



APITHERAPY

Also Known As:

Api-therapy, Api-treatment, Bee Therapy, Bee Treatment, Bee Venom Therapy, Honey Bee Venom Therapy.

Scientific Name:

None.

People Use This For:

Apitherapy is the use of honey bee products such as honey, bee venom, propolis, and royal jelly for medicinal purposes. Apitherapy is used for multiple sclerosis, osteoarthritis, rheumatoid arthritis, post-herpetic neuralgia, and bee sting desensitization. It is also used for cough, herpes simplex virus, premenstrual syndrome (PMS), sulcoplasty, allergic rhinitis, improving athletic performance, hyperlipidemia, and the common cold.

Topically, apitherapy, usually using honey, is used for burns, wound healing, and diabetic foot ulcers.

Safety:

LIKELY SAFE ...when apitherapy using bee venom is given by subcutaneous injection by a trained medical professional (2619, 6070). Purified bee venom for subcutaneous injection is an FDA-approved product (2619). ...when apitherapy using honey is taken orally and appropriately. Honey consumption is safe in adults and children over 1 year (13160, 14319). The concern about botulism pertains to infants and young children and not to adults (13160).

POSSIBLY SAFE ...when apitherapy using stings from live bees is administered. Live bee stings have been safely administered under medical supervision in doses up to 20 bee stings three times weekly for up to 24 weeks (13222). ...when apitherapy using royal jelly and bee pollen is taken orally and appropriately, short-term. Taking 2 tablets twice daily of a specific combination product containing royal jelly 6 mg, bee pollen extract 36 mg, and bee pollen plus pistil extract 120 mg (Femal, Natumin Pharma) per tablet for up to 2 months seems to be safe (12008); however, it's not known if other royal jelly doses and formulations are safe. ...when apitherapy using honey is applied topically and appropriately (395, 396, 397, 398, 399, 7847, 7849, 13133, 14317). There is insufficient reliable information available about the safety of apitherapy using propolis.

CHILDREN: POSSIBLY SAFE ...when apitherapy using honey is taken orally and appropriately, short-term. Single doses of honey have been safely used in children aged 2 years and older (15910). **POSSIBLY UNSAFE** ...when apitherapy using honey is given orally in infants or young children. Ingestion of raw honey contaminated with *Clostridium botulinum* spores can cause botulism poisoning in infants or young children under 12 months of age (13160); however, this is not a danger for older children or adults.

PREGNANCY AND LACTATION: **LIKELY SAFE** ...when apitherapy using honey is consumed in food amounts (13160). **POSSIBLY SAFE** ...when apitherapy using bee venom is given by subcutaneous injection by a trained medical professional. Significant adverse effects to fetus or mother have not been reported. However, some clinicians decrease maintenance dose by half during pregnancy (2619). **POSSIBLY UNSAFE** ...when apitherapy using bee venom is given by subcutaneous injection in high doses. High doses of bee venom can increase release of histamine, which can cause uterine contraction (2619); avoid using in high doses.

Effectiveness:

LIKELY EFFECTIVE

Bee sting allergy. Subcutaneous use of bee venom seems to be effective for bee sting desensitization in patients with severe allergy to bee stings. Bee venom immunotherapy provides 98% to 99% protection from systemic reactions to bee stings. Once immunotherapy is stopped, the risk of a systemic reaction over the next 5 to 10 years is about 5% to 15% (6043, 6075, 6076). Bee venom is an FDA-approved subcutaneous injectable product for the treatment of severe allergies to bee stings (2619).

POSSIBLY EFFECTIVE

Burns. Honey applied directly in gauze applications seems to improve formation of granulation tissue and speed healing time in partial thickness burns. It appears to compare favorably with silver sulfadiazine and moisture permeable polyurethane dressing (OpSite) (395, 396, 397, 398, 399, 14317). Surgical intervention with tangential excision and skin grafting appears to be more effective than honey for moderate burns (7848). Overall poor study design limits the reliability of these findings. Propolis used topically might also help for treating minor burns. There is preliminary evidence that a propolis skin cream is comparable to silver sulfadiazine for preventing infection. It might also be more effective in the re-epithelization and healing of minor burn wounds such as superficial second degree burns (8663).

Cough. Some evidence shows that taking 2.5-10 mL (0.5-2 teaspoons) at bedtime can significantly reduce nighttime cough frequency and severity, and improve sleep compared to placebo in children ages 2 years and older. Honey also appears to be at least as effective as the cough suppressant dextromethorphan in typical over-the-counter doses (15910).

Herpes simplex virus type 2 (HSV-2). A 3% propolis ointment seems to significantly improve healing of recurrent genital lesions caused by herpes simplex virus type 2 (HSV-2). There is some evidence that it might help heal lesions faster and more completely than 5% acyclovir ointment (1926).

Sulcoplasty. Propolis mouth rinse following sulcoplasty seems to improve healing and reduce pain and inflammation (799).

POSSIBLY INEFFECTIVE

Athletic performance. Taking bee pollen orally doesn't seem to increase athletic performance or stamina (7062, 7063).

Multiple sclerosis (MS). Administering live bee stings in graduated doses up to 20 stings given three times weekly does not seem to improve multiple sclerosis. Treatment for 24 weeks does not seem to reduce gadolinium-enhancing lesions on MRI or improve fatigue, disability, or quality of life (13222).

Osteoarthritis. Some early reports seemed to indicate a possible benefit of injected bee venom in the treatment of arthritis; however, results are conflicting and most clinical studies do not show a benefit (6045).

INSUFFICIENT RELIABLE EVIDENCE to RATE

Allergic rhinitis. Preliminary clinical research suggests that consuming honey one

tablespoon daily, in addition to standard treatment, does not significantly improve symptoms (14319).

Athletic performance. Some preliminary clinical evidence suggests that honey might normalize blood sugar following exercise and improve performance when given during exercise (7851).

Common cold. There is some evidence that propolis might be helpful for treating the common cold. Propolis might decrease the duration of cold symptoms by 2.5 times compared with placebo in patients with rhinovirus infection (6602).

Diabetic foot ulcers. Anecdotal reports suggest that applying topical raw honey can speed healing of otherwise non-healing diabetic foot ulcers, even in the presence methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE), and *Pseudomonas* infection. In one report, previously non-healing ulceration completely healed after applying honey dressings for 6-12 months and lower-limb amputation was prevented (13133).

Hyperlipidemia. There is preliminary evidence that royal jelly might lower cholesterol levels in people with hyperlipidemia (3515).

Premenstrual syndrome (PMS). Preliminary evidence suggests that a specific combination product (Femal, Natumin Pharma) seems to decrease some symptoms of PMS including irritability, weight gain, and edema when given over a period of 2 menstrual cycles. This product contains royal jelly 6 mg, bee pollen extract 36 mg, and bee pollen plus pistil extract 120 mg per tablet. It is given as 2 tablets twice daily (12008).

Wound healing. Preliminary research suggests that applying honey topically to infected post-surgical wounds speeds healing time, increases eradication of infection, and decreases hospital stay (14317). Preliminary evidence also suggests that applying honey topically can improve healing of mild skin ulceration, wounds, and sores (7847, 7849).

More evidence is needed to rate apitherapy for these uses.

Mechanism of Action:

Apitherapy is the use of honey bee products such as bee venom, honey, royal jelly, propolis, and bee pollen for medicinal purposes. These different bee products are used in a variety of different ways and for different uses. For a complete discussion of the mechanism of action, see detailed monographs for Bee Pollen, Bee Venom, Honey, Propolis, and Royal Jelly.

Bee pollen refers to the pollen from flowers that collects on the legs and bodies of worker bees. Proponents often claim that enzymes in bee pollen provide a variety of therapeutic benefits. However, any enzymes in bee pollen are likely to be digested in the gastrointestinal (GI) tract. There is no reliable evidence indicating that bee pollen enzymes or other constituents in bee pollen offer any therapeutic benefit.

Bee venom is primarily used for bee sting desensitization, multiple sclerosis, and osteoarthritis. Bee venom injections subcutaneously or by live bee stings are thought to stimulate an allergic response, decreases leukocyte sensitivity to the allergen, and increases the number of T-suppressor cells (2619). There were early suggestions that bee venom could be a useful treatment in patients with arthritis. This theory was largely due to purported anti-inflammatory effects of bee venom, and the observation that many beekeepers don't develop arthritis (6). While some components in bee venom have been shown to have anti-inflammatory effects, studies have also shown that some components of bee venom are pro-inflammatory. For example, activators of PLA2 such as melittin, are thought to cause an increase in the synthesis of cytokines (tumor necrosis factor and interleukin 1) and stimulate arachidonic acid release resulting in an immune or inflammatory response (6044, 6071).

Honey is produced by bees (*Apis mellifera*) from the nectar of several varieties of plants. Pharmacological activity can vary depending on the type of plant from which the nectar is obtained. For example, honey produced from poisonous plants can be poisonous (6).

Honey is thought to improve wound healing by promoting the formation of granulation tissue. It promotes the growth of epithelial cells by providing a barrier to moisture which helps keep the wound hydrated. Enzymes and hydrogen peroxide in honey can aid in debridement (395, 396, 399, 7849).

Propolis is a resinous material from poplar and conifer buds. Bees use it for maintaining their hives. Therapeutic uses of propolis are primarily attributed to antiviral, antibacterial, and antimycotic effects. Propolis contains flavonoids including pinocembrin, galangin, pinobanksin, and pinobanksin-3-acetate, which are thought to be responsible for its antimicrobial effects (5, 1926). Propolis extracts that contain the constituents pinocembrin and galangin have been shown to inhibit the growth and enzyme activity of *Streptococcus mutans*, an organism that causes dental caries (2631). Propolis also seems to have in vitro activity against a variety of bacteria that cause periodontal disease such as *Porphyromonas gingivalis*, *Prevotella intermedia*, *Actinobacillus actinomycetemcomitans*, and *Fusobacterium nucleatum* (8664).

Propolis might also have anti-inflammatory effects. There is preliminary evidence that it might suppress the lipoxygenase pathway of arachidonic acid metabolism and decrease the synthesis of prostaglandins and leukotrienes involved in inflammation (2630).

Royal jelly is a milky secretion produced by glands in the heads of nurse honey bees (*Apis mellifera*). The composition of royal jelly varies with geographical areas and climatic conditions. It typically contains about 60% to 70% water, 12% to 15% crude proteins, 10% to 16% sugar, 3% to 6% lipids, and 2% to 3% low molecular weight compounds such as vitamins, salts, and free amino acids (7313). Royal jelly is used for the development and nurturing of queen bees (6). There is very little scientific information available about its effects in humans. In animal models, royal jelly seems to have some antitumor activity (6) and antiatherogenic activity (3515).

Adverse Reactions:

Different products used in apitherapy can cause a wide variety of adverse reactions. For the complete discussion of adverse reactions see detailed monographs for Bee Pollen, Bee Venom, Honey, Propolis, and Royal Jelly.

Bee pollen seems to be well-tolerated in most patients. There is one report of dizziness in a patient who took a combination product containing royal jelly, bee pollen extract, and a bee pollen plus pistil extract (12008).

Patients with pollen allergies are at risk for serious allergic reactions. Allergic reactions can include itching, swelling, shortness of breath, light headedness, and anaphylaxis. Chronic allergy symptoms due to bee pollen include gastrointestinal (GI) and neurologic symptoms and eosinophilia (5, 6, 11). There have also been two cases of acute hepatitis associated with bee pollen use. One case involved ingestion of two tablespoons of pure bee pollen daily for several months. Another case involved ingestion of 14 tablets per day of a combination herbal product containing bee pollen, chaparral, and 19 other herbs for 6 weeks (1351). In this case it is not known if bee pollen or another herb might have caused the adverse event.

Bee venom is often administered subcutaneously. The most common adverse reactions including local erythema, swelling, and tenderness at the injection site are the most common reactions to bee venom treatment (1343, 13222). Less common adverse effects ranging from itching, urticaria, edema, malaise, flu-like symptoms, and

anxiety to anaphylaxis occur in about 20% of patients (1343, 13222). Adverse reactions most often occur during the dose increase phase of immunotherapy, particularly with rapid dose increases (1343, 6077). Risk of adverse effects seems to be increased in people treated with honeybee venom (1343, 6077). Women seem to have more severe and more frequent adverse effects (1343). Anaphylaxis is most likely to occur in extremely sensitive individuals or in the case of an overdose (2169, 6074, 6077). Other adverse reactions include chest tightness, palpitations, dizziness, nausea, vomiting, diarrhea, somnolence, respiratory distress, hypotension, confusion, fainting, and laryngeal edema or asthma (1343, 2619, 6070, 6078). Uncommon reactions are abdominal pain, incontinence, chest pain, or visual disturbances (6078). Rarely, coagulation abnormalities can occur, and are usually associated with severe reactions to bee stings (6046).

Honey can cause allergic reactions. Some honey is contaminated with *Clostridium botulinum* spores, which poses a risk to infants, but not older children or adults (6, 11). Botulinum spores can proliferate in the intestines of infants and cause botulism poisoning. Honey from the Black Sea coast of Turkey has been linked with a unique form of poisoning. Honey from this region sometimes contains excessive concentrations of acetylcholinesterase which can cause nausea, vomiting, dizziness, sweating, weakness, bradycardia, atrioventricular (AV) block, and hypotension within a few minutes to several hours after consumption. Fatalities have not been reported. Patients typically respond with fluids and reversal of cardiac conduction abnormalities with atropine. Honey containing this poison is sometimes called "mad honey" (12220). Topically, honey may cause excessive dryness of wounds, which could delay healing. This can be managed by application of saline packs as needed (7850).

Propolis can cause allergic reactions and acute oral mucositis with ulceration from the use of the propolis-containing lozenges (2632). Patients allergic to bees or bee products may be more likely to experience allergic reactions. Propolis has been linked to acute renal failure in one case report. In this report, a 59-year-old man with cholangiocarcinoma developed acute renal failure requiring hemodialysis after taking a Brazilian preparation of propolis 5 mL three times daily for 2 weeks. Renal function improved when propolis was discontinued. The patient restarted taking propolis and symptoms developed again and the patient again required hemodialysis. Symptoms of renal failure again improved when propolis was finally discontinued. This pattern suggests that propolis was the likely cause of renal failure in this patient. This product was not screened for contaminants; however, family members of this patient used the same product without apparent adverse effects (14300). Topically, propolis-containing products, including some cosmetics can cause eczematous contact dermatitis (2632, 15647).

Royal jelly appears to cause few side effects in nonallergic people (7314). There is one report of dizziness in a patient who took a combination product containing royal jelly, bee pollen extract, and a bee pollen plus pistil extract (12008). In people with a history of atopy or asthma, royal jelly appears to cause a high rate of allergic symptoms including pruritus, urticaria, eczema, eyelid and facial edema, conjunctivitis, rhinorrhea, dyspnea, and asthma (7314, 7315, 7316, 10623). In severe cases, royal jelly can cause status asthmaticus, anaphylaxis, and death (792, 7315, 7316, 10623, 10624). Allergic symptoms are associated with IgE-mediated hypersensitivity reactions (3513, 10623). Tell people with a history of allergy or asthma not to use royal jelly. There is also one case report of hemorrhagic colitis with abdominal pain, bloody diarrhea with concomitant hemorrhagic and edematous mucosa of the sigmoid colon after ingestion of royal jelly. Symptoms resolved within 2 weeks following discontinuation of royal jelly and conservative treatment (3516). Topically, skin irritation, exacerbation of dermatitis, or contact dermatitis may occur (791).

Interactions with Herbs & Supplements:

None known.

Interactions with Drugs:

IMMUNOSUPPRESSANTS

Interaction Rating = **Moderate** Be cautious with this combination
Severity = Moderate • Occurrence = Possible • Level of Evidence = D

Bee venom might stimulate immune system activity (6044, 6071). Theoretically, bee venom might interfere with immunosuppressant therapy. Immunosuppressant drugs include azathioprine (Imuran), basiliximab (Simulect), cyclosporine (Neoral, Sandimmune), daclizumab (Zenapax), muromonab-CD3 (OKT3, Orthoclone OKT3), mycophenolate (CellCept), tacrolimus (FK506, Prograf), sirolimus (Rapamune), prednisone (Deltasone, Orasone), corticosteroids (glucocorticoids), and others.

WARFARIN (Coumadin)

Interaction Rating = **Moderate** Be cautious with this combination
Severity = High • Occurrence = Possible • Level of Evidence = D

Royal jelly might increase the effects of warfarin and increase the risk of bleeding. In one case, an 87-year-old man, who was previously stabilized on warfarin, developed hematuria and was found to have an highly elevated INR of 7.29 after taking a royal jelly supplement for a week (14303). How royal jelly might increase the effects of warfarin is not known.

Interactions with Foods:

None known.

Interactions with Lab Tests:

PROTHROMBIN TIME (PT): Bee venom might increase the prothrombin time (PT) and partial thromboplastin time (PTT) (6046). The PLA2 component of bee venom seems to reduce the activity of clotting factors II, V, and VIII (6046). Royal jelly might also increase INR and PT in patients anticoagulated with warfarin. In one case, an 87-year-old man, who was previously stabilized on warfarin, developed hematuria and was found to have an highly elevated INR of 7.29 after taking a royal jelly supplement for a week (14303).

Interactions with Diseases or Conditions:

ASTHMA: Some sources suggest allergens in propolis may worsen asthma (3574); avoid using. In patients with asthma or atopy, royal jelly also causes a high rate of allergic symptoms including pruritus, urticaria, eczema, eyelid and facial edema, conjunctivitis, rhinorrhea, dyspnea, and asthma (7314, 7315, 7316, 10623). In severe cases, royal jelly can cause status asthmaticus, anaphylaxis, and death (792, 7315, 7316, 10623, 10624). Allergic symptoms have been associated with IgE-mediated hypersensitivity reactions (3513, 10623). Advise people with asthma or allergies not to use royal jelly.

ATOPY: In patients with asthma or atopy, royal jelly causes a high rate of allergic symptoms including pruritus, urticaria, eczema, eyelid and facial edema, conjunctivitis, rhinorrhea, dyspnea, and asthma (7314, 7315, 7316, 10623). In severe cases, royal jelly can cause status asthmaticus, anaphylaxis, and death (792, 7315, 7316, 10623, 10624). Allergic symptoms have been associated with IgE-mediated hypersensitivity reactions (3513, 10623). Advise people with asthma or allergies not to use royal jelly.

AUTOIMMUNE DISEASES: Some evidence suggests that bee venom might stimulate immune system activity (6044, 6071). Theoretically, bee venom might exacerbate autoimmune diseases by stimulating disease activity. Advise patients with autoimmune diseases such as multiple sclerosis (MS), systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), or others to avoid or use bee venom with caution.

DERMATITIS: Royal jelly might exacerbate dermatitis; avoid using (791).

POLLEN ALLERGY: Patients with pollen allergies are at risk for serious allergic reactions. Allergic reactions can include itching, swelling, shortness of breath, light

headedness, and anaphylaxis (5, 6).

Dosage/Administration:

ORAL: For cough, 2.5-10 mL (0.5-2 teaspoons) of honey at bedtime has been used (15910).

For hyperlipidemia, 50-100 mg per day has been used (3515). For premenstrual syndrome (PMS), two tablets twice daily of a specific combination containing royal jelly 6 mg, bee pollen extract 36 mg, and bee pollen plus pistil extract 120 mg (Femal, Natumin Pharma) per tablet for 2 menstrual cycles has been used (12008).

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PARENTERAL: Bee venom is used subcutaneously, intradermally, and intra-arterially for these uses. For arthritis, purified, sterile bee toxin (apitoxin 2 mg/mL) has been used starting with 0.05-0.1 mL. The dose is gradually increased to 0.25 mL, 0.5 mL, and 1 mL, with dose intervals usually from 5 to 7 days. For bee venom immunotherapy in people hypersensitive to bee stings, increased doses of venom are given at selected intervals, usually weekly (6078). There are many possible protocols for immunotherapy. Some start with 0.0001 or 0.001 mcg of venom extract (6077). This is continued until a maintenance dose is achieved, usually 100 micrograms per venom.

Once the maintenance dose is achieved, therapy can continue for years. Patients have varying sensitivities to venom and tolerability to immunotherapy, so it is not possible to provide a general dosing schedule for all patients. Venom immunotherapy should only be done by physicians thoroughly familiar with the use of these products, including the treatment of anaphylactic and other adverse reactions. It is also advised to have injectable epinephrine and emergency facilities nearby in case an anaphylactic reaction occurs (2619, 6074, 6078). Alcohol and tincture of iodine rapidly destroy the activity of bee venom and should not be applied at the site of injection. In China, bee venom is also commonly administered by electrophoresis, ultrasonophoresis, and acupuncture.

TOPICAL: For the treatment of burns, honey has been applied directly or as a dressing made from gauze impregnated with honey. The dressings have been left in place for up to 25 days, with wound inspection every 2 days (397, 398). When used directly, 15 to 30 mL of honey has been applied every 1 to 2 days, and covered with a dry sterile gauze and bandage (396, 399).

For diabetic foot ulcer, ordinary honey purchased from a supermarket has been used. It is applied in thick applications to a 4x4 gauze and placed on the ulceration and then wrapped (13133).

As a mouth rinse after sulcoplasty, a 5% aqueous alcohol solution of propolis is commonly used (799).

For herpetic lesions, 3% propolis ointment applied to the lesions 4 times daily has been used (1926).

Editor's Comments:

There is no training or licensing standard for practitioners of apitherapy in North America. In many instances, apitherapy is practiced by other licensed health professionals such as nurses, physicians, acupuncturists, or naturopaths.

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