Journal of Pharmaceutical, Chemical and Biological Sciences
ISSN: 2348-7658
Impact Factor (GIF): 0.615
Impact Factor (SJIF): 2.092
March-May 2016; 4(1):48-53

Review Article

Therapeutic Effect of Honey Bee Venom

Obioma B.L. Eze[1], Okwesili F.C. Nwodo[2], Victor N. Ogugua[2]

[1]Department of Biochemistry, Micheal Okpara University of Agriculture, Umudike, Abia State, Nigeria
[2]Department of Biochemistry, University of Nigeria Nsukka, Enugu State, Nigeria

***Corresponding Author:** Obioma B.L. Eze, Department of Biochemistry, Micheal Okpara University of Agriculture, Umudike, Abia State, Nigeria

Received: 15 February 2016 Revised: 22 February 2016 Accepted: 01 March 2016

ABSTRACT

The practice of using honey bee or its products (raw honey, royal jelly, pollen, propolis, bee venom and bees wax) for medical conditions is known as apitherapy. Apitherapy has been practiced in many cultures whereas bee venom therapy is the use of live bee stings (or injectable venom) to treat various diseases such as arthritis, multiple sclerosis, diseases of the central and peripheral nervous system, heart and blood system, skin diseases and other diseases. Honey bee venom is a complex mixture of a variety of peptides and proteins which has strong neurotoxic and immunogenic effects. It contains 18 active components, mellitin (40-50%) being the main active component has anti-inflammatory, anti-bacterial and anti-viral action. Apamine (2-3%) increases cortisol production in the adrenal gland. Adolapine (0.5-1%) acts as an anti-inflammatory and analgesic which block cyclooxygenase. The pain and swelling of the stings are caused by histamine (0.5-2%). Bee venom also contains neurotransmitter: dopamine (0.2-1%), serotonin (0.5-1%) and norepinephrine (0.1-0.5%). The component responsible for the allergic response; hyaluronidase (1-2%) and phospholipase A_2 (10-12%) and enzymes that activate immune cells and produce immunoglobin E (IgE). Mast-cell degranulating protein work to soften tissues and facilitate the flow of fluid. Protease-inhibitors (0.1-0.8%) act as anti-inflammatory and stop bleeding. The component of bee venom and its effect on human treatment are to be mention but a few. The median lethal dose (LD_{50}) is 2.8mg of bee venom per kg of body weight. Therefore bee stings are safe for treatment of human disease if carefully apply.

Keyword: Apitherapy; multiple sclerosis; immunoglobin E; neurotransmitter; neurotoxin

INTRODUCTION

Honeybee venom is produced by two glands associated with the sting apparatus of worker and queen bees. Its production increases during the first two weeks of their life and reaches a maximum when they become involved in hive defence and foraging. It diminishes as the bee gets older [1]. The queen bee's production of venom is highest on emergence, which allows her to be prepared for immediate battles with other queens. When a honey bee stings, it does not normally inject all of the 0.15 to 0.3 mg of venom held in a full venom sac [2]. Only when it stings an animal with skin as tough as ours will it lose its sting and the whole sting apparatus, including the venom sac, muscles and the nerve center. These nerves and muscles keep injecting

venom for a while until the venom sac is empty. The loss of such a considerable portion of its body is always fatal to the bees [2]. Honeybee venom is a transparent liquid which dries up easily at room temperature. It is characterized by its odourless nature-ornamental pungent smell, a bitter taste, hydrolytic blend of proteins with pH 5.0 to 5.5 that is used by bees for defence [3], [4]. Bee venom is soluble in water and insoluble in alcohol and ammonium sulphate. Its contact with air forms grayish-white crystals. Dried venom has a light yellow colour and some commercial preparations are brown, may be due to oxidation of some of the venom proteins. Bee venom contains a number of very volatile compounds which might lost during collection, it is a rich source of enzymes, peptides and biogenic amines [3], [5]. Bee venom contains at least 18 active substances. The most prevalent substance mellitin which is one of the most potent anti-inflammatory agents known and is 100 more potent than hydrocortisol. Adolapin is a strong anti-inflammatory that inhibits cyclooxygenase. Phospholipase A_2 degrade phospholipids of cellular membranes. It also decrease blood presure and inhibits blood coagulation. Hyaluronidase dilates the capillaries causing the spread of inflammtion [6]. Histamine is responsile for allergic respone. Protease-inhibitors act as anti-inflammatory agent and stop bleeding. Other biochemicals like Apamin, Compound X, and Mast Cell Degranulating Protein (MCDP) etc work to soften tissues and facilitate the flow of fluids. Also, there are measurable amounts of the neurotransmitters; Dopamine, Noradrenaline, and Seratonin [7].

THE COMPOSITION OF BEE VENOM

Table 1: Composition of Bee Venom and its percentage dry weight [20-23]

Substance Group	Component	% of dry weight
Peptides	melittin	40-50
	apamine	2-3
	MCD peptide	2-3
	secapine	0.5-2
	pamine	1-3
	minimine	2
	adolapine	0.5-1
	Procamine A,B	1-2
	Protease inhibitor	0.1-0.8
	Tertiapine, Cardiopep, melittin F	1-2
Proteins (enzymes)	Phospholipase A_2	10-12
	Phospholiase B	1
	Hyaluronidase	1-2
	phosphatase	1
	α-Glucosidase	0-6
phospholipids		1-3
Biogenic amines	Histamine	0.5-2
	Dopamine	0.2-1
	Noradrenaline	0.1-0.5
	Aminobutyric acid, α-amino acids	1
sugars	Glucose, fructose	2-4
Volatiles (pheromones)	Complex ethers	4-8
Minerals	P, Ca and Mg	3-4

MECHANISM OF ACTION

Honey bee venom therapy is not a single mechanism; it explains a wide range of treatment applications. Several mechanisms have been proposed. Components of bee venom describe the effectiveness of it for the treatment of different types of diseases. The immune system is a complicated web of communication between the “brain and bone marrow”. Bee venom stimulates key centres in the immune system by stimulating a nonspecific response. It appears to stimulate cortisone secretion, enhances antibody production, and affects cytokine production. It is also a powerful inhibitor of prostaglandin formation and antioxidant membrane [8]. The pharmacological effects of bee venom are based on its components. It has been found that phospholipase A_2 acts in a synergistic way with melittin to lyse erythrocytes. Phospholipase A_2 (PLA_2) has been implicated in the management of arthritis. It is the most destructive component of apitoxin. It is an enzyme that degrades the phospho-lipids which are made of cellular membranes. Prostaglandins which are form from cyclooxynase cycle regulate the body's inflammatory response. [9], [10]. Apamin has a high affinity for the central nervous system and is responsible for the beneficial results in treating Multiple Sclerosis patients [11]. It increases cortisol production in the adrenal gland, a mild neurotoxin. Melittin interferes with the cellular membrane enzyme phospholipase A_2 and is responsible for the beneficial result in treating arthritic patients and other disease [12]. MCD-peptide is a powerful anti-inflammatory agent. Adolapin acts as an anti-inflammatory and analgesic because it blocks cyclooxygenase. Hyaluronidase dilates the capillaries causing the spread of inflammation. Histamine involved in the allergic response. Dopa-mine and noradrenaline increase pulse rate. Protease-inhibitors act as anti-inflammatory agents and stop bleeding [10].

THERAPEUTIC USE

When use in a normal doses, bee venom can be of benefit in treating many number of ailments. Its therapeutic value was already known to many ancient civilizations. Based on recent researchers, bee venom destroys HIV and spare surrounding cells. Nanoparticles containing bee venom toxin which is melittin can destroy human immunodeficiency virus (HIV) without harming surrounding cells. According to [13], their finding is a major step toward creating a vaginal gel that can prevent HIV spread. Melittin which is a powerful toxin found in bee venom can poke holes in the protective viral envelope that surrounds the human immuno deficiency virus and other viruses. Free melittin can cause considerable damage. The scientists showed that nanoparticles loaded with melittin do not harm normal healthy cells. When Protective bumpers added to the nanoparticles surface, they come in contact with normal cells which tends to be much larger, the nanoparticles bounce off rather than attach themselves. HIV is much smaller than the nanoparticles and fits in between the bumpers. When HIV comes across a nanoparticle it goes in between the bumpers and comes into direct contact with its surface, which is coated with the bee toxin and then destroys it. "Melittin on the nanoparticles fuses with the viral envelope. The melittin forms little pore-like attack complexes and ruptures the envelope, stripping it off the virus. "While most anti-HIV medications work on inhibiting the virus' ability to replicate, this one attacks a vital part of its structure and kill it off Said [13]. Melittin nanoparticles may prevent and treat existing HIV infections. The researchers believe that the melittin-loaded nanoparticles have the potential for two types of therapies: A vaginal gel to prevent the spread of HIV infection and therapy for existing

HIV infections, particularly drug-resistant ones. The hepatitis B and C viruses, among several others, rely on the same type of protective envelope and could be targeted and destroyed by administering melittin-loaded nanoparticles. The gel also has the potential to target sperm, the researchers explained, making it a possible contraceptive medication [14]. scientists reported in the Journal of the Science of Food and Agriculture that honey bee products, including venom, could well have applications in cancer treatment and prevention while normal cells remain intact. when nanoparticles are loaded with melittin, it develops anti-cancer properties and have the capacity to kill tumor cells. In arthritis managegment, bee venom found to block the buiding of the pro-inflammatory substances; cytokinine, PGE-2, NO, Tumour Necrosis Factor TNF-2 and enzyme COX-2. It inhibits the proliferation of reuhmatoids synovial cells [8]. Parkinson's disease is a progressive disorder of the nervous system that affects movement. Bee venom help to improve the supply of blood and dopamine in the brian which increase brain blood vessels and reduces blood coagulation [6], [15]. Alzheimer is a disease that causes problems of memory, thinking and behaviour. Several behavioural and electrophysiological studies indicated that small conductance calcium-activated potassium Channels-blockade by apamin enhance neuro excitability, Synaptic plasticity and long-term potentiation in the CAI hippocampl region and apamin has proposed as a therapeutic agent in Alzheimer's disease treatment [16], [17]. Multiple Sclerosis (MS) is a disseminated sclerosus or encephalomyetis disseminate. It is a chronic inflammatory disease of the central nervous system that leads to substantial disability through deficits of sensation and of motor, autonomic, and neuro-cognitive function. Bee venom reduced the severity of experimental auto-immune enphalomylitis (EAE) while the therapeutic effects of bee venom on EAE disappeared when CD4-(+), CD25(+) FOXP3(+) T cells were depleted by using anti-CD25 antibody [18] suggested that bee venom could be a potential therapeutic agent for anti-inflammatory effects in an experimental animal of EAE.

DISCUSSION

Whereas the use of live bee sting or injectable venom is called bee venom therapy for the treatment of disease: multiple sclerosis, stimulate the function of immune system, affect the release of cortisol production [19]. The honey bee venom contains 88% water. The glucose, fructose and phospholipids contents of other venom are similar to those in bee venom. The component of bee venom responsible for pain in vertebrates is the toxic melittin, histamin and other biogenic amines which contribute to pain and itching [18]. Melittin is a strong anti-inflammatory agent and induces the production of cortisol in the body. Honey bee venom has been reported for the treatment/or prevention of many ailment of which the use of free melittin-component of honey bee venom inhibit CXCR4- and CCR5- dependent HIV-1 infection but considered to be toxic to normal cells [13] while the use of attached melittin nanoparticle has been proved to be safe for the treatment of HIV-1 and also unreactive against vaginal epithelial, reporter cells in vitro and prevents infection by both CXCR4 and CCR5 viral stain. Adolapin act as an anti-inflammatory and analgesic, it blocks cyclooxygenase. Apamin help to increase cortisol production in the adrenal gland. It acts as a mild neurotoxin. Phospholipase A_2 contain destructive component of apitoxin. It is an enzyme which degrades the phospholipids that is made of cellular membranes. It decrease blood pressure and inhibits blood coagulation. The bee venom is safe for human treatments. The median lethal dose (LD_{50}) for an adult human is 28mg of venom per kg of body weight. A person weighing 60kg has a 50% chance of surviving total injections of 168mg of bee venom. Stings

of 600 could be lethal for a person if bee injects all its venom and no stings are quickly removed at a maximun of 0.3mg venom per sting [19].

CONCLUSION

The use of honey bee venom for treatment of HIV and other ailments has been proved safe by recent researchers if use in a required dose.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing interests.

REFERENCES

1. Crane E. Bees and beekeeping: Scince, Practice and World Resources. Ithaca NY., USA: Cornstock Publication; 1990, p 593.
2. Schumacher M J et al. lethality of killer bee stings. Nature 1989; 337:413-418.
3. Krell. Value-addaed Products from Beekeeping. SAO Agricultural Services Bulletin. Rome: Food and Agriculture Organization of the United Nation; 1996.
4. Schmidt OJ and Bchmann SL. Other Products of the Hive, In: The Hive and the Honeybee. Graham JM ed. Hamilton, Illinois, USA,, Dadant and Sons, 1999; p 952.
5. Feraboli F. Apitherapy in orthopaedic disease, bee products. Prop Applications and Apitherapy 1997; 221-225.
6. Alvarez-Fischer D et al. Bee venom and its component apamin as neuroprotective agents in a parkinson disease mouse model. Plos one 2013; 8 (4). 67-84.
7. Benton AW, Mulfinger L. Method and compositions for the treatment of mammalian infections emploing medicaments comprising Hymenoptera venom or proteinaceous or polypeptide components thereof 56. USA patent 1989, (US 4 thin 822 thin 608):39.
8. Son DJ et al. Therapeutic application of anti-arthritis, pain-releasing, and anti-cancer effects of bee venom and its constituent compounds. Pharmacol Ther 2007; 115 (2):246-270.
9. Jeong JK. Bee venom phospholipase A_2 Prevents Prion Peptide Induced- Cell death in neuronal cells. Int J Mol Med 2011; 28 (5): 867-873.
10. Meier J, White J. Clinical toxicology of animal venoms and poisons. CRC Press, Inc; 2011.
11. Wesselius T et al. A randomized crossover study of bee sting therapy for multiple sclerosis. Neur 2005; 65(11):1764-1768.
12. Yiangou M et al. Modulation of alpha 1-acid glycoprotein (AGP) gene induction following honey bee venom administration to adjuvant arthritic (AA) rats; possible role of AGP on AA development. Clin Exp Immunol 1993; 94(1):156-62.
13. Hood JL et al. Cytolytic nanoparticles attenuate HIV-1 infectivity. Antiviral Thera 2013; 19: 95 - 103.
14. Croatian et al. Honey Bee products potent in cancer prevention, treatment. J Sci Food Agri 2004; 3: 154-89.
15. Kim et al. Bee Venom reduces neuroinflammation in the the mPTP-induced model of parkison's disease. Int J Neueosci 2011; 121(4):209-217.
16. Ikeda m. Selective reduction of {1251} apamin binding sites in Alzheimer hippocampus: a Qualitative autoradiographic study. Brain Res 1991; 567:51-56.
17. Romero-Curiel et al. Apamin induces plastic changes in hippocampal neurons in senile Sprague-Dawley rats. Synapse 2011; 65(10):1062-72.
18. Shramana B, Saswata A. Apitherapy. Int J Rec Res Life Sci 2015; 2 (3):45-61.
19. Mahmoud AA. Studies on Bee Venom and Its Medical Uses. Int J Advancement Res Tech 2012; 1(2): 1-15
20. Shkenderov S, Ivanov T. Pcelni Produkti. The Bee products in Bulgarian. Zemizdat Abstract in Honey Bibliography 1983; 1-238.

21. Banks BEC, Shipolini RA. Chemistry and pharmacology of honey-bee venom, In Piek, T ed. Venoms of the Hymenoptera, London, Academic Press; p 330.
22. Dotimas EM, Hider UR. Honeybee venom. Bee World 2008; 68 (2):51-70.
23. Urtubey N. Apitoxin: From Bee Venom to Apitoxin for Medical use. Argentina: Termasde RioGrande Santiago del Estero; 2005.

Cite this article as:
Obioma B.L. Eze, Okwesili F.C. Nwodo, Victor N. Ogugua. Therapeutic Effect of Honey Bee Venom. J Pharm Chem Biol Sci 2016; 4(1):48-53.