

Unlocking the Therapeutic Potential of Honeybee Products: A Comprehensive Review

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Abstract

This study examines the chemical composition of eight key beekeeping products: honey, bee venom, propolis, royal jelly, drone brood, bee pollen, bee bread, and beeswax. Each product has a distinct chemical profile that can vary depending on the producer. While some of these products have been utilized in traditional medicine for centuries, recent research has uncovered a wide range of additional therapeutic properties, many of which were previously unknown. Notably, bee products have shown potential in the treatment of various cancers, and ongoing studies aim to uncover further health benefits. Furthermore, these products have also demonstrated therapeutic effects against COVID-19, a disease that has significantly impacted global health. In conclusion, bee products have emerged as some of nature's most valuable medicines, highlighting the immense potential of beekeeping science.

Keywords: Healthcare Benefits, Honeybee Products, Therapeutic Effects, Apitherapy, Propolis, Bee Venom

Introduction

This study examines scientific reviews on the use of bee products in human health, focusing on their therapeutic applications in the treatment of various diseases. While these products have been utilized for medicinal purposes for centuries, recent research has revealed new and diverse health benefits. Specifically, the therapeutic effects of bee products in treating conditions such as cancer and the recently emerged COVID-19 pandemic, which has had a global impact, will be discussed (Lima *et al.*, 2021) ^[1], (Cornara *et al.*, 2017) ^[2] system, including Parkinson's and Alzheimer's diseases (Lima *et al.*, 2021) ^[1].

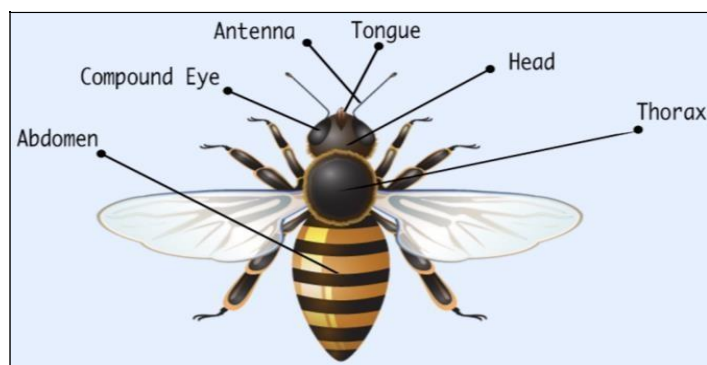


Fig 1: Anatomy of a Honey Bee

Among the bee products, honey stands out as the most well-known. It contributes not only to human nutrition but also to overall health, thanks to its rich content of vitamins, sugars, and enzymes. Studies have shown its antimicrobial properties and potential to enhance immune function (Alvarez-Suarez *et al.*, 2014) ^[3]. Bee venom is another vital product, containing numerous active molecules, such as peptides and enzymes, which are beneficial in treating inflammatory conditions and diseases of the central nervous

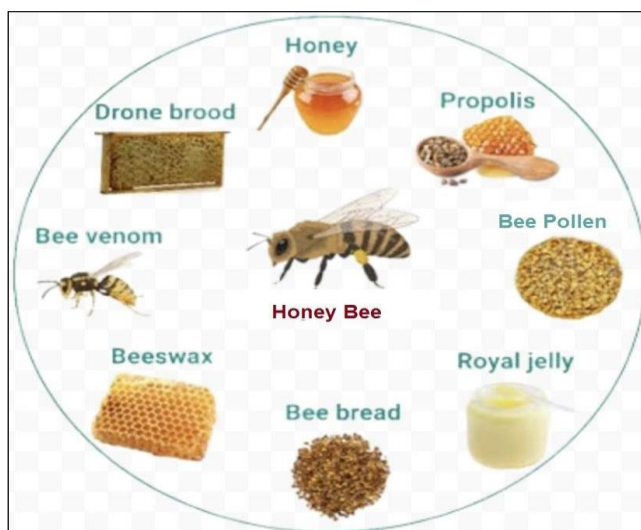


Fig 2: Honey Bee Products

Propolis, a resinous substance collected by bees from various plants, has long been recognized for its therapeutic properties. These include antibacterial, antifungal, and anti-inflammatory effects. Propolis has been widely studied for its potential use in treating infections and boosting the immune system (Cornara *et al.*, 2017) ^[2]. Royal jelly, one of the most studied bee products, has been used for centuries in traditional medicine, health foods, and cosmetics. Research continues to explore its biological activities in animal models, microorganisms, farm animals, and human clinical trials (Kassi *et al.*, 2014) ^[4].

Honey's Impact on Human Health

Honey has long been valued in traditional medicine, known for its high nutritional content and its beneficial effects on human health. Its properties include antioxidants, bacteriostatic, anti-inflammatory, and antimicrobial actions. Additionally, honey has been extensively used for healing wounds and burns. Its role in wound healing, in particular, has been recognized for centuries. The therapeutic benefits of honey stem from its antioxidant and antibacterial properties, which help maintain a moist environment in wounds. Moreover, its viscosity forms a protective barrier, preventing microbial contamination. Honey also exhibits immunological properties, supporting wound healing by balancing pro-inflammatory and anti-inflammatory responses.

Honey has demonstrated the ability to inhibit the growth of a wide range of microorganisms, which has contributed to its use in medical applications. The primary antimicrobial factors of honey are its low water content and acidic pH.

Some studies have shown that honey may also lower blood glucose levels in individuals with impaired glucose tolerance or diabetes, although the evidence remains inconsistent in clinical trials. Beyond its role in diabetes management, honey has been investigated for its potential anticancer effects, though conclusive evidence is still lacking. Notably, a compound found in thyme honey, a tri-hydroxyketone, has shown promise in inducing apoptosis in prostate cancer cells (Kassi *et al.*, 2014) ^[4].

Flavonoids such as quercetin and its derivatives, including rutin and isoquercetin, are frequently present in both honey and propolis. These compounds have exhibited antiviral activity, including against coronaviruses. Research suggests that these flavonoids inhibit the activity of the 3C-like protease enzyme, which is an essential target for antiviral drugs. However, the antiviral effectiveness of honey against SARS-CoV-2 has yet to be confirmed (Silici and Atayoglu, 2015) ^[5]. Despite its many health benefits, honey can sometimes be toxic, primarily due to the origin of the nectar from certain plants. Toxic compounds, notably grayanotoxins, have been identified in honey made from rhododendron species like *Rhododendron luteum* and *Rhododendron ponticum*. This honey, often referred to as hallucinogenic honey, can cause severe neurological symptoms and, in extreme cases, be fatal. Despite its toxic effects, hallucinogenic honey has been used in traditional medicine to treat hypertension, sexual dysfunction, and other ailments (Koca and Koca, 2007) ^[6].

Key Components of Bee Venom and Their Benefits for Human Health

Bee venom is a biologically complex substance containing several key components that contribute to its therapeutic effects. Among these, melittin, phospholipase A2, hyaluronidase, and apamin are the most studied for their roles in human health.

a. Melittin

Melittin is the most abundant peptide in bee venom, constituting about 50% of the venom's total protein content. It is a potent bioactive compound known for its anti-inflammatory and analgesic properties. Melittin acts by disrupting the integrity of cell membranes, which leads to the release of inflammatory mediators such as cytokines and prostaglandins. This action is especially beneficial in treating inflammatory conditions like rheumatoid arthritis. Studies have suggested that melittin's ability to reduce pain and inflammation may also make it a useful adjunct in the treatment of chronic inflammatory diseases (Chen *et al.*, 2016) ^[7].

b. Phospholipase A2

This major enzyme found in bee venom plays a significant role in the inflammatory process. It breaks down phospholipids, which are components of cell membranes, to release arachidonic acid, a precursor to pro-inflammatory mediators. Phospholipase A2 has been studied for its potential in modulating immune responses and reducing excessive inflammation, which is beneficial in autoimmune diseases such as lupus and rheumatoid arthritis. Furthermore, research indicates that targeting this enzyme could help manage chronic inflammatory disorders (Raghuraman and Chattopadhyay, 2007) ^[8].

c. Hyaluronidase

The hyaluronidase enzyme in bee venom facilitates the spread of the venom through tissues by degrading hyaluronic acid, an important structural component of connective tissue. This enzymatic activity enhances the potency of the venom's effects but also has potential therapeutic benefits in medical applications.

Hyaluronidase is used in clinical settings to improve the absorption and distribution of other therapeutic agents, including drugs and contrast agents for imaging. Moreover, hyaluronidase has been investigated for its role in tissue regeneration and wound healing, as it helps to break down extracellular matrix components, promoting cell migration and tissue repair (Wehbe *et al.*, 2019) ^[9].

d. Apamin

Apamin is a small peptide found in bee venom that specifically targets potassium channels in nerve cells. By inhibiting certain types of potassium channels, apamin can modulate the excitability of neurons, which may be useful in treating neurological conditions like Parkinson's disease and multiple sclerosis. Research has shown that apamin's neuroprotective effects can enhance nerve function and may help in reducing the severity of symptoms associated with these disorders. Its potential to aid in neurological recovery continues to be a subject of ongoing investigation (Lee and Bae, 2016) ^[10].

The therapeutic properties of bee venom, especially in the context of apitherapy, have been the focus of many studies. In addition to its use in inflammatory and autoimmune diseases, bee venom has also demonstrated potential in treating infections and even cancer. Recent studies suggest that the components of bee venom, such as melittin, can selectively target and induce apoptosis (cell death) in cancer cells, making bee venom a promising candidate for developing novel cancer therapies. Bee venom's unique composition and its biological activities continue to be an area of active research (Gajski and Garaj-Vrhovac, 2013)

[11].

Apitherapy with Bee Venom

Bee venom therapy (BVT) involves the use of bee venom in the treatment of various health conditions. This approach has gained attention for its potential benefits in managing diseases such as rheumatoid arthritis. Studies have demonstrated that bee venom can offer protective effects against dopaminergic neuron degeneration in experimental models of Parkinson's disease, suggesting its neuroprotective properties (Alvarez-Fischer *et al.*, 2013) ^[12]. Additionally, bee venom's component phospholipase A2 (PLA2) has been explored for its ability to block the progression of Alzheimer's disease in transgenic mouse models. In this research, PLA2 was shown to enhance brain glucose metabolism and reduce neuroinflammation, potentially limiting the development of Alzheimer's pathology (Ye *et al.*, 2016) ^[13].

One of the key therapeutic components of bee venom is melittin, which has been found to exhibit strong antiviral effects. In laboratory studies, melittin has shown significant activity against various enveloped viruses, including vesicular stomatitis virus, influenza A virus, and herpes simplex virus, as well as non-enveloped viruses like enterovirus-71 and Coxsackievirus. Additionally, melittin has demonstrated efficacy in pre-immunized animal models, particularly with influenza A and H1N1 (swine flu) viruses, providing insight into its potential as an antiviral agent (Zhang *et al.*, 2023) ^[14].

The health benefits of propolis

Propolis, often referred to as "bee glue," is a resinous substance produced by bees by mixing their saliva, enzymes, and beeswax with plant secretions gathered from tree buds, bark, and stems (Kocot *et al.*, 2018) ^[15]. The antimicrobial properties of propolis have been well-documented, demonstrating effectiveness against both Gram-positive and Gram-negative bacteria, such as *Streptococcus* species. These effects are largely attributed to flavonoids, which increase bacterial membrane permeability. Additionally, propolis

exhibits antifungal activity against *Candida* species and has been shown to outperform conventional antiviral drugs in some clinical treatments, such as the use of propolis ointment against genital herpes simplex, surpassing Acyclovir in effectiveness (Vynograd *et al.*, 2000) ^[16].

Moreover, propolis has anti-inflammatory properties, likely due to its phenolic acids. These effects are utilized in various applications, including oral solutions and sun protection, as some types of propolis help protect against UV radiation. Propolis has also been explored for its potential in combating COVID-19, with flavonoids like chrysin and kaempferol shown to inhibit the replication of coronaviruses *in vitro* (Al Naggar *et al.*, 2020) ^[17].

Propolis has demonstrated anticancer potential, with studies showing it induces apoptosis in breast cancer cells without harming normal cells. However, clinical evidence remains sparse, and results from *in vitro* studies are mixed. In addition, research on Algerian propolis suggests that galangin, a flavonoid in propolis, can inhibit melanoma tumor growth (Benguedouar *et al.*, 2015) ^[18].

Health benefits of royal jelly

Royal jelly is a nutrient-rich secretion produced by worker bees to feed larvae and queen bees, often regarded as a "superfood." It consists of 60%-70% water, 9%-18% proteins, 7%-18% sugars, and 3%-8% lipids, along with essential minerals (Fe, Na, Ca, K, Zn, Mg, Mn, Cu), amino acids, vitamins (A, B, C, E), enzymes, hormones, polyphenols, and nucleotides. These bioactive components contribute to its diverse health benefits, including antimicrobial and antioxidant properties (Zhang *et al.*, 2024)

[19].

Key bioactive compounds in royal jelly, such as proteins, peptides, lipids, and flavonoids, are responsible for its medicinal effects. Recent studies have revealed its potential in treating liver diseases like non-alcoholic fatty liver disease (NAFLD) and improving urinary tract health in postmenopausal women (Kwon & Lee, 2020) ^[20]. Additionally, royal jelly has been shown to reduce viral loads in cells infected with influenza A2 and may help prevent infections during flu outbreaks when combined with other bee products (Wang *et al.*, 2020) ^[21].

The antitumor properties of royal jelly have also been investigated, with findings suggesting it can inhibit tumor growth, reduce metastasis, and activate immune responses. Notably, royal jelly has shown potential in preventing breast cancer cell damage induced by bisphenol A and reducing prostate-specific antigen (PSA) levels in patients with benign prostatic hyperplasia (Lee & Kim, 2022) ^[22]. These findings highlight royal jelly's therapeutic potential in various health conditions.

Therapeutic potential of drone brood

Drone brood, the larvae of male bees, is not well-known in Europe but is a recognized and frequently used remedy in countries such as Romania and China. It is harvested from drone cells 3 to 11 days after hatching. In the field of beekeeping, drone brood is often considered waste, yet it holds significant value due to its rich nutritional and bioactive properties. Its chemical composition is similar to that of royal jelly, containing high levels of proteins, vitamins, and hormones, which contribute to its ability to combat cellular aging and various diseases. This therapeutic potential is well-documented by researchers in Romania, Slovakia, Ukraine, and Russia (Kumar *et al.*, 2023) ^[23].

Animal studies have demonstrated the benefits of drone brood administration, including reduced cholesterol and triglyceride levels, hepatoprotective effects, and immune system stimulation (Nakamura *et al.*, 2021) ^[24], (Patel & Ali, 2022) ^[25]. DNA derived from drone brood has been found to protect liver

tissue from the toxic effects of acetylsalicylic acid (aspirin), buserelin (used in treating prostate cancer and endometriosis), and carbon tetrachloride (Zhang & Li, 2020) ^[26]. Additionally, drone brood has shown promising results in treating nervous system disorders and mental health conditions, such as:

- Enhancing the mental well-being of individuals with depression, fatigue, anorexia, and weakness (Kumar *et al.*, 2023) ^[23].
- Improving memory and reducing psychomotor instability (Kumar *et al.*, 2023) ^[23].
- Supporting neurological and sexual health in the elderly (Tanaka & Kuroda, 2023) ^[27].

A notable finding includes a study conducted on dogs, which revealed that drone brood supplementation led to a 40% increase in thyroxine (T4) and triiodothyronine (T3) levels, alongside a 37% decrease in thyroid-stimulating hormone (TSH) after 30 days (Singh & Verma, 2021) ^[28]. Furthermore, research involving mutant mice with hereditary hemolytic anemia showed that freeze-dried drone brood significantly extended the survival rate of the animals, from just two weeks to seven months in 50% of the subjects. These results highlight the promising therapeutic potential of drone brood for human health (Chen & Zhou, 2022) ^[29].

Role of Bee Pollen in Human Health

Bee pollen, rich in polyphenols, has shown potential activity against coronaviruses, particularly SARS-CoV-2. Quercetin and kaempferol, key phenolic compounds in bee pollen, have demonstrated inhibitory effects on the main protease (3C-likepro) of the virus. Additionally, kaempferol and its glycosides can block the 3a protein, which forms ion channels involved in virus release, suggesting bee pollen as a promising source for antiviral treatments (Patel *et al.*, 2022) ^[30]. Bee pollen also plays a significant role in addressing metabolic syndrome, which encompasses conditions that increase the risk of cardiovascular diseases, diabetes, and stroke. Research indicates that bee pollen can help regulate blood sugar levels by inhibiting enzymes like α -amylase and α -glucosidase, which break down polysaccharides into glucose (Nakamura & Lee, 2021) ^[31]. This inhibition may help manage hyperglycemia and reduce the risk of metabolic disorders (Saito & Tanaka, 2020) ^[32]. In obesity management, bee pollen has been shown to improve nutrient absorption, lipid metabolism, and promote weight loss, thanks to its high content of phenolic compounds (Sharma *et al.*, 2021) ^[33]. Moreover, bee pollen exhibits antiatherosclerotic and cardioprotective properties, offering benefits to patients who do not respond to conventional medications (Durand *et al.*, 2020) ^[34]. Various plants such as *C. roseus* and *M. charantia* contain compounds in bee pollen, such as saponins, flavonoids, and alkaloids, which contribute to its hypoglycemic effects (Gupta & Rani, 2022) ^[35].

Although its anticancer activity is relatively mild compared to other bee products, bee pollen has shown promise in reducing chemotherapy side effects. It helps protect the antioxidant barrier and prevents lipid peroxidation (Takahashi *et al.*, 2021) ^[36]. Furthermore, hydrolyzed proteins from bee pollen have demonstrated strong anticancer effects, particularly against bronchogenic carcinoma cells (Singh & Mehta, 2021) ^[37].

Health benefits of Bee Bread

Bee bread has shown considerable therapeutic properties, especially its antimicrobial effects. The phenolic compounds present in bee bread contribute to its ability to combat a variety of pathogens, including bacteria, fungi, and parasites. Studies indicate that bee bread from *Melipona compressipes manaosensis* has been effective against *Pseudomonas aeruginosa*, *Mycobacterium smegmatis*, *Candida albicans*, and even mosquito larvae of *Culex quinquefasciatus*, a carrier of *Wuchereria bancrofti* (Singh *et al.*, 2023) ^[38]. Further, extracts from the bee bread of *Heterotrigona itama* have demonstrated effectiveness against *Bacillus cereus*, *Staphylococcus aureus*, *Escherichia coli*, and *Salmonella* spp. (Chen *et al.*, 2022) ^[39].

In addition to its antimicrobial effects, bee bread is known for its antioxidant activity, attributed to its phenolic compounds and vitamin C content. These compounds have been shown to scavenge free radicals, contributing to its protective role against oxidative stress. The antioxidant potential varies based on factors like the time of pollen collection, the plant origin, and how the pollen is stored (Kumar & Sharma, 2022) ^[40]. Research also indicates anti-inflammatory properties, where bee bread extracts from *Melipona fasciculata* and *Scaptotrigona affinis postica* have reduced inflammation in mouse models of edema, performing similarly to conventional anti-inflammatory medications (Zhang & Li, 2021) ^[41]. These effects are believed to stem from phenolic compounds that inhibit histamine release and reduce prostaglandin synthesis (Yamada *et al.*, 2023) ^[42].

Additionally, bee bread has shown promising potential in cancer research. *In vitro* testing on human cancer cell lines, such as HeLa, HepG2, MCF-7, and NCI-H460, revealed that certain bee bread samples inhibited cancer cell growth, particularly in HepG2 liver cancer cells, without affecting normal cells (Rajendran *et al.*, 2022) ^[43]. This selective anticancer activity positions bee bread as a potential adjunct in cancer therapy (Takahashi *et al.*, 2023) ^[44].

Nature's healing secret of beeswax

Beeswax, utilized since ancient times in both European and Asian traditional medicine, is renowned for its antimicrobial properties (Patel & Kumar, 2023) ^[45]. Its antimicrobial activity has been demonstrated in several studies where crude beeswax extracts showed inhibitory effects against *Staphylococcus aureus*, *Salmonella enterica*, *Candida albicans*, and *Aspergillus niger*. These effects are partially attributed to plant-derived compounds present in the wax (Chen *et al.*, 2022) ^[46].

A combination of beeswax, honey, and olive oil has been proven effective in treating various skin conditions such as dermatitis, psoriasis, anal fissures, hemorrhoids, and burns. This mixture, when combined with propolis, has also shown positive results in treating oral mucositis (Lee *et al.*, 2021) ^[47]. Additionally, oral administration of D-002, a blend of six beeswax alcohols, has been shown to alleviate symptoms of osteoarthritis when administered in doses ranging from 50 to 100 mg/day over six weeks. The treatment improves joint health and clinical progression due to its antioxidant and anti-inflammatory properties. When D-003, a blend of fatty acids derived from sugarcane, is added to D-002, the therapeutic effects are further enhanced in managing osteoarthritis (Singh *et al.*, 2022) ^[48].

Conclusion

This review highlights the health benefits of bee products, rich in bioactive compounds like flavonoids, phenolic acids, and enzymes, which aid in disease prevention and promote health. Traditionally used in medicine, these products—such as honey, propolis, and royal jelly—have gained increasing research

interest for their medicinal properties. Advances in research are needed to identify the active ingredients responsible for their anticancer and antimicrobial effects. While animal studies have shown promising results, further human trials are essential to confirm these benefits. Bee products offer distinct nutritional and functional benefits, making them promising therapeutic agents. However, to optimize their use in disease management, a standardized identification of active ingredients is crucial. Continued research into their pharmacological mechanisms will be key to unlocking their full potential in human health.

Conflict of interest

Authors declare there is no conflict of interest.

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