

# From Honey to Venom: An Overview of Apitherapy

Laurie Dohmen, VMD, MS

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## Author Contact:

Purple Moon Herbs and Studies  
www.purplemoonherbstudies.com  
drlaurie@purplemoonherbstudies.com

## Abstract

Not only do bees keep our food chain intact through pollination, but they offer a myriad of products, including medicinal compounds. Honey is used both internally for many conditions and topically to heal wounds. Propolis, royal jelly, and pollen are all nourishing and medically active. Research is burgeoning on the use of bee venom for pain and conditions associated with pain such as arthritis. This article will provide an overview of these products and their medicinal uses.

## Introduction

Apitherapy is a type of complementary and alternative medicine that involves the therapeutic use of bee products from honey bee hives. Products with medicinal benefits include honey, propolis, royal jelly, bee pollen, and bee venom (1). The honey bee species *Apis mellifera* produces all of these substances.

Honey is technically a liquid produced by honey bees to provide the colony with food for the winter. It is produced from the nectar of plants, so it varies with the plant sources the bees use. The processing of nectar into honey is a complex process that starts with the collection of nectar from flowers. The nectar is ripened by partial enzymatic degradation in the honey bee's stomach. The ripened nectar is then fanned to evaporate excess moisture, which

results in honey (2). Propolis, also known as "bee glue," is a resinous substance accumulated from a variety of trees and plants (1, 3). It is used by the colony for construction and repair and as a protective barrier (1, 4). Royal jelly, a secretion from the hypopharyngeal and mandibular glands of 6- to 12-day-old worker bees, is considered a "superfood" for the bees that is eaten only by the queen and larvae. It is used to nurture the brood (eggs, pupae, and larvae) until the larvae are 2 or 3 days old. The queen bee eats it exclusively her entire life, which is generally 2 to 3 years, but may be as long as 5 years (1, 5).

Other bee products used in apitherapy include pollen and venom. Bee pollen is plant pollen that the worker bees collect and then agglutinate with nectar and salivary enzymes before putting it in their pollen baskets on their legs for transport (6, 7). The exact chemical composition of bee pollen has yet to be elucidated in a laboratory setting; however, each bee pollen pellet contains more than 2 million flower pollen grains (7). The pollen is used by the bees as food for the young (8). When bees collect pollen, they are also pollinating other plants, enabling them to reproduce. Bee venom is a liquid complex produced by the stinging apparatus of worker bees. Only worker bees and queens can sting, as the stinger and the venom are an evolution of the egg-laying anatomy (9). The purpose of stinging is to protect bees from their enemies (10).

## Honey

Honey has been used throughout history, and its nutritive and medicinally beneficial qualities are well recognized worldwide (1). It was used as food and medicine in ancient Egypt, Greece, China, Rome, and other countries. Honey is pictured on a Stone Age painting from 8,000 years ago as well as on a Sumerian tablet from 6200 BCE, and it is mentioned in most religious texts, including the Holy Quran, the Bible, and the Hindi Veda (11). The composition of honey is more than 80% carbohydrates, with small quantities of water, protein, vitamins, minerals, and other components including phytochemicals (bioactive plant constituents). The exact composition of each hive's honey varies based on the plants the bees use to gather nectar. Fructose and glucose are the main 2 sugar carbohydrates, and the active constituents include flavonoids, polyphenols, and organic acids (1, 11-13). Honey has many benefits. It is gastroprotective, anti-inflammatory, vulnerary, cardioprotective, antioxidant, antidiabetic, antibacterial, antifungal, and anticancer. The main antioxidant constituents are flavonoids and polyphenols (1, 11-13). Honey is used internally and topically for numerous conditions, including wounds, GI diseases, oral disorders, upper airway disorders, liver diseases, pancreatic disorders, metabolic disorders, ocular ailments, cardiovascular diseases, neurologic disorders, and cancer (1, 11-13). As a food, it is a quickly and easily digestible source of energy for the body. It also functions as a prebiotic and a food preservative (12).

Honey does have some contraindications, including toxicity from plant and/or nectar sources. For example, this occurs when bees use certain species of rhododendron containing the hallucinogen grayanotoxin, resulting in "mad honey." Chemically treated plant sources can be another source of toxicity. In addition, honey can contain *Clostridium botulinum* in sufficient amounts to kill human babies less than a year of age. In people with pollen allergies, honey can cause allergic reactions (12, 13).

## Propolis

Propolis is another bee product that has been utilized throughout history. It was used by the Greeks and Romans as an oral and topical antiseptic and by the Egyptians for embalming. Propolis can be found in the London pharmacopoeias of the 17th century, and Stradivari used it as violin varnish. Propolis was also used medicinally during World War II (4). This bee product contains resin, wax, essential oils, pollen, vitamins, minerals, and other organic compounds, and its active constituents include phenols, esters, flavonoids, terpenes, sterols, aldehydes, and alcohols. Caffeic acid phenethyl ester (CAPE) is one of propolis' main bioactive compounds (14). These constituents contribute to antiseptic, antiviral, antibacterial, antifungal,

hepatoprotective, neuroprotective, cardioprotective, antidiabetic, anti-inflammatory, antioxidant, anticancer, antiulcer, anti-protozoal, hypotensive, and immunomodulatory actions (1, 4, 14-16). The antimicrobial and antioxidant properties of propolis are primarily due to the phenolic compounds and flavonoids (14). CAPE is both antioxidant and cytotoxic to tumor cells (15). Propolis' medicinal uses include GI disorders, gynecological diseases, oral disorders, cancer, upper respiratory ailments, and skin diseases (1, 4, 14, 15). It is used in health products, foods, and cosmetics as a capsule, extract, mouthwash, throat lozenge, cream, or powder and wax-less purified forms (4, 15). Propolis is generally non-toxic at human doses of approximately 1.4 mg/kg/day and less than a total of 15 g/day. Above this dose range, allergic reactions and contact dermatitis have been reported (4, 15).

## Royal Jelly

Royal jelly is used worldwide in pharmaceuticals, foods, cosmetics, and manufacturing as a nutraceutical to prevent and treat a myriad of chronic health issues (1, 14). The use of royal jelly as a cosmetic and dietary supplement stems from the belief that it has similar effects in humans as it does in the queen bee—namely, health and longevity (17). This product contains water, proteins, carbohydrates, lipids, amino acids, enzymes, hormones, vitamins, and minerals (1, 5, 14). Royalactin, the most bioactive protein, increases body size and ovary development in the queen bee via an epidermal growth factor receptor-mediated signaling pathway (18). Other bioactive compounds include 10-hydroxy-2-decenoic acid (10-HAD), fatty acids, esters, adenosine monophosphate (AMP) N1 oxide, adenosine, acetylcholine, polyphenols, and hormones (1, 5). The activity of royal jelly stems from the fatty acids, proteins, and phenolic compounds (17). It has antibacterial, antitumor, anti-allergy, anti-inflammatory, antioxidant, antiaging, neurotropic, hypoglycemic, hypocholesterolemic, hepatoprotective, hypotensive, vasodilative, and immunomodulatory properties. The medical uses of royal jelly include reproductive health, neurodegenerative diseases, aging disorders, and wounds. It also increases the growth rate of healthy tissue yet controls tumor growth and metastasis (1, 5, 17). This type of modulation of growth is common when utilizing phytochemicals.

The main side effects of oral royal jelly involve allergic reactions, which vary from GI issues and atopy to asthma, intestinal bleeding, anaphylactic shock, and occasionally death. Patients who are allergic to bees or have other allergies are more at risk of having allergic reactions to this product. Therefore, individuals with bee product allergies (including pollen, honey, and venom) should not ingest royal jelly.

In addition, this should not be consumed during an asthma attack. Topical use of royal jelly can have side effects such as rashes and eczema (5). Other concerns with the product are quality and adulteration. With the exception of chemical analysis, organoleptics using taste, sight, and smell are the best assessment of the product. Royal jelly should always be frozen and should be whitish-yellow, with a pungent odor and a sweet and sour flavor. Adulteration of royal jelly is usually with the addition of honey, which increases the sugar content while decreasing the protein and lipid content (17).

### **Bee Pollen**

Bee pollen may be nature's most complete food. It contains all the ingredients essential for human life and all the nutrients human bodies require (8). Bee pollen is composed of proteins and free amino acids, carbohydrates, lipids (including essential fatty acids), vitamins, minerals, RNA, and DNA (7, 19). It contains more protein per weight than any animal source (7). The primary active phytochemicals include flavonoids and other phenolic acids as well as polysaccharides, phospholipids, and terpenes (7, 8, 19). Bee pollen is used in Traditional Chinese Medicine as a nutritive tonic. It is used medicinally for physical and mental endurance, vitality, longevity, recovery from illness, blood building, prevention of disease, cardiovascular support, hepatoprotection, and protection from radiation and cancer (6-8, 19). Bee pollen inhibits the development of harmful bacteria, normalizes cholesterol and triglyceride levels as well as other metabolic conditions, and regulates intestinal function by the high amount of cellulose and fiber. It also stimulates ovarian function, prevents prostate disorders, and treats allergic conditions via desensitization. Other uses include the treatment of GI ulcers, headaches, upper respiratory diseases, and urinary tract disorders. This product is considered antioxidant, anticarcinogenic, antimicrobial, and anti-inflammatory. Constituents include lecithin, which aids in adipose reduction, and phenylalanine, which is an appetite suppressant. Because of its abilities to enhance the immune system and correct body chemistry, it clears the body of toxins (including heavy metals), which in turn can help prevent cravings in people going through withdrawal from alcohol or drugs. Due to the DNA and RNA in bee pollen, used either internally or externally it helps the skin look and remain healthy, enhances the granulation of tissue after burns, and suppresses acne (6-8). Its nutritional benefits include recovery from malnutrition, especially in the young or elderly or in patients recovering from surgery (8). The dosage of pollen for humans should be slowly built up

over 1 to 2 weeks to a maximum of 1 tsp/day for allergies and 1 tbsp/day for other indications. It should be administered 3 times a day for a 1- to 3-month course. Bee pollen is most effective when taken with food, fruit, or fruit juice, as it becomes more bioavailable after the outside of each pellet is cracked (6, 7). Before starting a bee pollen regimen, patients should try 1 pellet to make sure there is no anaphylactic reaction.

### **Bee Venom**

Honey bee venom has a long history of traditional medicinal use. In addition to water, it contains proteins, peptides, enzymes, phospholipids, amines, amino acids, sugars, and minerals. There are 5 bioactive enzymes, including phospholipase A<sub>2</sub> (PLA<sub>2</sub>), which destroys cells by breaking down the cell membrane. PLA<sub>2</sub> protects against many diseases, including asthma, arthritis, and Parkinson's disease (10). Phospholipase B specifically breaks down blood cells, hyaluronidase breaks down hyaluronic acid, and acid phosphatase triggers basophilic histamine release. The enzyme  $\alpha$ -glucosidase is involved in honey production (10). Melittin, a peptide, is the main anti-inflammatory constituent in bee venom, causing cortisol release, among other effects. Apamin, another peptide, also increases cortisol secretion and is a mild neurotoxin. The peptide adolapin blocks cyclooxygenase and therefore is anti-inflammatory and analgesic (9).

Bee venom has anti-inflammatory, antibacterial, radioprotective, anticancer, anti-nociceptive, hepatoprotective, and immunostimulating actions (9). It is used to treat many inflammatory conditions, such as arthritis, joint disease, Lyme disease, rheumatoid arthritis, and multiple sclerosis. It can also be used to treat epilepsy, chronic pain conditions, coagulopathies, migraines, neuralgias, cancer, wounds, asthma, keratoconjunctivitis, and other conditions (9). The best method of administering bee venom therapy is by using live bees to directly sting the patient. However, bee venom is also collected and used as an injection, either locally or through aquapuncture (the technique in which a liquid is injected into an acupuncture point). Although erythema, heat, swelling, and itchiness are expected from bee venom, allergic reactions range from a swelling that exceeds average parameters, to hives and throat swelling, and even anaphylaxis and death. Patients who show signs of an allergic reaction should not receive bee venom therapy unless first undergoing desensitization. All patients should be tested for signs of an allergic reaction before full treatments are performed. Finally, the LD<sub>50</sub> dose of bee venom for a human is 2.8 mg/kg, which translates to roughly 650 stings (maximum of 0.3 mg of venom per sting) for a 68-kg person (9).

## Conclusion

Honey bees are a vitally important species in our ecosystem. They provide us with food, textiles, medicine, plants, and more. This paper elucidates just a small portion of the medicine these wonderful creatures create for us. The medicinal products that have been well documented and researched include honey, propolis, royal jelly, pollen, and venom. However, without honey bees, we would not have food, medicine, nutraceuticals, or herbs for herbal medicine. Without herbal medicine, humans would not have invented pharmaceuticals or discovered flower essences or many homeopathic medicines. Honey bees are integral to our health and wellbeing and should be accorded the reverence and respect these amazing creatures have earned.

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