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A Review On Bee Venom And Its Medical Uses

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Abstract

One of the most important insects in the world is Apis mellifera, which shows a critical role in different environmental conditions. For thousands of years, diverse honeybee products have been used to cure human ailments in many civilizations, and their curative effects have been mentioned in several holy books. The worker bees and queen produce an apitoxin, which is a cytotoxic and colorless liquid of hemotoxic bitter. The bee venom or apitoxin contains different sugars, volatile pheromones, phospholipids, enzymes, peptides, amino acids, minerals, proteins, and other bioactive compounds. The present review aims to collect more information about the history of honeybee venom and its medicinal uses. The apitoxin or bee venom is medicinally utilized to control different human diseases such as cancer, fibrotic disease, liver fibrosis, Parkinson disease, Alzheimer disease, arthritis, HIV, and Lyme disease. The first report on the application of bee venom to treat human ailments was published in 1888, when European clinical research was conducted to determine the efficacy of honeybee venom in treating rheumatic disorders. According to several studies published in different scientific journals, honeybee venom has been applied to control different human diseases for several centuries. Thus, it can be decided that bee venom can be a potential future biomedicine to control different diseases such as cancer.

Keywords: Honey Bee, Bee Venom, Apamin, Apitoxin, Melittin.

1. Introduction

All female insects of the order Hymenoptera, which includes wasps, ants, and honeybees, generate bee venom, or apitoxin. Venom from honeybees is generated in the venom glands (acid glands) of worker bees and queen bees, which are situated in the venom sac. Apitoxin has a critical defensive function in the honeybee colony. Additionally, bee venom includes a variety of chemical substances with potential medicinal and biotechnological use (Abrantes et al., 2017). Apitoxin production increases throughout the first two weeks of an adult worker's life cycle and peaks when the bee workers begin to defend and feed the hive. However, when employees age, their ability to produce apitoxin decreases. On the other side, the queen bee's apitoxin production is greatest at emergence, since the bee venom must be prepared for instant combat with other queens (Devi et al., 2016). Apitoxin is responsible for toxic or allergic reactions, which are often triggered by molecules with a low molecular weight. As an immediate reaction, these compounds may cause significant pain, local inflammation, itching, and irritation that decreases after several hours (Bellik, 2015; Al-Ameri and Alhasan, 2020). Melittin is the primary component that causes allergic responses. However, Moreno and Giralt (2015) observed that the interaction of mastocytes with lg E causes a cascade of mediators to be released, including histamines, enzymes, leukotrienes, platelet activating factors, peptides, and other chemical substances.

Apitoxin has been used to treat numerous chronic conditions, including arthritis, tendinitis, fibrosis, rheumatism, bursitis, and multiple sclerosis, as an anticancer, antifungal, antiacne, anticoagulant, and anti-inflammatory drug (Sobral et al., 2016). The primary components of bee venom with low molecular weights are melittin, phospholipase, and apamines, and the concentrations of these apitoxin ingredients vary according on the bee's age, seasonality, and venom protein content (Azam et al., 2018). Apitoxin may be extracted using a bee venom collector, which causes bees to attack an electric collecting plate resting on a glass plate. Thus, the apitoxin in the volatile phase will evaporate onto the glass plate, and the brown-colored bee venom will be recovered in the last stage by scraping. On the other hand, apitoxin's brown hue needs be altered in order to get the typical white powder of bee venom (Abrantes et al., 2017).
As a result of the above, this research will concentrate on the existing scientific literature that demonstrates apitoxin's efficacy in regulating various human illnesses.

2. The constituents of apitoxin and their bioactivities as medicine

Bee products have been used medicinally since the earliest documented accounts. They have since been employed in modern folk medicine. Apitoxin and its chemical constituents, like other bee products, have been thoroughly studied and supported by experts in a number of nations, including the United States, China, Russia, and Northern European countries. Apitoxin has been demonstrated to be beneficial in a range of medical conditions, including arthritis and rheumatism, chronic pain, and cancer. There is a sizable amount of literature on the use of bee venom in treatment. The most investigated and well-known BV ingredients are detailed below, along with their key biological features and method of action.

2.1. Parkinson’s Disease (PD) and Alzheimer’s Disease

Recent research indicates that BV may protect dopaminergic neurons from degeneration in animal models of Parkinson's disease. BV was demonstrated to reduce neuroinflammation in a mouse model of Parkinson's disease (PD) generated with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MRTP). Acupuncture with BV substantially protected dopaminergic neurons against MPTP toxicity in mice models of Parkinson's disease (Doo et al., 2010; Kim et al., 2011). Additionally, BV protects SH-SY5Y human neuroblastoma cells from MRTP-induced apoptosis (Doo et al., 2012).
The neuroprotective properties of bee venom phospholipase A2 are attributed to its ability to reduce neuroinflammatory responses in a rat model of Parkinson's disease (Chung et al., 2012). Acupuncture with bee venom shown neuroprotective effects in a mouse model of Parkinson's disease (Kim et al., 2014). Additionally, another research revealed that the BV peptide apamin protects DA neurons in a model system of midbrain cultures that simulates Parkinson's disease's selective death of DA neurons. Apamin's protective impact was attributed to a little increase in the excitability of dopaminergic neurons, which resulted in a moderate and sustained rise in cytosolic calcium (Salthun-Lassalle et al., 2004).
Apitoxin may preserve dopaminergic neurons in an animal model that resembles the chronic degradation process associated with Parkinson's disease over a longer period of time, according to the present research. Apamin, a peptide isolated from bee venom that specifically blocks SK channels, duplicated just a portion of these protective effects. A clinical experiment is being done to determine the neuroprotective efficacy of bee venom (apamin) in individuals with Parkinson's disease (Alvarez-Fischer et al., 2013).
Ye et al. (2016) cited case studies in support of apamin's anti-dementia and anti-disease Alzheimer's capabilities. In Alzheimer patients, specific brain effects of BV have been found (Ikeda et al., 1991; Wehbe et al., 2019). Numerous studies have shown that apamin enhances neuron excitability, synaptic plasticity, and long-term potentiation in the hippocampal region of Cornu Ammonis (CA1). As a consequence, apamin

has been proposed as a possible therapy for Alzheimer's disease (Behnisch and Reymann, 1998; Romero-Curiel et al., 2011).

2.2. Multiple Sclerosis (MS)

Multiple sclerosis (MS) is a progressive neurological illness marked by inflammation of the central nervous system, demyelination, and axonal degeneration. BV treatment is often utilized to treat multiple sclerosis in hospitals in Japan, South Korea, Taiwan, and other Far Eastern nations. Castro et al. (2005) performed research to determine the safety of apitoxin extract as a possible therapy for progressive multiple sclerosis. Although this exploratory research indicates safety, owing to the limited sample size, no firm conclusions about effectiveness can be drawn. As a result, there is little evidence to support the use of apitoxin in the treatment of multiple sclerosis.

Individuals with multiple sclerosis (MS) are increasingly being treated with bee stings in the goal of stabilizing or ameliorating the sickness. A randomized cross-over experiment discovered that bee sting treatment had no impact on disease activity, disability, or fatigue in people with relapsed multiple sclerosis, and had no influence on their quality of life (Wesselius et al., 2005).

2.3. Amyotrophic Lateral Sclerosis (ALS)

South Korean researchers investigated whether BV can prevent motor neuron degeneration and microglial cell activation in hsoD1G93A mutant mice. In an animal model of ALS, their results indicated that BV may be a viable therapeutic agent with anti-neuroinflammatory characteristics (Yang et al., 2010).

In glutamate-stimulated cells, one research discovered that apitoxin prevents cell death and activation of pro-apoptotic signaling. Additionally, BV protects cells from damage by decreasing the JNK (June Nterminal Kinase) and p38 pathways. These results support the therapeutic potential of apitoxin in the treatment of glutamate-mediated syndromes and inflammatory illnesses. Although ALS is one among them, it is not the only one. Additional in vivo research is necessary to elucidate the mechanisms behind this action and to fully exploit BV's therapeutic potential (Lee et al., 2012).

2.4. Neuralgia

A case study describes the consequences of bee stings on a 51-year-old man's excruciating post-herpetic neuralgia. Three bees stung the patient, and one day later, the patient's excruciating post-herpetic neuralgia was fully cured, lasting for one and a half months. The researchers concluded that more study into BV therapy as a viable therapeutic option for post-herpetic neuralgia should be conducted (Janik et al., 2007).

New research done by specialists at the Korea Institute of Oriental Medicine suggested that cold allodynia, a kind of neuropathic pain, may be effective in treatment. The researchers discovered that diluted apitoxin significantly decreased cold allodynia in sciatic nerve chronic constriction injury (CCI) rats. These results were thought to be mediated via spinal adrenergic receptors. Through activation of the spinal 2-adrenoceptor, single or repeated stimulation of DVB may ameliorate CCI-induced cold allodynia (Kang et al., 2012; Choi et al., 2017; Kang et al., 2015).

2.5. HIV

Melittin is a very toxic toxin that is present in bee venom. It is capable of penetrating pores in the protective viral envelope around the human immunodeficiency virus and other viruses. When released in sufficient numbers, free melittin may do significant harm. Washington University School of Medicine researchers have showed that nanoparticles containing the bee venom toxin melittin are capable of destroying the HIV virus that causes AIDS. Recent research demonstrates that melittin on the nanoparticle's forms pore-like attack complexes with the viral envelopes. They break the virus's envelopes, removing them from the virus, and these nanoparticles have no adverse effect on normal cells (Hood et al., 2013).

2.6. Arthritis

Bee venom seems to offer a new source of hope for patients with rheumatoid arthritis. At least two pathways contribute to BV's anti-arthritic activity: (a) immunological regulation, most likely through antigen competition; and (b) anti-inflammatory effect via corticosteroids or another as-yet-unidentified mechanism (ELTedawy et al., 2020; Azam et al., 2018). One study compared the antinociceptive effectiveness of apitoxin injections into a specific acupoint (Zusanli) versus a non-acupoint in an animal model of chronic arthritis. It has been proven that injection of BV into the Zusanli acupoint has anti-inflammatory and antinociceptive properties in rats stimulated with Freund's adjuvant. These findings imply that apitoxin acupuncture may be a viable alternative medicine therapy for the treatment of chronic rheumatoid arthritis (Kwon et al., 2001; Kwon et al., 2002).

3. Conclusions

According to scientific evidence, honeybee venom should be regarded a potential therapeutic agent for the regulation of a variety of clinical processes. Bee venom has a long history of efficacy against a variety of essential ailments as a traditional kind of medication. Thus, with proper administration and composition of its components, it may be efficiently employed as a future-proof drug. Following a review of several pharmacological research studies on bee venom's ability to fight various diseases and disorders, it was discovered that the components of honeybee venom not only possessed a variety of bioactivities to boost immune defense, but also acted via a variety of distinct pathways depending on the disease encountered. Given the paucity of clinical trials and the need for more research, more scientific tests with bee venom therapy should be done in order to provide more compelling evidence for the bioactivities against illnesses. We may infer that honeybee venom has considerable potential as a pharmaceutical additive, and that humanity will profit much from this wonderful natural remedy.

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