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A Review on Various Pharmacological Uses of Honey Bee Venom; A Special Reference to Breast Cancer



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ABSTRACT

Apis mellifera or honey bee has lots of medicinal uses. Api therapy is nowadays used for so many human diseases. Insects which in the order Hymenoptera contain defensive substances, bee have a defensive compound called bee venom or api toxin that contains many biologically active compounds like enzymes and peptides. A growing number of evidence has demonstrated the anti-microbial, anti-inflammatory, analgesic, anti-carcinogenic, anticoagulant, radioprotective, antidiabetic and anti-atherosclerosis effects of bee venom therapy. Nowadays prevalence of cancer has been increased, especially breast cancer. 1 in every 28 women in the world is likely to get affected by the disease. Various research shows that bee venom component exerts anticancer effects on human breast cancer cells. The mechanisms of anticancer effects included cytotoxicity, apoptosis, cell lysis, cell targeting and gene expression regulation. However, bee venom has some safety tissues; for that new approaches have been developed to avoid these complications. The present review aims to refer to the pharmacological uses of bee venom; especially to the most relevant disease – breast cancer.

INTRODUCTION

Bees, one of the most widespread, social insects have both domestic and wild variety. In the 21st century, food and food product having medicinal properties are become popular all over the world; projected to reach a \$94.21 billion market by 2023 in the United State.^[1] Honey bee product - honey have food value with medicinal property. Because of that honey were used in antient time. But over the year, so may studies shows that bee products other than honey is also have medicinal value such products including, bees wax, royal jelly, propolis and venom. These all products are now used as part of apitherapy.^[2]

Bee venom is a substance secreted by a gland located in the abdominal cavity of the bees. In recent years, many studies have highlighted the importance of bee venom as a natural product. Bee venom has been used for the treatment of anti-inflammatory disorders, skin diseases, rheumatism, neurological disease, asthma, infectious disease, cancer etc. ^{[3][4]} Bee venom administration traditionally done by direct application that is, being stung by live bees. Now in apitherapy bee venom applied indirectly by an acupuncture needle or direct injection in inflamed area. Recent researches reveals the components of bee venom, so it promotes the study of possible therapeutic uses.^[5]

COMPOSITION OF BEE VENOM

Apitoxin or bee venom has different compounds and its composition is more complex. As per the studies, bee venom composition mainly includes melittin and phospholipase A₂. The other composition includes peptides like apamin, adolapin, mast cell degranulating peptides and enzyme like hyaluronidase as well as non-peptide components such as histamine, dopamine, and norepinephrine. Within all of these composites, at least there are more than 18 pharmacologically active compounds.^{[6] [7]}

From a pharmacological point of view bee venom is the most potent bee product. Many pharmacological effects of bee venom have been reported.^[8] This review paper will give insight into the various pharmacological actions of bee venom especially to breast cancer.

THERAPEUTIC USES OF BEE VENOM

ANTIOXIDANT PROPERTY

Bee venom has antioxidant property due to some of the components present init. The compounds which have the antioxidant property inhibit lipid peroxidation process and

increase superoxide dismutase activity. Studies shows that the compounds which are mainly responsible for antioxidant activity are melittin, PLA2, and apamin.^[9]

ANTIMICROBIAL PROPERTY

Bee venom possesses the anti-microbial compound melittin which is mainly responsible for antimicrobial activity. Also, PLA, vitellogenin have antimicrobial property. These compounds have the capacity to disrupt the biological membrane of microbes. Mainly bee venom is used for antibacterial and antifungal effect.^{[7][10][11]}

ANTI-INFLAMMATORY ACTIVITY

The main compound of bee venom melittin is having the capacity to reduce the excessive immune response and provide a new alternative for the control of inflammatory disease. Somew studies shoes that invitro, melittin can suppress the activation of nuclear NF-KB P65 and inhibit the P38 MAPK signal. In vivo, melittin also showed anti-inflammatory properties by the modulation of NF-KB and AP-1 transcription factor.^[12]

ANTIDIABETIC ACTIVITY

Bee venom also have effect on diabetic mellitus. This study was conducted on alloxan induced rats. This study revealed a significant decrease in glucose level accompanied by a significant increase in insulin level. Histological examination shows the improvement in the islet structure and marked regeneration of insulin secreting β cell. Bee venom have therapeutic and protective effects on the management of biochemical and histological changes in diabetic rats.^[13]

ANTIVIRAL ACTIVITY

Antiviral property of bee venom identified against a broad panel of viruses. The main component melittin significantly inhibited the replication of enveloped viruses such as influenza A virus, vesicular stomatitis virus, respiratory syncytial virus and herpes simplex virus. Also inhibits non-enveloped viruses such as enterovirus 71, coxsackie virus. Apart from bee venom virucidal activity, Bee venom can stimulate type I IFN, which subsequently could stimulate the antiviral state in the host cell and also inhibit the viral replication. Taken together these result bee venom has the potential to become a prophylactic or therapeutic agent for infectious viral disease.^[14]

ANTI-ARTHRITIC ACTIVITY

A study showed that subcutaneously administered bee venom suppresses the development of carrageenan-induced paw edema and adjuvant arthritis in the rats in a dose-related manner. Anti-arthritic action of bee venom involves alteration of the immune response probably via antigen competition and an anti-inflammatory action via corticosteroids through an as yet undetermined mechanism.^[15]

BREAST CANCER

Breast cancer is one of the most common malignant diseases in the female population all over the world. High prevalence and death rate of breast cancer have placed this disease at the top of life-threatening diseases in women.^[16] In 2021, a study estimated that 2.1 million newly diagnosed breast cancer cases would be in world wide. Life style, environmental factors, genetic factors are mainly responsible for increasing the prevalence of breast cancer cases^[17]. The most common treatment for breast cancer is radiotherapy, hormonal therapy, chemotherapy. Nowadays most of people are go with chemotherapy as treatment option. While the survival rate has increased due to treatment for breast cancer, the quality of life has decreased due to the side effects of chemotherapy.^[18] Depending upon the presence of molecular marker breast cancer can be divided into 3 subtypes. Treatment strategies are decided according to the above subtypes. Mainly chemotherapy, endocrine therapy, radiation therapy, surgery or a combination of all these are used as treatment methods.^[19]

Recently, the possibility of treatment has expanded to various area, especially in biotoxins. Bee venom is one of the substances which is used for the treatment of breast cancer. Bee venom consist of active ingredients like melittin, mast cell degranulating peptide, apamine, phospholipase A2, hyaluronidase and amino acids. Melittin is a chief component of bee venom and it can be easily inserted into the membrane by pore formation and perturbation in non-selective manner, resulting in antimicrobial and anti-tumour activity.^[20]

Honeybee venom and its main constituent melittin are proved to be good agents for breast cancer treatment by managing different conditions of tumour like inhibition of cell proliferation, cell growth, control of metastasis and apoptosis.^[21] Recent research shows that role of bee venom and melittin in suppressing the activation of growth factor receptors in HER2-enriched and triple-negative breast cancer.^[22]

CONCLUSION

In conclusion, this review article focuses on the pharmacological uses of honey bee venom especially to breast cancer. Now a days biotoxin are used for various treatments. Honey bee venom one of the biotoxins now used therapeutically for various disease. Quite recently studies reveal the targeted effect of melittin and honeybee venom in suppressing growth factor receptor activation in HER2-enriched and triple-negative breast cancer. This type of biotoxin is accessible worldwide and offers economical and easily available treatment solutions for developing countries. It is important to carry out further research to evaluate to ideal method of provision of melittin, level of toxicity, and average accepted dose.

REFERENCES

1. Srivastava S, Bhargava A. Functional foods and nutraceuticals in Biotechnology; new ideas, new development a textbook of modern technology.2012. first edition. Springer international publishing, Switzerland.
2. Enas M Ali. Contributions of some biological activities of honey bee venom. Journal of apiculture research. 2014, vol.53 (4), 441-451
3. Zhang S, Lia Y, Ye Y, Wang X R, Lin L T et al., Bee venom therapy; potential mechanisms and therapeutic applications. Toxicon .2018;148: 64-73.
4. Orsolio N, Bee venom in cancer therapy. Cancer and metastasis reviews. 2012; 31.173 – 194.
5. Grassberger M, Sherman R A, Gileva O S, Kim C M H. Biotherapy – history, principles & practice. springer; dordrecht, The netherlands, 2013.
6. Moreno M, Giralto E. Three valuable peptides from bee and wasp venoms for therapeutic and biological use; mellitin, apamin and Mastoparan. Toxins. 2015;7:1126-1150.
7. Abd El-Wahed A A, Khalifa S A M, Sheikh B. Y, Farag M A, Saeed A et. al., Bee venom composition: from chemistry to biological activity. Studies in natural products chemistry.2019;60:459-484.
8. Karsten Munstedt, Stefan Bongdnov. Bee products and their potential use in modern medicine. Journal of api product and apimedical science.2009;1(3):57-63.
9. Sorbal F, Sampaio A, Falcao S, Queiroz M J R P, Calhelha R C, Vilas – Boas M et al., Chemical characterization, antioxidant, anti-inflammatory and cytotoxic properties of bee venom collected in northeast Portugal. Food and chemical toxicology.2016;94:172-177.
10. Al-Ani I, Zimmermann S, Reichling J, Wink M. Pharmacological synergism of bee venom and melittin with antibiotics and plant secondary metabolites against multi-drug resistant microbial pathogens. Phytomedicine.2015.22.245-255.
11. Park H G, Lee K S, Kim B Y, Yoon H J, Choi Y S et al. Honey bee (*Apis cerana*) vitellogenin acts as an antimicrobial and anti-oxidant agent in the body and venom. Developmental and comparative immunology.2018.85.51-60.
12. Lee G, Bae H. Anti-inflammatory applications of melittin, a major component of bee venom; Detailed mechanism of action and adverse effects. Molecules. 2016;21:616
13. Ahmad K Hassan, Dina A EL-Kotby, Mohamed M Tawfik, Rasha E Badr, Iman M Bahgat. Antidiabetic effects of the Egyptian honey bee (*Apis mellifera*) venom in alloxan-induced diabetes rats. The journal of Basic and applied Zoology.2019;58
14. Md Bashir Uddin, Byeong-Hoon Lec, Chamilani Nikapitiya, Jae – Hoon Kim, Tae-Hwan kim, Hyun-cheol Lee, Choul Goo kim, Jong–Soo Lee, Chul- Joong Kim. Inhibitory effects of bee venom and its components against viruses invitro and invivo. Journal of microbiology.2016;54(12).853-866.
15. Yi-Han Chang, Marcia L Bliven. Anti-arthritis effect of bee venom. Agents and actions.1979;9:205-211.

16. Abdel-Salam I M, Abou-Bakr A A, Ashour M. Cytotoxic effect of aqueous ethanolic extract of *Luffa cylindrica* leaves on cancer stem cells (D44(+)/24(-)) in breast cancer patient with various molecular subtypes using tissue samples in vitro. *Journal of Ethnopharmacology*.2019;238:11877
17. Han Chen, Jiaping Yang, Yanlong Yang, Jianpeng Zhang, Yaoyu, Xiaoling L V. The natural products and extracts; anti triple -negative breast cancer in vitro. *chemistry and biodiversity*.2021;18(7):e2001047
18. Raguz S, Yague E. resistance to chemotherapy;new treatments and novel insights into an old problem. *British journal of cancer*.2008;99(3):387-391.
19. Adrienne G Waks, Eric P Winer. Breast cancer treatment:A review. *JAMA*. 2019;321 (3):288-300.
20. Wehbe R, Frangieh J, Rama M, Elobeid D, Subatier J M, Fajloun Z. Bee venom: an overview of main compounds and bioactivities for therapeutic interest. *Molecules*. 2019;24:2997.
21. Orsolich N. possible molecular targets of bee venom in the treatment of cancer: application and perspective. *Onco therapeutics*.2013;4:3-4.
22. Ciara Duffy , Anabel Sorolla , Edina Wany, Emily Golden, Eleanor Wood ward, Kathleen Davern, Diwei H O, Elizabeth Johnstone, Kevin Pflieger, Andrew Redfern, K. Swaminathan Iyer, Boris Baer & Pilar Blancafort . Honey bee venom and melittin suppress growth factor receptor activation in HER2 enriched triple-negative breast cancer. *NPJ Precis oncol*. 2020;4:24.