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THE REVIEW OF
NATURAL PRODUCTS

TOPIC:
BEE VENOM

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SCIENTIFIC NAME(S): Derived from *Apis Mellifera*

COMMON NAME(S): Bee venom, honeybee venom

SOURCE: Honeybee venom is obtained from *Apis Mellifera*, the common honeybee. Other venoms are derived from related members of the hymenoptera.

HISTORY: Anaphylaxis to insect stings is a relatively uncommon problem, believed to have affected only 0.4% of the general US population in the early 1990s. It is the cause of approximately 40 deaths per year in the United States.[1]

The allergic reactions are mediated by IgE antibodies directed at constituents of honeybee, yellow jacket, hornet and wasp venoms. In order to minimize the allergic reaction, hyposensitization immunotherapy techniques have been developed in which small doses of the venom are administered under controlled conditions over a period of months to years. Patients allergic to honeybee venom may be particularly sensitive to hymenoptera venoms in general and have been found to be at a significantly higher risk of developing systemic side effects to venom immunotherapy than patients who are sensitive to yellow jacket venom.[2]

More recently, it has been suggested that honeybee venom may alleviate the symptoms and slow the progression of immune-modulated diseases such as arthritis and multiple sclerosis.

CHEMISTRY: Bee venoms are complex mixtures of amino acids and polysaccharides. They are collected from the insects and diluted to standardized concentrations. Melittin, a phospholipase activating protein in bee venom, has been shown to induce neutrophil degranulation[3] and to both increase[3] and inhibit[4] the formation of superoxide. This difference in activity appears to be dependent upon the test method employed. Melittin induces neutrophil degranulation with subsequent superoxide formation;[3] however, melittin binds to calmodulin, and this effect is associated with an inhibition of the production of superoxide.[4]

The polypeptide adolapin isolated from bee venom inhibits inflammation in animals (carrageenan, prostaglandin and adjuvant rat paw edema models) and appears to inhibit the prostaglandin synthase systems.[5]

PHARMACOLOGY: *Immunotherapy:* Hypersensitivity to honeybee venom is mediated by a number of antibodies and immunomodulators, the most important of which appears to be IgE. The infusion of beekeepers' plasma has been shown to protect patients against systemic reactions that can occur during active immunotherapy.[6] Following infusion of this plasma, a decrease in the sensitivity to honeybee venom has been noted; in one study, this was accompanied by increases in the levels of anti-idiotypic antibodies and decreases in specific antibodies to honeybee venom (IgG and IgE). (The study was conducted over a 76-week period of immunotherapy with the venom.) These findings suggest that several mechanisms play an interrelated role in the development of immunity to honeybee venom.

Arthritis Therapy: For some time it has been speculated that honeybee venom may prevent the development or improve the status of patients with rheumatoid arthritis. This conclusion was based largely on anecdotal observations of a general lack of arthritis among beekeepers stung routinely during their lifetimes. In one survey of a random sampling of the general population, 83% of respondents believed that bee venom could be an effective treatment for arthritis based on information they had read in the popular press.[7]

Honeybee venom administered to rats with adjuvant arthritis resulted in a significant suppression of the disease.[8] Melittin has been shown to block the production of superoxide and hydrogen peroxide in human neutrophils. Melittin and other agents that bind calmodulin have been shown to decrease superoxide production. An elevated superoxide level has been suggested as a possible cause of oxidative damage to synovial fluid and other joint membranes. Therefore, agents that decrease the production of the superoxide may prevent or halt the progression of inflammatory diseases such as arthritis. Also, honey-

bee venom has been found to decrease the production of the inflammatory mediator interleukin-1 (IL-1) in rat splenocytes.[9] Honeybee venom treatment of rats with adjuvant arthritis inhibits certain macrophage activities and, thus, indirectly inhibits the activation of T and B cells.[9]

Other Uses: Other uses for bee venom, though poorly substantiated, include the treatment of diseases of the locomotor system,[10] particularly multiple sclerosis (MS). Despite widespread reports of true effectiveness of bee venom therapy for MS, there is no scientific consensus as to its safety and true effectiveness in the management of this disorder.

TOXICOLOGY: While single honeybee stings can cause anaphylaxis, the most severe reactions generally result from multiple stings. Signs and symptoms of multiple stings include urticaria (hives), nausea, vomiting, diarrhea, hypotension, confusion, seizures and renal failure. Treatment is supportive, with attention to blood pressure, renal function and maintaining an open airway. Stingers should be removed with gentle scraping to prevent further venom injection.[11] Because cardiac levels of noradrenaline have been found to increase dramatically in animals following injection with bee venom, it is suggested that all patients, regardless of sensitivity history, have cardiac monitoring if they are victims of multiple bee stings.[12] Rare cases of anuria and rhabdomyolysis/rhabdomyonecrosis have been reported.[13,14]

SUMMARY: Bee venom is used in hyposensitization immunotherapy for patients who are highly sensitive to the effects of bee stings. In addition, the venom finds use in the nontraditional treatment of arthritis and multiple sclerosis. The latter uses are based on observations of an anti-inflammatory and immunomodulating effect induced by bee venom.

PATIENT INFORMATION – Bee Venom

Uses: Bee venom is used to hyposensitize individuals highly sensitive to bee stings. There is some evidence it also helps inhibit or suppress arthritis and multiple sclerosis.

Side Effects: A single bee sting can produce anaphylaxis in sensitive individuals. Regardless of history, any patient with multiple stings should be monitored.

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