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A peek inside bee venom: Review on its pharmacological action

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Abstract
Bee venom is a chemical and biological composition of proteins, peptides, enzymes, and other compounds. Peptides mainly melittin, mast cell degranulating peptide (MCD), apamin found in bee venom can be used to treat a wide range of diseases, from cancer and chronic pain to neuromuscular and other disease conditions. We discussed Bee venom components and their uses in human illness treatment in this paper. Bee venom has been proven to have potential impacts on a variety of diseases, opening up new avenues for medication development. The findings in Homoeopathic literature are supported by a recent investigation on the active components of *Apis mellifica* and their pharmacological effects. As possible medication candidates in the therapy of human ailments, we summarise Bee venom's properties and detail its components and application in this paper.

Keywords: Bee venoms, melittin, pharmacological action, homoeopathy

Introduction
There is a wide variety of biologically active substances in venoms. As a result, it comes as no surprise that research aimed at identifying lead compounds for medicinal development has long included an emphasis on animal venoms. Animal venom, such as snake, spider, and wild bee venom, has long been used in homoeopathy to create medicinal compounds by turning it into nano-particles that are both safe and effective for use by patients. A significant amount of medicinal compounds is found in natural products such as Bee venoms. To cure a wide range of ailments, bee venom (BV) has long been utilised as an alternative medicine.
Bee venom has been used medicinally for 3000–5000 years in China. Hippocrates, the Greek physician, utilised bee venom to treat patients. The Russians Lokumski and Lubarski wrote "Bee venom, a remedy" in 1868, sparking interest in the effects of bee venom [1].
Research on the drug *Apis mellifica* derived components and pharmacological effects must be done in depth. Not only will this reveal the origin of the drug's effects, but it will open the door to synthesising therapeutically relevant compounds that can be used to treat patients successfully. Many of the medications used in homoeopathy are derived from animals. Ministry of AYUSH, Government of India has included *Apis mellifica* on the essential drug list (EDL) because of its importance for public health [2].
Bee venom compositions, advantages, and applications in experimental and clinical medicine are the focus of this paper. This *Apis mellifica* medication review will explain how it can help treat a wide range of human ailments. Important aspects of nano-forms of *Apis mellifica* (As a Homeopathic medicine) in medical treatment are also discussed in this review.

Homeopathic medicine from bee venom and description
The homoeopathic formulation consists of whole live honey bees *Apis mellifica* Linn (Family: Hymenopterae, Common names are Honey Bee, Common Hive Bee). In Homoeopathy, this drug proved by Brauns. *Apis mellifica* mother tincture prepared by the following method- Clean, wide-mouthed jar with live bees in it is preferred. Menstrum should be placed in and allowed to macerate for ten days while being stirred twice daily. Filter and drain out the tincture that develops. It's not a good idea to press on the bees. The drug strength changes with the time of year and season in which the bees are captured. Their poisons supposed to be weaker when they are dormant [3]. Materials required for preparing 1000 ml of mother tincture are(As per class 4)- *Apis mellifica*, moist magma containing solids 100 g, moisture 150 ml (250 g), Glycerin 225 ml, Purified Water 225 ml and Strong Alcohol 425 ml [3].

Sphare of action in homeopathy

Apis mellifica was describe by Dr. William Boericke to be effective in treating different conditions. Burning while urinating (example: UTI, AGN), involuntary stool passage on every motion, swollen fiery red tonsils, headache, Fever, for treating cancer, skin affection, Neurological disorder, indifference, and mania are some of the ailments that patients experience [4].

Compounds of bee venom and their action

Peptides, proteins, enzymes, and other small compounds constitute the majority of insect venoms that affect humans. The molecules that make up BV are more complex. Melittin, on the other hand, is the molecule in BV that has been linked to the most diverse range of biological activity. Over 20 bioactive compounds have been isolated and discovered in BV, with anti-inflammatory, anti-arthritis, anti-nociceptive, neuroprotective, anti-tumor, anti-microbial, anti-diabetic, and anti-rheumatic properties [5]. Among them peptides including melittin, mast cell degranulating peptide (MCD), apamin and adolapin, enzymes (phospholipase A_2), histamine, dopamine, and norepinephrine, and non-peptic compounds (carbohydrates) are important [5].

Table 1: Compounds of bee venom and their action

Compounds	Action
Melittin	Melittin stimulates the production of cortisol, a hormone that aids in the body's natural healing process. It works as an anti-inflammatory. As a result, bee venom therapy may be useful in the treatment of inflammatory illnesses like rheumatoid arthritis. South Korea investigated the molecular processes behind the therapeutic impact of bee venom on rheumatoid arthritis. Researchers from the "University of Exeter" discovered this component in bee venom that may help with joint pain [5].
	Bee venom and melittin have been shown to prevent prostate cancer *in vitro* and *in vivo*, and these effects may be mediated by the NF-B/caspase signalling pathway [6]. Bee venom can be designed to specifically target tumours and cancer cells, according to a study conducted at "Washington University in St Louis." After four to five injections of the nanobees, breast cancer tumours decreased by 25% and melanoma tumours reduced by 88 percent, compared to untreated mice [5].
	It exerts a variety of effects in various malignant cells, including cell cycle arrest, apoptosis, and growth inhibition, as well as antibacterial, anti-inflammatory, and antiviral characteristics. Melittin has antiviral properties against non-enveloped viruses (coxsackie virus and enterovirus-71) as well as a number of enveloped viruses (vesicular stomatitis virus, influenza A virus, herpes simplex virus) [7]. The protective envelope that covers HIV and other viruses can be pierced by bee venom. Scientists at Washington University School of Medicine in St. Louis have discovered that nanoparticles containing a toxin found in bee venom can kill HIV while leaving surrounding cells intact [5].
	El-Hanoun *et al*. reported an elevation in glutathione-S-transferase (GST) activity and glutathione (GSH) content in the treated rabbits, as well as a reduction in malondialdehyde (MDA) and TBARS levels, indicating the anti-oxidant action of honeybee venom [8].
Apamin	The principal impact is to block Ca2+-activated K+ channels selectively [9]. Apamin enhances synaptic plasticity and neuronal excitability by blocking channels at low concentrations [10]. The effect of apamin on tracheal contraction and the release of histamine from lung tissues was described by Ichii *et al*., who concluded that it reduces allergic airway inflammation [10]. Apamin also reduces nitric oxide-induced relaxation of the myometrium in non-pregnant women, according to a 2003 study [5].
MCD	It has anti-allergic effect by inhibiting the release of histamine from mast cells at low concentrations [5, 11].

Pharmacological action of bee venom

Anti-arthritis and anti-inflammatory activities

The major component of bee venom, melittin, is thought to have anti-inflammatory properties. Acne vulgaris, neuro-inflammation, Amyotrophic lateral sclerosis, arthritis, and liver inflammation have all been linked to this compound's anti-inflammatory properties [12]. Melittin was discovered to inhibit the protein 38 mitogen-activated protein kinase (p38 MAPK) signal and reduce the activation of nuclear factor kappa B (NF-B) p65 *in vitro*. As a result, NF-B and p38 signalling pathways may be involved in anti-inflammatory activities. Melittin displayed anti-inflammatory activities by modulating the transcription factors NF-B and activator protein 1 (AP-1) *in vivo* [13].

Recent research on the effects of BV on arthritis-inflicted rats demonstrated that the drug had therapeutic qualities against the disease. Inflammatory cytokines such IL-1, IL-6, TNF-, and others were shown to be lower than in the positive control [14].

Antibacterial and antiviral activity

Antibacterial activity of bee venom against Gram-positive and Gram-negative bacteria has been discovered. It works against penicillin-resistant Staphylococcus aureus strains. Bee venom is also anti-HIV, with strong antiviral properties. There have been studies on antifungal activities against various species of the Candida genus [5, 14].

In studies with HIV-1NLHX and HIV-1 NLYU2 virus strains, melittin in combination with nanoparticles inhibited infectivity and deactivated the viral package. Also, the interaction of melittin with virus surface and target cells, i.e., host cells that evade viral infectivity, helps to explain this action. Inhibition of viral replication by interferon type 1 activation is possible with melittin [14, 15].

To treat neurological diseases

The components of honeybee venom are effective treatments for diseases involving microglial activation. Microglia are a type of macrophage cell found in the brain that is involved in immune defence, CNS tissue repair, and normal brain homeostasis. BV decreased the synthesis of nitric oxide (NO), inducible nitric oxide synthase (iNOS), cyclooxygenase (COX)-2, prostaglandin E2 (PGE2), nuclear factor (NF)-kB, and pro-inflammatory cytokines [TNFa, IL1b, and IL6] in LPS-stimulated microglial cells [5, 14].

Table 2: Venom/compound research

Venom/compound	Research Outcome
Melittin	Improvement of motor behavior in the ALS mouse model and mitigation of microglial activity [5].
PLA2	Attenuated microglia activation and diminished CD4+ T cell infiltration in the brain of mouse with parkinsonism [5].
Apamin	Improvement of akinetic deficits produced by nigrostriatal dopaminergic lesions when injected directly into the subthalamic nucleus of parkinsonian rats [5].

Anticancer effects

The anti-tumor properties of bee venom and melittin have been discovered in a variety of cancer cell lines, including breast, liver, leukaemia, lung, melanoma, and prostate cancer [16-18]. The anti-cancer properties of bee venom and its main component melittin are multifaceted. First, the anti-tumor impact may be mediated by extrinsic and intrinsic apoptotic pathways. Bcl-2 associated x protein (Bax), caspase-3, caspase-9, and other death receptors have been shown to increase in expression and levels in response to bee venom and melittin. The anti-tumor actions of bee venom and melittin may also be mediated by NF-B and Ca2+/CaM signalling pathways. This inhibition results cell proliferation, angiogenesis, antiapoptosis, and metastasis. Bee venom was found to stimulate ROS production which induce intrinsic apoptosis [1, 19]. Increased mitochondrial membrane potential releases pro-apoptotic proteins in human gastric cancer cells (SGC-7901). Under a transition electron microscope, the apoptotic bodies formed by membrane disintegration and reduced microvilli (characteristic of mitochondrial mediated apoptosis). A549 cancer cells, ovarian (SKOV3 cancer cells), and bladder (TSGH-8301cells) cancer cells demonstrated enhanced cytotoxicity. A 2011 study concluded that bee venom components can decrease prostate cancer. Another 2007 study found that melittin reduces ovarian cancer tumours *in vivo* and suppresses ovarian cancer cell growth and proliferation *in vitro* [5, 20, 21].

Conclusion

Bee venom and its components have a wide range of biological and pharmacological effects. It has been used to treat a variety of illnesses in therapeutic settings. The components of bee venom are used to treat human illnesses in the form of nanoparticles. Recent study on the active components of *Apis mellifica* and their pharmacological effects supports the findings found in Homoeopathic literature. Recent advances in the analytical and biochemical realms, on the other hand, have allowed us to decipher the sources of pharmacological bioactivities. Overall, research on bee venom-based therapies appears to be highly impacted by the results of early homoeopathic practitioners, according to the available literature. Medical research can rely on the homoeopathic literature for drug development in the realm of animal-based treatments in the future.

Conflict of Interest

Not available

Financial Support

Not available

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