.11	5.49±0.22	0.623

Hematocrit (HCT)	47.94±0.89	47.31±0.86	48.48±1.91	0.949
Biochemical parameters				
Triglyceride	**129.71±15.16** [a]	**114.88±14.21** [a]	**94.2±4.97** [b]	**0.008**
Cholesterol	145.14±9.41	165.44±11.44	158±6.66	0.923
HDL-Cholesterol	40.80±1.86	48.77±3.22	46.96±3.46	0.133
LDL-Cholesterol	78.4±8.70	93.68±12.04	92.60±6.02	0.644
BUN	12.22±0.70	12.08±0.71	15.22±1.01	0.408
Creatinine	0.98±0.02	0.87±0.02	0.98±0.04	0.362
Uric acid	4.94±0.43	5.43±0.28	5.68±0.57	0.882
Calcium	9.57±0.13	9.65±0.10	9.68±0.14	0.191
Sodium	140.57±0.42	139.55±0.64	139.2±1.46	0.412
Potassium	4.65±0.15	4.92±0.25	4.59±0.10	0.340
Chloride	102±0.89	102.08±0.79	102±0.96	0.893
Bilirubin	0.74±0.14	0.65±0.014	0.65±0.08	0.265
GGT	**20.57±1.92** [b]	**18.44±1.87** [ab]	**16.20±1.85** [a]	**0.034**
LDH	175±7.14	167.77±7.36	200.4±20.2	0.075
AST	16.57±1.25	18.44±1.56	18±2.16	0.875
ALT	17.71±3.17	22.66±4.69	15.80±1.35	0.362
Total protein	7.14±0.22	7.57±0.05	7.12±0.18	0.350
ALP	74.85±6.55	79.11±5.40	70.80±4.91	0.847
Glucose	99.28±8.15	91.55±1.06	91.60±3.85	0.387

X ±SD: mean ± standard deviation; The letters in the lines (a-b) indicate the significance of the difference between the groups (P<0.05).

When the urine and CBC tests of the volunteers who completed the 30th day of the study were examined, there was no statistically significant difference between the groups, but a significant difference was found between the groups in terms of biochemical tests, triglyceride, HDL cholesterol, calcium, GGT and LDH enzymes (p<0.05), (Table 4). While the triglyceride value of blood fats was 121.66 mg/dL in the olive oil group, it decreased to 114.25 mg/dL in the group consuming 2.5 ml OEP and to 77.80 mg/dl in the group consuming 5 ml OEP. HDL cholesterol value was 40.95 mg/dL in the group consuming only olive oil, while it was 47.85 mg/dL in the group consuming 2.5 ml OEP and 49.48 mg/dL in the group consuming 5 ml OEP. The average calcium value of the group consuming olive oil was higher than the group consuming 2.5 ml OEP, but lower than the group consuming 5 ml OEP. The enzyme activities of GGT and LDH, which are two important liver enzymes, differed between the groups. In terms of GGT enzyme activity, the average of the groups consuming 2.5 and 5 ml OEP was found to be lower than the group consuming olive oil, while the LDH enzyme activity was found to be lower than the group consuming olive oil (p<0.05). These values were included in the reference values (Table 3).

Table 2. Comparison of the groups consuming olive oil and olive oil-based propolis on the 30th day of the experiment

Parameter	**Olive oil**	**OEP1**	**OEP2**	**P**
Urine				
pH	5.50±0.22	5.75±0.25	5.80±0.37	0.398
Erythrocyte	0.50±0.050	0.50±0.026	0.40±0.04	0.956
Hematological parameters				
WBC	7.04±0.48	6.23±0.311	6.97±0.90	0.221
Hemoglobin (HBG)	16.11±0.24	16.13±0.26	16.08±0.46	0.989
Platelet (PLT)	243.83±14.27	266±14.47	233.6±4.86	0.174
Erythrocyte (RBC)	5.16±0.02	5.30±0.06	5.29±0.19	0.329
Hematocrit (HCT)	46.83±0.52	46.81±0.50	46.42±1.36	0.865
Biochemical parameters				
Triglyceride	**121.66±6.55** [a]	**114.25±8.58** [a]	**77.80±2.32** [b]	**0.000**

Cholesterol	157.33±2.20	162.12±10.68	153.0±3.53	0.817
HDL-Cholesterol	**40.95±1.20** [a]	**47.85±2.42** [ab]	**49.48±2,05** [b]	**0.008**
LDL-Cholesterol	95.43±3.42	97.97±9.46	87.96±2.68	0.351
BUN	10.88±0.58	12.11±1.02	13.22±0.77	0.095
Creatinine	0.96±0.021	0.88±0.04	0.88±0.33	0.094
Uric acid	5.40±0.12	5,33±0,29	5,18±0,19	0.712
Calcium	**9.57±0.10**[ab]	**9.35±0.11**[a]	**9.67±0.03** [b]	**0.040**
Sodium	141.83±0.43	140.25±0.99	140.80±0.45	0.167
Potassium	4.51±0.07	4.31±0.07	4.44±0.068	0.137
Chloride	101.16±0.58	101.75±0.64	101.20±0.64	0.762
Bilirubin	0.79±0.10	0.56±0.05	0.59±0.08	0.056
GGT	**22.11±1.02** [b]	**17.25±1.19** [a]	**16.40±0.60** [a]	**0.001**
LDH	**172.83±7.19** [b]	**141.37±5.10** [a]	**166.40±13.61** [b]	**0.007**
AST	19.16±0.86	17.75±1.68	17.60±1.82	0.727
ALT	24.66±3.15	19.0±3.81	14.80±1.78	0.072
Total protein	7.14±0.11	7.31±0.08	7.07±0.04	0.126
ALP	73.83±5.19	73.37±3.57	69.20±1.88	0.642
Glucose	93.50±3.70	86.50±1.99	88.40±0.91	0.140

X ±SD: mean ± standard deviation; The letters in the lines (a-b) indicate the significance of the difference between the groups (P<0.05).

Table 3. Reference values of biochemical parameters

Parameters	**Reference**	**Parameters**	**Reference**
Ph-Urine	5-6	Uric acidt mg/dL	3.5-7.2/E
Erythrocyte-Urine /mL	<3	Ca-mg/dL	8.8-10.6
WBC 10^3/µL	4.8-10.8	Na-mmol/L	136-146
Hgb-Hemoglobin g/dL	14-18 (E)	K-mmol/L	3.5-5.1
PLT-Platelet 10^3/µL	130-400	Cl-mmol/L	98-106
RBC 103/µL	4.2-5.4	Total bilirubin mg/dL	0.3-1.2
HCT-Hematocrit %	42-52(E)	GGT-U/L	0-55/E
Triglyceride mg/dL	35-150	LDH-U/L	0-248/E
Cholesterolmg/dL	120-200	AST-U/L	0-35
Cholesterol-HDL mg/dL	40-60	Alt-U/L	0-45
Cholesterol-LDL mg/dL	<130	Total protein g/dL	6.6-8.3
BUN mg/dL	7.9-21	Alp- U/L	30-120
Creatinine mg/dL	0.66-1.09	Glucose mg/dL	75-106

4. Discussion

Since it is not possible to consume propolis in its raw form, it must be extracted and the wax and other wastes must be removed. For this reason, propolis is extracted and processed using different solvents (ethyl alcohol, propylene glycol, glycerol) to make it suitable for consumption. Until recent years, the ethanolic extract of propolis has been the most preferred extract in both scientific studies and commercial products due to its high solubility all over the world. However, while its sharp and resinous taste limits its use in the cosmetic and pharmaceutical industry, the high concentration (70-80%) ethyl alcohol content of the products is not considered medically appropriate for use in ophthalmology, pediatrics, diabetes and cancer patients and people with alcohol intolerance (Kubilene, et al. 2015) and searched for a harmless extraction solvent. Most studies have compared the efficacy of different solvents. In a study where the antibacterial and antifungal activities of commercial propolis extracts obtained with different solvents were tested, oil, ethanol and propylene glycol extracts of propolis all showed antimicrobial effects against the tested bacteria, yeast and dermatophytes. It has been shown that the /glycerol solution can maintain this effect for only a few days (Tosi et al. 1996). In another study, propolis collected from Lithuania was dissolved with distilled water, ethanol and propylene glycol, and the most effective solvent in terms of total phenolic

content was found to be ethyl alcohol, the least effective was water and propylene glycol was found to be moderate (Ramanauskiene et al. 2011). While the antioxidant activity of propolis is mostly attributed to the flavonoids in its structure, crude propolis produced by Trigona bees grown in Indonesia (Sulawesi region) was extracted with different solvents (water, ethanol, propylene glycol, olive oil and coconut oil) and its flavonoid content was determined. According to the results they obtained, the researchers emphasized that using oil as a solvent in the extraction of propolis has a flavonoid content similar to the ethanol extract, and that both olive oil and coconut oil can be used in propolis extraction (Pujirahayu et al. 2019). Olive oil extracts of propolis had better antioxidant activity at 0.01% levels compared to butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT), while the highest antioxidant activity was found to be 0.08%. In the study, it was concluded that the antioxidant activity of propolis increased with concentration and olive oil extract could be considered as a new natural antioxidant source (Özcan et al. 2003). In another study, the antioxidant, antiradical and antipyretic effects and total phenolic content of the poplar type olive oil extract (OOEP) of propolis were determined. ferulic acid, p-coumaric acid and vanillin were determined. In the study, it was determined that as the propolis concentration increased, the total phenolic content, antioxidant and antiradical activity also increased. Olive oil extract of propolis showed antipyretic effect in rats in which hyperthermia was induced by yeast. Researchers have shown that olive oil extract of propolis has antioxidant, antiradical and antipyretic effects and reported that it is a healthier alternative to alcoholic extracts (Silici and Baysa , 2020). In a master's thesis conducted by Şahin (2019), the highest bioactivity was obtained with cold-pressed unrefined olive oil as a result of extraction of propolis with olive oil prepared with different processing procedures. It was determined that the extraction was done. However, in a study in which the phenolic components of extra virgin olive oil produced in Turkey were determined, tyrosol, hydroxytyrosol, vanillic acid, p-coumaric acid, cinnamic acid, luteolin and apigenin compounds were reported (Alkan et al. 2012). Similarly, in the chromatographic analysis of extra virgin olive oil in Spain by HPLC, it was determined that it contains phenolic compounds such as hydroxytyrosol, tyrosol, vanillic acid, p-coumaric acid, decarboxymethyl oleuropein, pinoresinol, cinnamic acid, luteolin and apigenin (Jimenez-Lopez et al. 2020).

As a result of this clinical study, as a result of the consumption of olive oil-based propolis by healthy male volunteers for 15 and 30 days, a statistically significant decrease was observed in the level of triglyceride from blood lipids, while an increase in the level of HDL-cholesterol was detected. Hyperlipidemia means that the cholesterol and triglyceride levels in the blood plasma are higher than the expected normal values. Determination of cardiovascular (vessel-vascular system) risk scores is very important for the clinical diagnosis of hyperlipidemia. There are many studies supporting this research result regarding the lowering effect of propolis on blood lipids. For example, in a study evaluating the effect of water extract of Libya-derived propolis on the detrimental effects of sodium nitrite-induced hematotoxicity and hyperlipidemia in guinea pigs, it was reported that the application of propolis provided a significant improvement in all hematological and lipid profile parameters and atherogenic ratio parameters36. The effects of ethanol extract of Iranian origin propolis on some biochemical factors in rats were determined. Glucose, triglyceride, aspartate aminotransferase, alanine aminotransferase activity were measured in the blood serum of rats, while the blood glucose level did not change significantly, the triglyceride level decreased but the AST level increased in the 100 mg/kg propolis group. For this reason, researchers emphasized that while propolis ethanol extract has a moderate effect on blood biochemical parameters, excessive consumption may harm people with liver disease (Azab et al. 2014). In a study investigating the effect of propolis ethanol extract on the growth performance of weaned piglets in Croatia, it was reported that while propolis had a positive effect on blood lipids, it caused an increase in liver

enzymes38. Another study is about to evaluate the effect of pollen and propolis added to the broiler diet. At the end of the 21st day of feeding, the results showed that propolis significantly reduced blood sugar, cholesterol and calcium levels, as well as triglyceride levels, while causing an increase in sodium, chlorine, phosphorus and globulin levels (Gheybi et al. 2016). The antilipidemic peroxidative effect of Brazilian propolis ethanol extract was evaluated on the inhibitory effect of the extract on the formation of hydroperoxide and endoperoxide type lipid peroxides during heating of polyunsaturated oil. Propolis ethanol extract dose-dependently inhibited lipid peroxidation reactions in rat liver microsomes. Researchers have stated that propolis ethanol extract can have an antilipidemic peroxidative effect at very low doses (Stolic et al. 2019; Klaric et al.2018). Wistar Kyoto rats and spontaneously hypertensive rats followed a 4-week diet and the effect of Brazilian propolis and ecomia plant (*Eucommia uloides* OLIVER, tochu) was investigated, and propolis caused a significant decrease in systolic blood pressure in the hypertensive rats group (Orsolic et al.2019). Again, it has been observed that propolis provides relief in acetylcholine-induced hypertensive animals, and it has been stated that propolis has an antihypersensitive effect by providing acetylcholine-induced vasodilation (Kubota et al. 2014). However, in a study using propolis of Brazilian origin, Brazilian propolis was given to rats at different doses for 30, 90 and 150 days, and as a result of the study, the cholesterol, HDL-cholesterol, total lipid, triglyceride levels and AST and LDH enzyme activities of the rats were compared with the control group. No change has been identified. Researchers have reported that propolis does not have a negative effect on biochemical parameters and that its long-term use does not cause any heart damage (Shinohara et al. 2002; Mani et al. 2006). It has been determined that propolis given to carp (*Cyprinus carpio*, Linnaeus) fish exposed to arsenic reduces biochemical values such as elevated triglycerides, urea, total cholesterol, ALT, and LDH (Selamoğlu-Talas et al. 2012). In another study, it was determined that propolis, pollen and CAPE could show positive effects on the heart, adrenal medulla and hypothalamus of hypertensive rats (Ekhteiari et al. 2018).

5. Conclusion

In this clinical study conducted for the first time in healthy male volunteers with olive oil-based poplar type propolis, after 15 and 30 days of use, there were statistical differences in terms of triglyceride level, decrease in GGT and LDH enzyme activity and increase in HDL-cholesterol level, but all tested parameters were within reference limits. has been included in. More importantly, these changes did not appear to adversely affect the health of the volunteers clinically. This clinical study is the first study conducted with healthy volunteers on propolis in our country, however, there is a need for more clinical studies on propolis, which has a large number of biological activities.

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This study was financially supported by Erciyes University Scientific Research Projects.

Oral Presentation

Effect of Short and Long-Term Use of Commercial Propolis Extracts on Liver Enzymes in Rats

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Abstract

Many commercial preparations have been developed due to the determination of the beneficial biological effects of propolis in the health field. In these propolis products, different solvents are used in extraction and in the final product. It is thought that long-term use of these solvents can damage vital tissues such as the liver. The aim of this study is to determine the effects of using commercial propolis extracts that are widely used and sold for one to three months on liver enzymes. In the study, 56 adults female Wistar albino rats were divided into 7 groups. For 30 and 90 days, propolis ethyl alcohol, propylene glycol and water-based propolis (250 mg / kg / day) were given to the groups orally by gavage. At the end of the research, liver enzyme levels such as GGT, AST, ALT, ALP were determined in blood samples taken from rats. According to the results obtained; At the end of the first month, the enzyme activities of the rats in the alcohol-based propolis group were found to be significantly higher than those of the control and other groups in terms of LDH, AST, ALT and ALP enzymes.

Keywords: Propolis, Ethanol, Propylene Glycol, Extraction.

1. Introduction

Propolis is a bee product produced from plant resins collected by honeybees. Bees are used for purposes such as plastering the walls of the hive to prevent the development of microorganisms in the hive, closing the cracks and cracks in the hive, keeping the humidity and temperature constant in the hive, mummifying them to prevent stinking of dead insects and animals that die in the hive and are too large to be carried outside the hive, and to make the hive entrance hole smaller They use propolis. Covering the cells of the comb with a thin layer of propolis is to protect the young (larva and pupa) from infections. Thus, an antibacterial, antifungal and antiviral environment is provided in the hive (Bankova et al. 2018; Silici, 2020). The relationship between honeybees and plants in the evolutionary process is extraordinary. Many plants protect their leaves, flowers, fruits and buds from cold and microorganism attack by producing a resinous compound with strong antimicrobial, waterproof and heat-insulating properties. This resinous substance, which is usually secreted from the colletary tissue of plants, is collected by honeybees (*Apis mellifera* L.) with the help of their jaws (mandible), mixed with wax and saliva, turned into pellets and transported to the hive in the pollen basket (corbicula). In this state, the chemical structure of the resin differs, so it is called propolis. In fact, considering its function in nature, the resin produced by the plant is necessary for the protection of the plant bud from micro-organisms and the continuation of the generation, while propolis is essential for the protection and survival of the honeybee (Silici, 2020). The color of propolis ranges from green, red, yellow, and brown, depending on the plant source, collection time, and storage time. Its smell is characteristic of its own. Its taste is intensely aromatic and astringent in its raw form. It becomes hard in the refrigerator and freezer becomes sticky at room temperature. Due to its sticky feature, it easily penetrates the skin, interacts with the oil and

proteins of the skin and becomes difficult to clean from the skin. In general, there are 50% resin and herbal balm in its natural structure, 30% beeswax, 10% essential and aromatic oils, 10% pollen and other organic substances (Burdock, 1998).

Solvents used in commercial propolis extraction are handled in two groups as organic (water and oil) and alcoholic (ethylalcohol, propylene glycol, glycol, glycerol etc.). Ethyl alcohol is the most frequently used solvent, both in scientific research and as a commercial formulation. Propolis has a high solubility in ethyl alcohol. However, high solubility can sometimes cause undesirable compounds to be obtained. It also poses a problem for patients who are sensitive to alcohol (such as those with alcohol intolerance), diabetics, cancer patients and children, and those who do not want to use alcohol-containing products for religious reasons. The lowest alcohol grade used in propolis alcohol extraction is 70%. Although the daily consumption of propolis ethanol extract is small, it can pose a risk in long-term use. Although there are very few commercial products in the world, propylene glycol is also used in propolis extraction. Propylene glycol (PG) is a clear, colorless, water-soluble alcohol used as an adjuvant in parenteral and non-parenteral pharmaceutical formulations containing water-insoluble active ingredients. It is also used in cosmetics and the food industry as a humectant (E1520), as a food preservative, and as a vehicle for flavors in preference to ethanol (Morshed et al. 1991; 1998). Propylene glycol (1,2 propanediol) has been reported to have low toxicity in adults, but has haematological, renal and cardiac toxicity (blood, kidney and cardiac toxicity) according to CNS (central nervous system) reports. Absorption of products containing propylene glycol applied to wounds has been reported to cause hyperosmolality in serum. It has been understood that hyperosmality of unknown cause in premature infants is due to multivitamin preparations used in parenteral nutrition and propylene glycol intake. It has been shown that propylene glycol intake can cause many health problems, especially in infants (Yu et al. 1985; O'Donnell et al. 2000; Shehab et al. 2009)

For all these reasons, researchers have sought natural and harmless extraction solvents in recent years. Most studies have compared the efficacy of different solvents. Tosi et al. (1996) reported that all of the extracts prepared with oil, ethanol and porpylene glycol and glycerin solutions of propolis showed antibacterial and antifungal activity (especially against bacteria, yeast and dermatophytes), while the glycerin solution provided inhibition for only a few days and the others for more than 2 weeks. Konishi et al. (2004) stated that although the most common propolis extraction process uses ethanol as a solvent, this extraction has disadvantages due to its very strong resinous taste, some people's intolerance to alcohol, and adverse effects. The organ that can be most affected by these negative effects is the liver.

The liver is the largest and most important metabolic organ in our body, which consists of different functional and anatomical structures. liver enzymes; ALT (alanine aminotransferase), AST (aspartate aminotransferase), GGT (gamma-glutamyl transpeptidase) and ALP (alkaline phosphatase). While the first two enzymes are synthesized in hepatocytes, the last two enzymes are synthesized in bile duct epithelial cells. There are numerous causes of elevated liver enzymes in symptomatic and asymptomatic patients. Although ALT and AST may originate from other tissues, they are enzymes that are released in hepatocyte damage in the blood following hepatocellular injury. The liver is more vulnerable to ethanol-induced damage than other organs in the body, because ethanol is mainly metabolized in the liver (Ozel et al., 2010; Zhou, 2010). Increased reactive oxygen species (ROS) alter the prooxidant-antioxidant balance and may cause increased lipid peroxidation in the gastrointestinal tract, liver, heart and brain tissues (Lieber, 1991).

Therefore, in this study, it was aimed to determine the effect of commercial propolis extracts prepared with alcohol and its derivatives, which are used as solvents in extraction or in the final product, on liver enzymes in 30 and 90 days of consumption.

2. Materials and Methods

2.1. Material

2.1.1. Experimental Animals

The research was carried out with the approval of the Ethics Committee from the Erciyes University Animal Experiments Local Ethics Committee. Experimental animals were housed in Erciyes University Hakan Çetinsaya Experimental and Clinical Research Center, rats kept in cages were kept in standard laboratory conditions (12 hrs light, 12 hours dark and 25 +/-3) fed standard commercial pellets, feed and water. given libitum. After the experiment, the rats whose blood samples were taken from the heart were sacrificed under ketamine xylazine anesthesia.

2.1.2. Propolis

Commercial propolis samples used in the research were made by purchasing products that are widely sold and preferred by the consumer.

2.2. Method

Group 1: Control (90 days) (n=8)
Group 2: Propolis water extract (250 mg/kg/day) by oral gavage for 30 days (n=8)
Group 3: Propolis water extract (250 mg/kg/day) by oral gavage for 90 days (n=8)
Group 4: Propolis ethanol extract (250 mg/kg/day) by oral gavage for 30 days (n=8)
Group 5: Propolis ethanol extract (250 mg/kg/day) by oral gavage for 90 days (n=8)
6.Group: Propylene glycol extract of propolis (0.1 gr /day /rat) (90 days) (n=8)
Group 7: Propylene glycol extract of propolis (250 mg/kg/day) by oral gavage for 90 days (n=8)
On the 30th and 90th days after the gavage of the extracts, 1 cc blood was taken from the heart and liver enzyme analyzes were performed.

2.2.2. Biochemical Analysis

Aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP), gamma glutamyl Transferase (GGT) enzyme activities were determined using a Cobas 8000 series analyzer (Roche Diagnostics, Mannheim, Germany) spectrophotometer (Ohkawa et al. 1979)

2.3. Statistical Analysis

Statistical analyzes in the study were determined by SPSS, One Way ANOVA, Post-hoc Tukey test, and the significance level was $p<0.05$.

3. Results

On the 30th day of the experiment, the weights of the rats (Table 1) and the liver enzyme levels detected in the blood samples (Table 2) were determined. According to the results, a statistically significant weight loss was observed in rats given alcohol-based propolis at the end of the 30th day compared to the control and other treatment groups ($p<0.05$).
At the end of one-month (30th day), the lactate dehydrogenase (LDH) enzyme was found to be statistically significantly higher in rats given alcohol-based propolis compared to the control and other treatment groups. High levels of this enzyme are indicative of cell death and tissue damage. Although there is a numerical increase in other enzyme activities besides GGT, it is not statistically significant ($p<0.05$).
While the rats in the control group took 18 grams (during normal development) for 3 months, an average of 8 grams in the alcohol-based group and 9 grams in the propylene glycol-based

group, while no weight gain was observed in the water-based propolis group. Weight gain was statistically significant at the end of the 90th day in the control group and rats given propylene glycol-based propolis ($p<0.05$).

As a result of giving different propolis extracts to the rats in the experimental groups for 3 months (90 days between 27.02.2020-27.05.2020), the difference between all enzyme levels except GGT enzyme is statistically significant ($p<0.05$). In terms of AST, ALT and ALP enzymes, the enzyme levels of the rats in the alcohol-based propolis group were found to be statistically significantly higher than the control and other groups. However, while the lactate dehydrogenase enzyme (LDH) was not different from the control group in the water-based propolis group, it was significantly increased in the groups given propylene glycol and alcohol-based propolis. It reached the highest level in the group given alcohol-based propolis.

Table 1. The weights of the rats in the experimental groups at the beginning of the trial and at the end of the 30th day (g) EEP: ethanol extract of propolis, PEP; propylene glycol extract of propolis WEP: water extract of propolis

Groups	**0. day**	**30. day**	**P**
Control	169.08±3.35	172.60±2.32	0.241
EEP	188.22±5,30	173.14±2.00	0.017
PEP	161.61±3,08	165.30±4.34	0.325
WEP	156.53±3,39	158.00±5.16	0.501

Table 2. Liver enzyme activities of the rats in the 2nd experimental groups at the end of the 30th day

Liver enzymes	Control	EEP	PEP	WEP	P
AST	170.33±34.16	292.50±61.83	285.83±74.40	278.16±41,.28	0.296
ALT	47.33± 2.84	132.50±49.12	107.83±43.16	53.00±2.33	0.152
ALP	48.00±7.09	65.66±9.47	73.50±3.94	64.66±9.35	0.197
LDH	840.66±88.95^{a}	2652.66±341.11^{b}	1718,50±490.92^{a}	1295.33±111.51^{a}	0.001*
GGT	2.66±1.19	1.16±0.40	1,66±0.95	1.50±0.50	0.383

Table 3. The weights of the rats in the experimental groups at the beginning of the trial and at the end of the 90th day (g)

Groups	Day	90. day	P
Control	175.0±2.44	193.25±1.10	0.001
EEP	166.5±3.55	174.0±4.86	0.106
PEP	161.0±2.30	170.1±2.64	0.031
WEP	159.85±3.34	159±5.98	0.280

Table 4. Liver enzyme activities of rats in experimental groups at the end of the 90th day

Liver enzymes	Control	EEP	PEP	WEP	P
AST	121.25±11,25^{a}	359.00±50.34^{b}	207.71±24.83^{a}	171.85±15.96^{a}	0.000
ALT	41.75±1,43^{a}	63.50±2.44^{b}	51.14±2.95^{a}	48.00±2.34^{a}	0.010
ALP	41.00±2,12^{a}	27.16±5.14^{b}	60.14±10.64^{a}	55.71±5.73^{a}	0.005
LDH	967.75±139,2^{a}	3104.00±208.75^{c}	2240.42±120.1^{b}	1602.71±70.26^{a}	0.000
GGT	2.500±0,025	1.6667±0.66	1.4286±0.48	1.2857±0.52	0.555

4. Discussion

Many factors are effective on the phenolic composition of the extract obtained during the extraction of propolis.

The liver-protecting effect of different propolis extracts at different times (one day, one week and one month) has been demonstrated by numerous scientific studies. Numerous drugs and

chemicals are the cause of permanent liver damage. For example, Gonzalez et al. (1994) tested the effects of propolis extract in a model of acute hepatotoxicity induced by high-dose oral (600 mg/kg) paracetamol in mice. At the end of the experiment, propolis significantly decreased the ALT activity that was elevated by paracetamol in the serum of mice and increased the concentration of reduced glutathione consumed by paracetamol in the mouse liver. Çetin et al. (2011) investigated the protective role of propolis on methotrexate (MTK)-induced liver damage in rats, and when 100 mg/kg propolis was given for 10 days, it decreased the increased MDA level caused by MTK, and significantly decreased SOD, GSH-Px and CAT levels. At the end of the experiment, the researchers determined that the oxidative stress caused by MTK decreased with the administration of propolis. In addition, the protective effects of propolis against oxidative stress in liver mitochondria in rats Guimarães et al. (2012) researched by. Pre-administration of Brazilian propolis ethanol extract (50 or 100 mg kg) to stressed rats protected against hepatic injury and increased hepatic lipid peroxide and NO levels, decreased myeloperoxidase activity. Oršolić et al. (2012) investigated the antioxidant effect of water (WSDP) and ethanolic (EEP) extracts of propolis on kidney and liver function in alloxan-induced diabetic mice. Propolis was able to prevent diabetic nephropathy and liver toxicity by inhibiting lipid peroxidation in vivo. Tanvir et al. (2019) In a study in which they investigated the phenolic composition of propolis produced in Bangladesh and its effects against tetracycline-induced hepatonephrotoxicity in rats; While tetracycline caused severe liver and kidney damage, propolis provided maintenance of cell membrane integrity, regulation of lipid profile and preservation of tissue structure, and also prevented changes in biochemical parameters caused by tetracycline. Najafi et al. (2007), water extract of propolis (WEP) inhibited the growth of different cell lines such as McCoy, HeLa, SP20, HEp-2 and BHK21, while stimulating the development of normal cells of human lymphocyte, rat kidney, liver and spleen. However, due to the cytoprotective, antioxidant and anti-inflammatory effects of caffeic acid phenethyl ester (CAPE), the most active component of propolis, it has shown protective effects against hepatocyte (main parenchymal cell of the liver) damage. The hepatoprotective capacity of CAPE has been investigated in numerous studies. Esrefoglu et al. (2012) reported that CAPE application increased the aging-related tissue catalase (CAT) activity in rat liver tissue. Macías-Pérez et al. (2013) showed that CAPE protects against lipid peroxidation, necrosis, abnormal cell proliferation and p65 activation.

While many studies have shown the liver protective effect of propolis, the effect of propolis consumption, which is used as a solvent in propolis extract and in the final product, on liver enzymes in long-term use has not been evaluated. In this study, it was determined that ethanol-based propolis statistically increased LDH enzyme levels in one month use and LDH, AST, ALT and ALP enzyme levels in three months use.

Ethanol is hepatotoxic via redox changes produced by NADH produced in its oxidation via the alcohol dehydrogenase pathway, which affects the metabolism of lipids, carbohydrates, proteins and purines. When ethanol and other drugs are given together, the hepatic vitamin A level drops dramatically. In addition, microsomal induction results in increased acetaldehyde production. Acetaldehyde causes damage through the formation of protein production, resulting in antibody production, enzyme inactivation, decreased DNA repair, changes in microtubules and plasma membranes, and significant oxygen utilization impairment in mitochondria. Acetaldehyde is also the cause of glutathione depletion and lipid peroxidation. Although the biochemical changes caused by ethyl alcohol occur by different mechanisms, there may be an effect in the liver tissue that can range from mild inflammation to toxic liver damage. AST and ALT are used for hepatocellular damage, ALP and GGT 5 nucleotidase enzyme activities are used for hepatobiliary function tests (Stolz 1990; Weisiger, 1992). ALT is a cytosolic enzyme and is relatively liver specific. AST is both a cytosolic and mitochondrial isoenzyme and is

found in the liver, as well as in striated muscles, brain, pancreas, and blood cells. Aminotransferases are useful in the diagnosis of liver diseases and are sensitive indicators of liver cell damage (Pratt et al., 2002). GGT is found in hepatocytes and biliary epithelial cells. GGT elevation can be detected in pancreatic diseases, myocardial infarction, kidney failure, chronic obstructive pulmonary disease, diabetes mellitus, and alcohol use (Goldberg et al., 1975). The lactate dehydrogenase (LDH) enzyme is the key enzyme of glycolysis and catalyzes lactate production. This enzyme is common in all tissues and clinically, activity measurements of LDH isoenzymes are more useful than total activity measurements.

In this study, the increase in LDH caused by the use of alcohol-based propolis regularly for one month, and the increase in ALT, AST and ALP and LDH enzymes for 3 months shows that long-term use of products containing high levels of alcohol in phytotherapy or apitherapy products may be objectionable. Similarly, in a study examining the effect of propolis, whose botanical origin is chestnut (*Castanea sativa*), Kolankaya et al. (2002) investigated the protective role of chestnut propolis of Turkey origin on oxidative stress caused by alcohol consumption. Ethanolic extract of propolis was given to male rats by gavage at a dose of 200 mg/kg/day for 15 days. At the end of the experiment, serum lipid levels, enzyme activities and other biochemical parameters were examined. Compared to the alcohol group, the ALP and AST enzyme activities decreased while the LDH enzyme activity increased.

5. Conclusion

As a result, although alcohol-containing products are preferred as a solvent in propolis extraction or in the final product due to their high solvent properties, it should be considered that these products may carry risks in long-term use. Instead, it is promising that the extracts using natural solvents such as water and oil, together with the new extraction methods developed, are both effective and do not have such side effects.

6. References

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This study was financially supported by Erciyes University Scientific Research Projects.

Oral Presentation

Effects of Apitherapy on Th1/Th2 Balance in Rats with Type II Collagen-induced Arthritis

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Abstract

To observe the effects of apitherapy on Th1/Th2 balance and expression of related specific transcription factors and cytokines in rats with type II collagen-induced arthritis (CIA). Fifty female SD rats were divided into five groups: normal, model, apitherapy, methotrexate and etanercept groups. Except for the normal group, rats were induced by immunizing with type II collagen to establish CIA model. Four groups of CIA rats were treated by saline, apitherapy, methotrexate (2.5mg/kg/w) or etanercept (6mg/kg/w) subcutaneous injection at "Zusanli" acupoint per week for 4 weeks respectively. Recorded the changes of arthritis index and observed the histological changes of knee joint by staining with H&E. The expression of T-bet and GATA-3 mRNA of spleen were detected by Real-time PCR. The concentration of serum cytokine IFN-γ, IL-10 and IL-4 were detected by ELISA. On the 28st day after booster immunization, the toe joints, feet and ankle of rats appeared swelling, and the CIA model was successfully established. After 4 weeks treatment, compared with model group, apitherapy alleviated the arthritis index and the damage of synovium and cartilage of knee joints. The results of Real-time PCR showed that T-bet mRNA expression and T-bet/GATA-3 ratio were declined in apitherapy group ($P < 0.05$). The ELISA results showed that the concentration of IFN-γ was decreased and the concentration of IL-10 and IL-4 were increased in apitherapy group ($P < 0.05$). Apitherapy alleviates the arthritis index and ameliorates the knee joints damage of CIA model. The mechanism possibly related to restoration of the balance between Th1/Th2 by regulating the expression of T-bet mRNA and T-bet/GATA-3 ratio and the concentration of IFN-γ, IL-10 and IL-4.

Keywords: Apitherapy, Th1/Th2 Balance, Type II Collagen-Induced Arthritis

Oral Presentation

Importance of Honeybee Health in Apitherapy From Veterinary Perspective

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Abstract

The products obtained by beekeeping activities are recognized as natural products in all historical development. However, the fact that most of the bee products are lipophilic (absorbent) causes these products to become polluted quickly due to environmental conditions and to become risky in terms of residue. Especially the use of drugs against bee diseases and pests (untimely and unlicensed use of pesticides under the stairs, pesticides), agricultural, veterinary ectoparasitic and environmental drugs (heavy metals) not licensed for bees, exhaust, gases, industrial pollutants and even smoke sources used for the colony (hydrocarbons) are important pollutants. Such careless use will do more harm than good. Treatment and prophylaxis with bee products have become widespread in modern medicine and veterinary medicine. Especially in recent years, the use of bee products for treatment and protection has been increasing in the field of veterinary medicine. Treatment with natural products is important to reduce the undesirable effects of synthetic chemicals. As a result, it is possible to use bee products for treatment and prophylaxis in the field of Medicine by working with healthy honeybees.

Keywords: Honeybee health, Apitherapy, Veterinary Perspective

Oral Presentation

Using Facilities of Propolis in Cattle Breeding: Preventing Neonatal Diarrhea and Promoting Growth of Calves

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Abstract

The purpose of this study was to determine the effects of propolis on growth performance and neonatal diarrhea of calves. Five females and five male calves from both control and propolis treatment groups, 20 Holstein calves, had been used, totally. Calves in both control and treatment groups were fed with same amount of milk once in a day Propolis tincture were given to calves 2cc in a day after milk feeding. The research prosecutioned for 35 days. Daily weight gains of females in control and propolis treatment groups were found to be 312.8 g/day and 392.83 g/day. Daily weight gains of males in both groups were found to be 458.31 g/day and 470.50 g/day. Daily weight gain was found significant ($P< 0.05$) in females. Significant differences had been obtained in both body and shoulder length parameters between control and treatment groups of females ($P< 0.05$). The only statistically important difference had been appeared between two groups of males for withers height. Neonatal diarrhea were not observed in propolis administration group. The results of the research showed that the effect of propolis administration was important on growth of calves and is very expectant for preventing neonatal diarrhea that cause a serious economic loss.

Keywords: Propolis, neonatal calf, growth, body measurements, diarrhea

1. Introduction

The reproductive efficiency of herd depends on livability of new born calves. The better growth performance of calves made it possible to utilize them as a brood-stock in early ages. Utilizing the young calves as brood-stock would shorten the unproductive period and increase the income of farm gradually (Webster, 1986; Etgen et al., 1987; Thickett et al., 1988). Various methods can be utilized in order to reach the target weight gain and growth. Thus, farmers are using various energy- protein rates, feed additives and hormones for feeding calves in order to succeed this aim (Thickett et al., 1988). Today, such methods are not accepted by consumer because of their inversely effect on human health. The farmers are seeking for natural methods in growth of promotion. Propolis is a bee product that has antibacterial, antibiotic, antioxidant, antimicrobial, antiparasitic and antiseptic properties in its structure (Stangaciu, 1999). The positive effects and preventive properties of propolis on dangerous pathogenic bacteries and viral infections have been reported by several researchers (Gluhovski et al., 1976; Popeskovic et al., 1976; Popravko, 1976; Kaal, 1991; Nowotnick, 1993; Donadieu, 1994; Stangaciu, 1999). It has not known adverse effects of propolis on human and animal health, except possible rarely seldom allergies. Our study have based on the study of Gubicza and Molnar (1987) and Kwon et al., (1999). These researchers examined the preventative and treated effect of propolis usage on neonatal calf diarrhea. The aim of our study was to examine the effect of propolis on growth rate and prevention of neonatal diarrhea of newborn calves.

2. Methods

Twenty Holstein calves that were born in winter period in Menemen Agricultural Research Institute, Izmir were utilized as research material. Five female and male calves had been used in both control and propolis group. Twenty calves were randomly assigned to the groups as five in propolis treatment and five in control groups for each gender.

Calves were allocated with their mothers and fed colostrums for the first three days after the birth (Tümer, 1983). After they housed in portable individual calf pen and milk was given to calves one in a day from bucket with a nipple at 8.30-10.00 am. Calves were reared with limited milk for 5 weeks. Milk were increased until 3rd week then decreased from 3rd week to the final of the 5th week (Fowler, 1968, Foley et al., 1973). All calves were weaned at the end of the 5th week. Each calf had drunk 154 kg milk in five weeks. Besides, clover hay were given adlibitum to calves after the second weeks, water was available from the first week. Clover hay consumption was not recorded.

The raw propolis was Pinus spp. origin from Izmir and nearby, stored at -18 ºC in deepfreeze until using. Raw propolis was grinded in mini coffee machine and made as granule form. After grinding, 500 g propolis was weighted and dissolved in 1 lt of ethyl alcohol (70%) in dark and tightly closed bottle. The bottle was shaked 4 times in a day regularly as manual and left in dark place at room temperature for 15 days. Then, the propolis solution was filtered and left in incubator in 55-60ºC for 10 minutes for evaporating the alcohol particularly. After this step, it is filtered and preparation of propolis tincture was completed. Propolis tincture was given to calves 2 cc using syringe (5cc) with spiral pipette from the first day of birth until the end of the trial. Syringe was cleaned with alcohol before and after using. Calves in trial were weighted after birth, at the 1st week, at the 3rd week and the end of research (at the 5th week). Also body measurements (withers height, body length, sacrum height, shoulder length, chest length, sacrum length, chest depth, chest perimeter, front shin girth perimeter, leg perimeter, head length, forehead length and width, face length) were recorded at the 2nd day of birth and at the end of the research. Fecal score was visually monitored daily using the method described by Larson et al. (1977), regarding the fluidity of feces. Feces were classified as normal (1) soft (2) loose (3), watery (4) or liquid consistency (5).

Data were analyzed with SPSS, (1997) statistic program using following model. Treatment were introduced as independent variables, birth weight were used as co-variable. Means were compared with Scheffe test. Fecal score values were analysed using chi-square test. (Bek and Efe, 1989).

$$Yi = \mu + ti + b\,(x-x) + ei$$

Yi= observation of traits
μ = general mean
ti = the effect of treatment
b = regression coefficient of birth weight for observed traits
ei = error

3. Results

Lsmeans and standard error of live weight gain and body measurements for control and propolis groups of female and male calves were presented in Table 1. During trial, total live weight gain mean was found 10.95 and 13.75 kg for female calves, 16.04 and 16.47 kg for male claves in control and propolis groups, respectively. Daily weight gain means were 312.88 and 392.83 g for female calves, 458.31 and 470.31 g for male calves in control and propolis groups,

respectively. Although, propolis had significant effect on female calves for total and daily weight gain ($P<0.05$), there was no significant difference between control and propolis groups for male calves. It was shown the birth weight, weight at 7th, 21st and 35th days (final weight) of female and male calves for control and propolis groups in Figure 1. Variance analysis results have been showed that, differences for birth weight, weight at 7th, 21st day between control and propolis groups were non-significant. Significant difference was determined between two groups in females for weight at 35th day.

In our research, higher body measurements were observed in propolis group compared with control group. Final withers height of female for propolis and control group was 75.88 and 70.50 cm, final withers height of male for propolis and control group was 79.79 and 82.37 cm, respectively. Final withers height difference between two groups for males was found significant ($P<0.05$) but was no significant for females. Besides, body length differences between two groups were found significant only for female calves ($P<0.05$). Final body length was found 74.66 and 77.74 cm for female calves, 81.51 and 79.99 cm for male calves in control and propolis groups, respectively. Sacrum height, chest and sacrum length were found higher in propolis group than in control group. Sacrum height, chest and sacrum length of female calves in propolis group were 77.96 cm, 30.51 cm and 26.76 cm; 77.04; 43.40; 26.35 cm in control group, respectively. Sacrum height, chest and sacrum length of male calves in propolis group were 83.24, 46.96 and 32.74 cm respectively, 83.24, 46.96 and 32.74 cm respectively in control group. Although, shoulder length was found higher in propolis groups compared with in control groups for females (30.51 cm versus 28.79 cm) but shoulder length in males was higher in control group (30.50 cm versus 30.62 cm). Chest perimeter both in females and males was higher in control group compared with propolis group (respectively for propolis and control group 90.31 cm versus 92.29 cm in females, 94.49 cm versus 95.14 cm in males). Chest depth was particularly higher in control group for females (31.00 cm versus 30.99 cm), higher in propolis group for males (31.67 cm versus 32.74 cm). Front shin girth perimeter for females was found higher in propolis group compared with control group (11.89 cm versus 12.11 cm), but males showed higher values in control groups compared with propolis group (12.83 cm versus 12.24 cm). Leg perimeter for females in control group (43.42 and 43.08 for control and propolis group), for males in propolis group was particularly high (44.17 and 44.37 08 for control and propolis group). Head and forehead length, forehead width, face length was higher in both females and males of propolis group compared with control group. Head and forehead length, forehead width, face length of female calves in control group were 22.16, 12.75, 13.10, 9.42 cm, in propolis group 22.84, 12.86, 13.40, 9.98 cm, respectively. The same measurements of male calves in control group were 23.13, 13.25, 13.78 and 9.88 cm, in propolis group were 23.50, 13.40, 13.87 and 10.09 cm (Table 1). On the other hand, during trial period, diarrhea events were observed in control group also one male calf died. But it had not observed any diarrhea events in propolis group (Table 2). Fecal score in propolis group differed significantly than control group in second and third week ($P<0.05$). It was observed that after weaning the calves in propolis group remained with the score close to 1, with an indication of health in calves.

Table 1. Lsmeans and standard error of body measurements and live weight for propolis and control group according to gender.

	Female calves				Male calves			
MEASUREMENTS	Control		Propolis		Control		Propolis	
	Initial	Final	Initial	Final	Initial	Final	Initial	Final
Live weight, (kg)	**39.50±2.20**	**51.70±0.72b**	**42.00±2.20**	**54.50±0.72a**	**45.75±1.28**	**63.37±2.26**	**48.60±1.15**	**63.80±1.98**
Withers height, (cm)	**69.00±0.98**	**75.88±1.37**	**70.50±0.98**	**77.72±1.37**	**73.00±0.98**	**79.79±0.66b**	**75.80±0.88**	**82.37±0.58a**
Body length, (cm)	**67.80±1.92**	**74.66±0.86b**	**71.20±1.92**	**77.74±0.86a**	**72.13±0.83**	**81.51±1.28**	**70.90±0.74**	**79.99±1.13**
Sacrum height, (cm)	**72.60±1.01**	**77.04±1.11**	**72.60±1.01**	**77.96±1.11**	**75.00±0.83**	**81.19±0.85**	**77.60±0.74**	**83.24±0.75**
Shoulder length, (cm)	**26.00±1.24**	**28.79±0.44b**	**25.40±1.24**	**30.51±0.44 a**	**27.75±0.38**	**30.62±0.39**	**27.40±0.34**	**30.50±0.34**
Chest length, (cm)	**39.70±1.17**	**43.40±0.57**	**39.90±1.17**	**44.79±0.57**	**42.00±0.88**	**45.92±0.73**	**42.30±0.79**	**46.96±0.64**
Sacrum length, (cm)	**24.90±0.69**	**26.35±0.40**	**24.20±0.69**	**26.76±0.40**	**26.50±0.74**	**28.09±0.47**	**25.90±0.66**	**28.82±0.41**
Chest depth, (cm)	**27.80±0.88**	**31.00±0.70**	**27.10±0.88**	**30.99±0.70**	**28.38±0.61**	**31.67±0.76**	**29.70±0.55**	**32.74±0.66**
Chest perimeter, (cm)	**79.80±1.62**	**92.29±1.19**	**79.60±1.62**	**90.31±1.19**	**82.25±1.15**	**95.14±1.25**	**82.20±1.03**	**94.49±1.09**
Front shin girth perimeter, (cm)	**11.90±0.22**	**11.89±0.32**	**11.45±0.22**	**12.11±0.32**	**12.38±0.18**	**12.83±0.18**	**12.10±0.16**	**12.24±0.16**
Leg perimeter, (cm)	**38.00±0.99**	**43.42±1.01**	**37.90±0.99**	**43.08±1.01**	**41.50±0.42**	**44.17±0.72**	**41.00±0.38**	**44.37±0.63**
Head length, (cm)	**21.20±0.50**	**22.16±0.51**	**21.10±0.50**	**22.84±0.51**	**22.13±0.38**	**23.13±0.27**	**22.70±0.34**	**23.50±0.23**
Forehead length, (cm)	**12.20±0.25**	**12.75±0.37**	**11.60±0.25**	**12.86±0.37**	**12.25±0.42**	**13.25±0.21**	**12.90±0.38**	**13.40±0.19**
Forehead width (cm)	**12.80±0.24**	**13.10±0.34**	**13.00±0.24**	**13.40±0.34**	**12.50±0.31**	**13.78±0.25**	**13.40±0.28**	**13.87±0.22**
Face length, (cm)	**9.00±0.45**	**9.42±0.31**	**9.50±0.45**	**9.98±0.31**	**9.88±0.27**	**9.88±0.35**	**9.80±0.24**	**10.09±0.31**
1st week live weight, (kg)	**41.82±0.37**		**42.94±0.37**		**52.09±0.77**		**50.83±0.68**	
3rd week live weight (kg)	**45.55±0.52**		**46.45±0.52**		**56.18±1.37**		**57.25±1.20**	
Total live weight gain, (kg)	**10.95±0.72b**		**13.75±0.72a**		**16.04±2.26**		**16.47±1.48**	
Daily weight gain, (g)	**312.88±20.63b**		**392.83±20.63a**		**458.31±64.53**		**470.50±56.67**	

abc: Means of the final measurements in the same row within each gender, with different letters differ significantly (P<0.05)

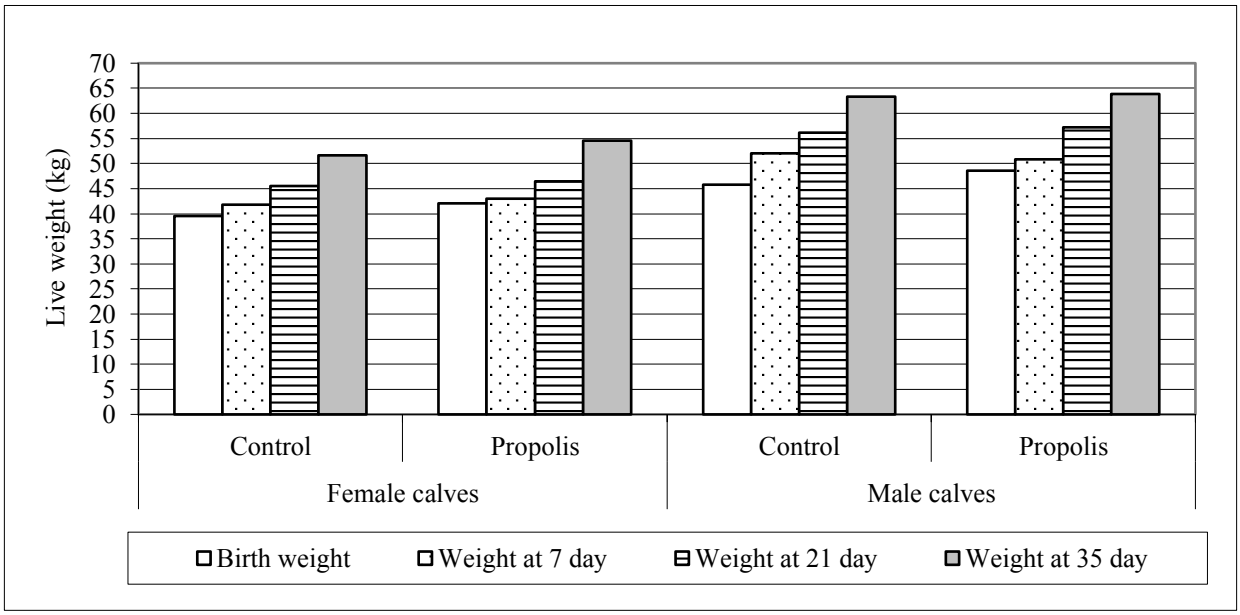

Figure 1. Live weight in control and propolis groups according to gender.

Table 2. Fecal score of calves (1=normal – 4=watery).

	Fecal	Female (%)		Male (%)		General (%)	
Week	Score	Control	Propolis	Control	Propolis	Control	Propolis
	1	**30**	**50**	**44.4**	**44.4**	**36.8**	**47.4**
1	2						
	3	**10**			**11.1**	**5.3**	
	4	**10**				**5.3**	
P		**0.287**		**0.343**		**0.361**	
	1		**30**	**11.1**	**44.4**	**5.3**	**36.8**
2	2		**20**	**11.1**	**11.1**	**31.6**	**15.8**
	3	**50**		**22.2**		**10.5**	
P		**0.04**		**0.155**		**0.02**	
	1	**10**	**50**	**11.1**	**55.6**	**10.5**	**52.6**
3	2	**40**		**22.2**		**31.6**	
	4			**11.1**		**5.3**	
P		**0.01**		**0.06**		**0.002**	
	1	**50**	**50**	**22.2**	**55.6**	**36.8**	**52.6**
4	2			**11.1**		**5.3**	
	4			**11.1**		**5.3**	
P				**0.20**		**0.289**	
	1	**50**	**50**	**22.2**	**55.6**	**36.8**	**52.6**
5	2			**11.1**		**5.3**	
	4			**11.1**		**5.3**	
P				**0.20**		**0.289**	

4. Discussions and Conclusion

The main cause of body weight losses, delaying growth, even calf losses during neonatal period is diarrhea originated from E. Coli. (Aytuğ, 1991). According to Webster, (1986), calves primarily should be stay alive before weaning then they should be prevent from severe diseases in order not to delaying of growth. Likewise, Kaya et al., (2000) have found higher daily live gain in calves which were reared with acidified whole milk because of any diarrhea event was no realized compared with in calves which were reared normal milk. But researcher reported that daily weight differences between these groups found to be non-significant. The literature considers that the calf has diarrhea when fecal score is above 3 (Larson et al., 1977). Most of the fecal score data observed throughout the experimental period of propolis group, was below 2, confirming propolis prevent calves from diarrhea and improve live weight gain and growth. Likewise, Kwon et al, (1999) reported that propolis could be used for both preventive and treatment in neonatal calf diarrhea. Also, Kaal, (1991), Greceanu and Enciu, (1976) reported that propolis was very effective natural product for many pathogen bacteria types. Hegazi and Abd El-Hady (1996) reported that propolis has positive effect on growth of livestock. Besides, Corleteanu (1976) found that calves treated with propolis have better growth performance than calves in control group whereas Sarker and Yang (2010) found lowest weight observed in propolis fed calves, controversary.

As a result of this study, it was shown that propolis serve to rear healthy calves and also improve live weight gain and growth. In our study, very low dose (2 cc) propolis tincture has been given to calves. In order to show its effect on growth exactly, different doses of propolis should be used in trials. But it is evident that propolis is a suitable natural product for ecological animal production.

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Oral Presentation

Complex Pathologies in Animals. Approach to Integrative Veterinary Medicine, with emphasis on Scientific Apitherapy and Traditional Chinese Medicine

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Abstract

The approach to Complex Pathologies from an Integrative point of view of Veterinary Medicine, allows to Synergize therapies, while reducing excess chemical treatments and hospitalization days. The Mixed Integrative Protocols are in the clinical study stage, and involve Scientific Apitherapy, Traditional Chinese Medicine and Allopathic Medicine in their different specialties. Based on traditional Chinese medicine and biomedical results on the use of bee products in various species of mammals, using the properties of each beehive product and their synergy, I developed different Treatment Protocols for different pathologies. Far above Apitherapy, the protocols combine many different therapeutic tools (Scientific Apitherapy, Traditional Chinese Medicine, Modern Allopathic Medicine, Phyto-Diet therapy, Physiotherapy, Habitat management, etc.), to treat and support many animal species. However, Apitherapy has been decisive in the therapeutic results. Twenty years of work in Integrative Clinical Veterinary Medicine show that beehive products are fundamental elements in the excellent results offered by Centrovetera - Apitherapy Veterinary Medical Center. To obtain the best results, we must pay attention to the quality of the bee products and the specific protocol for the needs of each patient. To achieve the first, in the practical and private work of Centrovetera, we include the supply of the "best" beehive products for "api-phyto-medical formulations" for animals, to walk from pathology to health. The presentation graphically shows examples of Integrative Treatments, including beehive products in different animal patients and applied by different routes. To simplify presentation, patients were ordered by medical specialties.

Keywords: Apitherapy, Apitherapy in Veterinary Medicine, Bee products for apitherapy, Apipuncture, Clinical Integrative Veterinary Medicine

Oral Presentation

Propylene Glycol (Propolis Extraction Solvent) Danger in Pregnant and Their Babies

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Abstract

Propolis is a bee product with many beneficial biological activities. Since it cannot be used in its raw form, it must be extracted, and different extraction solvents are used for this purpose. Propolylene glycol is one of these solvents, although it is not used very often. In this study, the effects of propylene glycol extracted with propylene glycol, which may cause a health risk, were investigated in pregnant and newborn rats. When the groups given propolis were compared with the control group, the difference between triglyceride, cholesterol, HDL and LDL values was found to be statistically significant. While the triglyceride level increased approximately 2.6 times in the glycol-propolis group compared to the control group, this value was higher than in the water-propolis group. Interestingly, cholesterol level was found to be low in both propolis-treated groups compared to the control group, while HDL level was statistically significantly lower in both propolis groups. LDL level of blood lipids was found to be quite high when compared to the control and water propolis groups ($p<0.01$). As a result, legal regulations and scientific studies should be taken into account in the preparation and consumption of the extract and it should be healthy for the consumer.

Keywords: Propylene Glycol, Propolis, Pregnant, Rat

1. Introduction

Propylene glycol (PG) is a clear, colorless, water-soluble alcohol (1,2-propanediol) used as an adjuvant in parenteral and non-parenteral pharmaceutical formulations containing water-insoluble active ingredients; phenobarbital, phenytoin and diazepam (EMEA/CHMP/PEG/194810/20052). It is also used in cosmetics and the food industry as a humectant (E1520), as a food preservative, and as a vehicle for flavorings in preference to ethanol. It is included in the list of food additives generally recognized as safe (GRAS) by the US Food and Drug Agency (NTP-CERHR, 2004). Propylene glycol is a synthetic chemical liquid that absorbs water. It is used to make polyester compounds and as a base for de-icing solutions. Propylene glycol is used as an antifreeze by the chemical, food and pharmaceutical industries. It is used in some medicines, cosmetics and food products to absorb extra water and retain moisture. It is a solvent for the paint and plastic industries and for color and flavor in foods. It is a clear, colorless, slightly syrupy liquid at room temperature. In order for it to evaporate, it must be heated and shaken.

Propylene glycol is approved for use at certain levels in food, cosmetic and pharmaceutical products. It passes into the blood through inhalation, skin contact or ingestion and is broken down in the body within 48 hours. The general population may be exposed to propylene glycol; It is a component of many products widely used in commercial formulations of food, pharmaceutical and cosmetic products (Morshed et al. 1989), as a de-icing agent and in heat transfer fluids, to produce artificial smoke or mist at rock concerts. Systemic and immunological, lymphoreticular, neurological, reproductive, developmental, genotoxic and carcinogenic effects on exposure were evaluated in 3 periods, acute (14 days or less), moderate

(15-364 days), and chronic (365 days or more). Results from studies with experimental animals have shown that moderate or chronic exposure to propylene glycol leads to hemolysis of red blood cells (Christopher et al. 1989). Hemolysis in red blood cells, decrease in hemoglobin and hematocrit values and decrease in total red blood cell count at different doses are among the reported results. Results from studies have shown that there may be species differences regarding the effect of propylene glycol on red blood cells. It is unclear whether hepatotoxicity occurs after acute exposure to high levels of propylene glycol. The body weight of rats given 2.942 mg/kg propylene glycol by gavage for 10 days decreased by 41%, while exposure for 20-30 days resulted in an increase in body weight. High levels of propylene glycol in plasma can lead to an increase in osmoral space. If oxidatively present in sufficient quantity, it is converted to lactic and pyruvic acid, which contributes to methanolic acidosis. There are also studies that cause an increase in lactate in the blood (Morshed et al. 1994). In one case, a woman with a history of kidney failure due to cocaine use and complaining of acute dyspnea was administered sedation with intravenous lorazepam 65, 313 and 305 mg daily infusions for 3 days; Forty-eight hours after the infusion, the patient was found to have hyperlactatemia, hyperosmolality, and anion gap metabolic acidosis with increased osmolality, and the potential source of the metabolic abnormality was propylene glycol, a component of the intravenous formulation of lorazepam (Cawley, 2001). No studies have been found on the effects on the reproductive system in humans after oral exposure. However, in a study on the Chinese Hamster Ovary cell line (CHO), to evaluate the possible genotoxicity of three cryoprotectants commonly used for oocyte vitrification; Propylene glycol caused chromosomal mutations by in vitro DNA damage, and these results showed that high propylene glycol concentrations could cause in vitro chromosomal damage in eukaryotic cells. Death has also been reported after acute exposure to propylene glycol (Clark et al. 1979; Dorman and Hascchek 1991, Ruddick 1972). There are also numerous reports of sensitization after dermal exposure. However, metabolic abnormalities occur at levels between 58-127 mg, while clinical problems occur at 104 and 144 mg levels (Wilson et al. 2005; Arroliga et al. 2004). Although propylene glycol is generally considered non-toxic, there have been reports of toxic effects in animals and humans. Indicated toxic effects include seizures, collapse, cardiac arrhythmia and asystole, hepatic injury, kidney injury, hemolysis, and serum hyperosmolality with a marked osmolar space. Serum hyperosmolality has been previously reported in small premature infants who received large doses of propylene glycol during feeding (Macdonald et al., 1987). Proximal tubular necrosis has been reported as the cause of propylene glycol-induced acute kidney injury (Morshed et al. 1989). 2-15 ml of acute propylene glycol showed adverse neurological reactions in patients who were positive to the propylene glycol patch test (Hannuksela and Forstern 1978). In the case of acute propylene glycol poisoning, neurotoxic symptoms were in the form of stupor and recurrent convulsions. In the neurology clinic, propylene glycol at a dose of 887 mg/kg for 3 days and acutely showed varying degrees of neurotoxicity in 16 patients (Yu et al. 1985). The estimated half-life of propylene glycol is 3.8 hours, meaning that multiple dosages will cause accumulation of propylene glycol (Yu et al. 1985).

he estimated half-life of propylene glycol is 3.8 hours, meaning that multiple dosages will cause accumulation of propylene glycol (Yu et al. 1985). In a study on oral LD50 values of propylene glycol, lethargy and coma were observed in rats before death (Clark et al. 1979). Cats receiving high doses had decreased activity, developed depression and mild to moderate ataxia, and high levels of D-lactate were found in their blood. Side effects occur after topical, oral and intravenous administration of PG (Fligner et al. 1985; Martin et al. 1970; Arulanantham et al. 1978; Glasgow et al. 1983). Side effects include central nervous system toxicity, hyperosmolarity, hemolysis, cardiac arrhythmia and lactic acidosis (Tuohy et al. 2003). For example, side effects have also been associated with oral and intravenous multivitamin

preparations containing PG. Unresponsiveness, tachypnea, tachycardia, diaphoresis, and hypoglycemia were observed in a 15-month-old boy who received high doses of vitamin C containing PG (Martin et al. 1970). Seizures have also been observed following intake of PG containing vitamin D (Arulanantham et al. 1978). Hyperosmolarity in young infants has also been reported after intravenous administration of a multivitamin preparation containing PG (Glasgow et al. 1983). The clinically defined level is unclear, as there is no acceptable propylene glycol level. The World Health Organization (WHO) has recommended a maximum consumption of 25 mg/kg/day (1.8 g/day for 75 kg men) for use as a food additive, but this value is not for use as a drug solvent (Wilson et al. 2005). EFSA has similar notices. The Food and Drug Administration (FDA) has classified propylene glycol as an additive "generally recognized as safe" for use in food. A safe intravenous dose of PG has not been reported in the literature. However, it has been shown that it can be toxic when the serum level containing PG is higher than 18 mg/dl (Arbour et al. 2000). Other investigators have reported that toxicity is seen when serum PG concentration is 25 mg/dl (Barnes et al. 2006). The World Health Organization (WHO) has determined the acceptable daily PG intake as PG.

2. Materials and Methods

2.1. Animals

Healthy Wistar albino pregnant and newborn rats (n=96) were used in the experiment. It was confirmed by smear test that the rats were pregnant. Animals were kept under standard laboratory conditions (12 hours light, 12 hours dark under 25 ± 3 ºC) and fed with pellet feed. The study was approved by the Erciyes University Animal Experiments Local Ethics Committee (20/064), and all experimental stages were organized in accordance with the recommendations in the Guidelines for the Care and Use of Laboratory Animals approved by the National Institutes of Health (USA) and Declaration of Helsinki.

2.2. Application of Propolis Extract

The research was carried out with the approval of Erciyes University Experimental Animals Local Ethics Committee dated 04.03.2020 and numbered 20/064. 72 Wistar albino rats were used in the study. Of these rats, 24 were pregnant, 24 whose mothers did not take propolis during pregnancy and lactation. The difference between the neonatal period and the young adult period (neonatal-weaning-periadolescent-young adult)7.-63. daily rats, and 24 of them are rats between the neonatal period and the young adult period of mothers given propolis during pregnancy and lactation. Water and glycol-based propolis was given by gavage for 21 days to rats during pregnancy, for 66 days to rats whose mothers were given propolis during pregnancy and lactation (21+21 days), and for 66 days to rats whose mothers were not given propolis. At the end of the application, blood samples were taken from the rats under anesthesia and tested.

2.3. Blood Collection

Following the administration of propolis extracts for 20 days in pregnant women and 60 days in newborns, 1 cc blood was taken from the hearts of the animals. It was stored for analysis of biochemical parameters.

2.4. Biochemical Analysis

The effect of propolis on the blood of propylene glycol, water and olive oil extracts was biochemically evaluated. Complete blood count (hemogram test) was performed in blood samples obtained from pregnant and newborn rats. Blood lipids (triglycerides, cholesterol),

BUN, creatine and uric acid levels were determined. The levels of liver enzymes (GGT, LDH, AST, ALT, ALP) in the blood were examined.

2.5. Statistical Evaluation

SPSS 16.0 (Statistical Package for the Social Sciences) Software package program was used for the analysis of the data obtained as a result of the experimental stages. Data are expressed as arithmetic mean standard error. Paired comparisons were made using two-way ANOVA analysis of variance and Post-hoc Tukey multiple comparison test. The significance level was determined as $\alpha = 0.05$ in all statistical tests.

3. Results

Rats that were found to be pregnant as a result of matings were given propolis during the 21-day gestation period. According to the results obtained, the effect of commercial propolis extracts extracted with glycol and water on blood lipids is evident. When the groups given propolis were compared with the control group, the difference between triglyceride, cholesterol, HDL and LDL values was found to be statistically significant. While the triglyceride level increased approximately 2.6 times in the glycol-propolis group compared to the control group, this value was higher than in the water-propolis group. Interestingly, cholesterol level was found to be low in both propolis-treated groups compared to the control group, while HDL level was statistically significantly lower in both propolis groups. LDL level of blood lipids was found to be quite high when compared to the control and propolis groups ($p<0.01$).

When the kidney function tests were examined as a result of giving propolis to pregnant rats; The BUN value showed a statistically significant difference between the groups and this value was found to be high in the glycol-propolis group. Liver function test parameters AST, ALT and ALP activities showed significant differences between the groups. While the AST activity of the rats in the water-propolis group decreased compared to the control group, this activity was significantly higher in the glycol-propolis group. While ALT and ALP enzyme activities were found to be similar to the control group in the water-propolis group, the activities of these enzymes were also found to be high in the glycol-propolis group.

Between the neonatal period and the young adult period (neonatal-weaning-periadolescent-young adult) whose mothers were not given propolis during pregnancy or lactation period. The rats were given propolis between days When the blood lipid levels of the rats given propolis during this period were compared with the control group, a statistically significant difference was found ($p<0.001$). Triglyceride, cholesterol and LDL levels were found to be statistically significantly higher in the glycol-propolis given group than in the control and water-propolis groups. HDL level was found to be lower than these groups. In terms of kidney functions, uric acid level was found to be significantly lower in the water-propolis group compared to the control and glycol-propolis groups ($p<0.01$). In terms of enzyme levels measured to determine liver functions, the LDH enzyme level of the rats in the glycol-propolis group was approximately 2 times higher than the control group ($p<0.01$), while the LDH activity of the rats in the water-propolis group was found to be close to the control group. ALT enzyme activity was found to be lower in the water-propolis group compared to the control and glycol-propolis groups. There was no statistically significant difference between the groups in terms of blood parameters ($p>0.05$).

The values of the groups given propolis during the neonatal-young adult period during which the mothers given propolis during the 21-day pregnancy and 21-day lactation period gave birth and breastfed were compared. All parameters tested for blood lipids differed between groups. While triglyceride, cholesterol and LDL levels of the groups given glycol-propolis were statistically significantly higher than the control and water-propolis groups, HDL levels were

found to be low ($p<0.05$). In terms of kidney functions, the uric acid level of the group given water-propolis was found to decrease significantly compared to the control group and the group given glycol-propolis. Liver function tests differed between LDH, ALP and ALT groups. The activities of these tested enzymes were found to be significantly higher in the glycol-propolis given group than in the control and water-propolis group. Three pregnant rats from the PEP group died.

4. Discussion

The solvent should be able to dissolve and take phenolic substances, which are the most important bioactive components of propolis. Phenolic acids and their esters, flavonoids, volatile organic compounds, alcohols, ketones, steroids, terpenoids, amino acids, etc. in the structure of propolis. (Cunha et al. 2018, Havsteen et al. 2002, Bankova et al. 2000, Marcucci et al. 2000, Line 2018) the polarities of the components are different. The most important factor in the solubility of a molecule in any solvent is its polarity. The principle of "like dissolves like" as it is widely known is also valid in propolis extraction. Extraction is difficult in solute:solvent pairs with far polarity.

According to the EMA/CHMP/704195/2013 report of the European Medicines Agency, considering the potential toxicity risks that propylene glycol may cause in the central nervous system, cardiovascular system and/or respiratory system, 1 mg/kg for 0-1month-old babies born naturally; 50 mg/kg in children aged 1 month to 4 years; Maximum daily use limits of 500 mg/kg are given for children aged 5-7 years and adults. According to the European Food Safety Authority (EFSA) 414, 1-22 report, the daily intake limits for polyethylene glycol (EFSA, 2006) are 2 mg/kg as a food supplement. When the Turkish Food Codex Communiqué on Extraction Solvents Used in the Production of Foodstuffs and Food Ingredients (Communiqué no: 2013/45) is examined, it is seen that hexane is present but must be completely removed. However, limits of polyethylene glycol (E 1521) and propylene glycol (E1520) as additives are given in the Communiqué on Food Additives (Communiqué no: 2013/49). In this communiqué, the maximum amount for E1520 from all sources in food for E 1518 and E 1520 is reported as 3000 mg/kg (total per person). It has also been reported that if propylene glycol is used as a carrier, the final product should be at most 1000 mg/kg. Along with all this, there is no limit determination in the Turkish Food Codex as in EFSA and EMA.

In this study, 6 offspring of pregnant rats given PEP died. It also had a negative effect on blood parameters when given to pregnant and newborns. For this reason, it is important for food safety that propolis products used to gain and maintain health do not carry the least risk. In addition, sensitivity should be higher in risky groups such as pregnant and newborn.

5. Conclusion

The fact that the solvent used is non-toxic, consumable, whether it can be removed after extraction, daily intake, absorption in the body, products released when metabolized, and their excretion are extremely important, as well as to obtain a product with high biological activity in making the appropriate extraction and obtaining an effective extract. For this reason, there should be no doubt about propolis extracts that are commercially produced and sold on the market as food supplements. Solvent-independent standardization creates serious errors when preparing standards for extracts. Legal regulations and scientific studies should be taken into account in the preparation and consumption of the extract and it should be healthy for the consumer. In this study, it was shown that propolis extracts prepared with propylene glycol may have negative effects on hematological and biochemical parameters in pregnant and newborn rats.

Table 1. Hematological and biochemical parameters

	Pregnant Rats			Infant rats (mother doesnt consume propolis)			Infant rats (Mother consume propolis)		
Parameters	**Control**	**PEP**	**WEP**	**Control**	**PEP**	**WEP**	**Control**	**PEP**	**WEP**
Triglyceride (mg/dl)	88.0±19.0^{a}	205.0±42.0^{b}	150.0±35.0^{b}	45.83±7.26^{a}	68.16±9.91^{b}	41.23±4.73^{a}	45.83±7.26^{a}	71.16±9.91^{b}	40.83±4.71^{a}
Cholesterol (mg/dl)	72.0±10.0^{a}	30.0±3.65^{b}	23.0±3.61^{b}	67.83±3.48^{a}	95.85±2.46^{b}	68.0±5.85^{a}	70.16±2.99^{a}	90.16±3.11^{b}	76.16±5.66^{a}
HDL-C (mg/dl)	48.65±2.61^{a}	8.70±3.41^{b}	6.60±3.04^{b}	66.36±2.92^{b}	47.11±2.22^{a}	55.11±2.60^{a}	60.86±3.11^{a}	48.55±2.30^{b}	56.78±3.69^{a}
LDL-C (mg/dl)	5.75±0.65^{a}	19.60±6.46^{b}	13.61±4.34^{b}	11.21±1.35^{a}	16.58±2.0^{b}	10.0±2.65^{a}	12.26±1.36^{a}	14.98±2.65^{b}	11.21±2.96^{a}
BUN mg/dl	17.15±3.75^{a}	22.5±1.65^{b}	18.75±0.98^{a}	16.88±0.96	17.76±1.66	16.25±0.89	17.0±1.22	17.31±1.59	16.63±1.17
Creatinine mg/dl	0.45±0.09	0.47±0.04	0.42±0.01	0.30±0.04	0.33±0.04	0.22±0.02	0.32±0.04	0.29±0.05	0.26±0.02
Uric acid mg/dl	3.30±0.9	3.68±1.18	2.96±0.61	5.01±1.10^{a}	6.09±0.66^{a}	3.0±0.47^{b}	5.28±1.20^{a}	5.48±0.83^{a}	2.66±0.29^{b}
GGT (µ/L)	1.50±0.50	1.45±0.34	1.46±0.22	1.83±0.07	1.50±0.05	1.30±0.49	1.33±0.21	1.66±0.49	1.68±0.42
LDH (µ/L)	1526.0±144^{a}	1988.0±400.0^{b}	920.0±171.0	960.0±167.0^{a}	1849.0±256.^{b}	814.0±189.0^{a}	1895.0±25.7^{a}	2898.0±60.7^{b}	1785.0±36.5^{a}
AST (µ/L)	190±13.5^{ab}	233.0±38.62^{a}	129.0±16.77^{b}	197.0±20.0	163.0±15.0	131.0±16.0	166.0±14.9	158.0±13.0	125.0±13.0
ALT (µ/L)	52.0±2.0^{a}	73.16±2.86^{b}	43.16±5.88^{a}	48.0±4.0^{a}	44.0±2.0^{a}	31.0±1.2^{b}	41.0±5.0^{a}	55.0±8.0^{b}	33.0±3.0^{a}
ALP (µ/L)	84.5±23.50^{a}	130.0±10.49^{b}	85.16±7.4^{a}	116.0±12.0	137.0±8.0	147.0±13.0	123.0±16.0^{a}	289.0±2.0^{b}	166.0±9.0^{a}
WBC $10^3/\mu L$	2.93±0.70	3.80±0.48	3.23±0.44	3.83±0.5	3.31±0.55	3.5±0.2	3.67±0.64	3.60±0.5	3.50±0.19
Hemoglobin g/dl	17.35±0.15^{b}	16.73±0.16^{a}	16.70±0.51^{a}	16.12±0.6	16.15±0.34	18.09±0.5	16.21±0.61	16.26±0.37	17.48±0.62
Platelet $10^3/\mu L$	323.0±17.6^{b}	840.0±10.5^{a}	685.0±14.9^{ab}	565.0±161.0	633.0±121.0	634.0±178.0	572.0±142.0	623.0±121.0	636.0±177.0
Monocyte $10^3/\mu L$	0.13±0.01	0.12±0.01	0.13±0.06	0.15±0.04	0.16±0.03	0.15±0.02	0.16±0.05	0.16±0.05	0.11±0.01
Bazophil $10^3/\mu L$	0.0±0.0	0.01±0.0	0.008±0.0	0.81±0.23	1.15±0.2	1.13±0.23	0.06±0.04	0.01±0.00	0.01±0.0
Neutrophil $10^3/\mu L$	0.53±0.02	1.26±0.12	1.30±0.31	0.71±0.02	1.14±0.03	1.13±0.01	0.82±0.22	1.15±0.27	1.35±0.18
Eozinophil$10^3/\mu L$	0.16±0.004	0.12±0.07	0.31±0.01	0.11±0.05	0.25±0.07	0.24±0.08	0.10±0.05	0.23±0.06	0.24±0.08
Lymphocyte $10^3/\mu L$	2.08±0.54	2.29±0.31	2.52±0.14	2.67±0.3	2.27±0.3	2.14±0.13	2.78±0.36	2.26±0.33	2.18±0.14
RBC	9.13±0.12	8.40±0.14	9.10±0.36	8.14±0.43	8.32±0.14	9.53±0.42	7.89±0.36^{a}	8.44±0.2^{ab}	9.55±0.42^{b}
Hematocrit %	56.15±0.05^{b}	53.38±0.56^{a}	52.37±2.48^{a}	53.12±1.37	48.07±2.13	54.01±2.24	52.51±1.18	49.60±2.02	53.9±2.14

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Oral Presentation

Bioactive Compounds of Brazilian Propolis and Its Mechanisms of Action in Cell

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Abstract

Propolis is a natural resin produced by bees from secretions or exudates from medicinal plants that surround the hive environment. This resin is rich in bioactive compounds, many of which are bio-transformed from the incorporation of salivary secretions from bees. In the world there are several different types with specific botanical origins, and their own chemical characterization. In Brazil the largest production of propolis type is *Baccharis dracunculifolia* (popularly known as Alecrim-do-campo) as a botanical origin. This propolis has a greenish tint and is rich in Artepillin C, as its main chemical marker. These bioactive compounds have innumerable biological activities, including anti-inflammatory, antimicrobial and antioxidant activity, which give Brazil's green propolis a high commercial and human health added value. Many of these compounds are considered to be senolytics, as they reduce cell aging and promote healthy longevity, preserving the physiological responses in human cells. The present work demonstrates the various mechanisms by which green propolis and its prenylated compounds are able to prevent the occurrence of cell senescence and body aging.

Keywords: Propolis, Compounds, Brazilian, Cell, Action

Oral Presentation

Bee Venom, Pain Memory and Tissue Degeneration: Basic and Clinical Correlation

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Abstract

Disease development over the months and years involves structural and functional transformations in the different organs and tissues of the body. The modification of transcription factors such as nuclear factor kappa-beta, STAT, mTOR and the release of growth factors from tissues are frequently affected in chronic and degenerative diseases. Bee venom has direct actions that regulate these molecular functions in the body. This presentation explores these mechanisms and how, in series of patients with osteoarthritis, fibromyalgia and autoimmune diseases, this has produced relevant clinical benefits and the arrest of the degenerative progression of the disease.

Keywords: Bee Venom, Pain Memory, Regulation

Oral Presentation

Uses and Applications of Beehive Products in Dentistry

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Abstract

The use of beehive products in dentistry, especially propolis, but also honey, wax, apitoxin, pollen and royal jelly help in the treatment and prevention of various dental diseases. The propolis with constituents of flavonoids and caffeic acid and other constituents it has high anti-inflammatory, antibacterial, analgesic capacity. The application in endodontics, periodontal treatment, dental surgery is very useful due to the aforementioned capacities, as well as not generating resistance from the microorganisms that cause various oral diseases. The use of propolis in endodontics is done in the form of a 5% alcoholic solution to irrigate the canal and to leave as a medication between consultations. In the case of periodontal treatment, it is used to irrigate the periodontal sock, replacing chlorhexidine. In the case of use in operative dentistry, the development of dental cements containing propolis has taken place, taking advantage of its properties to stimulate the stem cells of the dental pulp.

Keywords: Odontology, Dentistry, Propolis, Endodontics, Chlorhexidine

Oral Presentation

Impact of Nutritional Genomics and Apitherapy on Healthy and Pathological Aging

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Abstract

In recent decades there has been an increase in world population and life expectancy. During the last century the world population has quadrupled, and estimates indicate that in the coming decades it will double again. Senescence, the process by which the cell enters a state of permanent cell cycle paralysis, involves generalized molecular changes, increasing risk of vulnerability, loss of vigor, disease and death. These changes take place in a cell, in an organ or in the whole organism during the entire vital period, these deleterious changes associated with age affect the members of the immune system and immunosenescence causes poor response to vaccines and susceptibility to cancer and infections. Comorbidity in the elderly aggravates the suffering of chronic degenerative diseases, so the knowledge and management of these clinical entities should be the domain of the physicians responsible for the primary care of the elderly. The products of the hive are very useful in the process of cellular aging. There are several mechanisms through which they act: Bee venom (inhibition of nuclear factor KB, inhibition of pro-inflammatory cytokines) propolis (activation of NRF2 for the synthesis of antioxidants, inhibits glycosylation, reduction of telomere shortening) honey (protection of mitochondrial DNA) royal jelly (modulator via AMPK, sirtuins-Mtor prevention of cellular senescence).

Keywords: Apitherapy, Nutrition, Genomics, Geriatrics, Anti-Aging, Health

Oral Presentation

Injectable Apitoxin in Oncology

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Abstract

I started studying and investigating the world of Apitherapy as a university undergraduate in 1978. On account of its success in the treatments I investigated, I have been using Apitherapy as a therapeutic resource since 1993. In this presentation I will analyze an oncological case (SCHWANOMA). I will begin by signaling the patient´s physical limitations caused by the disease. Secondly, I will go over the laboratory analyses that determined the pathology and will account for the choice of Apitoxin as the only medication for its treatment. In addition, I will review the protocol to follow before the use of Apitoxin, more specifically the intradermal skin testing. And finally, the medical treatment including the indications, dose and concentration, the surgical procedures and the after-surgery treatment.

Keywords: Veterinary, Cancer, Oncology, Apitherapy, Bee Venom

Oral Presentation

Diabetes: Non-Infectious Pandemic of The Modern Era. Approach and Treatment with Apitoxin

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Abstract

Diabetes Mellitus is a disease spread worldwide, with a high incidence and mortality. The WHO estimates that 8.5% of the world's population suffers from it, with poor and developing countries being the most affected. Its morbidity is even higher, generating diseases in the nervous, cardiovascular and renal systems, among others. Diagnosing, treating and controlling the different types of diabetes is a health priority around the world, and in apitherapy we have a powerful tool for its approach. In multiple scientific studies that we will analyze, it has been shown that bee venom decreases the glycosylation of hemoglobin in diabetic subjects, as well as it acts by inhibiting the inflammation of the beta cells of the pancreatic islets, thus increasing the secretion of pancreatic insulin and decreasing hence the blood glucose level. Melittin and phospholipase A2 have also been shown to directly stimulate monophasic insulin production in pancreatic cells in the islets of Langerhans. In patients with diabetic peripheral neuropathy, studies with a control population revealed on ultra-structural examination that apitoxin reversed axonal, myelin damage and degenerative changes in axonal mitochondria of Schwann cells that occurred in diabetic subjects. We consider that apitherapy, as an integrative natural medicine, should be offered to diabetic patients as a complementary therapy to conventional treatments and changes in lifestyle. We will discuss suggested treatment schemes for different types of diabetes and patients.

Keywords: Diabetes, Apitoxin, Treatment

Oral Presentation

Optimal Use and Applications of Apitherapy Protocols Based on Statistical and Ethical Evidence (ABEE)

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Abstract

Apitherapy is the tool that has the greatest therapeutic potential and the wide capacity to adapt to any medical treatment system, it provides support in all stages of the pathology. This is due to the fact that it has several modulating functions at the cellular level, extracellular matrix, tissues, organs and structural and energetic systems, thus achieving harmony in the immune barrier. Among the hive products, bee venom enters the bloodstream by nature and is considered invasive, therefore it will be the most careful and its responsible use requires standardized protocols and procedures to minimize risks and adverse effects, thus achieving acceptable results. in the shortest possible time. The sensitivity test is the first step that must be taken for the process of induction to bee venom, always trying to be the least invasive. The use of a minimum dose protocol induces the patient to achieve therapeutic results with the least exposure, thus achieving two effects: 1. Response and adaptation inherent to bee venom (short term). 2. Inherent organic response and adaptation of the individual, the same that will ensure well-being in the medium and long term. Identifying the sensitivity test and determining the sensitivity percentage and the tolerance percentage is essential to establish the minimum dose protocol and therefore a safe process within the therapeutic field. The sensitivity test constitutes the fundamental pillar for each process of bee venom application and in the scientific evidence it even provides predictive values of the organic state and response of the individual instantly and in the future. In these studies, and presentations, the main guidelines on the bee venom sensitivity test will be established, as well as its current alternatives, interpretation and even diagnostic approach.

Keywords: Apitherapy, Sensitivity Test, Protocols, ABEE, Statistics

Oral Presentation

Dissemination of Microparticles Of Propolis And Essential Oils for The Treatment and Prevention of Respiratory Infections

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Abstract

Propolis have a complex composition of flavonoids, terpenes and phenolic acids with antibacterial, anti-inflammatory, expectorant secretion slap and immunoregulatory action. In the pharmaceutical industry, we find the association of propolis with essential oils with antibacterial, antiviral and antifungal effect, in addition to the relief of symptoms associated with respiratory infections, such as rhinorrhea, cough with expectoration and Bronchospasm. The most common route of administration is oral, but we have experienced rapid improvements with inhalation. In this work, we will present the association of propolis tincture at 3.5%, essential oils of Eucalyptus Globulus and Minthostachys mollis administered by an ultrasonic diffuser of volatile microparticles, as a treatment of symptoms in upper and lower respiratory tract infections. We use 3.5% propolis extract in alcoholic tincture 5 drops per 100ml, Eucalyptus globulus essential oil 3 drops per 100ml, Minthostachys mollis essential oil 3 drops per 100ml and sterile water sufficient amount dilution. The scent diffuser was placed in a closed room of approximately 15m2, for a period of 4 hours. We had 4 cases with acute bacterial bronchitis, with demanding cough and expectoration. Improvement of symptoms was observed within the first 4 hours of diffusion exposure, such as decreased cough frequency and more fluid expectoration. Currently, casework is limited, but replication of the method is planned in schools of initial education, so that the improvement of symptoms and the decrease in the rate of contagion can be measured.

Keywords: Propolis, Micro Particles, Cough, Eucalyptus Globulus, Minthostachys Mollis

Oral Presentation

A Decade of Research on Mexican Propolis

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Abstract

The objective of this work is to present the results of our work team in the last 10 years, on the investigation of the antimicrobial activity of Mexican propolis, using propolis from different States of the Republic, creating the Official Mexican Propolis Standard (NOM 003-SAG / GAN / 2017) and the Propolis Analysis Service Laboratory, the first in Mexico to provide service to beekeepers. Its chemical content was established by Gas Chromatography coupled to Mass Spectrometry (GC-MS), highlighting the presence of flavonoids responsible for the high antimicrobial activity. Antibacterial activity was evaluated in Staphylococcus aureus, Salmonella tiphy, Pantoea agglomerans (Enterobacter agglomerans), Streptococcus agalactiae, Bacillus subtilis, Staphylococcus epidermidis. Corynebacterium pseudotuberculosis, Escherichia coli, Enterobacter aerogenes, Shigella dysenteriae, Yersinia enterocolytica, Pseudomonas aeroginosa, Klebsiella pneumoniae, Vibrio cholera, Pasteurella multocida from rabbits, Pasteurella multocida of porcine origin. Antimycotic activity was evaluated in Microsporum canis, Microsporum gypseum, Trichophyton mentagrophytes, Saprolegnia spp, Aspergillus flavus, Aspergillus fumigatus, Aspergillus niger, Fusarium moniliforme, Candida albicans, Cryptococcus neoformans y Malassezia pachydermatous. The antiviral activity was evaluated with the Aujeszky virus (PRV) and the canine Distemper Virus. Structural alterations have been observed by electron microscopy in Pasteurella multocida, Candida albicans, Cryptococcus neoformans, and Malassezia pachydermatous. Likewise, products have been developed against superficial mycosis, canine otitis and respiratory diseases in rabbits based on propolis.

Keywords: Research, Propolis, Mexico, Antimicrobial Activity

Oral Presentation

Apitherapy Applied in Aesthetics (aesthetic api): Skin and Acne

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Abstract

1. Protocol: first week • Allergy test (apitoxin, royal jelly, honey and pollen) • Apitherapy sessions (1st session on the day of the assessment and the 2nd after four days). • Deep facial cleansing (cleansing, exfoliation and extraction) • Application of a decongestant mask (honey, propolis and aloe vera) • Apply a cold hydroplastic mask to create vasoconstriction (close the pores and seal). • Apply a collagen or repair gel to help reduce inflammation. • Lastly, apply sunscreen. 2. Deep Facial Cleaning - Cleaning Exfoliation Extraction. 3. Decongestive Mask (Propoleal Honey and Aloe Vera). 4. Application of Cold Hydroplastic Mask (Vasoconstruction And Seal Pores). 5. Collagen or Repairing Gel (Helps Deflamming). 6. Acne Scar. 7. Treatment for Acne Scars Deep Cleansing Cell renewal (dermabrasion) after 5 days. Mask (honey, aloe vera, royal jelly) every 8 days. Apitherapy sessions. 8. What Is Dermoabrasion? Aesthetic technique that consists of the mechanical removal of the affected skin layers, so that the final result is a face with a smooth texture. It is a procedure that serves to blur the scars left by acne, when the sequelae are strong, it greatly reduces the visibility of the scars. Aesthetic technique that consists of the mechanical removal of the affected skin layers, so that the final result is a face with a smooth texture. It is a procedure that serves to blur the scars left by acne, when the sequelae are strong, reduces the visibility of scars greatly. 9. Before - after 2 sessions. 10. Expression lines, nutrition and hydration In aesthetic Api, the bee sting is used as an injector for multiple applications, it is reused between two and up to five small punctures on the areas to be treated on the face; especially in the orbicularis oculi, between the eyebrows and the perioral area, that is, around the lips and mouth. 11. Stinger - micro points. Apitoxin is applied to stimulate the microcirculation (oxygenation) of the tissues and the renewal of the 100% natural hyaluronic acid produced by the body itself. 12. Cold collagen veil to seal. 13. Nutrition - Fruits, Vegetables and Honey - Salads with Pollen - Shakes with Pollen And Aloe Ver.

Keywords: Protocol, Aesthetics, Apitherapy, Beehive Products

Oral Presentation

Importance of Beehive products in the Prevention and Treatment of COVID-19

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Abstract

If we analyze carefully the statistics, we will see that 95% of the population has no, or very few problems with the SARS-Cov-2 infections, while only 5% of the infected people have problems if they have a low immune system, have co-infections, advanced co-morbidities or have an old age. So, logically, the focus should be, besides using various antiviral methods (physical, biochemical or chemical) to ameliorate the functioning of the immune system, to reduce the co-infections and keep under good control the co-morbidities. Such a complex task can be realized only by using, ideally on an individual base ("one patient one treatment protocol"), complex remedies that contains inside hundreds of different nutrients, micro-nutrients and pharmacologically active substances that can cover all major needs of the human body. The medicinal beehive products are perfect for such a complex task, are cheap, well tolerated, have less or no adverse reactions and can be used, in synergy with other integrative medicine methods like phytotherapy, aromatherapy, including at hospital level, to save the lives of thousands of people.

Keywords: Immune System, Medicinal Bee Products, COVID-19, Prevention

Oral Presentation

The Importance of Propolis in COVID-19 Treatment

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Abstract

Propolis is a multi-functional bee product with a rich in flavonoids. Propolis became the most preferred supplement in the Covid-19 pandemic due to its antiviral, antimicrobial, antioxidant and immunomodulator properties. According to literature studies, only 2 published article has in Web of Science until now. But it is possible to access about hundred articles in silico, pre-clinical and clinical studied published in Google academic. Every day the number of studies increases exponentially. With the first studies were in silico, the ability of the active components of propolis (flavonoids) to bind to Angiotensin-converting enzyme (ACE-II)-related carboxypeptidase receptors was examined. Our previous molecular docking study results had indicated that myricetin, quercetin, caffeic acid phenethyl ester and hesperidin have highly binding constants to ACE-II. The second study was in vitro screening ELISA test against the spike S1 protein (SARS Cov-2): ACE-2 inhibition KIT with ethanolic Anatolian propolis. In vitro studies have been supported our findings in the literature. As a result, it is seen that propolis active components have a high potential with their properties such as competitive inhibition against ACE-II receptors, Protein Kinase (PAK1) inhibition, inhibition against proteases, the virus spike protein binding ability. In addition, in some case report studies has been pointed out that the duration of hospital stay was decreased.

Keywords: Propolis, COVID-19, Pandemic

Oral Presentation

EPP-AF Propolis Reduced the Time of Hospitalization of COVID-19 Patients - Pilot, Randomized and Controlled Clinical Trial

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Abstract

The COVID-19 pandemic has renewed interest in propolis products worldwide. It was known that propolis components have inhibitory effects on the ACE2, TMPRSS2 and PAK1 signaling pathways, which would interfere with SARS-CoV-2 virus attachment to the host cell and reduce the risk of exaggerated and often fatal lung inflammation. Additionally, antiviral activity of propolis had been previously proven "in vitro" and "in vivo". In pre-clinical studies, propolis promoted immunoregulation of pro-inflammatory cytokines, including reduction in the levels of IL-6, IL-1-beta and TNF-α, and increased levels of the regulatory cytokine IL-10. Additionally, clinical trials had demonstrated antioxidant properties and a lack of interference with medicines. Propolis products with consistent bioactive properties are currently available, including a standardized Brazilian green propolis extract (EPP-AF® - Apis Flora Indl. Coml. Ltda., Ribeirão Preto, SP, Brazil), facilitating objective and comparable studies. In a randomized, controlled, open-label, single-center trial, hospitalized adult COVID-19 patients were treated with propolis as an adjunct therapy at Hospital São Rafael, Salvador, BA, Brazil in June and July 2020. Patients (n = 124) were allocated to receive standard care plus an oral dose of 400 mg or 800 mg/day of EPP-AF® propolis for seven days, or standard care alone. Standard care included all necessary interventions, as determined by the attending physician. The length of hospital stay post-intervention was shorter in both propolis groups than in the control group; lower dose, median 7 days versus 12 days for the control group (95% confidence interval [CI] −6.23 to −0.07; p = 0.049) and higher dose, median 6 days versus 12 days of control (95% CI −7.00 to −1.09; p = 0.009). With the higher dose of propolis, there was a lower rate of acute kidney injury than in the controls (4.8 vs 23.8%), (odds ratio [OR] 0.18; 95% CI 0.03–0.84; p = 0.048). Considering the proposed endpoints, we can conclude that propolis reduced the hospitalization time of COVID-19 patients.

Keywords: Green Propolis, EPP-AF Propolis, COVID-19, Clinical Trial, SARS-Cov-2

Oral Presentation

COVID-19 and Anatolian Propolis: A Case Report

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Abstract

As an age-old folk remedy, it is widely accepted that propolis has natural anti-inflammatory properties. Anatolian propolis is a different form among bee products group. Propolis has taken its current place as a food supplement during the pandemic period and new studies on propolis against covid-19 have gained momentum. 38-year-old male patient, who served as a medical secretary, first complained of a tickling in his throat. RT-PCR was requested from the patient who presented with this complaint and was in the high-risk profession. The routine blood values and Thorax CT results of the patient whose test was positive were normal. Medical treatment recommended in the Ministry of Health guidelines was initiated for the patient. The patient's cough complaint started 3 days later, and his complaint got worse on the 5th day. A control thorax CT was requested from the patient whose fever did not decrease simultaneously and extensive bilateral ground glass areas were formed. The patient was hospitalized, and moxifloxacin was added to his treatment; However, after 72 hours, the patient's fever continued. The patient started respiratory failure and his general condition worsened. It was decided to follow the patient in the intensive care unit (ICU) and tocilizumab and continue positive airway pressure (CPAP) support was started. Although 2 days passed, the patient's oxygenation and clinic status did not improve. For this reason, BEEO'UP 30% Anatolian propolis 80 drops / day was applied to the patient. At the end of the third day, improvement began in the patient's oxygenation, blood parameters and radiological findings. For 5 days, the patient was followed up with IV moxifloxacin, 60 mg steroid, CPAP, inhaler treatments, low molecular weight heparin (LMWH) and BEEO'UP 30% Anatolian propolis. The patient's clinic improved, and the patient was taken to the service on the 7th day of his admission to the ICU. The patient was discharged on the 10th day of hospitalization. At the health check-up 1 month later, the patient had no complaints except for forced exertion dyspnea, blood parameters normalized and abnormal radiological findings in Thorax CT completely regressed. Surely, in this disease with many unknowns, it may not be correct to attribute the remarkable rapid and sequel-free recovery in this case to the use of Anatolian propolis alone. However, in such cases where there are no other treatment options left, in addition to the treatment recommended in the guideline, there is no harm in using Anatolian propolis, and even benefit will be gained due to its proven antioxidant and antiviral effect. This phenomenon has provided hope for further study plans. As a result, Anatolian propolis can be added to the existing treatment protocol in patients diagnosed with Covid due to its easy, safe and low cost. There is a need for multi-center, large-population studies on the use of Anatolian propolis in Covid-19 prophylaxis, treatment and post-covid-19 period, and even to prevent complications. With the promising picture created by this case, we continue our work more comprehensively. We look forward to announcing our results. It is hoped that in the future there will be drug studies that will provide definitive treatment with one or more of the specific compounds of Anatolian propolis.

Keywords: Anatolian, Propolis, COVID-19, Food Supplement

Oral Presentation

Propolis in COVID-19 Infection

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Abstract

The COVID-19 outbreak has been a cause of concern around the world due to its negative effects on both human health and the economy. Since it is more contagious than other diseases with a worldwide impact, it has required measures such as restricting travel between cities and countries, closing places and businesses where people can contact such as schools and cafes. Although countries adopt different public health strategies to prevent the spread of the diseases, the virus continues to spread through asymptomatic ways. In this process, various products such as vitamins and minerals, mainly herbal products, are recommended, but most of these must be tested in clinical studies before being used widely and safely. Isolation and home stay measures are not sustainable in terms of economy and other requirements, especially in poor countries. As people trying to return to normal life, they decrease social distance thus the risk of infection increases. In this situation, people need reliable alternatives to prevent or alleviate the disease, and adjuvant therapy is accepted because it is cheap and widely available and rarely has side effects. Indeed, given the large number of deaths and permanent damages caused by the COVID-19 outbreak, there is a need for treatment that are proven to be safe, that could potentially inhibit the virus, reduce its contagiousness and/or alleviate symptoms of infection. In scientific studies, propolis and some of its components in the pathophysiology of the disease caused by SARS-CoV-2, with the entry of the virus into the cell, immunomodulation of monocytes (macrophages (reduction and immunization of IL-1 beta and IL-6 production), reduction of transcription factors, reduction of NF-KB and JAK2/STAT3, blocking PAK1, which indicates fibrosis caused by inflammatory activities and reduction of TMPRSS2 and ACE2. In this sense, apitherapy attracts attention as potential candidates, especially propolis and its components that can help reduce the pathophysiology consequences of SARS-CoV-2 infection.

Keywords: COVID, propolis, PAK1

1. Introduction

Infection with SARS-CoV-2, the virus that causes COVID-19, is characterized by binding between viral proteins and angiotensin-converting enzyme (ACE-2) (Wan et al. 2020). Activation of spike protein, transmembrane serine protease 2 (TMPRSS2), which plays an important role in viral infection (Hoffmann et al. 2020). After entry into the living organism, up-regulation of PAK1, a kinase that mediates endocytosis, coronavirus infection, lung inflammation, lung fibrosis, and other critical death-causing factors, takes place. An increase in PAK1 level suppresses the adaptive immune response and facilitates viral replication (Maruta et al. 2020; Xu et al. 2005). SARS-CoV-2 infection is associated with active proinflammatory cytokines, which lead to the development of atypical pneumonia with increased chemokine level, rapid respiratory disorder and pulmonary failure, spectrum, immunological/inflammatory phenomena are known to be important, and these mechanisms

are associated with organ dysfunction rather than viral load (Ding et al. 2004; Stebbing et al. 2020). Qin et al. (2020) in their observational studies, they reported that serum levels of proinflammatory cytokines such as IL-6, IL-1 and TNF-alpha were higher in severe COVID-19 patients than in mild ones (Hori et al. 2013). In studies conducted to date, there are studies that propolis can reduce the symptoms of inflammatory diseases by affecting various metabolic cycles (Hori et al. 2013; Machado et al. 2012). Various comorbidities, such as hypertension and diabetes, have required patients with severe symptoms of COVID-19 to seek intensive care. The mortality rate of COVID-19 patients was found to be much higher in patients with cardiovascular diseases, chronic respiratory disease and diabetes (Guan et al. 2020; Stein et al. 2020). There are studies on the effect of propolis in diabetes, hypertension and cardiovascular diseases (Fuilang et al. 2005; Fang et al. 2013) its reduction in viral replication and its anti-inflammatory effect provide evidence that it may be effective in SARS-CoV-2 infection (Shimizu et al. 2011; Ansorge et al. 2003; Chan et al. 2013).

Propolis is produced from resin containing phytochemicals produced by honeybees to protect plants from pathogens, and contains phenols and terpenoids (Langenheim et al. 1994, Toreti et al. 2013). The compounds noted for the inhibition of coronavirus in propolis are quercetin, myrcetin, and caffeic acid. There is a need for products that do not change in their bioactive components, are safe, have minimal interaction with pharmaceutical drugs, and whose effectiveness has been proven by clinical studies. The fact that propolis, which has scientifically proven antimicrobial (including antiviral), anti-inflammatory, immunomodulatory, antioxidant and antitumoral effects, is considered as an adjuvant treatment in SARS-CoV-2 infection, is inexpensive, common, and rarely causes undesirable effects.

The use of propolis in the treatment of COVID-19 is due to its prominence among natural medicine alternatives, the fact that many studies have been conducted on propolis and it is already widely consumed in many countries. Therefore, propolis with wide pharmacological activities is a food supplement that can be used both as a preservative and as a support for treatment. Potentially some propolis compounds can interact with SARS-Cov-2 MPRO. In a study evaluating potential therapeutics to inactivate the virus and reduce the damage it causes, the genetic code of the coronavirus and the mechanisms underlying the damage caused by SARS-CoV2 were examined. MPRO (3 chymotrypsin-like cysteine enzyme), the main protease of the coronavirus, is required for the life cycle of polyproteins and the target is the inhibition of the active site of this enzyme. Caffeic acid phenethyl ester (CAPE), galangin, chrysin and caffeic acid in propolis are potential compounds that act on this viral target (Hashem et al. 2020) It is thought that propolis can potentially inhibit or reduce host cell SARS-CoV2 spread by interacting with ACE2 and TMPRSS2. SARS-CoV-2 strongly binds to the angiotensin converting enzyme (ACE2), uses this enzyme as a receptor for invasion and replication in the host cell and causes damage (Hoffmann et al. 2020; Xu et al. 2005). In this case, ACE inhibitors are prescribed as drug alternatives. However, the harmful effects of ACE inhibitors and angiotensin receptor blockers (ARBs) have been a concern for the treatment of patients with COVID-19. Inhibition of the ACE2 enzyme is an important target in the treatment of SARS-CoV2 infection Mehra et al. 2020; Vardhan et al. 2020; Sanchis-Gomar et al. 2019)

In the study, they found that routine had the highest binding energy to ACE2, followed by myricetin, caffeic acid phenethyl ester, hesperidin, and pinocembrin. Oses et al. (2020) evaluated different propolis types in terms of ACE inhibition and found that more than 90% of the propolis types they tested showed strong ACE inhibition. They showed that the propolis components catechin and p-coumaric acid gave the best results. ACE2 and TMPRSS2 at the host cell surface are used by SARS-CoV2 to continue invasion and replication through interaction with glycoproteins. Vardhan and Sahoo (2020) RNA-dependent RNA polymerase (RdRp) uses molecular insertion procedures with targets such as ACE2 and glycoproteins.

compared the effects of the molecule with hydroxychloroquine. As a result of the research, limonene was the most active ingredient, while quercetin and kaempferol in the structure of propolis gave high scores. Kaempferol reduced the expression of TMPRSS2 in prostate cancer, which showed a potential mechanism of action for its antitumoral effect (Da et al. 2019). In addition to antiviral activity, kaempferol It is anticipated as an effective component against COVID-19 as it potentially interacts with ACE2, RdRp and spike glycoprotein (SGp) and plays a role in inhibition of TMPRSS2(Da et al. 2019; Debiaggi et al. 1990). By blocking PAK-1, propolis potentially prevents lung fibrosis and restores normal immune response. The pathogenic kinase PAK1 is key, seen among possible targets in controlling COVID-19 damage. While it is a key component in malaria and viral infections, when activated abnormally it plays a role in conditions such as cancer, inflammation, and immunosuppression. PAK1 activation includes lung fibrosis, an aggravating factor in COVID-19, and is activated by RAC (Maruta et al. 2020) Xu et al. (2005) reported that caffeic acid phenethyl ester (CAPE), one of the components of propolis, can inactivate RAC, resulting in inhibition of PAK1.4 PAK1 inactivation can weaken the pathogenesis of coronavirus. B and T cells are lymphocytes that produce specific antibodies against viruses and foreign substances, and PAK1 While contributing to its suppression, PAK1 inhibitors help both fight the virus and restore the normal immune response. Poplar propolis mainly contains flavonoid compounds, while green propolis (*Baccharis dracunculifolia*) contains various flavonoids such as artepillin C, baccharin and drupanin and prenylated phenylpropanoids. It has been reported that both types of propolis inhibit PAK1 (Messerli et al. 2009).

Some studies have shown that propolis can act as an immune stimulant with its ability to improve the immune response. Its components increased neutralizing antibody titers, activated phagocytosis, and increased IFN-alpha levels and lymphocyte (Fernandes et al. 2015; Mahmoud et al. 2017). Shiumuzi et al. (2008) found an increase in IFN-alpha levels by CAPE is a potent inhibitor of NF-kB activation in myelomonocytic cells. Ansorge et al. (2003) showed that propolis, CAPE, quercetin, hesperidin and other propolis flavonoids can increase TGF-alpha, an important anti-inflammatory cytokine, while inhibiting cytokine production of T cells such as Th1 and Th2. It has been shown that CAPE can alleviate inflammation and is important for the development of proinflammatory Th17, together with the immunomodulatory effect of inhibiting IL-6 phosphorylation and STAT3.

The antiviral activity of propolis has been demonstrated against influenza, herpes simplex virus type 2 and HIV.35-38 Shimizu et al. (2008) evaluated 3 propolis types with different chemical structures using a murine model of herpes simplex virus type 1, all three extracts both showed anti-HSV1 effects and stimulated immunological activity against intradermal HSV-1 infection in mice. In another study, the antiviral activity of propolis Tested on DNA and RNA viruses (poliovirus, herpes simplex virus and adenovirus) in an in vitro model. The best results were obtained against poliovirus and herpes virus by inhibiting the herpes virus by 99.9% at a propolis concentration of 30 µg/ml (Amoros et al.1992; Harish et al. 1997)

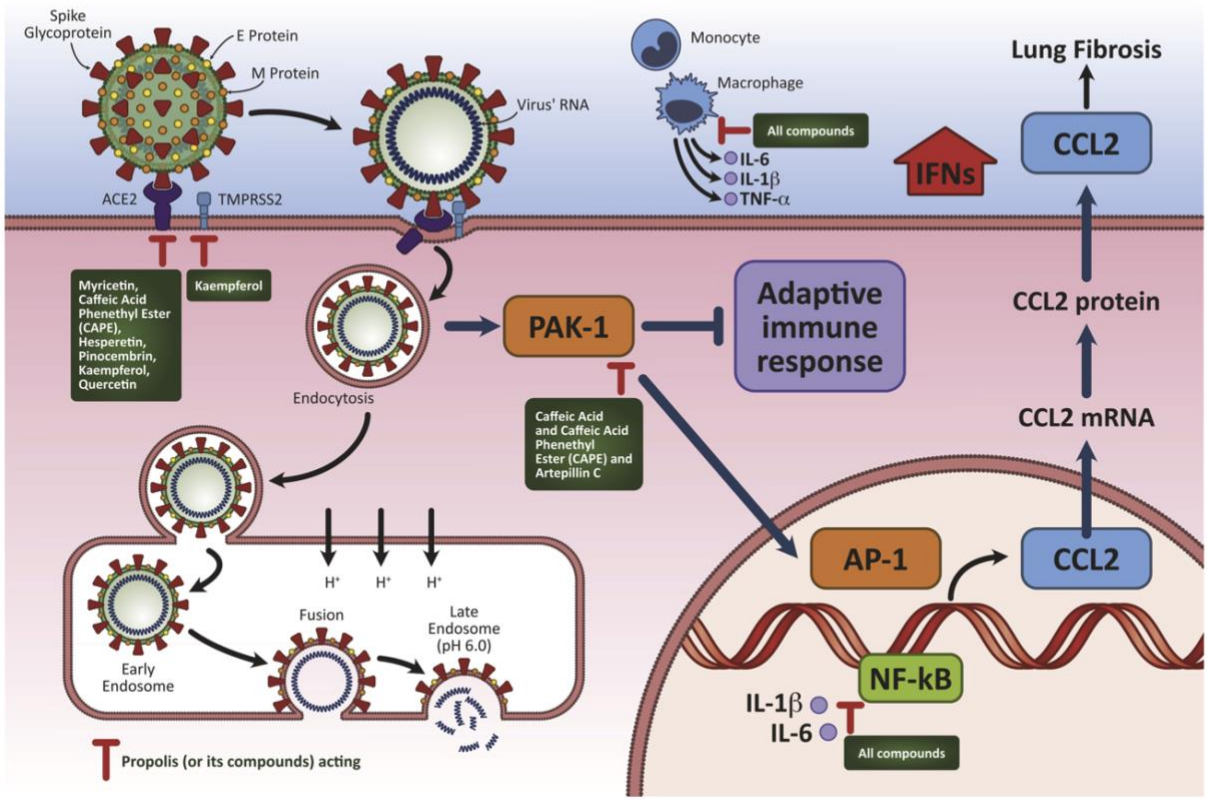

Figure 1. Major pathways through which propolis can interfere with SARS-CoV-2 attachment to the host cell, viral replication, and pathophysiological consequences. SARS-CoV-2 entry into target cells requires spike protein binding to ACE2 and activation by TMPRSS2. After binding, several signals are triggered, allowing viral endocytosis and PAK1 activation, which reduces the adaptive immune response and antibody production against the virus. PAK1 also stimulates CCL2 production, which generates a fibrotic response. Viral infection induces nuclear transition factor NF-KB activation, generating local pro-inflammatory cytokine production. Propolis-derived compounds downregulate the expression of TMPRSS2 and the anchoring ACE2, which limits entry of the virus. Furthermore, they promote NF-KB and monocyte/macrophage immunomodulation, reducing pro-inflammatory cytokine overproduction, and they reduce PAK1 activation, increasing the production of antibodies against SARS-CoV-2 (Beretta et al. 2020).

2. Discussion

Vegetative and geographical factors, bee species, seasonal and climatic differences, differences in solvent and extraction processes affect its structure and composition. The standardization problem exists not only in apitherapy products, but also in phytotherapy products. As a matter of fact, there are differences in raw materials when working with herbal products, because season, tillage and other environmental factors can be limiting factors. Since it is not possible to have the same raw material lots in such products, safety and efficacy studies and minimum standardization are essential. However, there are also standardized propolis products.

3. Conclusion

Considering the damages of the COVID-19 epidemic on both human health and economy all over the world, there is a need for supportive treatments to prevent SARS-CoV2 infection and to reduce the damage it will cause. One of these treatments, one of the Apitherapy products, propolis stands out in this regard. The anti-inflammatory and immunomodulatory effects of

propolis, including PAK1 inhibition, have been demonstrated in scientific studies. Propolis inhibits the binding of SARS-CoV-2 virus to its main target, ACE2. It is also reported that propolis components such as routine, kaempferol, myricetin, especially CAPE, have a strong interaction with ACE2, and that kaempferol reduces the expression of TMPRSS. In accordance with the criteria adopted by the World Health Organization, propolis can be used simultaneously with drugs without the risk of inactivation. However, studies on its antiviral effect on the virus are needed.

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Oral Presentation

Apitherapy against COVID-19 infections

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Abstract

Propolis, a resin mixture collected by honeybees from various herbal sources, contains many useful biological compounds. There are many studies showings that propolis has antibacterial, antioxidant and anti-inflammatory activities. The extraction procedures and solvents are important for the sources of phenolic and flavonoid contents. The extraction time sometimes increases the phenolic yield and sometimes decreases it. It is seen that the solvent effect on the extraction yield is very high. In this study, water and propylene glycol were used and total phenolic, flavonoid, dry extract amount, and antioxidant capacities were compared.

Keywords: Propolis, Coronaviruses, Extraction Procedures, Antioxidant Capacities.

1. Introduction

Propolis, a resinous material produced by honeybees from plant exudates, has long been used in traditional herbal medicine and is widely consumed as a health aid and immune system booster. The COVID-19 pandemic has renewed interest in propolis products worldwide; fortunately, various aspects of the SARS-CoV-2 infection mechanism are potential targets for propolis compounds. SARS-CoV-2 entry into host cells is characterized by viral spike protein interaction with cellular angiotensin-converting enzyme 2 (ACE2) and serine protease TMPRSS2. Propolis components have inhibitory effects on the ACE2, TMPRSS2 and PAK1 signaling pathways; in addition, antiviral activity has been proven in vitro and in vivo. Propolis has also shown promise as an aid in the treatment of various of comorbidities that are particularly dangerous in COVID-19 patients, including respiratory diseases, hypertension, diabetes, and cancer. Standardized propolis products with consistent bioactive properties are now available. Given the current emergency caused by the COVID-19 pandemic and limited therapeutic options, propolis is presented as a promising and relevant therapeutic option that is safe, easy to administrate orally and is readily available as a natural supplement and functional food. Natural products, which have historically been widely used to help avoid and alleviate diseases (Saklani and Samuel 2008), are among the options being considered as an adjuvant treatment for SARS-CoV-2 infection (Maruta and Hong 2020), because they are generally inexpensive, widely available, and rarely have undesirable side effects. Plant defense substances collected by bees include phenols and terpenoids. Phytochemical compounds that show promise for the inhibition of coronavirus in humans include quercetin, myricetin, and caffeic acid, all components of propolis (Mani et al 2020). The composition of propolis varies according to the plant species available in each region (Bankova 2013). As this variability can affect their medicinal properties, standardized propolis products have been developed to help meet the need for a product that does not vary in the main bioactive components and is safe, with minimal interaction with pharmaceutical drugs and proven efficacy in clinical trials (Beratta et al 2017). Along this line, Hashem evaluated various natural compounds with an in-

silico approach (molecular docking) to try to find useful options for treating SARS-CoV-2 infection. Curiously, caffeic acid phenethyl ester (CAPE), galanginin, chrysin and caffeic acid, substances found in several different types of propolis around the world, appeared as potential drugs against this viral target (Hashem 2020).

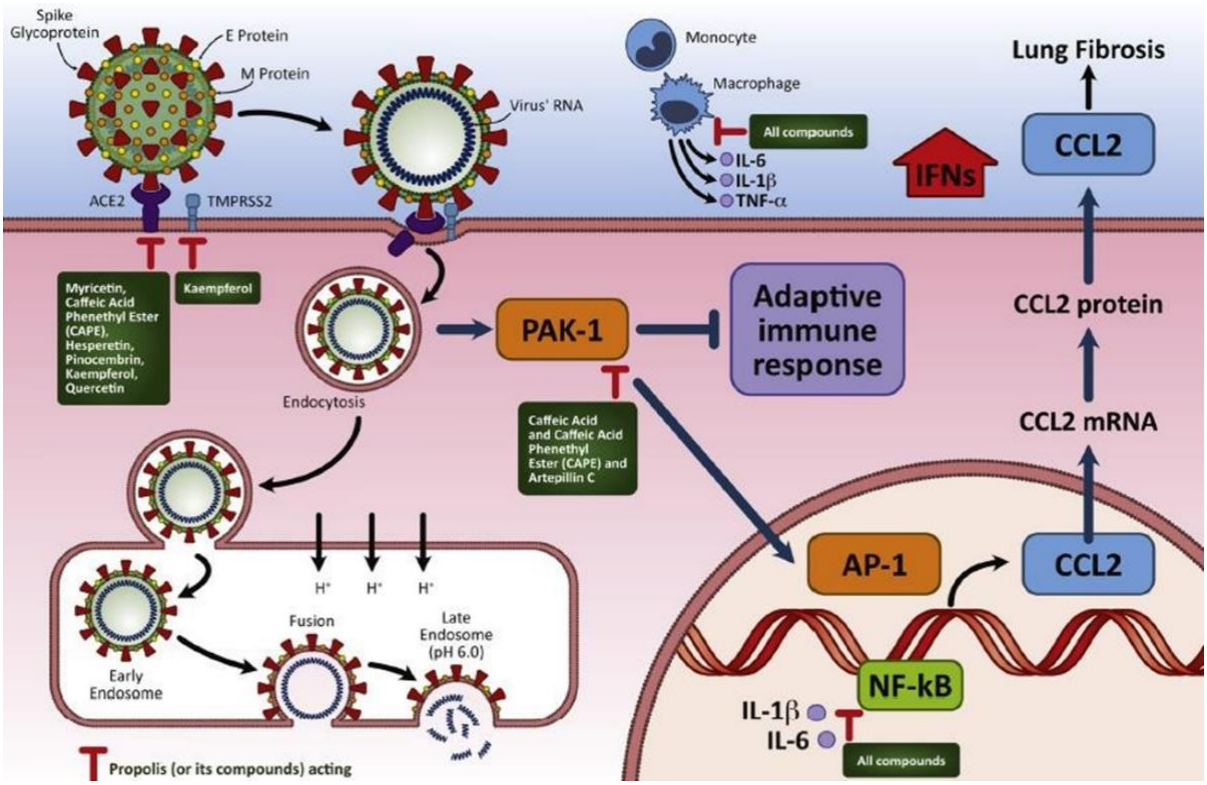


Figure 1. Major pathways through which propolis can interfere with SARS-CoV-2 attachment to the host cell, viral replication, and pathophysiological consequences. SARS-CoV-2 entry into target cells requires spike protein binding to ACE2 and activation by TMPRSS2. After binding, several signals are triggered, allowing viral endocytosis and PAK1 activation, which reduces the adaptive immune response and antibody production against the virus. PAK1 also stimulates CCL2 production, which generates a fibrotic response. Viral infection induces nuclear transition factor NF-KB activation, generating local pro-inflammatory cytokine production. Propolis-derived compounds downregulate the expression of TMPRSS2 and the anchoring ACE2, which limits the entry of the virus. Furthermore, they promote NF-KB and monocyte/macrophage immunomodulation, reducing pro-inflammatory cytokine overproduction, and they reduce PAK1 activation, increasing the production of antibodies against SARS-CoV-2 (Beratta 2020).

2. Materials and Methods

2.1. Chemicals and solvents

Silica gel, formic acid, acetonitrile, trichloroacetic acid (TCA), 2-thiobarbituric acid (TBA), EDTA, $K_3Fe(CN)_6$, sodium phosphate, K_2HPO_4, KH_2PO_4, ascorbic acid, $DPPH^{\cdot}$, linoleic acid, α-tocopherol, $FeCl_2$, $FeCl_3$ and $Na_2S_2O_3$ were obtained from Sigma Chemical Co. The organic solvents (ethyl acetate, methanol, hexane, di-chloromethane, chloroform, *n*-butanol used in analyses were of HPLC grade and purchased from E. Merck. All the other chemicals were supplied from other commercial sources.

2.2. Samples

Crude propolis samples were obtained from beekeepers interested in natural beekeeping in different geographic regions of Turkeys in 2019. Propolis samples were extracted with water (WEP) and propylene glycol (PEP). The obtained extracts were stored at +4 temperature to be used in the experiment.

2.3. Preparation of samples

Propolis samples collected from different provinces of Turkey were stored at -80 degrees, 10 gr of dry propolis was boiled in distilled water in a reflux system for 2 hours and subjected to aqueous ethyl acetate and *n*-butanol extraction, respectively (Demirtaş et al. 2013; İpek, Özen and Demirtaş, 2017). The water extract was filtered off and extracted with ethyl acetate. This process was continued until substantial amounts of the aqueous components were transferred to ethyl acetate. When this process was performed three times, the extraction was completed with ethyl acetate. The remaining water extract was subjected to the same extraction as the *n*-butanol extract (Figure 1). WEP and PEP were separated from the solvent by rotary evaporation to obtain dry crude extracts.

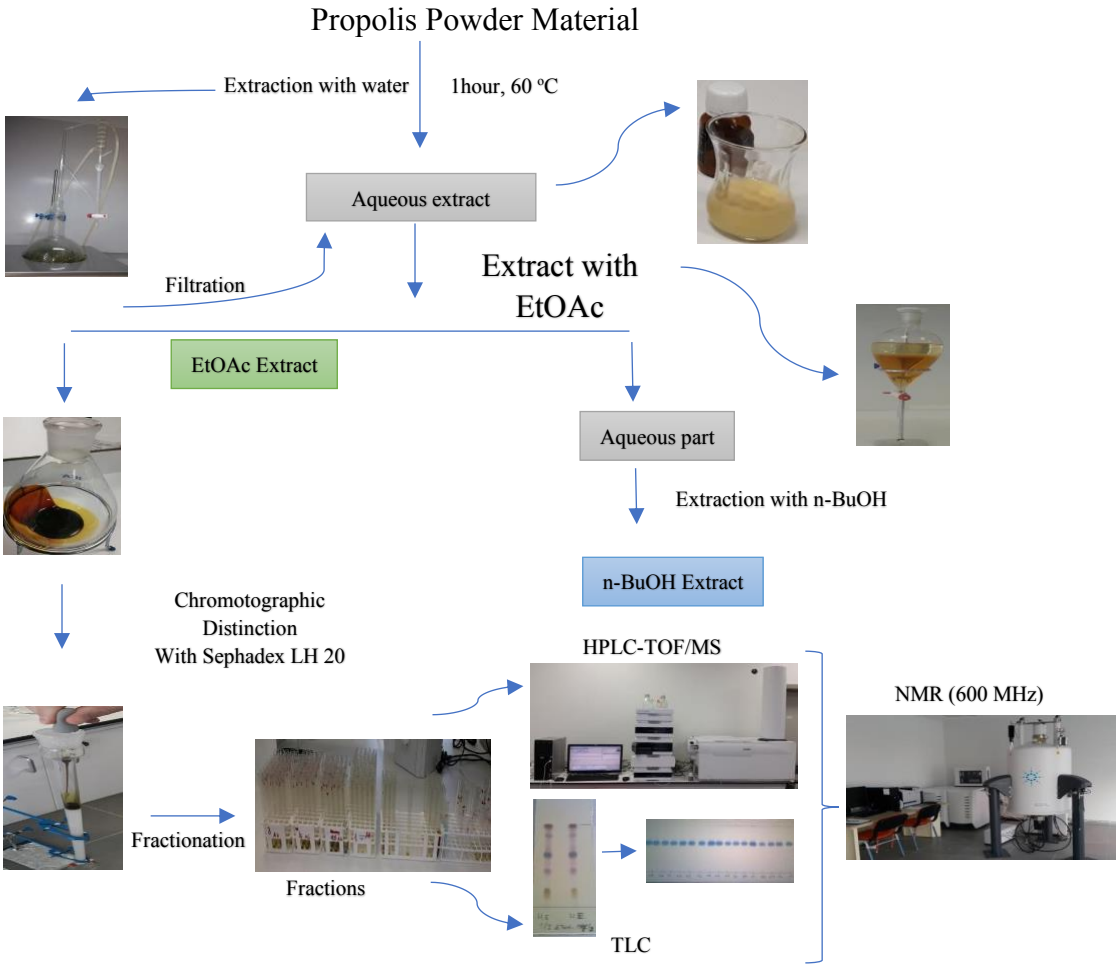


Figure 2. Extraction and isolation steps applied to propolis

2.4. Determination of antioxidant activities

2.4.1. Reducing power

Ferric cyanide (Fe^{3+}) reducing antioxidant test (FRAP) was performed by modifying the method reported by Oyaizu (1986). When ferric ions (Fe^{3+}) are reduced to ferrous ions (Fe^{2+}) at 700 nm, the complex is formed and is a method of spectrophotometric measurement of this complex. Reduction capacity (Cu^{2+}) for Cupric ions was determined by the cupric ions reduction assay (CUPRAC) in previous studies (Bursal et al 2012).

2.4.2. DPPH$^{\bullet}$ radical scavenging activity

DPPH$^{\bullet}$ scavenging activities of methanol and water fractions of HPL and EAL were determined according to the method performed by Blois (1958). In the method, the stable DPPH$^{\bullet}$is removed by the free radical removal activity of the sample. Extract of 20 µg/mL was prepared from the samples then the volume with ethanol was adjusted to 1 mL. Then the prepared DPPH$^{\bullet}$ solution was added and left in the dark for 30 minutes. DPPH$^{\bullet}$ removal activity of the sample after incubation was measured spectrophotometrically (Necip and Işık 2019).

2.4.3 ABTS$^{\bullet+}$ radical scavenging activity

In this method, a sample is added to a preprepared ABTS$^{\bullet+}$ solution and after 30 minutes, the remaining cationic ABTS radical was measured spectrophotometrically at 734 nm. Then, 1 mL of cationic ABTS$^{\bullet+}$ solution was added to the sample at different concentrations. Absorbance was determined 30 minutes after mixing and for each concentration, radical removal percentage was calculated (Ak and Gülçin, 2012).

2.5. Chemical contents

2.5.1. Determination of total phenol compound amounts

Total amounts of phenolic compounds in gallic acid equivalents (GAE) were determined using the Folin-Ciocalteu reagent. For this; 0.2 ml of 50% Folin-Ciocalteu reagent was added to 0.1 ml extract and left for 3 min. Then, 2% Na_2CO_3 was added to this mixture and left to incubate for 45 min at room temperature. Absorbance values were measured spectrophotometrically at 760 nm wavelength after incubation. The amount of GAE (gallic acid equivalent corresponding to the measured absorbance value was calculated. Results were given as mg GAE/g propolis. Absorbance versus concentration was plotted, a linear plot was determined, and the R^2 value was calculated. This method is widely used in determining the antioxidant capacity of foods and in antioxidant studies.

2.5.2. LC-MS / MS content analysis

A 1260 Infinity II LC system model high-performance liquid chromatography (HPLC) coupled with mass spectrometry was used to a perform qualitative evaluation of the composition by mass spectrometry and chromatography conditions. Reverse-phase HPLC is equipped with a column furnace (1260 TCC), dual pumps (1260 Thousand Pump) and a degasser (1260 Degasser). Chromatographic conditions were optimized to ensure optimum separation for the composition and to overcome quenching effects. Therefore, the chromatographic separation was performed on a reverse phase Agilent Poroshell 120 EC-C18 model (100 mm x 3.0 mm, 2.7 µm) analytical column. The column temperature was set to 25 °C. Elution gradient, channel: A (water + 5 mM ammonium formate) and channel B (acetonitrile + 0.1% formic acid), solvent flow rate and injection volume were set at 0.250 mL/min and 5 µL.

3. Results

Phenolic compounds which were widespread in propolis were analyzed by LC-MS/MS method. Phenolic compounds are used in plant foods for taste, flavor, color and stability. They are also considered to be important factors in reducing the risk of chronic disease and supporting medical treatment (Arapitsas, 2012). The total phenolic content of propolis constitutes 6% to 43% of the dry matter (Table 1).

Table 1. The quantitative analysis results of water and propylene glycol extracts of propolis

Compounds, mg/g	1.Day	15.Day	30.Day		1.Day	15.Day	30.Day
Ascorbic acid	0	0.681	0.766		0	0	0
Gallic acid	0.059	0.034	0.115		0	0	0
4-Hydroxyibenzoic acid	0.774	0.762	0.813		0	1.002	0.711
Vanillic acid	0.386	0.316	0.646		0.173	0.257	0.489
Caffeic acid	0.076	0.075	25.265		0.551	6.425	5.809
Apigenin-7-O-Glikozid	0	8.321	0		0	0.321	0.222
Rosmarinic acid	0.269	0	0.281		0.272	0.268	0.276
p-coumaric acid	0.131	0.771	3.093		0.537	4.391	3.987
4-Hydroxybenzaldehyde	0.101	0.101	0.104		0.101	0.103	0.105
Trans-ferulic acid	0.381	0.773	2.311		1.022	5.043	4.447
Protocatechuic acid	0.319	0.308	0.309		0.379	0.331	0.321
Quarcetin	0.032	0.005	0.031		0.592	2.968	3.245
Apigenin	0.031	0	0.032		2.332	17.603	17.512
Naringenin	0.064	0.176	0.421		0.542	2.641	3.013
Trans-cinnamic acid	0	0	0.286		0	0.438	0.502
Kaempferol	0	0	0		1.911	7.094	8.678

Total phenolic and flavonoid contents of water and propylene glycol extracts of propolis (WEP and PEP) samples from each region (15 samples) are given in Table 2. Total phenolic contents in WEP at day 1, day 15 and day 30, respectively. It ranges from 0.97 mg GAE/g to 156.34 mg GAE/g, 0.97 mg GAE/g to 238.6 mg GAE/g, and 19.25 mg GAE/g to 431.08 mg GAE/g. Total phenolic contents in PEP at day 1, day 15 and day 30, respectively. It ranges from 19.78 mg GAE/g to 212.26 mg GAE/g, 44.52 mg GAE/g to 248.28 mg GAE/g, and 64.95 mg GAE/g to 238.6 mg GAE/g.

Table 2. Total Phenolic Content of water and propylene glycol extracts of propolis (mg GAE/g)

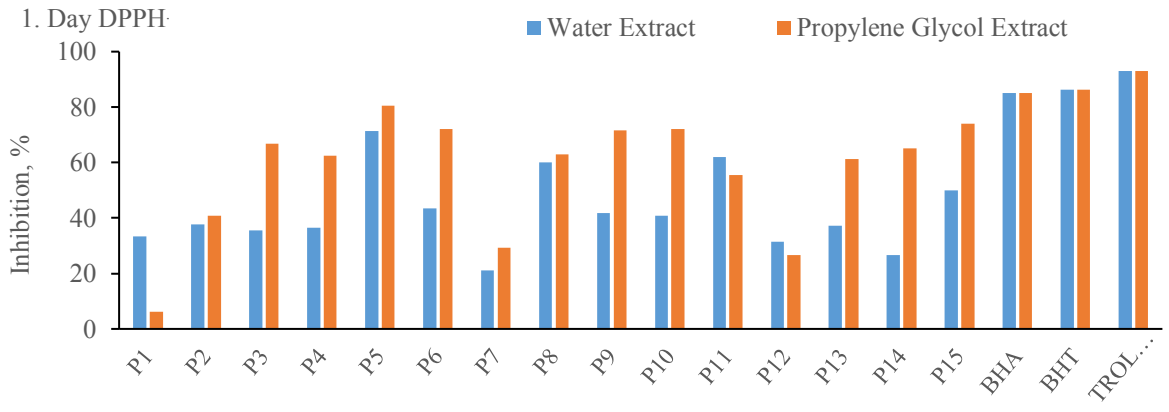
Samples, (mg GAE/g)	Water Extracts			Propylene Glycol Exctracts		
	1.Day	15.Day	30.Day	1.Day	15.Day	30.Day
P1	1.51	0.97	32.15	19.78	44.52	64.95
P2	13.33	238.6	55.27	75.16	79.46	84.84
P3	39.68	20.32	38.6	117.1	81.61	83.76
P4	107.42	98.82	19.25	123.01	147.74	169.25
P5	156.34	156.34	70.32	212.26	248.28	238.6
P6	63.87	208.49	77.31	126.24	150.43	177.31
P7	6.88	17.1	431.08	32.15	53.66	38.06
P8	25.7	88.06	164.95	157.42	113.33	125.16
P9	71.4	127.31	134.84	191.83	205.27	228.39
P10	6.34	230	131.61	175.7	141.29	209.03
P11	68.71	126.24	98.28	147.74	71.94	177.85
P12	0.97	52.58	38.06	56.34	147.2	72.47
P13	91.83	145.05	93.44	143.44	151.51	180
P14	5.81	52.58	114.41	174.62	119.25	136.45
P15	52.58	163.87	77.31	162.8	172.47	207.42

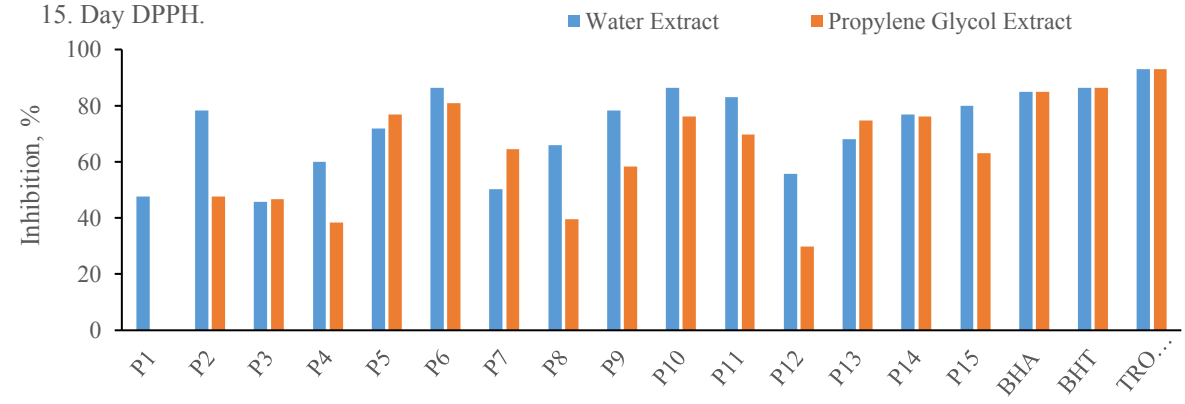
Table 3. Dry Propolis Quantities (mg/g)

Samples, mg	**Water Extracts**			**Propylene Glycol Extracts**		
	1.Day	15.Day	30.Day	1.Day	15.Day	30.Day
P1	33.3	33.04	14.82	ND*	492.06	287.28
P2	30.3	40.7	19	230.1	292.8	238.14
P3	59.94	50.16	38.4	163.68	172.36	459.36
P4	85.47	91.3	80.4	275.6	324.52	235.72
P5	45.98	66.3	39.6	443.8	500.5	331.08
P6	68.82	85.2	53.1	441.6	441.32	167.7
P7	56.61	49.82	26.5	244.76	295.2	471.04
P8	61.61	77.72	71.92	309.6	454.08	394.68
P9	82.14	102.06	88.2	456.3	437.76	249.6
P10	39.93	46.36	27.5	141.52	183.28	404.8
P11	43.43	54.52	46.4	305.52	349.14	373.52
P12	37.31	29.4	17.28	229.68	306.34	297.48
P13	45.98	48.1	32.5	511.88	471	157.3
P14	62.92	58	49	253.26	291.06	246.24
P15	68.12	76.88	55.12	300.3	335.24	352.8

ND: not detected

Antioxidant capacity measurement methods may be classified as hydrogen atom transfer (HAT)-based, electron transfer (ET)-based and mixed mode (ET- and HAT-based) assays. DPPH and ABTS are based on HAT, and also CUPRAC and FRAP are based on ET. (Apak et al. 2016). Purplish DPPH color changes to light yellow hydrazine. Color change occurs with reducing or antioxidant molecules and is measured spectrophotometrically at 517 nm. This bright color is due to the action of antioxidant molecules.





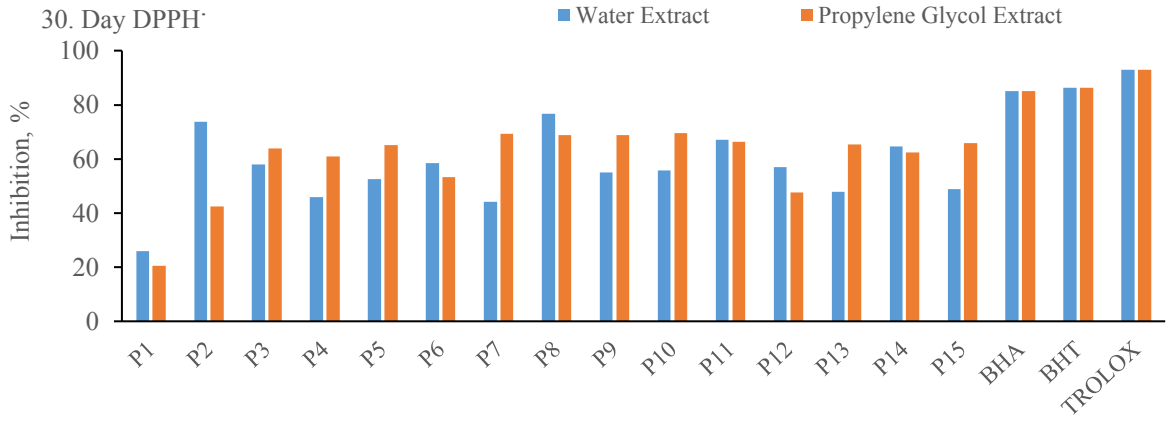
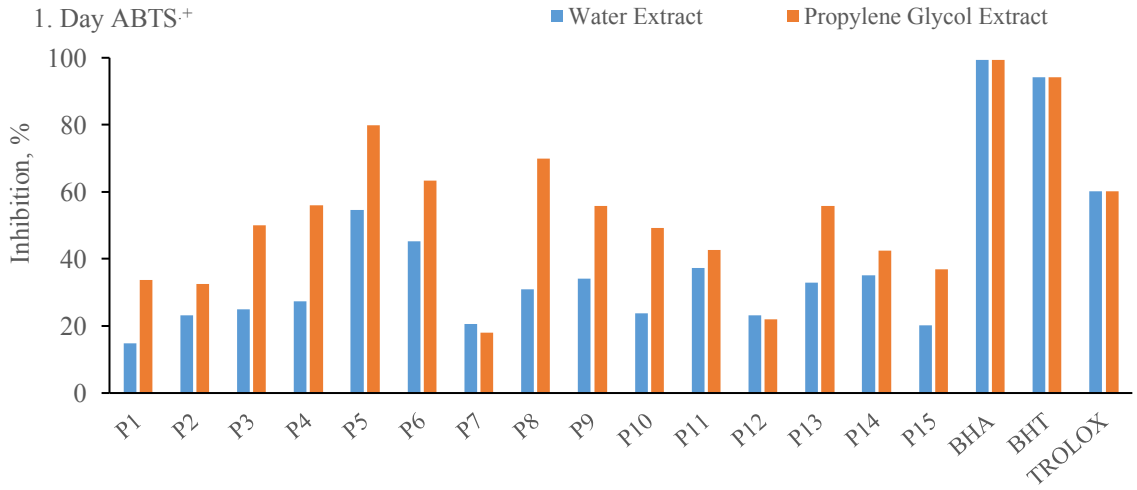
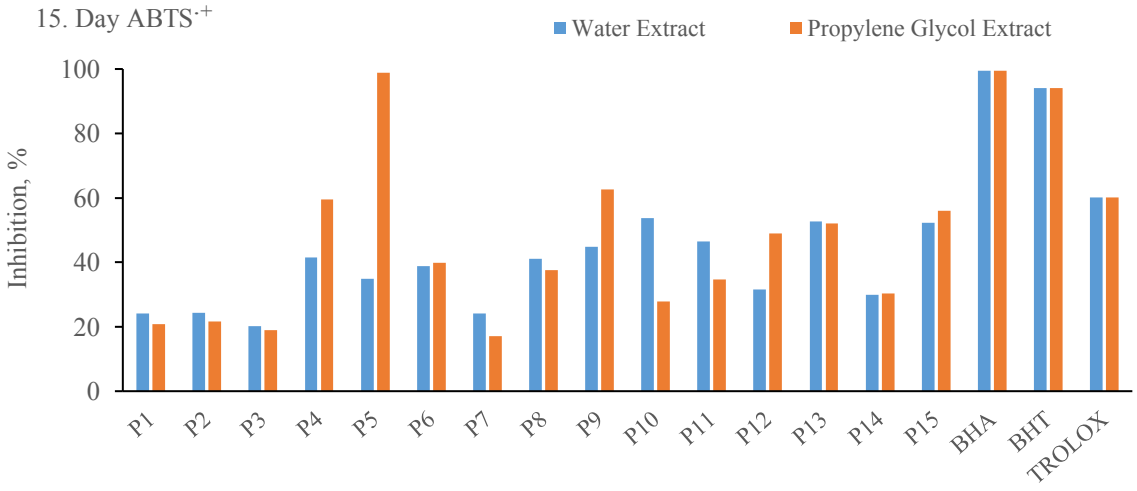


Figure 3. DPPH• scavenging activities of WEP and PEP





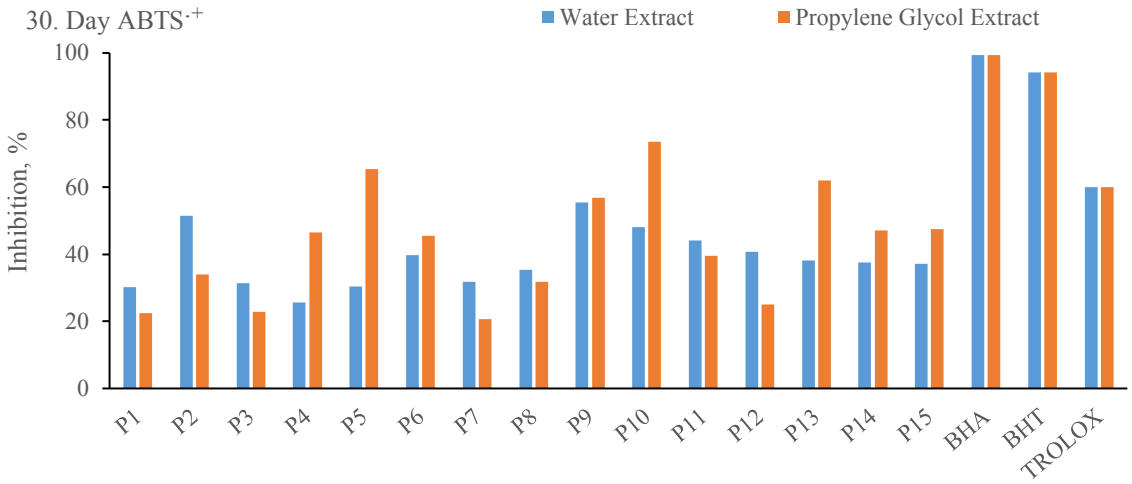
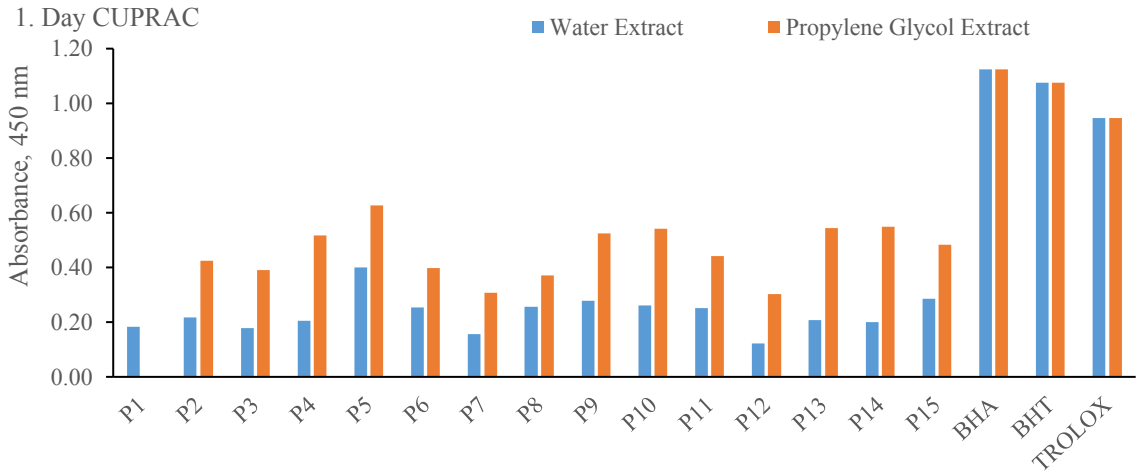


Figure 4. ABTS·+ scavenging activity ABTS of WEP and PEP

Reducing power characteristics of P1, P2, P3, P4, P5, P6, P7, P8, P9, P10, P11, P12, P13, P14, P15 and reference antioxidants Trolox, BHA and BHT are given in Figures 5 and 6. According to the result of CUPRAC method, the absorbance values at 450 nm varied between, 0.25 to 1.20 and 0.16 to 0.63 and for PEP and WEP, respectively. The standard antioxidants BHT, BHA and trolox were found to be 1.08, 1.12 and 0.95, respectively. Absorbance values at 700 nm according to the FRAP method varied between 0.055 to 0.295 for PEP and 0.02 to 0.11 WEP. The standard antioxidants were found to be BHT, BHA and trolox as 0.119, 0.31 and 0.275, respectively. A high absorbance value indicates a high reduction.



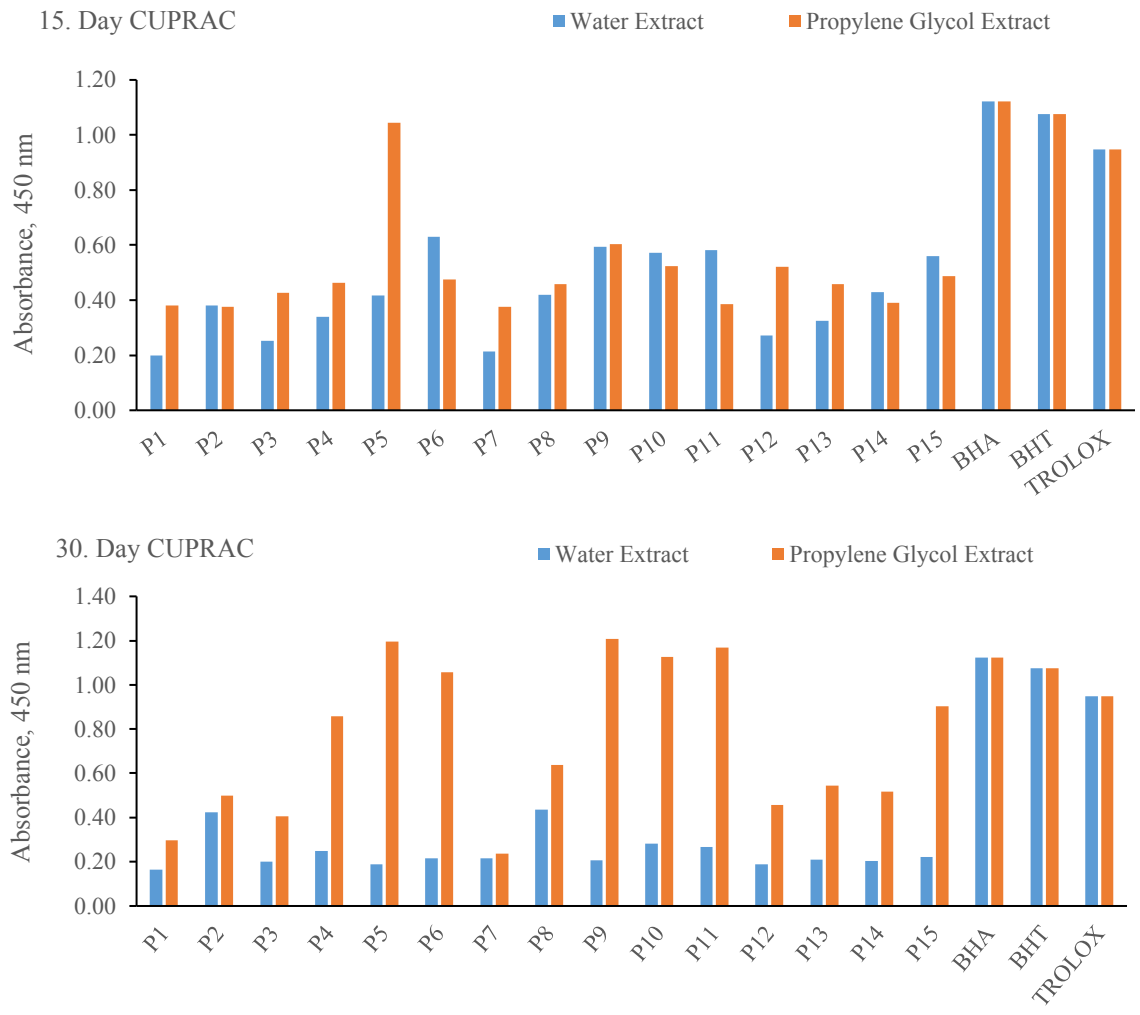
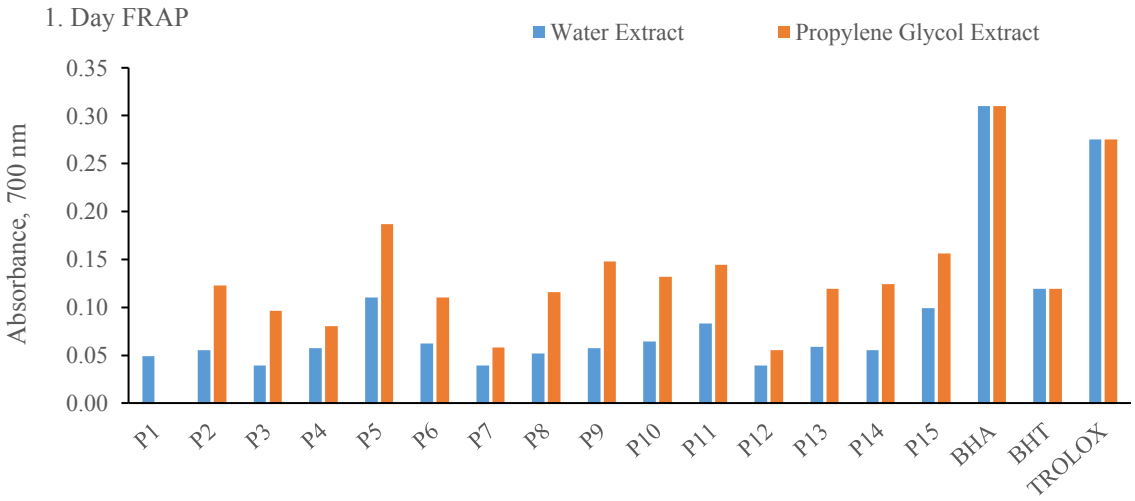


Figure 5. Metal-reducing capacity with CUPRAC assays of WEP and PEP



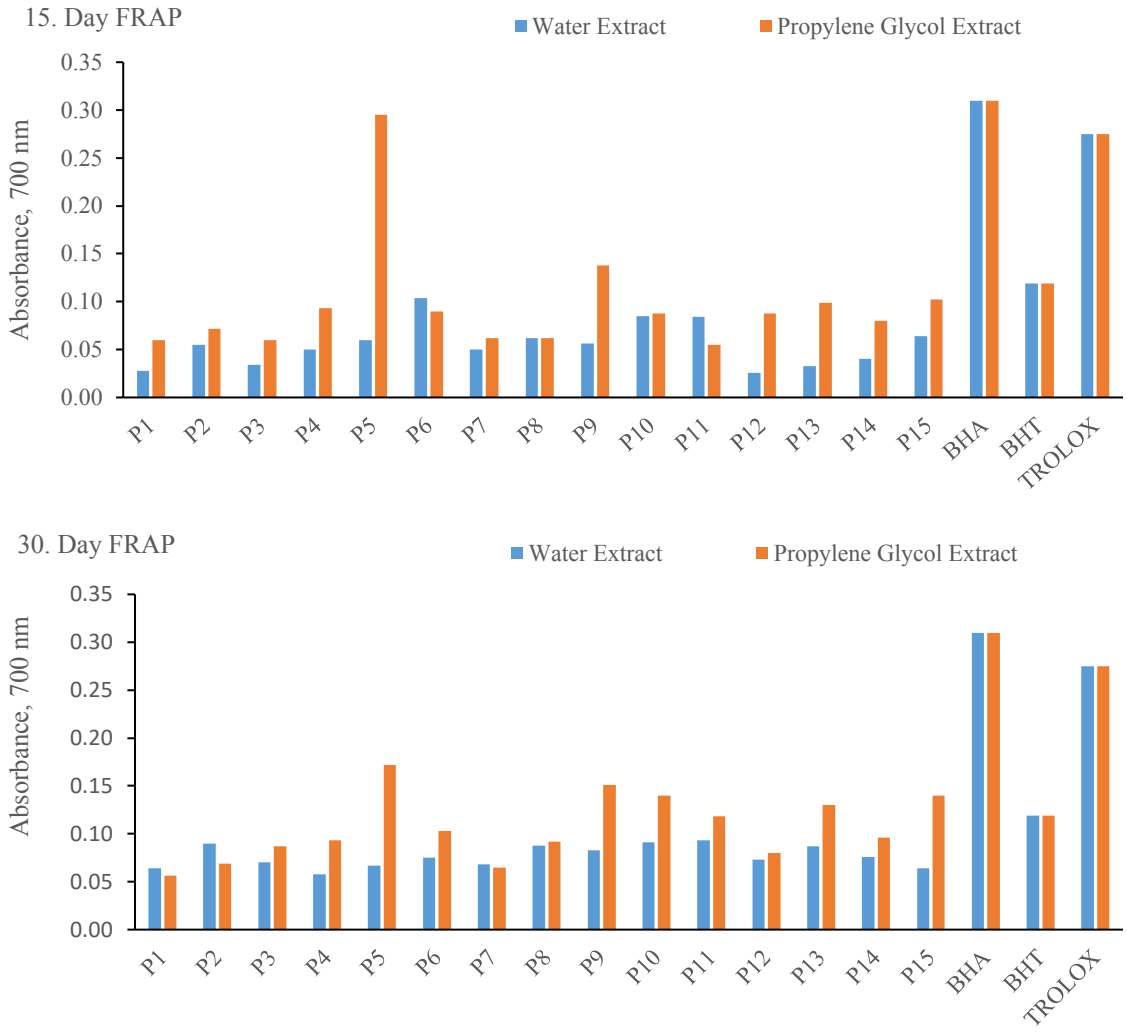


Figure 6. Metal-reducing capacity with FRAP assays of WEP and PEP

4. Discussion

Propolis is a highly complex mixture, containing more than 350 chemical moieties, many of which have documented beneficial health outcomes. The main constituents of propolis include resins, waxes, essential oils, and pollen, as well as various organic compounds, among which are phenolic compounds, flavonoids, terpenes, esters, aromatic aldehydes and alcohols, and several specific antioxidant compounds including beta-carotene, caffeic acid, and kaempferol. The studies evaluating the effect of propolis on coronaviruses are scarce. We investigated the in vitro effect of fifteen propolis samples for phenolics, flavonoids and crude quantities on several antioxidants' capacities, employing the technique of DPPH, radical scavenging activity ABTS, metal-reducing capacity with CUPRAC and FRAP of water and propylene extracted propolis (WPE, and PEP, respectively). Ascorbic acid, gallic acid and caffeic acid quantities of WPE were higher than PEP. The corona viruses' effect on either the infectivity or replication of any of the viruses studied had already published that the caffeic acid and caffeic acid phenethyl ester is effective on Covid-19. SARS researchers have been paying particular attention to quercetin, a flavanol found in propolis, since quercetin in conjunction with vitamin C is an effective aminopeptidase inhibitor. Quercetin and its derivatives inhibit in vitro, the SARS-CoV-1 and MERS-CoV main protease. Quercetin also modulates the cellular unfolded protein response (UPR). As coronaviruses can utilize the UPR to complete their entire replication cycle, quercetin may have anti-coronavirus effects.

5. Conclusion

Apitherapy is not dose-dependent, but stimulant dependent. The use of propolis and other bee products in the fight against Covid-19 should be expanded (Propolis should be taken at least 5 times a day). Studies on transforming bee products into functional products and increasing their bioavailability as well as the purification and conversion of plant-derived and valuable chemicals into functional products are not enough. R&D studies should be focused on the production of innovative, high value-added and industrial-scale bee products. It is essential to produce target-oriented and using new generation technologies. To make Bee Products usable, multi-functional and target-oriented production models should be developed. In addition to R&D and P&D studies in Bee Products, new methods are required for industrial-scale production.

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Oral Presentation

COVID-19 and Propolis

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Abstract

Covid-19 is a virus that stroke the human society globally. The life changed drastically. But biologically, a number of therapy types have simple and fast solutions for this infection. One of them is apitherapy. Few of the bee products proved fast actions in curing Covid-19 infection. From one year we recommended propolis tincture PT (30% European propolis in 65° ethanol solution), as prophylaxis and cure, considering it is largely available on the Romanian market. Doses for prophylaxis: Generally: 3 ml/day for the contacts with Covid-19 persons, without symptoms: 2 x 3 ml/day PT Doses for treatment: - For people with light or moderate symptoms: 3 doses/day of 3-4-5 ml, according to the weight. - For severe symptoms, we observed a faster to complete recovery without sequels, by taking 6 x 5 ml/day. We recommended to mix PT with honey for a faster action. Results for prophylaxis - about 97 % of consumers didn't have a symptomatic infection - direct contacts: didn't become symptomatic. Results for treatment: 1. people with light or moderate symptoms: recovered in few days. 2. people with severe symptoms who started fastly the intake: recovered in about one week. 3. those with severe symptoms who delayed 4-7 days the intake, recovered in longer time, and some had pulmonary sequels, recovered gradually in about few months. Those on numbers 1. and 2. had no pulmonary, renal or other organs sequels.

Keywords: COVID-19, Propolis, Tincture, Pulmonary, Sequels

Oral Presentation

Propolis in Cancer: Scientific Evidences

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Abstract

Propolis has been recognized for centuries. In the historical documents from ancient Greeks, Romans, and Egyptians the healing potential of propolis was mentioned and had been used as a medicine against diverse health problems. Despite its long history in medical practice, Propolis has only recently attracted the attention of the scientific community. Among the various pharmacological effects were determined so far, many of its healing benefits have been attributed to particularly its antimicrobial, antioxidant, anti-inflammatory activities. There is recently a significantly growing scientific interest to discover the possible role of propolis in cancer prophylaxis and therapy. A PubMed search with a keyword to find the published papers related to its medicinal specifications has revealed that there are 3645 scientific papers and 27% of them reported its possible contribution to cancer prophylaxis and treatment. Accordingly, propolis has been reported to show the following effects on cancer cells; hinders uncontrolled growth of cancer cells, provides selective apoptosis of cancer cells, interferes with a specific cancer signaling pathway, reduces angiogenesis, prevents metastasis, regulates tumor microenvironment. On the other hand, propolis may also indirectly reduce the cancer risk by strengthening the body's resistance, supporting the immune system. Moreover, propolis may provide an adjuvant effect to increase the efficiency of Chemotherapy/Radiotherapy treatments by increasing the sensibility of cancer cells to therapeutic agents. There is also strong evidence that propolis may reduce the risk for organ damage and may help to rebalance blood biochemical values during Chemotherapy/Radiotherapy treatments. This presentation aimed to discuss the possible role of propolis in the prophylaxis and therapy of cancer.

Keywords: Propolis, Cancer, Adjuvant, Organ Damage

Oral Presentation

Propolis in Breast Cancer

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Abstract

Breast cancer is the most commonly diagnosed cancer in women and the second leading cause of cancer related deaths. Although increased awareness and screening applications reduced mortality, the numbers are still increasing. Moreover, the more aggressive types are more common among women under 45 years of age, which lack of efficient therapy approaches and de novo or acquired resistance to therapy stands out as a significant challenge. Therefore, researches are turning into natural products with no adverse effects and high efficiency. Propolis, a resinous bee product, contains a diverse range of phenolic compounds depending on the region with anticarcinogenic effects. In a previous study, we have demonstrated that different propolis samples collected from different regions show different effects due to their varying phenolic content, some are even ineffective. The most effective sample stands out with the low doses of a highly diverse phenolic content. These different phenolic compounds target various cellular mechanisms simultaneously. This is referred to as 'confusing the complex system with many weak hits', which is the best approach regarding the precarious nature of cancer. In our more recent study, we investigated the gene expression patterns of Anatolian propolis that had been found the most effective on various breast cancer cell lines. Although gene expression patterns of propolis treated cells differ, immune response, cell cycle and apoptotic pathways stand out. Finally, propolis seems very promising in cancer treatment; however, propolis samples may be contaminated with pesticides or heavy metals. Therefore, content analysis is crucial and propolis with high diversity of phenolic content should be preferred.

Keywords: Propolis, Breast Cancer, Microarray

#Istanbul Development Agency (ISTKA/2010/KBO-62).

Oral Presentation

Bee Venom and Melittin in Possible Cancer Treatment

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Abstract

It is well known that natural products and secondary metabolites can inhibit cancer cell growth and metastasis by activating different pathways including apoptosis. These were suggested that natural compounds as an alternative medicine may be used for treatment of human cancers. One of the best example of the natural products is Honeybee (*Apis mellifera*) venom. It contains various molecular weight peptides and proteins (melittin, apamin, adolapin), biologically active amines (histamine, epinephrine) and several non-peptide components including lipids, carbohydrates and free amino acids. Bee venom has been used skin diseases, the relief of pain and the treatment of chronic inflammatory diseases, such as rheumatoid arthritis in oriental traditional medicine. Cell culture and animal studies showed that bee venom (BV) has anti-cancer activity. Studies in our lab showed that Bee venom obtained from Anatolian honeybee showed cytotoxic and apoptotic response in variety of cancer cell lines, including prostate, colon, liver and cervix. Moreover, it was very effective in treatment of hepatocarcinoma in diethyl nitrosamine-induced liver cancer animal model. Anticancer activity of bee venom is attributed to its main component, namely melittin. Recent research showed that this small peptide can involve in inhibition of cancer cell proliferation, metastasis, angiogenesis and induction of apoptosis and necrosis. All these results show that bee venom and its main component melittin may be possible candidates of cancer treatment agents. However, further studies will be required to reduce their side effects and to increase their efficacy for therapeutic applications.

Keywords: Bee venom, Melittin, Cancer, Apoptosis, Cytotoxicity

Oral Presentation

Antitumoral Effect of Anatolian Honeybee Venom on Glial Tumor Cell

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Abstract

Honeybee venom is a special mixture of protein, lipid and low molecules that honeybees secrete by their venom glands in order to defend their colonies against the enemies and inject through their sting. Bee venom has been using in traditional and complementary medicine for centuries to treat immune-related diseases. The most active ingredients of honeybee venom determined as; melittin, apamin and phospholipase A2. This specific mixture has been known by its positive effects on chronic pain, arthritis, antitumor, skin diseases and neurodegenerative diseases. Malignant (high-grade) gliomas are fast-moving brain tumors consisting of anaplastic oligodendroglioma, anaplastic astrocytoma, mixed anaplastic oligoastrocytoma and glioblastoma (Louis et.al., 2007). There is no clear treatment strategy in the progression of primary glioblastoma. Current treatments can significantly decrease the survival and life quality of patients. For that reason, new treatments in traditional complementary medicine are being studied. In this study, it was aimed to determine the antitumoral effect of Anatolian bee venom on glial tumor cells. The lyophilized bee venom prepared at 0.7, 1.5, 3.0, 6.0, and 12.5 µg/mL doses and applied to three study groups of 24, 48 and 72 hours which formed and evaluated with the WST-1 kit. As a result of the study, it was determined that Anatolian honeybee venom has an antitumoral effect on C6 cells. Based on this result, it is planned to reveal the mechanism of action of bee venom on C6 cells through molecular pathways in our future studies.

Keywords: Antitumoral Effets, Bee Venom, Glial Tumor Cell, WST-1

Oral Presentation

Use of Beehive Products to Prevent and/or Treat Basal Cell Carcinoma

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Abstract

Basal cell carcinoma (BCC)is an extremely common form of skin cancer that is normally treated in allopathic medicine by surgical removal (MOHs surgery), burning or freezing out of the skin. If extensively required, this treatment can often lead to disfiguring surgery and there is a high incidence of the BCC returning. This paper is about a treatment of extensive facial BCC using bee products in combination with high-tech cold plasma. The treatment was at the insistence of the patient delaying conventional treatment as she did not want to be facially disfigured. The treatment was performed with the co-operation of her doctor and the results documented in this paper were very encouraging. This paper explores the tumor shrinking properties of propolis, bee venom and cold plasma. The treatment was able to eradicate the topical BCC sores, rejuvenating the skin and was supported using specially formulated topical propolis and bee venom cream. Propolis and bee venom have documented benefits for stimulating collagen and elastin as well as apoptosis. The subject also took internal propolis capsules to help prevent recurrence of the BCC. This paper documents how all three – propolis, bee venom and cold plasma- have been successfully proven to perform to shrink and prevent tumors and appeared to do so with this procedure. As far as we are aware this treatment has not been attempted previously.

Keywords: Basal Cell Carcinoma, Beehive Products, Prevention, Treatment

Oral Presentation

Relationship between Telomere Length and Beekeepers

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Abstract

Though it is believed that beekeepers live longer is present since ages, there is dearth of research exploring on the longevity of life in beekeepers. Telomeres are the tandem repeat sequence of TTAGGG associated with telomere-associated proteins called shelterin. With every cell division, there is shortening of telomeres because the DNA replication machinery cannot copy the ends of the linear molecules. Telomere length is considered to be a marker of biological ageing and shorter telomere length has been associated with ageing and human ageing-related diseases. Due to this reason, telomere length can act as a good indicator for measuring the longevity of life biologically. Hence, this research was set out to investigate the telomere length in 30 male beekeepers and 30 male non-beekeepers using Southern analysis of terminal restriction fragments and to associate them with their longevity of life based on TeloTAGGG Telomere Length Assay. The results showed that the telomere length of beekeepers was significantly longer than those of non-beekeepers ($p < 0.05$) which suggested that beekeepers may have longer life span in comparison to non-beekeepers. It was also found that the consumption of bee products for a long period and frequent consumption of bee products per day were associated with the length of telomere. An increase of year in consuming bee products was associated with a mean increase of 0.258 kbp in telomere length. Moreover, an increase in frequency of eating bee products per day was also associated with a mean increase of 2.66 kbp in telomere length. Hence, it can be hypothesized that bee products may play a role in the maintenance of telomere length.

Keywords: Telomere length, Longevity, Beekeepers, Southern blot.

Oral Presentation

Apitherapeutical Properties of Major Proteins of Royal Jelly in Light of Epigenetics

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Abstract

The most important component of royal jelly (RJ) in terms of apiterapy is a family of nine major protein referred to as MRJP or easier to name apalbumin. They have multiple pharmacological activities: such as life extensions, antiallergic, antitumor, antihypercholesterolemic, antihypertensive, anti-inflammatory effects and other. They are a model for the development of multifunctional drugs by using knowledge of the sequence of bee genome and epigenetics. The honeybee's genome represents a superpower among the genomes. The bee-worker or queen are formed from exactly the same DNA sequence by the action of an external epigenetic factor in RJ. They differ in appearance, perform completely different jobs, and the queen lives 10 times longer than her worker bees. The bee genome responds very flexibly to nutritional signals during the larval development of the bee. The key to recognition of these phenomena is in epigenetic changes - chemical labels that, when added or removed from DNA, change the activity of genes, without changing the order of nucleotides in DNA. For example, DNA methylation accompanies many diseases, especially in the aging process. The bee appears in epigenetics in two roles. In the first, it presents itself as a model for understanding the general laws of epigenetics. In the second role, it acts as a source of epigenetic substances that have a beneficial effect on human vitality and longevity. We can consider these substances as potential drugs - and I will tentatively call this drug Epigenomicum. I get the courage to say this: In the future, a patient would connect with prescribed drug manufacturer's website and using his or her individual program that contains a nucleotide sequence of his DNA, the patient will receive active substance of the drug, i.e. epigenomicum, which "epigenetically marks DNA or removes an unwanted mark", thus achieving the desired therapeutic effect.

Keywords: Honeybee, Royal Jelly, Proteins, Epigenetics, Longevity, Epigenomicum

Oral Presentation

Sustainable Productions Farms, the Ideal Home for Bees

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Abstract

The objective of this project is to become the starting point for a sustainable tourism development through the implementation of friendly agriculture that, will allow the farmer the option of producing fruits and vegetables organically and at the same time and the most important action plan: promoting the care of bees, who according to the Royal Geographical Society of London, are considered the most relevant species for life on the planet. However, they are threatened by the very action of human activities. For their part, with this they will be able to find healthy food, without chemicals, making this their home. For all the aforementioned to be a reality, tourism will be established as the essential base, whose alternatives generated from apitherapy, will be able to demonstrate the importance of bees. The project began with 17 enterprises that consider bees as part of their family, which are located in Ecuador, zone 1, specifically in the provinces of: Carchi, Imbabura and Esmeraldas, most of which are farms with differences necessary to implement in the future a conscious tourist api route. The first action implemented was to organize its members in a legalized association for the Superintendency of Popular and Solidarity Economy. So that funds can be raised from non-governmental organizations, to achieve actions aimed at strengthening enterprises and above all to achieve a welfare action and access to the rights of bees. At the moment, its implementation is carried out in the first Sustainable Production Unit which is made up of 20 hives that have been cared for more than 20 years by a rural family. The alternative for this UPS is to implement a beekeeping garden that, will be used for environmental education, likewise, it already has crops of uvilla and chili pepper, which will solve the economic needs of the family. In this case the uvilla will be processed and exported as fruit dehydrated and the chili will be processed by an entrepreneur from the region. On the other hand, it is necessary to propose solutions that allow an opportunity for these generous peasant women, whose main function in nature is save the world.

Keywords: Sustainable production, Bees, Rural enterprises.

Oral Presentation

Sustainable Pollen Production in Colombia and Verification of its Attributes as a Nutritional Supplement

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Abstract

Colombia is a tropical country located in the northwestern corner of South America, where solar radiation arrives perpendicularly throughout the year. This condition, in addition to the presence of plains and mountain systems, generates a great variety of climates and microclimates. The mountain chain of the Andes crosses the country; there is a large part of the natural wealth, population and economic activity. As one ascends the mountain, there is a progressive decrease in annual average temperatures, at an average rate of 1.8 °C per 100 meters above sea level. The main pollen-producing region of the country (40 kg / hive. year), is in the high mountain, at 2,600 meters above sea level, in an extensive flat area of the eastern Andes, called the Cundi-boyacense High plateau, where the average daily solar radiation of 5000 Wh / m2. Through various research and extension projects, it has been possible to improve production practices to ensure the safety of pollen, studies have been carried out on its composition and bioactive characteristics and progress has been made in sustainability indicators to meet the requirements for its commercialization at national and international level. It was found that, without deterioration of its nutritional properties, it is possible to dehydrate pollen, a costly stage due to energy consumption, replacing the use of electric dryers with chambers where solar radiation is used in a passive way, that is, without the use of photovoltaic cells, but taking advantage of the effect of the solar radiation on decreasing the relative humidity of the air confined in the chamber and its subsequent effect on the activation of convection and on the removal of moisture from pollen to the air. It was also found that the pollen produced in this High plateau, ready for commercialization, contains on average (dry basis) 23.8% protein, 6.9% lipids, 14.5% dietary fiber, 2.5% ash and 23.8% carbohydrates. Within minerals: 90 ppm Na, 5030 ppm K, 495 ppm Mg, 1700 ppm Ca, 45 ppm Mg, 47 ppm Zn, 63 ppm Fe and 9 ppm Cu. The lipid conformation was determined: 34.9% SFA, 8.9% MUFA and 56.2% PUFA. With respect to pollen from other sources, the fatty acid content stands out: 44.1% ω−3 (identified as C18: 3 ω− 3 α-linolenic acid) and 11.9% of ω−6, with a relationship (ω−3) / ω−6) = 3.7. In addition, this pollen contains carotenoids, 221 µg Zea / g, a value between 5 and 10 times higher than that of pollen from other sources. The antioxidant activity is 89 µmol TE / g, a value equivalent to 10 times that of recognized fruits, which can be explained by the high solar radiation in the area. Due to the magnitude of the values found, and with a daily portion of 10 g, the pollen produced in Colombia can be considered a nutritional supplement in terms of dietary fiber, potassium, calcium, iron, ω−33 fatty acids, carotenoids and antioxidant activity, in addition to its low sodium content.

Keywords: Pollen, Composition, Bioactive Properties, Solar Dehydration, Fatty Acids

Oral Presentation

Quality Control in Products Made with Apitoxin

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Abstract

Apitoxin or bee venom (Apis mellifera) has been used by man as a therapeutic alternative for 3000 years to treat a large number of rheumatologic and autoimmune diseases such as arthritis, osteoarthritis, osteoporosis, lupus, multiple sclerosis among others. These therapies have evolved from a simple bee sting to the dosage and preparation of products that provide an effective and focused action. Within the industry, selecting the best raw material is the cornerstone to produce a quality product, especially if it is of animal origin. Analysis is required that provides the certainty of its good condition and innocuousness, an option to determine the quality of the raw material as well as of finished products is the method of separation and identification of chemical components of bee venom by HPLC that provides a more diagnostic accurate of the characteristics of the samples and the quantification of the active principle in finished products.

Keywords: Bee Venom Products, Quality, Production

Oral Presentation

Reflections, News and Recommendations in Therapy with Products from the Beehive

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Abstract

We will talk about this ecosystem of the hive from its appearance on earth until today, how it has been transformed and the scope it currently has, we will talk about the presence of this procedure and its documentation in the scientific field, we will address the main obstacle in the population As consultants, we will analyze the realities worldwide in how it is carried out, we will propose how to improve and update this important procedure in today's life. We will briefly review the products that the hive gives us the traditional ones and the new proposals to get the most out of it for the benefit of human health, we will call on our allies the beekeepers to provide therapeutic resources that are currently not commercial, we will address the routes of administration of some products of the hive mainly apitoxin, honey, royal jelly, propolis. We will review the good to do with our consultants in their first contact with apitherapy, the information that the apitherapist will provide and the record of acceptance by the patient, we will propose how to apply puncture techniques of apitoxin to control adverse sensitivity processes and thus offer greater security In therapy, we will mention the importance of its registration, monitoring and evolution of the therapies of each of the patients, we will call for the integration of a collegiate group with sufficient experience to create the bases of a standard model in the application of the apitherapy.

Keywords: Beehive Products, Recommendations, Apitherapist

Oral Presentation

Conservation of Native Stingless Bees in Mexico and Its Relationship with Modern Therapy

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Abstract

The native stingless bees, belonging to the Meliponini tribe (Apidae), represent for Mexico a biocultural legacy because they have been and continue to be cultivated by indigenous peoples, in addition to a growing interest of the general population to cultivate them due to their docility and to the therapeutic value of its products. For this reason, the present work aims to show the relationship existing in the conservation of these bees with the therapeutic value of products such as virgin honey, pollen and propolis that these bees produce. The record of meliponine species in Mexico and their distribution in the country is taken into account, as well as the growing cultivation activity where colonies of bees are transported to different areas, due to the fact that they do not have a stinger and ignoring that they require a habitat. special in which they have evolved for millions of years. This evolution has implied associating with tropical and subtropical plants, which have been used in the ancestral pharmacopoeia of indigenous peoples and from which bees take the resources to make their own products. Fact that has been ignored by people who have not been adequately trained, taking different species of stingless bees to places where despite the similar climate conditions that may exist, they do not find the original floral resources and not only condemn them to long-term death but not to be productive. The main ailments in which the products of native stingless bees are used today with very good results are mentioned. Some examples are shown that when there is production, their products (honey, propolis, etc.) may not show the original organoleptic characteristics, as well as the therapeutic effectiveness that have always characterized these insects. Despite the need for studies of this type, calls have been made not to transport colonies out of their natural habitat; However, the desire to commercialize their products and use them in alternative therapies have clouded this conservation of the colonies, whether wild or in cultivation.

Keywords: Melipona, Apis, Mexico, Apitherapy, Derivate, Stingless

Oral Presentation

Treatment with Meliponiterapia and Natural Medicine in Pressure Ulcers

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Abstract

The honey of native bees without sting or meliponas is a very important product nowadays since it has properties of medicinal interest due to the flora that they visit to collect resources and in return pollinate the plants. The pre-Hispanic cultures of Mesoamerica, Mayan, Totonac and others perfected meliponiculture for thousands of years and used honey to cure various health conditions, thus initiating meliponitherapy. The antibacterial properties are due in part to its hygroscopic capacity and the presence of various enzymes, as well as many phenolic compounds, flavonoids, and others. Antimicrobial activity is one of the main biological properties of honey from bees. The osmotic effect due to the high sugar content of honey gives it antibacterial activity, however various microbiological studies indicate that honey has other more effective antibacterial components. The enzyme glucose oxidase allows glucose to react with free oxygen and water molecules, generating gluconic acid and hydrogen peroxide. Worldwide, Apis sp honey has traditionally been used as a natural therapy, however recent studies on stingless honey have discovered that it is therapeutically more effective and is therefore an alternative in various medical treatments against pathogenic microorganisms. On the other hand, the increase in resistance to antibiotics leads to the use of natural treatments such as Melipona honey. The honeys of various Meliponinos have proven to be effective as bactericidal treatments of species such as Pseudomonas aeruginosa, Staphylococcus aureus, Bacillus subtilis, Candida albicans, Streptococcus's neoformans, Escherichia coli, Salmonella typhi among others. The methodology used was to apply Melipona honey to various wounds and ulcers, first performing aseptic cleaning, then the application of Melipona honey and closing with gauze covered with wax and propolis. The treated patients had wounds and ulcers which worsened with conventional medical treatments, so they went to apitherapy where Melipona honey is used mainly for treatment of wound infection, achieving better wound healing and closure, allowing granulation, stimulated epithelialization. for the Melipona honey. It is concluded that Melipona honey is very effective since it inhibits the growth of bacteria that cause many complications in common wounds.

Keywords: Melipona, Pressure Ulcers, Natural Medicine

Oral Presentation

Medicinal Uses and Vision of the Products of Meliponini Bees in Mexico

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Abstract

For centuries, the Maya people of the Yucatan Peninsula have had a close relationship with the native stingless bees, *Meliponini,* mainly with the *Melipona beecheii* bee, through its breeding and care, and they used the honey as a medicinal product of great curative power, endowing it with religious and mythical faculties. The honey was used for all type of sicknesses as a principal element to restore the health of the patients. It is frequently mentioned in the traditional Maya recipes, for its use to heal ailments of the respiratory, digestive, circulatory and immunological systems. It was also applied to remedy illnesses of the sense organs such as the skin, eyes and ears, the mouth, tongue, gums, and teeth. An important employment is to heal the sicknesses called "fevers" and dangerous diseases belonging to the Maya world vision, with special characteristics and supernatural etiology.

Keywords: native bees, stingless bees, *Melipona beecheii,* native honey, virgin honey.

Oral Presentation

Importance of Bee Products in Nutrition

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Abstract

Honey, pollen, bee bread, royal jelly and propolis have high dietetic and nutritional value and beneficial effects to human health. Honey is good source of energy and carbohydrates as well as minerals and vitamins. Also, honey contains antioxidants, aromatic components, and enzymes. The source of flower nectar categorizes different types of honey, according to some data there are hundreds of types of honey, and each boasts special health and nutritional benefits. Nutritional properties of honey also depend on the type and content of pollen grains and other ingredients. People commonly take bee pollen for nutrition. Bee pollen contains many BAC-like carotenoids, polyphenols, flavonoids, alkaloids, glycosides, as well vitamins, minerals and other antioxidants. Numerus studies have linked bee pollen and its compounds to health benefits such as decreased inflammation, as well as improved immunity, menopausal symptoms and wound healing. Pollen is a functional food for human consumption with a wide range of functional properties, such as antioxidant, antimicrobial, anti-inflammatory, anti-radiation and hepatoprotective activity. The chemical composition of propolis, as well as the content of biologically active compounds in it, depends on its botanical and geographical origin, the type of bees, as well as the season in which propolis is collected. Propolis is available today in numerous preparations, which can be in the form of capsules, drops, sprays, creams, powders and lozenges. It has a preventive effect on sore throats and periodontitis. The natural form is the best form, but it is very unstable and also the active ingredients are labile. The Royal jelly is immunomodulatory agent, stimulates cell growth and stimulates cell growth in the brain.

Keywords: Nutrition, Benefit, Bee Products

Oral Presentation

Principles of Api-nutrition

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Abstract

Nutrition has been a concern of mankind since ancient times. An old Ayurvedic proverb states "When the diet is bad, medicine is not helpful. When the diet is correct, medicine is not necessary". Research on health, disease and longevity clearly shows that people who follow mainly a whole-food plant-based diet, have significantly better long-term health results. It has been shown that this kind of diet make people feel well nourished, full of vitality able to have a long, happy and healthy life. Therefore, we sought to find a balanced diet that would fulfil the body`s complete needs. This is what API-NUTRITION suggests - combining the principles of a healthy diet with bee products daily. Raw bee-products meet important requirements for a healthy diet: they contain various nutrients and micronutrients: proteins, fatty acids, glucose, antioxidants, minerals, vitamins, pre- and probiotics, enzymes, including telomerase, the "longevity enzyme". Bee products are accepted as "functional food", meaning that beyond their basic nutritional features they bring a positive contribution to our health. We know already that bee products strengthen the immunity, help the body fight with bacteria, increases the level of the beneficial bacteria in the gut, stimulate the tissue regeneration, and consequently protect overall body health. Using them properly we maintain and improve our health, life quality and life span. This presentation will offer basics of Api-nutrition and results obtained with it.

Keywords: Api-Nutrition, Bee products, Functional food, Health

Oral Presentation

Apitherapy, Fermented Honeybee Products

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Abstract

This study aims to examine the results of the relationship between honeybee main products and by-products and traditional, natural, or industrial fermentation. Thus, humanity will be able to encounter more healing products. Storing and consuming honeybee products by fermenting will provide people with better quality and beneficial living environments to meet their health and nutritional needs in a longer and safer manner. Fermented honeybee products are beneficial not only to humanity but also to bees in the fight against viruses, bacteria, fungi, and similar microorganisms of the immune system. A whole new level of protection and resistance to bee diseases can result in the success of fermented bee products. For example, a microbiota element in the digestive system of bees can prevent brood rot in bees, while the natural fermentation formation of bee pollen into bee bread (Perga) can bring new approaches to maturation and storage of nutrients.

Keywords: Honeybee Products, Fermentation, Health Benefits,

1. Fermentation of honey

As it is known, the sugars that are densely found in honey constitute a little more than 80% of the total carbohydrates (honey sugars). Thanks to the invertase enzymes in bees, the sucrose taken with nectar undergoes changes and turns into glucose (dextrose) and fructose (levulose) and forms inverted honey sugar. Sucrose, maltose, and other reduced sugars and high molecular Erlose and Melezitose sugars also take their place in honey sugars. In other words, the concept of tea sugar in the market and the sugars in honey are not the same. In addition, the glycemic index values are low <55, medium 55-70 values according to the source of honey, while the high glycemic index for tea sugar is> 70.[1]

The structure of honey is enriched with organic acids and natural nitrogenous substances, amino acids, minerals, pigments, aromatic and flavoring esters, alcohol and aldehydes, tannins and enzymes, and proteins and vitamins. Since these structural features can change in each honey, evaluations should be made with precision in monofloral or multi-floral honey and commercial honey.[2]

In the natural structure of honey, water can be found between 17% and 20%. During the spontaneous ventilation during the transfer of the nectar collected by the foraging bees to the young bees in the hive from the mandibles to the mandibles, or with the social bee consciousness, the immature honey with a high-water rate placed in the honeycomb chambers is evaporated by flapping its wings and evaporating the humidity at the most reasonable level. Efforts are made to reduce it to around 17s. The secret of honey is that during this process, honey with high humidity is uncovered and taken before it is matured by the unethical behavior of beekeepers with high commercial ambition, if the water rate in honey remains higher than 18%, fermented honey caused by naturally occurring yeasts will occur. The maturation of honey is essential for bees. In other words, while the honeycomb chambers are filled with honey, the

water content in it is 60% in nectar, and after it is reduced to 17-20% in honey, it is glazed in a way not to take the air. These physicochemical processes performed by bees in their short lives actually show that honey is produced by chemist bees working with zero error.
The chemical composition of nectar, which is a sugary mixture, is also changed by the enzymes in the bee's stomach. The main sugar of nectar is Sucrose, which is a disaccharide. Unlike all other sugar types, the sucrose molecule atoms are linked by 2 saccharide rings, while the bee's invertase enzymes split each sucrose molecule into two smaller molecules: glucose and fructose. These two resulting monosaccharides have a higher solubility than sucrose. Thus, bees obtain honey with better quality and appropriate viscosity. The structure of honey, which can give high energy, is very easily digested for both human and bee feeding. The harmony of the water ratio counteracts the growth of yeast and bacteria in the honey, with the possibility of osmosis. In short, honey is a formation suitable for lean food and health with excellent functions.[3]
The relationship between fermentation and bee products naturally depends on the water ratio in the honey and the bacterial environment of the environment in the hive. Enzymes found in the bee's digestive system and a few bacteria such as Lactobacillus play a role in some important formations. But the essentially important structure of honeybees, such as mitochondria and using very valuable life elements such as amino acids, initially explains that their relationship with fermentation will be compatible. In addition, it should not be forgotten that it is an environmentally friendly entity that uses energy economically with minimum waste.

2. Fermented Bee Products

2.1. Honey vinegar

Since honey is the most expensive and valuable raw material used in vinegar production, Honey Vinegar should be considered very carefully. It is obtained by bacterial and chemical oxidation of ethanol (also with the effect of bioactive elements) resulting from the other fermentation of invert sugars in honey vinegar.[4] When analyzed by grouping according to all other raw materials used in the production of vinegar, it appears to have a structure in which the most valuable compounds compared to an apple, wine, rice, and others are obtained.[5] The raw and auxiliary materials used in the production of vinegar create differences in the quality of the kinds of vinegar. For example, apple cider vinegar is characterized by high levels of malic acid and alanine, while both orange and rice vinegar are rich in lactic acid. In honey vinegar, the difference in honey sources changes the quality of the vinegar. In addition, the flavor and smell, and acidity of vinegar in oak barrels or different wooden containers vary. Plastic and aluminum containers should not be used for vinegar.
The amount of water used in honey vinegar and monofloral honey affects the density of phenolic components. Besides valuable phenolic compounds, honey kinds of vinegar, which have high antioxidant activity and antimicrobial effects, can also be used to obtain alkaline environments that increase intercellular permeability.

2.2. Mead

Drinks made with honey are among the most well-known products of beekeeping in folk culture and not only sherbets with which honey is mixed. In addition to the use of honey to sweeten foodstuffs, it has also been used for preservation and as a sign of wealth in history. There are many examples in ancient Maya, Sumerian, Egyptian and Greek civilizations such as Rakomela, Metaxa, and so on.
Mead; Although it is a low alcohol drink, it is considered a beekeeping product to stay out of taxes and other regulations. It is a traditional low alcohol honey drink preferred in monasteries

among the vineyards. It is often described as honey wine or mead. A honey beer is a similar mild alcoholic honey drink in Africa.[6]
Mead, or honey wine or liqueur; It is made by brewing honey, water, and fermented yeast. The types of mead known with different names are as follows.
Mulsum / Omphacomel / Pyment: Grape wine flavored with honey.
Balche / Pitarrilla: Mead fermented with Balche tree bark.
Capsicumel: Pepper fermented mead
Cyser: Honey and apple fermentation drink
Hydromel: Light honey drink
Melomel: Fruit honey drink
Metheglin: The fermentation of elderberry flower, spices, herbs, and honey by combining with water.
Ethiopian Tej: Powdered leaf and bark mead
There are many recipes for mead making. Honey, water, yeast food, citric acid, tannin (thuja powder) are heated at 65.5 degrees. This mixture is placed in a glass bottle and rested with yeast at approximately 21 degrees. The fermentation, which remains after 4 or 5 days, continues at 18 degrees. This beverage, which is obtained by choosing herbs and spices for taste and smell, is stored in clean bottles or jars in cool places so that it is not airtight. Citrus honey is preferred because it is a light honey with an aroma.
Although Mead is a derivative product, it is the physicochemical composition and microbiota of honey that bring the water and other fermenting substances involved in the process to different changes and present a new taste and benefit to consumers.

2.3. Sirkencubin

It is a Mevlevi and Ottoman sherbet made of vinegar and honey under the same conditions without waiting too long. The disappearance of vinegar in the sea of honey in Mesnevi's Volume V, page 166, line 2024 is compared to the test of a lover dervish. In fact, when both vinegar and honey are combined in the water environment in physical life, they disappear, and the fact that honey is a part of a realm that has a different taste and benefit by completely changing its physicochemistry with new particles shows its submission to dynamism. In the traditions of the Turkish people, it is referred to by the combination of two Persian words (the word ***serke*** and the word ***angabin***). Sirkencübin or Sirkengebin, meaning vinegar honey sherbet, is a honey drink used by the people and is believed to be healing. However, it would be beneficial to conduct and develop a food chemistry analysis anywhere.[7] It is very easy to make. Mix 1 liter of warm water, 5 spoons of honey, and 5 spoons of vinegar. Honey vinegar, apple, or grape vinegar can also be used. For a glass of water, a teaspoon of honey and an equal amount of vinegar are mixed and can be drunk one night later. It can be repeatedly tried to indigestion or to keep fit. This mixture is considered a very simple hygienic application for sustainable living. Its other name is Mevlana Sherbet. Additive spices make this mixture normal Honey Sherbet.

2.4. Fermented Propolis

As it is known, propolis has recently been used in the fight against all diseases, as raw as it is taken from the beehive or by tincture with other chemical solvents, especially ethyl alcohol, powdered Propolis mixed with honey or evaporating in Api-air.
Chemical applications for obtaining fermented propolis extract have reached industrial dimensions by going beyond traditional production and bringing new opportunities to producers and consumers by obtaining many patents. Tinctures of ethanol and water mixtures in various proportions are vacuumed and dried with the addition of microcrystalline cellulose

up to ten times the possible soluble particles in it and turned into powder propolis by mill gravity. The powder is pasteurized after adding twenty times its weight of water to the propolis. Bacteria such as yeast, bacillus, lactobacilli, and acetobacter, and aspergillus are inoculated, and their fermentation is completed by the waiting period.[9]
Fermented propolis has achieved water solubility by stripping its adhesion compared to propolis extracts. By separating from ethanol, it eliminated the use problems of the elderly and children. While public health improves the well-being of people with ease of use, its contribution to the economy will also increase.

2.5. Perga and Pollen

Pollen is an excellent food that bees bring to the hive while collecting nectar from flowers, when they cause pollination, by wetting the spilled flower powders by wetting the mouth mandibles, collecting them through their front legs, placing them in the pollen-collecting mechanisms on their hind legs. It contains small amounts of lipids, necessary amounts of natural proteins, carbohydrates, plenty of vitamins and minerals, as well as all of the amino acids and enzymes. Bees hatch their larvae; They feed on royal jelly, honey, and pollen. However, after the pollen arrives in the hive, it takes 2-3 more processes following the collection from the flowers. During these processes, the bacteria and enzymes in the fluids that come out of the bees' bellies cause the pollen to crack and disintegrate the outer shells and the rich mixture in it to ferment.[10]
Many microorganisms take part in the transformation of pollen into Perga. Bacteria and yeasts, with the enzymes they secrete, facilitate the digestion of bee bread and increase the biological recovery. It has been observed that microorganisms similar to each other are effective in the digestive system of the honeybee, bee pollen, and bee bread. Lactobacillus, Bifidobacterium bacterial species, and as yeast Candida spp. and Torulopsis spp. While Bacillus species secrete enzymes of different genes, Candida Species contribute to fermentation by secreting proteases and phospholipases enzymes. It is a food with high total phenolic content, total flavonoid content, and total antioxidant capacity.
Perga can be applied for pediatric purposes, especially in premature children up to the age of 10, as well as children with anemia, pneumonia, and bacterial infections. Bee bread helps in the treatment of blood pressure and chronic constipation with its high content of acetylcholine. It helps to increase the physical and mental strength of individuals. It also has antiseptic and germicidal properties. It is useful in the treatment of bleeding gum protection. With its contribution to reproductive hormones, it helps men to improve their sexual life and increase their muscle strength.

3. Results

The fermentation process is reaching a very important place in both the food and health industries. Whether traditional, modern or industrial, different sizes of features show that the relationship between bee products and fermentation will continue. In fact, there is no doubt that folk culture and traditional structure will preserve the more aesthetic and artistic structure in terms of taste, flavor and healing, and organic understanding in fermented bee products and maintain the competition. However, the economy and industrial processes have to increase the supply by following technological developments to keep up with the rising demands of the societies for fermented bee products by producing on a large scale. In the fermented bee products sector, Turkey should make every effort to keep a place worthy of our country in the world.

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Oral Presentation

Applications of Apitherapy in Urology

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Abstract

Apitherapy products are honey, bee pollen, bee bread, royal jelly, apilarnil, propolis and bee venom. Bee polen has been used in the treatment of moderate benign prostatic hyperplasia (BPH). There are many clinical studies conducted with drugs containing Gibberellin, which is contained in pollen. Pollen extract has also been found effective in the treatment of 16 prostatitis patients with hematospermia. Phytosterols in pollen prevent benign prostatic hyperplasia. Beta carotene in pollen reduces the risk of cancer. Effect of bee venom in BPH has been shown in experimental studies. There are many studies conducted on infertility with pollen. Bee polen is affective on ovarian cells and testicular cells. Bee pollen and date palm pollen ameliorate the sperm quality in diabetic rats. Royal jelly contributes to animal reproduction. It reduces the testicular damage caused by hydroxyurea group of medications used in cancer. It reduces the damage of cadmium to testicles. In a study performed on 83 infertile males treated with royal jelly; it has increased the sperm quality. Sexual desire increased as well. In a study performed on 83 infertile males treated with royal jelly; it has increased the sperm quality. Sexual desire increased as well. Caffeic acid (CAPE) in propolis reduces the testicular damage caused by cadmium. Propolis reduces the testicular damage caused by paclitaxel (taxon). In addition, application of apipuncture can be used in erectile dysfunction. Propolis and cranberry have been found useful in recurring cystitis. Propolis has been found effective in bladder cancer cell culture. It has been found effective in prostate cancer cell culture. Royal jelly increases the efficiency of molecular therapy medications used in advanced stage kidney cancer; reduces their adverse effects.

Keywords: Benign prostatic hyperplasia, Bee pollen, Infertility, Royal jelly, Cystitis, Propolis

Oral Presentation

Application Hints for The Use of Bee Venom Summarizing Some Case Studies Treatment for Ligament and Sinew Injuries

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Abstract

The use of bee venom for a lot of applications like rheumatism, autoimmune diseases or inflammatory processes as well known. In this contribution it should be described when it is recommendable to use bee venom for ligament and sinew injuries, which are often associated to sports or overload like tennis elbow. In these cases, bee venom can work greatly beneficial: Pain is stopped. The healing process will be enhanced. Inflammation is avoided. Nevertheless, that treatment has some intrinsic footholds which shouldn't be overlooked. Pain is an alarm signal to protect the body against overload. Locking this kind of alarm system means that in case of continuing overload more severe damage can happen. This contribution covers the necessary apitherapeutic actions. On the other hand, these actions have to balanced out in order to reach satisfying results.

Keywords: Bee Venom Therapy, Ligament and Sinew Injuries

Oral Presentation

Clinical Study of Propolis in the Treatment of Diabetes and Its Complications

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Abstract

A large number of experimental studies on white mice show that oral propolis has the obvious effect of regulating blood glucose. In addition, the application of propolis on the wound can kill bacteria, diminish inflammation, and promote wound healing.

Keywords: Blood glucose, Bacteria, Inflammation, Wound

Oral Presentation

Why Should Apitherapy Be Used in the Treatments?

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Abstract

"What is eaten and drunk is one of the causes of illness" Avicenna said. Nutrition is not an action only. "The human genome has a complex network. Genetic and environmental factors are completely intertwined. To attribute health problems to genetic predisposition is to ignore society's responsibility for diseases. "says the scientists who are working in the gen project. If we do not want to be sick, we must know the ways of protection. Nutrition and lifestyle changes are always included in the treatment guidelines of all chronic diseases in the world and in the first step of treatment. Because health is "A state of complete well-being physically, spiritually and mentally". In this context, apitherapy; In the stages of health protection, improvement and nutrition with bee products; Bee sound is in maintaining and repairing spiritual well-being with its amazing sound frequency; Hive air fulfills all the parameters of the definition of health with its use in the prevention and rehabilitation of lung diseases and degenerative nervous system diseases. Everything in our body is the based-on frequency and stimulation. If you give suitable stimulus the body gives you answers. During this pandemic period, we have seen that the most important issue is a having healthy body and not getting sick. If we want to be healthy, we must be conscious that the miracle of nature, so bees and their products must be in the knowledge scale of people and physicians. If preventive medicine is important, apitherapy effects cannot be denied.

Keywords: Apitherapy, Bee products, Venopuncture, Bee voice, Hive air

Oral Presentation

Palliative Care and Apitherapy

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Abstract

Today, new difficult processes that influence both patients' and their families' comfort and quality of life due to many diseases becoming chronic, increased number of chronic diseases and lengthened survival have emerged. These difficult processes have put an emphasis on the importance of palliative care, which includes multidimensional care that patient and families need. The objective of palliative care is to prevent, to alleviate or to eliminate the symptoms that disease causes and thus to offer patients and their families a life of high quality. To achieve that objective; evidence-based pharmacological and non-pharmacological traditional and complementary medicine methods are used in palliative care. As the necessity of palliative care is better understood, regulations to improve palliative care services have lately been accelerated in our country as well as over the world and "Apitherapy"–one of the traditional and complementary medicine methods- is used in palliative care settings. In this presentation, it is discussed how apitherapy is used in palliative care practices.

Keywords: Palliative Care, Apitherapy, Symptom Control

Oral Presentation

Role of Apitherapy in Rehabilitation of The Patients with Obesity and Diabetes Type 2

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Abstract

Obesity and type 2 diabetes (T2DM) are common noncommunicable diseases worldwide. The treatment of obesity and T2DM is complex. Both obesity and T2DM can be treated by lifestyle interventions, dietary modification, pharmacological correction. Apitherapy have the potential for use in the treatment of both obesity and T2DM. Out of all apitherapeutic products, application of propolis in complex treatment regimens for obesity and T2DM was associated with the best results. In particular, patients receiving metformin and supplemental propolis of 300 mg/day were found to have a significant decrease in blood glucose levels 2 hours after a meal (postprandial glycemia), a decrease in plasma insulin concentration (respectively, a decrease in insulin resistance), and a decrease in inflammatory cytokine concentration. Also, the effect of propolis in patients with obesity and type 2 diabetes was characterized by improvements of liver function (decreased markers of cytolysis of hepatocytes ALT, AST), improved lipid profile (decreasing of cholesterol and triglycerides).

Keywords: Rehabilitation, Obesity, Diabetes

Oral Presentation

The Importance of Apiphytotherapy in the Surgical Approach of Open Arthritis - Case Report, Implications and Perspectives

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Abstract

Honey has proven multiple properties and effects favorable for wound healing. These actions can be very useful in cases of open arthritis, especially infected with multiresistant germs, when the local defense of the organism is deficient and other resources are limited. The work presents the application of a combination of honey and thyme volatile oil in a patient with open suppurating wrist arthritis due to a grade III-IV burn by electrocution at the level of the right hand and forearm. The lesions were deep, with necrosis of soft tissues and the opening and infection of the right wrist. The previous surgical treatment comprised multiple debridements, skin grafts and regional flap to cover the open joint of the right wrist, with bone exposure. Bacteriological analyzes from infected wounds revealed multidrug-resistant germs, such as Acinetobacter and MRSA. Combination of polyflora honey and 1% thyme volatile oil was applied topically pre and especially postoperatively at the level of the right wrist. The wound evolution was favorable, with remission of infection and progressive closure of the opened and infected wrist joint. The present case report is a difficult case of deep burn through electrocution, with invalidating injuries. It highlights the efficacy of the combination between the surgical treatment and the topical applications of honey with thyme volatile oil. The combinations of honey and volatile oils could be recommended in severe and infected wounds, due to the multiple actions on wound healing provided by honeybee products, together with the antiseptic action of volatile oils. These actions can be extremely favorable in problematic cases of wounds with bone exposure or open fractures, especially infected with multiresistant germs, with difficult healing, poor local defense and limited loco-regional resources. The combination of honey and thyme volatile oil represents a potent compound with wound healing and anti-infectious effects and can be applied especially in these difficult cases.

Keywords: Honey, Arthritis, Thyme volatile oil, Wound healing

Oral Presentation

Potential of Apitherapy in Preventive Medicine

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Abstract

The World Health Organization's Traditional Medicine Strategy for 2014-2023 encourages the member countries to develop their national health policies as integrated as possible. Apitherapy is the use of honeybees and bee products for health purposes. The main bee products are honey, beeswax, bee pollen, royal jelly, propolis and bee venom. Honey and bee pollen contain health promoting food ingredients and functional food components. Preventive medicine is the maintenance and promotion of health and the reduction of risk factors that result in diseases. Chronic diseases are the leading causes of poor health and long-term disability. However, many of the chronic diseases can potentially be prevented or delayed through primary prevention activities. The antioxidants play diverse physiological role in body by inhibiting the process of oxidation. They delay, prevent, or remove oxidative damage to a target molecule or directly scavenge Reactive Oxygen Species or indirectly acts as inhibitor of their production. They play important role in the prevention of free radical formation and helps in reducing various disorders. The immunomodulation effect of apitherapy products with high antioxidant content has highlighted the use of apitherapy applications especially in preventive medicine. This presentation reviews the literature on the apitherapy products and their potential in preventive medicine.

Keywords: Apitherapy, Antioxidants, Bee products, Chronic diseases, Preventive medicine

Oral Presentation

Use of Bee Products for a Healthy Skin

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Abstract

The aim of our short communication is to give information about the use of bee products in prevention and therapy of the most common skin disorders like acne, rosacea, furunculosis. We have developed a small brand of natural skin products which are the fusion of herbs, bee products, natural oils and lactic acid bacteria. Beside skin treatment, we developed a range of food products with natural herbal pigments conservated by honey and lactic fermentation. The combination of herbal antioxidants, pigments, lactic acid bacteria together with cosmetics is able to keep the skin healthy and young looking.

Keywords: Bee products, Skin, Cosmetics

Oral Presentation

Skin Health and Dermo-Cosmetics in Apitherapy: Exploring Possibilities for Expanded Use of Bee Products in Skin Rejuvenation Treatments and Formulations

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Abstract

Bee products are well known for their beneficial ingredients when it comes to skin rejuvenation, but are they hiding in plain sight? The recent "green rush" to research why the much-demonized plant, cannabis, is so effective as medicine has uncovered many helpful compounds that are well known to exist in bee products. The idea is then offered, why do not apitherapists capitalize on this new research into old compounds and make opportunities to market bee products alongside these fashionable "new" compounds "discovered" by the cannabis industry. Aromatherapists and plant medicine experts are also familiar with the plant compounds and terpenes in cannabis, but the wealth of new research inspired by the so called "green rush" can only aid apitherapists with new information to utilize and reformulate ancient bee products especially for skin treatments. There is also the possibility of exploring new skin treatments combining ancient bee compounds with ever evolving high-tech skin rejuvenation devices.

Keywords: Apitherapy, Skin, Bee products

Oral Presentation

Honeybee Silk: A Valuable Biomaterial

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Abstract

Silks are outstanding natural protein compounds produced by great number of insects and spiders. Honeybee silk is produced from the salivary glands. The honeybee salivary glands, also known as labial glands, are composed of two parts, both of which connect to the mouth. Honeybee silk has varied amino acid composition and composed of four fibrous proteins encoded by four small and non-repetitive fiber genes. Honeybee silk has α-helix and β-sheet structures. It is recently confirmed that the α-helical conformation predominates the principal molecular structure of honeybee silk. The molecular structure of α-helix proteins maximizes the robustness with minimal use of building materials for honeycombs. Honeybees, just before pupation, the larva cover the waxen walls of their cells with silk. Although wax is the primary building material for the nest, the honeycombs become modified with continued addition of silk and propolis. The spinning of silk by honeybees refers to the process of producing an insoluble filament from an aqueous protein solution. The silks are structurally strong and quite extensible with the 132 MPa breaking stress; 204% breaking strain values. In the effort toward biomimicking of functional materials, honeybee silk as valuable biomaterial has attracted extensive attention. Revealing how natural honeybee silk structure form its mechanical properties can help design of biomimicking studies. Therefore, this study aimed to review the relationship between mechanical properties of honeybee silk and its biological function.

Keywords: Bee silk, building material, α-helix, breaking stress

1. Introduction

Silks are defined as protein fibers spun by a number of arthropod lineages such as honey bees, wasps, silkworms, spiders (Nguyen et al., 2019; Hepburn et al., 2013). The structure, composition and properties of silks show changing depending on where it was collected from sources. Most of the 113,000 species of Lepidoptera and to over 30,000 species of spiders can produce silk (Nguyen et al., 2019). In addition, silkworm, crickets, bees, wasps, fleas, lacewings, scorpions, mites, flies and glowworms are also known to produce silks (Pereira et al., 2015). However, the most known sources of silks are spiders, domestic silkworms, and wild silkworms. They are recently gained extensive applications as industry materials as well as biomaterials especially in tissue engineering owing to their excellent mechanical properties, biocompatibility and biodegradability. In the recent years, they are recently gained extensive applications as industry materials especially in tissue engineering (Kumar et al 2016; Shi et al., 2008).

Honeybee silk is generated from salivary glands named as labial glands (Weisman et al., 2010). Jay (1964) reported that silk is produced by bees during the larva make random head movements in all directions inside the cell. The honeybee labial glands are composed of two parts, both of which connect to the mouth. The mature larva conceals waxen walls of their cells with silk by spinning the fibers randomly, and then enter the pupation (Hepburn et al., 2013).

Thus, the honeycomb made of beeswax workers honeybee silk excreted by the larval bee (Kameda and Tamada, 2009). With each future generation covering the walls with silk, the cells become smaller and an increase in the mass ratio of silk compared to wax is observed (Chauvin 1962). Because of this situation the silk can be separated from the wax in old hatching combs only by chemical and/or heat treatment (Hepburn et al., 2013). Honeybee silk plays an important role in improving the mechanical properties of honeybee combs (Kumar et al., 2016). In this review, we describe the relationship between mechanical properties of honeybee silk and its biological function especially can be used as natural biomaterial in tissue engineering.

1.1. Honeybee Silk Protein

X-ray fiber diffraction data indicated that honeybee silk included ά-helical proteins assembled into order coiled-coil conformation and the meridian reflections are about 28 nm (Rudal 1962). Honeybees silk protein composed four fibrous at approximately equal levels and non-repetitive proteins (approximately 32 kDa) (Kumar et al., 2016). These structures are important that in silk synthesis and function. Honeybee silk proteins are presented rich in Ala residues are caused that very close spacing of helices in coiled coils. A current study demonstrated that honeybee silk proteins have both a-helix and b-sheet structures, however, the a-helix structure is predominate (Kamada and Tamada, 2009), conversely, the dominant molecular structure in silk of silkworm cocoon and spider is extended β-sheets crystallites (Sutherland et al., 2011). Therefore, micelles or crystallites form a series of coiled-coils with four threads parallel to the fiber axis, ensure making the honey bee's silk an alpha helical fibroin (Hepburn et al., 2013). Honeybee fibroin is crystalline compared to other insect silks, when hydrated they show only half the stiffness of dry fibers although they are equal strength. Moreover, it was reported that honeybee silk was tougher and unlike silkworm silk, it still retained its properties even when wet (Hepburn et al. 1979).

1.2. Use of Honeybee Silk in Tissue Engineering

Currently silk proteins are a more biocompatible biomaterial than some widely utilized biological polymers. Silk fibroin (SF) are a biomaterial that has been used as a suture in wound treatment for centuries. SF-based biomaterials are benefited in different applications such as vascular tissue regeneration, skin wound treatment and bone tissue scaffolds owing to their unique mechanical properties, biocompatibility and biodegradability (Farokhi et al., 2018; Qi et al., 2017). The field of tissue engineering is in need of materials that mimic the structure, biological and mechanical functions of the extracellular matrix, as a consequence both synthetic and natural polymers have been commonly used as biomaterials (Sutherland et al., 2019; Wittmer et al., 2011).

While synthetic materials such as polycaprolactones, polyethylene glycol, polylactic acid, ceramics, and metals are more easily produced simple processing and modifications, they generally deficient from the chemical cues support cell attachment and proliferation (Place et al., 2009; Wittmer et al., 2011). To overcome this problem, natural polymers such as alginate, collagen, chitosan, proteoglycans, and silkworm silk are benefited from which offer better biocompatibility, cell attachment and proliferation. But this time, the reproducibility of natural products is difficult with the variation from batch to batch (Kemp, 2009; Seal et al., 2001; Silver et al., 1992; Sutherland et al., 2019). There is increasing interest in the produce of structural proteins like as honeybee silk, spider silk, and bacterial collagen by recombinant technology. Thus, they can be produced with high reproducibility protein aggregates under controlled conditions and then converted into solid-state material forms (An et al., 2014; Weisman et al., 2010). Because the amino acid sequence of recombinant proteins is dictated by a DNA template, it can be easily modified by standard molecular biology techniques (Sutherland et al., 2019). In the near future characterized honeybees silk protein are small (300–600 amino acids)

and have low levels of repetition so is well suitable for recombinant production (Poole et al., 2013; Campbell et al., 2014). In contrast, silkworm and spider silks proteins have the large size (>10 kbp) and highly repetitive sequences making it recalcitrant to expression and cause to low protein yields (Sutherland et al., 2019; Poole et al., 2013; Weisman et al., 2010). Thanks to their small size, the honeybee silk proteins have been produced on a large scale in transgenic systems and the recombinant proteins are fabricated as sponges, films, and fibers (Huson et al., 2012; Sutherland et al., 2018; Walker et al., 2013). Furthermore, genetic variation of homologous bee proteins indicates that the sequence can be greatly altered and still function as a "silk" material (Poole et al., 2013). Bee silk is ideally suited to producing biomaterials especially for tissue engineering because it can be produced at high levels by *E. coli* fermentation and processed into different materials, and its natural variation can provide to add different functions such as cell attachment site and other biological recognition motifs (Sutherland et al., 2019).

Sutherland et al (2019) investigated the biocompatibility and immunogenic response to materials generated from the recombinant honeybee silk protein by fermentation in *Escherichia coli.* Analysis results showed that honeybee silk protein can be produced recombinantly by fermentation in *E. coli* and it can be easily purified. It was observed that both the soluble protein and the formed solid material were not cytotoxic in the cells in vitro. In addition, a focal lymphohistiocytic granuloma formation was observed just as in implanted silkworm silk when bee silk was subcutaneously implanted. Here it was expressed recombinant honeybee silk protein is biologically harmless when implanted subdermally. The authors stated that the new protein-based materials are suitable for the rational design and therefore ideal for biomedical application materials.

In another study, some properties such as mechanical properties and the solid-state structure of materials produced from a single honeybee silk protein are compared with the properties of natural silk and materials produced from four recombinant proteins (Sutherland et al., 2011). As a result of the study, it has been shown that fibers artificially generated from a single recombinant silk protein successfully exhibit the structural and mechanical properties of native silk. This result demonstrated that the properties of natural honeybee silk spun from four different proteins can be achieved with a single recombinant protein, thus greatly simplifying the production of natural silk-like material with recombinant technology.

Weisman et al. (2010) studied on tried to optimize the heterologous expression conditions in order to produce honeybee protein in high yield. Additionally, to evaluate honeybee silk as a biomimetic material, recombinant silk threads were drawn, and their mechanical properties were investigated. Results indicated that full-length unrevised recombinant honeybee silk proteins of very high yield and purity can be fabricated in inclusion bodies by fermentation of *E coli*, and produced recombinant proteins self-associate into a coiled coil structure similar to natural honeybee silk. Thus, it is thought that recombinant silk fibers that provide the mechanical properties of natural silk protein can be produced using a biomimetic spinning system, which is not very difficult.

Poole et al. (2013) investigated the generation of self-assembled recombinant honeybee silk proteins and process that can be used to ensure the continuity of the flexible fibers produced from them. They used transgenic honeybee silk proteins in the study and reported that the orientation of the drawn b-layers perpendicular to the fiber axis differs from silkworm and spider silk, and this feature probably supports the flexible properties of the fibers. Recombinant bee silk proteins can be used in numerous fields, as many production conditions can be checked, such as the amount of β layer bonds can be controlled by coagulation conditions and molecular alignments can be controlled with some shrinkage. Also, production of materials that can maintain their stability in strong protein denaturants can be made from silk fiber. The ability of honeybee silk proteins to be produced recombinantly indicates that they can be used in

especially in areas where biomimetic properties are desired in many different industrial products and medicinal materials.

2. Conclusion

Honeybee silk, which is used by bee larvae to mechanically strengthen the hive, has many similar properties to the commonly known silkworm or spider silk. However, its amino acid composition variation and structure create a different surface chemistry and enable it to be used in different applications. Many of study indicated that honeybee silk can be successfully produced high level and efficiency using recombinant DNA technology, also reported that the recombinant process is easier to apply than silkworm and spider silk. It is thought that honeybee silk can be listed as promising candidate for the development and design of new generation biomaterials for various practical applications.

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Oral Presentation

Honey Nebulization Against Respiratory Diseases in Children

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Abstract

Honey, as a natural product produced by honeybees, has anti-microbial, antioxidant, anti-inflammatory, and immune-modulator effects. Evaluation of the effects of nebulization of honey solution on some respiratory diseases in pediatrics. The most frequent honey used was the ziziphus one. The honey was dissolved in normal (0.9%) saline to get concentrations ranging from 2.5 to 10%. An ultrasound nebulizer was used. Each patient received from 1 to 6 nebulization sessions/day, and the duration of each session was 30 min. The age of the patients ranged from 3 months to 14.5 years, and they were of both sexes. They had the following respiratory illnesses: acute bronchial asthma (more than 500 children); pneumonia (6 patients); and croup (5 patients). This study started on 2000 and still ongoing. Since 2000 more than 5000 nebulization sessions were given to children suffering from different respiratory disorders. In addition to honey nebulization, each patient ingested 5ml honey/kg/day. The honey therapy, both oral and by nebulization, continued until resolution of all symptoms related to the underlying respiratory disease. No toxicity was observed with honey therapy, either oral or nebulized. In all diseases, honey nebulization resulted initially in increased frequency of cough, which was usually productive and was sometimes associated with vomiting of sputum. The increased frequency of cough with expectoration was temporary and was almost always followed by improvement of symptoms. Especially in bronchial asthma, initial negative or misleading reactions to honey nebulization sometimes included in addition to cough, wheezing and respiratory distress. The duration and severity of the initial negative reactions were proportionate to the severity of the underlying disease. These negative reactions are termed false negative reactions because they were transient, and they did not result in deterioration of the disease. They are also termed misleading reactions because they may be misinterpreted as toxicity or allergy from honey, but they are almost always followed by improvement. The success rate of this mode of therapy in the patients enrolled in this study and continued the honey therapy was almost 98.5% in acute bronchial asthma, 100% in pneumonia, and 100% in croup. Honey therapy (oral and nebulization) was the sole treatment used; no medicines were given including, antibiotics, steroids or bronchodilators. Increased frequency of cough, with or without chest wheezes and respiratory distress, associating honey nebulization is a benign, false negative misleading reaction, which is almost always followed by improvement. In the respiratory diseases mentioned in this paper, we should not prescribe medicines, which suppress cough or lead to dryness of secretions because getting rid of sputum helps recovery, whereas keeping the sputum inside the bronchial tree delays recovery and may result in worsening of the disease.

Keywords: Honey, Nebulization, Respiratory Diseases, Children

Oral Presentation

The Child's Reaction to Bee Stings: Kindergarten Responsibility (or Educator's Responsibility)

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Abstract

The present research establishes the legal responsibility of professional staff of kindergartens in the event of a bee sting at a time when the child is included in the program of educational organization. Determining the weight of the importance of measures to ensure safety in order to create professional guidelines for professionals of educational institutions, which should serve as principles and international legal acts in the implementation of the professional pedagogical program API kindergarten. In determining legal liability, a case study was conducted in the field of adverse reactions to bee venom and a case study in the field of case law and legal basis. It should be noted that in the case of suboptimal attention and care for preventive measures that provide the highest possible level of safety in the vicinity of bees, professionals cannot be held criminally liable in the event of a sting, regardless of the severity of a possible atypical reaction. It is impossible to prevent the sting from occurring at any time, and the body's reaction of the child is always beyond the reach of human influence. It should be noted that in the case of optimal attention and care for preventive measures that provide the highest possible level of safety in the vicinity of bees, professionals are unlikely to expect to bear liability in the event of a sting, insofar as all measures for ensuring safety and procedures for the formation of professional guidelines for professional workers of educational institutions are provided, which should serve as principles and internal legal acts in the implementation of the professional pedagogical program API kindergarten.

Keywords: API Kindergarten, Pedagogy, Bee Venom, Anaphylaxis, Legal Basis

Oral Presentation

Bee Products for Children

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Abstract

Children's needs are very specific and their response to a health condition is significantly faster than adults. Nowadays, foods are increasingly poor in nutrients and most often contaminated with chemicals. That means we need to pay more attention to the nutrition of the child. Bee products are lately attracting the attention of the consumers, but also of the researchers due to their marvelous characteristics: significant effects on human health and nutrition. For example, raw pollen and bee bread due to their complex composition are accepted as superfoods. Raw honey not only replace sugar in daily diet, but offers a variety of phytonutrients that can play important roles for maintaining a good health: enzymes, probiotics, antioxidants, etc. Propolis has very good antimicrobial and anti-inflammatory properties. Royal jelly and apilarnil are very good for body and brain development, for premature babies, immune problems, etc. Introducing bee products in children's diet helps to maintain a good state of health and harmonious development. Their taste is well accepted and appreciated by kids, which is important for a good compliance. The use of bee products has shown very good effects in boosting immunity: children who start in kindergarten or school are protected from recurrent infectious. This presentation will show some of our experience introducing bee products as part of the diet and remedies for common issues that infants and toddlers might face.

Keywords: Apitherapy, Nutrition, Bee Products, Children

Oral Presentation

Propolis in Oral Health

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Abstract

Due to its antimicrobial, antioxidant, anti-inflammatory, and antiproliferative properties, propolis has immense potential in dentistry, oral health management, and medicine. Propolis containing products are effective in reducing and /or inhibiting the growth of S.mutans and other caries (decay) causing bacteria in human clinical trials. Based on large numbers of invitro, invivo, animal model studies, and human clinical trials, propolis use is considered safe and having a high therapeutic effect. However, propolis (like other bee- related products) can induce allergic reactions. Cases of contact dermatitis and other allergic reactions have been noted. The presentation will show the clinical application of propolis in dentistry, for use by dentists, specialists and patients for self-care.

Keywords: Oral Health, Dentistry, Propolis

Oral Presentation

From the Hive to the Office: Use of Propolis in Dentistry

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Abstract

From many years ago, humans have been used beehive products to treat many buccal diseases. The use of standardized 5% propolis is one of the products it been used for dental treatments. The antibacterial, anti-inflammatory, analgesic proprieties of propolis is used for endodontic treatment for irrigating and medication between session, for periodontal treatment the use of propolis during the periodontal surgery is used for irrigation. In operative dentistry the develop of new dental cements with propolis are introducing in dentistry, the capacity of the propolis to stimulate the steam cells in the dental pulp. This use is in deep caries lessons or in a small pulp exposure is better than calcium hydroxide. The antifungal property of propolis can be used for buccal candidiasis treatment in topical treatment and in systemic treatment. The use of standardized propolis is very important for the security and safe treatment because we need to use the same product all the time for the different uses and clinic situations because propolis constituents change along the year and the geographic place.

Keywords: Root Canal Treatment, Periodontal Treatment, Standardized, Operative Dentistry

Oral Presentation

The Propolis Influence on the Dental Plaque Accumulation and on the Dental Plaque and SARS-CoV-2 Interrelation.

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Abstract

Dental plaque is the community of microorganisms found on a tooth as a biofilm. They are embedded in a matrix of polymers of both host and bacterial origin. Microbial dental plaque causes an acute and chronic inflammation of tissues surrounding the teeth. That leads to promotion of periodontal diseases, which constitute a predisposition to negative consequences connected with Covid-19. Among the mechanisms explaining the association between oral pathogens and the severity of the course of the SARS-CoV-2 infection there are aspiration of oral pathogens into the lower respiratory tract, modification of the respiratory tract mucosal surfaces, secretion of proinflammatory cytokines, expression of ACE-2 receptors in the oral mucosa, the increased viral attachment mediated by Galectin-3 as well as the increased plasma D-dimer level. Keeping the oral health in good condition may allow to decrease the severity of Covid-19 symptoms and reduce the associated morbidity. Therefore, propolis as a natural substance useful in dentistry and oral health management can bring advantages in maintaining oral health. Propolis possesses antibacterial, anti-inflammatory, antifungal, antiviral and antioxidant activity. Propolis ethanol extract has been used as a component of toothpaste, mouth rinses and throat lozenges. Due to its bacteriostatic, bactericidal and anti-adherent actions, propolis may prevent the dental caries occurrence caused by pathogenic microorganisms.

Keywords: dental plaque, propolis, Covid-19, anti-inflammatory effect, antibacterial effect, anti-adherent effect

Oral Presentation

Api-tourism & Api-wellbeing in Slovenia

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Abstract

Api-tourism with its innovative and creative approach on the one hand provides for unforgettable experiences, and on the other includes a significant educational aspect, as it raises people's awareness of the importance of preserving bees, preserving humanity. Api-tourism is a partner product developed by Aritours, ApiRoutes travel company and Slovenian Beekeeping Association. Created with aim to raise the awareness of the important role of the bees for humankind – No Bees No life! By developing beekeeping-tourism offer where everyone can learn about the honeybees, their community, work, bee products; we create travels that educate & inspire. Visitors learn how important is healthy and locally produced food, we teach about Apinutricism and other api-culinary products. By entering bee house full with aerosol from the hive we enrich knowledge about the use and effects of bees, bee products and apitherapy. Tanja Arih Korošec, the front man of api-tourism & api-wellbeing programs, she is also a strategic partner of SBA and Slovenian beekeeping academy: educational programs on apitourism, api-wellbeing, apinutricism, and she is a coordinator of Apimondia working group for api-tourism at Apimondia, International beekeeping organization. Apitours, ApiRoutes is accredited travel company for Api-tours and Api-wellbeing programs providing professional tours, excursion, educational programs, leadership programs, team buildings for bee -lovers, travel enthusiast. Slovenia is taking a leading role in implementation of Slovenian api-tourism model on worldwide level.

Keywords: Api-tourism, Api-wellbeing, Slovenia

Oral Presentation

Apitherapy Tourism, a New Form of Health-Related Tourism

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Abstract

The bees have no frontiers but the apitherapists located in various countries all over the world live inside their borders, have their own language, culture, and personal experiences in beekeeping and apitherapy and many of them are isolated from the rest of the world. There are for example excellent apitherapy practitioners I meat in small villages located in Russia, South Korea, China, Germany, Mexico, or Brazil… Practically, the lifetime knowledge of these precious people can be accessed only by visiting them and staying with them for at least a couple of days, asking them, face to face, with the help of local translators, how they prevent and treat human and animal diseases with their local bees and local beehive products. If we want to have not only "dry" theoretical knowledge, from books or scientific congresses, but also concrete, detailed practical "secrets" on various methods of administration, on making specific preparations, etc., we must take into consideration to travel to as many as possible such places, and thus participate to what I call a new form of tourism, "Apitherapy Tourism". Thanks to the bees and wonderful people I have had the chance and honor to meet during the last 30 years of apitherapy practice, I travelled to over 50 countries from all "bee continents", except for Australia. Once the Covid-19 dark era will be gone, we should be able to plan together various Apitherapy Tours on each major continent, together with our friends, organizing international conferences, but also round tables, practical workshops, and visits to remote areas where we will find apitherapy practitioners of great value. A good start is to take part to all our future major, international events to be organized in various countries by various national apitherapy associations and also by Apimondia. A direct contact with apitherapy practitioners from all over the world will mean not only getting practical knowledge, but also getting wonderful friendships that will last all our lifetimes.

Keywords: Apitherapy Practitioners, Remote Areas, Practical Knowledge, Api-Tourism

Oral Presentation

Current Issues and Suggetions on Regional Beekepeings Activities

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Abstract

Beekeeping strategic plans should be formed and followed for short and long terms. It should be done with collaboration of the associations and stakeholders, under the coordination of ministries. Each region should have the records of actual production data on bee products. The number of hives is increasing day by day, the existing flora may not be enough, and we may not even protect the existing bees due to the approaching drought. Setting artificial flora may not be the solution. Municipalities and public institutions' bee-hive tenders should be limited. The stability of existing bees and beekeepers is more important than new ones. Training is provided free of charge by public institutions and organizations, those who want to be a beekeeper can start this profession with 2-3 beehives with their own means. At the end of the year, if the bees donot survive, they may perish and cause more harm than good to the economy. Each regional beekeeper uses beehives of different sizes, although the hive standard is “Langstroth”- in many regions. There are problems in buying and selling these beehives or bee frames. Hives made of poor-quality trees become unusable after 2-3 years under nomadic beekeeping conditions. Standardization certificate and wood quality should be sought in workshops that make beehives, including carpentry shops. Queen bee enterprises should be inspected more frequently, queen bee quality criteria should be measured, foreign origin queen bees should not be brought to the country, urgent decisions should be taken. A sector that has not yet grasped the importance of Digital Marketing in the new world system should be able to quickly take its place. The beekeeping industry should work with experts in the digital sense so that it can sell its products outside the region where they are produced, whether cooperatively or individually. Public spots should be prepared regarding contribution of beekeping to fruit set and quality should be explained by the Ministry of Agriculture and Forestry in visual and written media. When the beekeepers increase their pollen production, the number of such enterprises will increase. As the production increases within the scope of Expanding the Production of Bee Products carried out by the General Directorate of Livestock, the sectors that will supply the products to companies that want to export by collecting will also develop. Chemical applications used in the control of varroa should be reduced. Biotechnical methods and organic compounds should be used. The products in the industrial agriculture to be used must be environmentally friendly. In the integrated control, the pest should be prevented from entering the production areas. It is seen that the pest population is reduced by 10% with biological control in agricultural areas. Use of beneficial insects in agricultural areas should be expanded. The products to be used in apitherapy should be produced with an organic and contracted production model. Joint studies should be carried out with the associations and ministries. Apitherapy on humans; It should be applied by physicians and an assistant team. Further projects on apitherapy should be organ by the Ministry of Health.

Keywords: Beekeeping, Organic, Biotechnical, Quality

1st JOINT INTERNATIONAL APITHERAPY CONGRESS PROCEEDINGS BOOK

ONLINE, 20-26 MAY 2021

ISBN: 978-605-4123-57-5

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