



## The Physiological Effects of Bee Venom and Its Medical Uses

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### ABSTRACT

Bee products have been used by man for centuries. Numerous properties and a wide range of activity of each bee product brings the possibility of using them in the therapy of many diseases. However, more research is needed on the composition of bee products, because the mechanism of their action has not yet been fully understood. This review provides information indicating a wide range of therapeutic properties of bee venom. Numerous substances found in this venom, through various mechanisms, have beneficial and positive effects on the functioning of the human body. The most important being the protein melittin, which has a powerful anti-inflammatory action. This suggests their possible use in many medical specialties. The number of threats to honey bee is increasing all over the world, which is becoming more and more susceptible to diseases and pathogens. Bees are thought to be threatened by: bacteria, viruses, parasites, pesticides used in agriculture, environmental changes, or genetically modified organisms. Also, increasing environmental pollution contributes to the extinction of bee families, which in the future will translate into low yields.

### Keywords:

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### Introduction

From the beginning, people have been using the goods that nature gives them. For centuries, we have developed, as a species, the skill of breeding animals and benefiting from the care of them. One of the species whose breeding we managed to master is the honey bee (*Apis mellifera*).

In a form similar to the current one, bees appeared on the earth about 100 million years ago. The area of their occurrence covers all continents except Antarctica. Because of this, the lives of humans and bees have been inseparably connected.

About 78% of plant species in a moderate climate zone are pollinated by a honey bee, which contributes to creation of about 1/3 of

the food produced. The global population of bees is between 80 and 100 million breeding hives, of which each contains between 10,000 and 60,000 individuals. However, it is increasingly emphasized that their population is decreasing [1, 2].

The number of threats to honey bee is increasing all over the world, which is becoming more and more susceptible to diseases and pathogens. Bees are thought to be threatened by: bacteria, viruses, parasites, pesticides used in agriculture, environmental changes, or genetically modified organisms. Also, increasing environmental pollution contributes to the extinction of bee families, which in the future will translate into low yields [3]

Bee products, which include honey, royal jelly, bee glue (called propolis), bee pollen, bee wax and bee venom have been used by man for centuries not only as food products but also as natural medical substances. [\(Apitherapy – the medical use\)](#)

### Apitherapy

Apitherapy is the therapeutic use of bee products is a branch of alternative medicine, or folk medicine, which uses their natural healing qualities [4] [\(Apitherapy – the medical use\)](#). It is the use of bee products such as honey, pollen, propolis, royal jelly, bee venom, wax and to prevent or treat illness and promote healing. [\(Apitherapy: Usage And Experience\)](#) [5]

Apitherapy originates in the areas of present-day Russia or ancient China. However, its foundations can already be found in ancient Egypt or Greece, where bee products were used as cosmetics and preparations to facilitate wound healing. [\(Apitherapy – the medical use\)](#). The roots of apitherapy can be traced back more than 6000 years to medicine in ancient Egypt. The Greeks and Romans also used bee products for medicinal purposes. [\(Apitherapy: Usage And Experience\)](#)

### Bee venom:

Bee venom also called apitoxin is produced in bee venom glands serving as a defensive element. Its properties have been known to

humanity since ancient times. Venom production begins after two or three days of adult bee life and with age decreases.

### [\(Apitherapy – the medical use\)](#)

Early collection methods required surgical removal of the venom gland or squeezing each individual bee until a droplet could be collected from the tip of the sting. Since the early 1960's, extraction by the electro-shock method has been continuously improved and is now standard procedure [6].



Even dried bee venom should be stored refrigerated or preferably frozen and it should always be kept in dark bottles in the dark. All producers and buyers should closely observe these conditions. Dried bee venom can be kept frozen for several months, but should not be kept refrigerated for more than a few weeks. Liquid venom and diluted venom can be stored for similar periods if maintained in well-sealed, dark glass containers. [\(VALUE-ADDED PRODUCTS\)](#)

### Physical and chemical properties

It is a transparent liquid that can also turn yellow, odorless, but has a sharp, bitter taste. This is a water-soluble substance, while it is insoluble in alcohol and ammonium sulfate. The venom's pH ranges 4.5-5.5 and its specific weight is 1.13. It dries quickly in contact with air, forming a yellow-brown powder [55, 56].

From all the substances in venom, the largest percentage is water, the amount of which is 88%. In addition to water, its main components are peptides such as mellitin, apamin, mast cell deregulating (MCD) peptide, promelittin, the enzymes hyaluronidase and phospholipase A2, and it comprises 10-12% of peptides. Other substances included in apitoxin are low-molecular compounds such as histamine, sinkaline, glycerol, noradrenaline, amino acids, carbohydrates, phospholipids, physiologically active amines and volatile compounds. [\(Apitherapy – the medical use\)](#)

### Physiologically effects and medical uses

There is an increasing interest of consumers and pharmaceutical and food industries in products originating from honeybees. All of these substances have been reported to possess medicinal properties.

These substances are responsible for the properties and activity of apitoxin. The diversity of these compounds means that bee venom has the largest range of biological activities among all bee products.

One of the main peptides (52% of all apitoxin peptides) contained in bee venom is melitin, which has numerous potential therapeutic properties and relatively low toxicity. It has a strong anti-inflammatory effect by inhibiting phospholipase enzymatic activity and increases cortisol production in the body by stimulating the pituitary gland to produce ACTH.

The possibility of its use is also seen in the therapy of HIV infection - it destroys the infectivity of the virus particle. However, its use is limited because of its toxic effect on cell membranes. This problem was solved by using nanoparticles that react only with virus components.

Mellitin also has antioxidant potential by inhibiting the production of hydrogen peroxide by neutrophils. Along with other substances contained in bee venom, it is antibacterial, particularly strong against Gram-positive bacteria.

Research on the mechanism and inhibitory effects of bee venom and melitin on melanoma

cells by Lim *et al.* showed that these substances strongly inhibited the proliferation, migration, invasion of cancer cells and melanin production, as well as increased the activity of the apoptotic pathway dependent on caspases 3 and 9, showing role of melitin as a potential compound used in the treatment of melanoma.

Bee venom has long been used as a natural remedy for rheumatoid arthritis. Its healing effect has been quite well understood - components of bee venom inhibit the chronic inflammatory response which rheumatoid arthritis based on.

Venom components, among others adolapin are inhibitors of pro-inflammatory substances such as: Tumor Necrosis Factor TNF-2, Prostaglandin E2 PGE-2, enzymes like Cyclooxygenase-2 COX-2 and many other cytokines.

In a study by Kocyigit *et al.* it was shown that administration of honey bee venom to rats suffering from rheumatoid arthritis causes an increase in IFN- $\gamma$  and a decrease in the level of pro-inflammatory factors, thus causing a therapeutic effect.

Among the peptides included in bee venom we can also find apamine, which blocks K<sup>+</sup> channels activated by Ca<sup>2+</sup> ions. Apamine has a neuroprotective effect, which may have a positive impact on the functioning of the nervous system in Parkinson's disease. In addition, calcium-induced blockade of potassium channels induced by apamine may result in neuronal stimulation, enhance synaptic plasticity and induce long-term potential of the hippocampal area, which may be used in the treatment of Alzheimer's disease.

In studies conducted on mice suffering from experimental autoimmune encephalomyelitis (EAE), which is the model most similar to human myelodegenerative diseases such as multiple sclerosis MS, administration of bee venom had a beneficial effect stimulating the immune system. Both in vitro and in vivo studies in EAE mice have increased the population of CD4 (+), CD25 (+), Foxp3 (+) T cells, which may result in a reduction of the inflammatory response and make bee venom a potential agent therapeutic.

Other uses of apitoxin include skin diseases such as psoriasis, dermatitis, boils, and eye diseases - iritis or optic neuritis. In the treatment of skin diseases, bee venom is used as ointments and creams, while in ophthalmology it is a component of drops. Bee venom is also used as subcutaneous injections.



### Antimicrobial properties

Bee venom contains several physiologically active components. Among them, melittin, is a very nonspecific cytolytic peptide that attacks all lipid membranes leading to significant toxicity. Also, phospholipase A2 is the most destructive component of apitoxin. It is an enzyme which degrades the phospholipids which cellular membranes are made of.

The antibacterial properties of bee venom as a natural antibacterial agent have been extensively studied, and bee venom therapy has been suggested to be used as an alternative to antibiotic therapy

A strong antibacterial activity of bee venom against both Gram negative and Gram-positive bacteria has been reported. Nakatuji et al. also reported that bee venom could control the

growth of *Staphylococcus aureus*. Moreover, bee venom also exhibited antibacterial activities against skin bacteria such as *Propionibacterium acnes*, *Staphylococcus epidermidis* and *Streptococcus pyogenes*. In a study done by Yu et al. it has been found that bee venom exhibited prominent antifungal activities against *Trichophyton mentagrophytes* and *Trichophyton rubrum* which is much stronger than that of fluconazole, one of the commercial antifungal drugs used in the treatment and prevention of superficial and systemic fungal infections.

### Conclusion

Bee products have been used by man for centuries. Numerous properties and a wide range of activity of each bee product brings the possibility of using them in the therapy of many diseases. However, more research is needed on the composition of bee products, because the mechanism of their action has not yet been fully understood. This review provides information indicating a wide range of therapeutic properties of bee venom. Numerous substances found in this venom, through various mechanisms, have beneficial and positive effects on the functioning of the human body. The most important being the protein melittin, which has a powerful anti-inflammatory action. This suggests their possible use in many medical specialties.

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