Biospectra : ISSN: 0973-7057, Vol. 19(1), March, 2024, pp. 271-276

An International Biannual Refereed Journal of Life Sciences

Plant Science

ISSN : 0973-7057

Exploring the therapeutic potential of bee venom: A review of composition and clinical uses

Pankaj Nath Yogi[a], Jaishree Meena[b], Shweta Bhodiwal[c] & Tansukh Barupal[d]*

[a]Department of Botany, S.P.C Government College, Bhim, Rajasthan, India

[b]Department of Botany, SPNKS Govt. PG College, Dausa, Rajasthan, India

[c]Department of Botany, IIS (Deemed to be University), Jaipur, Rajasthan, India

[d]Department of Botany, The Gurukul College, Budal, MLSU, Udaipur, Rajasthan, India

Received : 10th January, 2024 ; Revised : 11th February, 2024

DOI:-https://doi.org/10.5281/zenodo.14257411

Abstract- The medical application of honeybee products, such as propolis, honey, pollen, beeswax, honey, and, most importantly, bee venom, is known as apitherapy. This research reviewed bee venom and its potential therapeutic uses. Since ancient times, traditional medicine has employed bee venom therapy, which involves applying the venom to cure a variety of diseases. A number of physiologically active peptides, including melittin (a major component of BV), apamin, adolapin, mast cell degranulating peptide, and enzymes (phospholipase A2 and hyaluronidase) as well as non-peptide components, like histamine, dopamine, and norepinephrine, are found in bee venom, which is produced by the venom gland located in the abdominal cavity. Bee venom offers therapeutic properties against a range of ailments, including skin conditions, disorders of the neurological system, heart and blood irregularities, and arthritis. Additionally, bee venom has been employed extensively in the past several years to treat tumours as well as a number of immune-related illnesses. Research needs to be done further to determine the precise component and intended action of bee venom therapy in order to take advantage on its promising potential.

Key words: Bee Venom, Apitherapy, Melittin, Tumour, Neurological.

INTRODUCTION

Apitherapy is a form of alternative healthcare that treats a variety of human illnesses by using honeybee products, most notably bee venom.[1,2] Various religious texts, including the Bible, the holy Quran, and the Veda, attest to the healing properties of honey and other bee products.[3] Since the late 1800s, research has been conducted on bee venom (BV) to investigate the possible medicinal use of the biomolecules that comprise it. A gland in the bees' (*Apis mellifera* L.) abdomen cavity secretes this material.[4] One small fact that demonstrates the potential application of BV in various therapies is connected to beekeepers that experience a correlation between being stung by bees frequently and experiencing exceptionally high rates of diseases like arthritis and other conditions affecting the muscles and joints. Oriental traditional medicine has been using BV to treat inflammatory illnesses since 3000 BCE.[5] Hippocrates (460-370 BC) was the first person in Europe to refer to BV as a remedy for baldness and to coin the word "apitherapy." Ivan the Terrible was

*Corresponding author :
Phone : 9983235235
E-mail : tansukhbarupal@gmail.com

among the first people to employ BV to cure ailments like gout in the fifteenth century.[6] Consequently, BV has been traditionally associated with the therapeutic management of rheumatism, skin conditions, and anti-inflammatory disorders. However, it has also demonstrated utility in the treatment of neurological conditions, asthma, arthritis, and infectious diseases like malaria.[4]

Because a single bee only has a little amount of venom and must sting in order to extract it, gathering a sizable amount of BV is difficult. In 1954, Markovic and Molnar utilised electroshocks and squeezed to cause the bees to sting in order to tackle this issue.[7] The method's effectiveness led to the creation of stinging bee traps, which allow for the collection of venom with the least amount of negative effects on the bees' and hive's health.[8] The earlier one that was described by Benton *et al.*, (1963)[7] is the source of modern methods and traps. The process's effectiveness is greatly dependent on the shock's intensity, the substance that the bees sting, how long it lasts, and how long it takes between shocks.[9] In lab settings, BV is obtained through reservoir disruption and/or hand milking; however, electroshock traps are employed when additional BV is required. The bee sting can be simulated directly with an injection of BV into the inflammatory area, or indirectly with acupuncture needles.[4] The fact that BV is now widely recognised for its usage in treating pathological disorders and that its primary components are understood encourages research into potential therapeutic applications through both *in vitro* and *in vivo* investigations.[5]

COMPOSITION

Peptides, proteins, enzymes, and other smaller compounds make up the majority of insect venoms that strike humans. These molecules also make up BV, however BV's makeup is more intricate. Amino acids (aa), peptides, proteins, enzymes, carbohydrates, biogenic amines, volatile chemicals, phospholipids, and pheromones are the foundation of this complex mixture. Furthermore, since water makes up more than 80% of BV, it is extremely watery.[4,10] At least one of these composites has more than eighteen pharmacologically active substances. The two most prevalent BV components are phospholipase A2 (PLA2) and melittin. Melittin is a peptide that makes up between 50 and 60 percent of the dry weight (DW), with BV having a higher abundance of this component. Furthermore, melittin is the most lethal BV chemical despite having the greatest variety of biological activities with noteworthy clinical and therapeutic effects.[10,11] The enzyme PLA2, which makes up around 10-12% of BV, is the second component that is more prevalent and has the second-highest level of biological activity. Nonetheless, this enzyme is the most allergenic factor, producing allergenic sensitization in 57-97% of the allergic patients.[12]

Additional substances with a minimal presence in BV but notable physiologic activity include peptides like apoptin, mast cell-degranulation peptide (MCD), secapin, adolapin, and enzymes like hyaluronidase. The 18 aa neurotoxic peptide known as aptamin has the ability to inhibit the K^+ channel that is triggered by Ca^{2+}. MCD comprises 22 aa, or roughly 1%-3% of BV. It also exhibits potent anti-inflammatory properties. Three appealing biological properties of secapin are its anti-microbial, anti-elastolytic, and anti-fibrinolytic properties. Adolapin is a polypeptide with analgesic and anti-inflammatory properties. Finally, it has been determined that hyaluronidase functions as a spreading factor, facilitating the penetration of cells by other BV factors.[13,14]

THERAPEUTIC VALUES OF BEE VENOM

A well-known and pharmacologically active byproduct of the hive, BV is produced by the venom glands connected to the worker and queen sting apparatuses, kept in the venom reservoir, and delivered through the apparatus during stinging. Because of its anti-oxidants, anti-coagulants, anti-inflammatory qualities, and bioactive ingredients like phospholipase and melittin, BV is primarily used to treat a variety of inflammatory conditions, including cancer, arthritis, nervous system disorders, abnormalities of the heart and blood system, skin conditions, and other conditions.[15] Bee venom can also be used therapeutically to treat a variety of conditions, such as multiple sclerosis, osteoarthritis, rheumatoid arthritis, bursitis, tendinitis, dissolving scar tissue, postherpetic neuralgia, Lyme disease, and osteoarthritis.[16]

3.1 BV to treat Arthritis

According to Krylov *et al*., (2007)[17], bee venom (BV) inhibits the growth of rheumatoid synovial cells and blocks the production of pro-inflammatory chemicals such as cytokine, PGE-2, NO, tumour necrosis factor (TNF-2) and enzyme COX-2. Good success rates, ranging from 60% to 90%, have been attained after using various venom administration techniques, such as bee stings, api-punctures, injections, electrophoresis, and application using ultrasound waves (phonophoresis). Over the past ten years,

api-puncture has emerged as a novel arthritis treatment method.[18] Furthermore, as patients' X-rays demonstrate, bee venom functions by reducing pain and inflammation rather than altering rheumatic deformity.[17] Additionally, BV is used to treat a variety of pain conditions, including rheumatoid arthritis, knee osteoarthritis, acute ankle sprains, wrist sprains, low back pain, herniated lumbar pain, disc pain, shoulder pain following a stroke, and bee sting (BS) and api-puncture (AP) therapy, which have been shown to be effective in treating all of these conditions.[19] Bee venom therapy (BV) is superior than hormone therapy, according to researchers, because the former has undesirable side effects like decreased activity of these essential hormone glands, while the latter continuously stimulates the functioning of hormonal systems.[20]

3.2 BV as anti-cancer

The two compounds that have been identified and isolated as the main contributors of BV's anti-cancer properties are melittin and phospholipase A2 (PLA2). While numerous research have reported the antitumoural effects of melittin and PLA2, the two main ingredients in the venom of the species Apis mellifera. Since BV functions as melittin in cells to combat many cancer forms, a potent anticancer peptide may be a preferable option over entire BV.[21] Melittin is a multifunctional component of BV that lowers and stabilises membrane surface tension, stimulates smooth muscles, activates the hypophysis and adrenal glands, increases capillary permeability, lowers blood coagulation, lowers blood pressure, is immunostimulatory and immunosuppressive, protects against radiation, affects the central nervous system, and has anticancer properties.[20] On the other hand, neuropathy brought on by cancer chemotherapy was managed with melittin and acupuncture using bee venom. Furthermore, a number of cancer cells are susceptible to the cytotoxic effects of the bee venom peptide lasioglossin II *in vitro*.[22,23]

3.3 BV against diseases of Nervous System

According to Hwang *et al.*, (2015)[24], BV is used to treat a variety of neurological disorders, including Parkinson's disease, amyotropic lateral sclerosis (ALS), Multiple Sclerosis (MS), Alzheimer's disease, and Alzheimer's disease. BV has distinct effects on the central and peripheral nervous systems. The action of glutamate transporters is altered in many neurodegenerative disorders, such as Parkinson's disease, Alzheimer's disease, and amyotrophic lateral sclerosis, due to changes in glutamate, the primary excitatory neurotransmitter in the central nervous system. However, because it prevents cell death and greatly reduces the cellular toxicity of glutamate, BV is useful in lowering the toxicity of glutamatergic cells in neurodegenerative illnesses. Additionally, pretreatment with BV changed the activation of MAP kinase after glutamate exposure.[25]

3.4 BV to treat Heart and Blood System Abnormalities

BV decreases blood pressure, acts as an antiarhythmic against fibrinolytic and blood coagulation, improves blood microcirculation, boosts coronary and peripheral blood circulation, and stimulates the production of erythrocytes.[26] According to Krylov *et al*. (2007)[17], it is also used to treat arteriosclerosis, endarteritis (a persistent inflammation of the inner layer of the arteries), hypertension, and angina pectoris arrhythmia.

3.5 BV to treat Skin Disease

According to research, BV is effective in treating a wide range of skin conditions, including dermatitis, psoriasis, acne, cicatrices, baldness, furunculosis (recurrent boils), opthamology, gastroenterology, pulmonology, asthma, bronchitis, otorinolaringology, pharingytis, tonsillitis, ear nerveneuritis, endocrinology, urology, and gynaecology.[27]

CONCLUSION

Bee venom, a complex biological substance produced by honeybees, has demonstrated significant therapeutic potential due to its unique composition. Comprising a diverse array of bioactive compounds, including peptides (such as melittin and apamin), enzymes (such as phospholipase A2), and proteins, bee venom exerts a range of biological effects. These include anti-inflammatory, analgesic, and immunomodulatory properties. Therapeutically, bee venom has been explored for its efficacy in treating conditions such as arthritis, multiple sclerosis, and chronic pain. The active compounds in bee venom work synergistically to modulate immune responses and reduce inflammation, presenting a novel approach to managing various health issues. Clinical research and anecdotal evidence suggest that bee venom therapy, while promising, requires further investigation to fully understand its mechanisms and optimize treatment protocols.

REFERENCES

1. **Ahmed O., Fahim H., Mahmoud A. & Ahmed E. A. E. 2018.** Bee venom and hesperidin effectively mitigate complete Freund's adjuvant-induced arthritis via immunomodulation and enhancement of antioxidant defense system. *Archives of Rheumatology*, **33(2):** 198.
2. **Carpena M., Nuñez-Estevez B., Soria-Lopez A., & Simal-Gandara J. 2020.** Bee venom: an updating review of its bioactive molecules and its health applications. *Nutrients*, **12(11):** 3360.
3. **El-Banby M. A. 1987.** *Honeybees in the Koran and in medicine* (No. Ed. 2, pp. 205-pp).
4. **Abd El-Wahed A. A., Khalifa S. A., Sheikh B. Y., Farag M. A., Saeed A., Larik F. A., ... & El-Seedi H. R. 2019.** Bee venom composition: From chemistry to biological activity. *Studies in natural products chemistry*, **60:** 459-484.
5. **Zhang S., Liu Y., Ye Y., Wang X. R., Lin L. T., Xiao L. Y., ... & Liu C. Z. 2018.** Bee venom therapy: Potential mechanisms and therapeutic applications. *Toxicon*, **148:** 64-73.
6. **Hellner M., Winter D., von Georgi R., & Münstedt K. 2008.** Apitherapy: Usage and experience in German beekeepers. *Evidence Based Complementary and Alternative Medicine*, **5(4):**475-479.
7. **Benton A. W., Morse R. A., & Stewart J. D. 1963.** Venom collection from honey bees. *Science*, **142(3589):**228-230.
8. **Bicudo de Almeida-Muradian L., Monika Barth O., Dietemann V., Eyer M., Freitas A. D. S. D., Martel A. C., ... & Gasparotto Sattler J. A. 2020.** Standard methods for *Apis mellifera* honey research. *Journal of Apicultural Research*, **59(3):** 1-62.
9. **Krell R. 1996.** Value-added products from beekeeping. In FAO Agriculture Server Bulletin; No. 124; Food and Agriculture Organization of the United Nations: Rome, Italy, ISBN 92-5-103819-8.
10. **Pucca M. B., Cerni F. A., Oliveira I. S., Jenkins T. P., Argemí L., Sørensen C. V., ... & Laustsen A. H. 2019.** Bee updated: current knowledge on bee venom and bee envenoming therapy. *Frontiers in immunology*, **10:** 2090.
11. **Raghuraman H., & Chattopadhyay A. 2007.** Melittin: a membrane-active peptide with diverse functions. *Bioscience reports*, **27(4-5):** 189-223.
12. **Jakob T., Rafei-Shamsabadi D., Spillner E. & Müller S. 2017.** Diagnostik der Hymenopterengiftallergie: aktuelle Konzepte und Entwicklungen mit besonderem Fokus auf die molekulare Allergiediagnostik. *Allergo Journal*, **26:** 33-50.
13. **Lee K. S., Kim B. Y., Yoon H. J., Choi Y. S. & Jin B. R. 2016.** Secapin, a bee venom peptide, exhibits anti-fibrinolytic, anti-elastolytic, and anti-microbial activities. *Developmental & Comparative Immunology*, **63:** 27-35.
14. **Mourre C., Fournier C., & Soumireu-Mourat B. 1997.** Apamin, a blocker of the calcium-activated potassium channel, induces neurodegeneration of Purkinje cells exclusively. *Brain research*, **778(2):** 405-408.
15. **Castro H. J., Mendez-Inocencio J. I., Omidvar B., Omidvar J., Santilli J., Nielsen Jr H. S., ... & Bellanti J. A. 2005.** A phase I study of the safety of honeybee venom extract as a possible treatment for patients with progressive forms of multiple sclerosis. *In Allergy & Asthma Proceedings*. **26(6)**.
16. **Ram S. K. M., Jayapal N., Nanaiah P., Aswal G. S., Ramnarayan B. K., & Taher S. M. 2014.** The therapeutic benefits of bee venom. *Int J Curr Microbiol App Sci*, **3:** 377-381.
17. **Krylov V., Agafonov A., Krivtsov N., Lebedev V., Burimistrova L., Oshevenski L., & Sokolski S. 2007.** Theory and agents of apitherapy. *Moscow: Comme it faut Publishers*.
18. **Urtubey N. 2005.** Apitoxin: from bee venom to apitoxin for medical use. *Termas de Rio Grande Santiago del Estero, Argentina*.
19. **Lee J. D., Park H. J., Chae Y., & Lim S. 2005.** An overview of bee venom acupuncture in the treatment of arthritis. *Evidence Based Complementary and Alternative Medicine*, **2(1):** 79-84.
20. **Bogdanov S. 2015.** Bee venom: composition, health, medicine: a review. *Peptides*, **1:** 1-20.

21. **Oršoliæ N. 2012.** Bee venom in cancer therapy. *Cancer and metastasis reviews*, **31:** 173-194.

22. **Park J. H., Kim K. H., Kim S. J., Lee W. R., Lee K. G., & Park K. K. 2010.** Bee venom protects hepatocytes from tumor necrosis factor-á and actinomycin D. *Archives of Pharmacal Research*, **33:** 215-223.

23. **Bandyopadhyay S., Lee M., Sivaraman J., & Chatterjee C. 2013.** Model membrane interaction and DNA-binding of antimicrobial peptide Lasioglossin II derived from bee venom. *Biochemical and biophysical research communications*, **430(1):** 1-6.

24. **Hwang D. S., Kim S. K., & Bae H. 2015.** Therapeutic effects of bee venom on immunological and neurological diseases. *Toxins*, **7(7):** 2413-2421.

25. **Lee S. M., Yang E. J., Choi S. M., Kim S. H., Baek M. G., & Jiang J. H. 2012.** Effects of Bee Venom on Glutamate Induced Toxicity in Neuronal and Glial Cells. *Evidence Based Complementary and Alternative Medicine*, **2012(1):** 368196.

26. **Savilov K. 2010.** Bee venom: physico-chemical properties. Biological and pharmacological effects. Use in medical practice. *Theoretical and practical basics of apitherapy (Russian), Roszdrav*, 135-162.

27. **Hegazi A. G., Abd Raboh F. A., Ramzy N. E., Shaaban D. M., & Khader D. Y. 2013.** Bee venom and propolis as new treatment modality in patients with localized plaque psoriasis. *International Research Journal of Medicine and Medical Sciences*, **1(1):** 27-33.

***