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COMPREHENSIVE DATABASE

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BEE VENOM

Also Known As:

Apis Venenum Purum, Apitoxin, Bald-Faced Hornet, Bumblebee Venom, Honeybee Venom, Mixed Vespids, Pure Bee Venom, Wasp Venom, White-Faced Hornet, Yellow Hornet, Yellow-Jacket Venom.

Scientific Name:

Apis mellifera (Honeybee); Bombus terrestis (Bumblebee); Vespula maculata (Hornet, Wasp).
Family: Apidae; Vespidae.

People Use This For:

Parenterally, bee venom is used for rheumatoid arthritis, neuralgias, multiple sclerosis, desensitization to bee stings (venom immunotherapy), tendonitis and tendosynovitis, and muscle conditions such as fibromyositis and enthesitis.

Safety:

LIKELY SAFE ...when used by subcutaneous injection by a trained medical professional (2619, 6070). Purified bee venom for subcutaneous injection is an FDA approved product (2619).

POSSIBLY SAFE ...when applied using stings from live bees. 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).

PREGNANCY AND LACTATION: POSSIBLY SAFE ...when used 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 used 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 INEFFECTIVE

Multiple sclerosis (MS). Administering live bee stings in graduated doses up to 20 stings given three times weekly does not seem to improve multiples 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).

There is insufficient reliable information available about the effectiveness of bee venom for its other uses.

Mechanism of Action:

Bee venom contains several physiologically active components. Two of the most toxic compounds are melittin and phospholipase A2 (PLA2). Melittin constitutes 30% to 50% of dry bee venom (6041, 6045, 6046), and PLA2 makes up about 10% to 12% of bee venom (6041). Melitin is a potent hemolytic (6042, 6045) that causes mast cell degranulation and activates PLA2 (6045). Other constituents in bee venom include hyaluronidase, apamin, mast cell degranulating peptide (MCD peptide), procamine, secapin, tertiapin, and other small peptides including adolapin (6). Some other components are histamine, dopamine, and noradrenaline (6041). In desensitization to bee stings, hymenoptera venom stimulates an allergenic 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).

PLA2 is an enzyme which catalyzes the hydrolysis of phospholipid bonds, destroying the major component of cell membranes and leading to cell death (6041, 6046). PLA2 causes smooth muscle contraction, blood pressure reduction, increased capillary permeability, and mast cell destruction. PLA2 also reduces blood coagulation, possibly by reducing the activity of coagulation factors II, V, and VIII (6046). Melittin might also be partially responsible for bee venom's anticoagulant effects (6046). Some components in bee venom seem to cause neutrophil degranulation and superoxide production (6, 6044), but other actions of bee venom components seem to decrease superoxide production (6, 6041, 6045, 6072). The formation of superoxide anions can be destructive to tissues. The melittin component of bee venom possesses antimicrobial activity, but due to its hemolytic effects, melittin is unsuitable as a treatment for infections (6042). Hyaluronidase is an enzyme which hydrolyzes hyaluronic acid. The adhesive properties of hyaluronic acid hold cells together, so once hydrolyzed, other venom components can penetrate into the cell. For this reason, hyaluronidase is termed a spreading factor (6041). Apamin is a neurotoxin (6045). It blocks many inhibitory effects, including alpha-adrenergic, cholinergic, and neurotensin-induced relaxation, by blocking calcium-dependent potassium channels (6041). MCD peptide is chemically similar to apamin. It causes mast cell degranulation and release of histamine at extremely low concentrations. Histamine causes dilation and increased permeability of capillaries (6041). The constituent adolapin inhibits inflammation and the prostaglandin-synthase system (6). In animals, whole bee venom, melittin, and apamin have also been shown to cause increases in cortisol levels (6039, 6040). The mechanism of other peptides is not yet understood (6041).

Adverse Reactions:

Parenterally, 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).

Interactions with Herbs & Supplements:

None known.

Interactions with Drugs:

IMMUNOSUPPRESSANTS
Interaction Rating = **Moderate** Be cautious with this combination
Severity = High • 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.

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).

Interactions with Diseases or Conditions:

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.

Dosage / Administration:

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.l 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.

Editor's Comments:

Avoid confusion with bee pollen, honey, and royal jelly. Other venoms are derived from related members of the insect order, Hymenoptera (6).

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