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Кафедра клінічної фармакології**

**АКТУАЛЬНІ ПИТАННЯ
КЛІНІЧНОЇ ФАРМАКОЛОГІЇ ТА КЛІНІЧНОЇ ФАРМАЦІЇ
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SYNERGISTIC EFFECTS OF NATURAL PRODUCTS IN MODULATION OF GUT MICROBIOTA

**Tarapata Michael, Kukhtenko Oleksandr,
Manskiy Oleksandr, Bezrukaviy Yevgen**

*National University of Pharmacy, Kharkiv, Ukraine
The Department of Pharmacy and Industrial Technology
automcorporation@gmail.com*

The 21st century is characterized by a significant demographic shift towards an aging global population. While lifespan has increased, this has not been proportionally matched by an increase in healthspan, leading to a greater burden of age-related chronic diseases such as cardiovascular disease, type 2 diabetes, neurodegenerative disorders, and cancer. A common denominator underlying many of these conditions is a state of chronic, low-grade, systemic inflammation, termed "inflammaging". This process is intricately linked to a decline in immune function (immunosenescence) and an accumulation of cellular damage from oxidative stress.

In the quest for strategies to extend healthspan, two fields of research have gained considerable traction: the modulation of the gut microbiota and the therapeutic application of natural products. The human gut is home to trillions of microorganisms that collectively function as a metabolic organ, essential for nutrient digestion, vitamin synthesis, pathogen defense, and maturation of the immune system. Dysbiosis, an imbalance in this microbial community, is strongly associated with inflammation, metabolic dysfunction, and increased susceptibility to disease. Interventions aimed at restoring a balanced microbiome-eubiosis are therefore a primary therapeutic target.

Apitherapy, the medicinal use of products derived from honeybees, offers a rich source of bioactive compounds. Honey, propolis, royal jelly, and bee pollen have been used in traditional medicine for centuries and are now being validated by modern science for their potent antioxidant, anti-inflammatory, antimicrobial, and immunomodulatory properties. These effects are attributed to a complex array of bioactives, including flavonoids, phenolic acids, enzymes, and unique fatty acids. While bee products and gut health modulators have been studied extensively in isolation, the investigation of their combined, synergistic effects represents a promising and relatively underexplored frontier. Bee products possess properties that make them ideal partners for probiotics, prebiotics, and other biotics. For instance, honey contains oligosaccharides that can serve as prebiotics, selectively fueling the growth of beneficial bacteria, while propolis exhibits antimicrobial activity that can suppress pathogens, creating a favorable environment for probiotics to thrive. This research examines the mechanistic basis for combining bee products with gut microbiota modulators to prevent sickness and promote healthy aging.

Aim of the Study. This review explores how natural bee products and gut microbiota modulators can work together to prevent illness and slow the aging process. It focuses on:

Defining key concepts (probiotics, prebiotics, synbiotics, postbiotics)

Analyzing how bee products influence the gut microbiome

Describing their combined roles in maintaining gut barrier integrity, modulating immunity, and reducing inflammation and oxidative stress

Highlighting opportunities for new, integrated “api-synbiotic” formulations.

Materials and Methods. Pure honey, propolis, and royal jelly were collected from certified apiaries. Standard probiotic strains (*Lactobacillus*, *Bifidobacterium*) and prebiotic substrates (inulin, fructo-oligosaccharides) were used for analysis. All materials were of analytical grade.

Results and Discussion.

1. **Bee Products as Gut Modulators.** Honey contains oligosaccharides that act as prebiotics, promoting beneficial bacteria and producing short-chain fatty acids vital for colon health. Its mild antimicrobial properties selectively inhibit harmful pathogens while supporting friendly microbes. Propolis, rich in flavonoids and phenolic acids, exerts strong antimicrobial effects, reducing pathogens and supporting beneficial species such as *Akkermansia muciniphila*. Royal jelly and bee pollen, rich in proteins, fatty acids, and polyphenols, further support immune balance and microbial diversity.

2. **Synergistic Effects in Disease Prevention.** **Gut Barrier Support:** Bee products reduce intestinal inflammation, while probiotics and postbiotics reinforce tight junctions, together strengthening the gut barrier. Propolis inhibits harmful microbes, allowing probiotics to colonize and maintain balance.

Immune Regulation: Probiotics promote balanced immune responses, and bee compounds like CAPE and 10-HDA suppress excessive inflammation, creating a coordinated defense against chronic diseases.

3. **Anti-Aging Mechanisms.** Combining bee products with microbiota modulators helps break the cycle of inflammaging by strengthening the gut barrier, enhancing SCFA production, and reducing oxidative stress. Bee polyphenols provide antioxidants, while a healthy microbiome supports the body’s natural defenses.

This synergy supports the concept of “api-synbiotics”-integrated formulations that combine probiotics with honey-derived prebiotics and propolis extracts for enhanced efficacy.

Conclusions. Combining bee products with gut microbiota modulators offers a powerful, multi-targeted strategy to improve gut health, strengthen immunity, and slow aging. The main benefits include:

- restoration of microbial balance,
- enhanced gut barrier and reduced inflammation,
- stronger immune regulation,
- protection against oxidative stress.

Future research should focus on standardizing bee product extracts, identifying optimal probiotic combinations, and conducting clinical trials to confirm these effects in humans. The integration of apitherapy with microbiome science offers a promising pathway to extend not just lifespan, but healthspan-supporting vitality and resilience throughout aging.