International Journal of Entomology Research
www.entomologyjournals.com
ISSN: 2455-4758
Received: 11-04-2025, Accepted: 12-05-2025, Published: 27-05-2025
Volume 10, Issue 5, 2025, Page No. 91-95

Therapeutic and pharmacological relevance of stingless bee pollen in human health: A review

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Abstract
Stingless bee pollen, produced through the fermentation of plant pollen with bee salivary enzymes and honey in cerumen pots, is gaining attention for its rich nutritional and therapeutic profile. Predominantly found in tropical regions like South America, Australia, and Southeast Asia, this pollen is increasingly used as a dietary supplement due to its abundance of bioactive compounds. It contains a diverse array of phytochemicals, including flavonoids, polyphenols, carotenoids, phytosterols, glutathione, Mangiferonic acid, vitamins C and E, along with various enzymes and coenzymes. These constituents contribute to a wide range of pharmacological activities—antioxidant, anti-inflammatory, antimicrobial, anticarcinogenic, antidiabetic, and anti-allergenic effects. Preliminary studies also suggest its role in immune modulation, highlighting its potential in preventive health. Despite promising evidence, further large-scale clinical studies are essential to substantiate these claims. This review compiles current findings on the pharmacological applications of stingless bee pollen and explores its under-investigated medicinal potential, supporting its value as a natural therapeutic and nutraceuticals.

Keywords: Stingless bee pollen, bioactive compounds, pharmacological applications, therapeutic potential, nutraceuticals, immune modulation

Introduction

Stingless bees, belonging to the family Apidae within the superfamily Apoidea, are a group of highly evolved social insects. Fossil evidence indicates that these bees have existed for at least 80 million years, with specimens preserved in ancient amber. Today, more than 600 species, classified under 61 genera, are recognized worldwide. Their highest species diversity is found in tropical regions, particularly Southeast Asia, Australia, Central and South America, and parts of Africa. These bees exhibit advanced eusocial behavior, characterized by cooperative brood care, division of labor, and overlapping generations. They are known for producing honey and beeswax, and for collecting pollen and plant resins to support their colonies. Stingless bees construct intricate nests and employ effective defense mechanisms despite lacking functional stingers. Among the numerous species, approximately 40 are considered particularly valuable for their ability to produce honey, making them of interest for both ecological and commercial purposes. (Al-Hatamleh *et al*., 2020) [1]

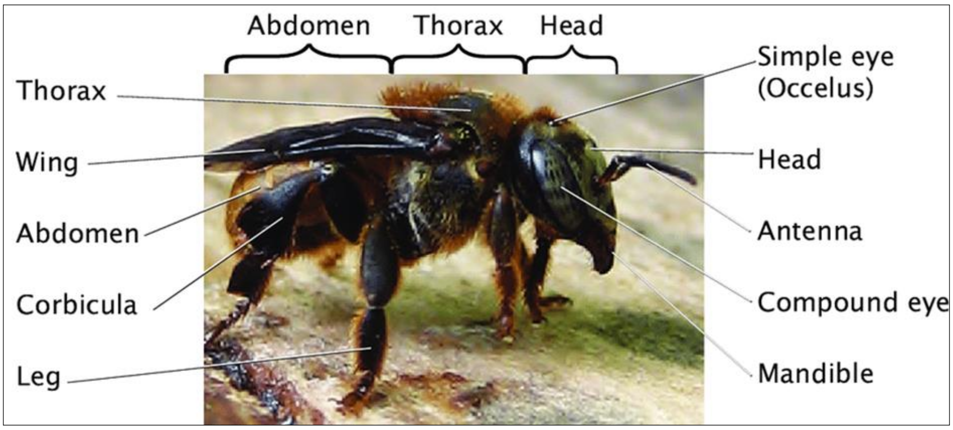

Fig 1: External Morphology of Stingless Bee

The practice of rearing stingless bees is known as meliponiculture. Although the use of these bees by humans dates back to ancient times, historical documentation of this practice remains limited in the archaeological record.

Stingless bees forage for floral nectar from a variety of local plant species and enhance it through biochemical processes involving enzymes and secretions from their cephalic glands, including saliva. Fig. 1. External Morphology of Stingless Bee illustrates the distinct external features that support these behaviors, such as their reduced wing structure and specialized head and mouthparts (Kwapong *et al*., 2010) [2].

One of the key products obtained from stingless bee colonies is bee pollen, which undergoes a natural maturation process within the hive. This process, aided by native microbes and bee-derived enzymes, gives the pollen a distinctive taste profile—often described as a combination of sweet and sour—and contributes to its medicinal value. These unique characteristics make stingless bee pollen both nutritionally valuable and therapeutically promising. Stingless bees are known not only for producing honey but also for generating other bioactive products such as propolis and bee pollen, each offering distinct therapeutic properties (Figure 2). This review explores the medicinal value of stingless bee pollen in depth, presenting recent findings on its biological effects, health-promoting properties, and its growing potential in the fields of therapeutics and functional nutrition. (Chuttong *et al*., 2016; Syafrizal *et al*., 2020) [3, 4]

Fig 2: Stingless Bee Products (Honey, Bee Pollen, Propolis)

Stingless Bee Pollen

Stingless bee pollen, derived from stingless bees, is increasingly recognized as a valuable food supplement. This natural substance forms when bees combine floral pollen with secretions from their glands and mix it with nectar or honey. Essentially, bee pollen consists of flower pollen grains, nectar, and bee secretions. Importantly, beekeepers can harvest this product without causing harm to the hive. Due to its growing popularity, stingless bee pollen is regarded as a promising apitherapeutic agent, with potential applications in both medical and nutritional fields. Honey, one of the sweetest and most flavorful bee products, shares a composition and properties somewhat similar to those of stingless bee pollen. It is produced by honeybees using nectar from flowering plants or secretions from living plant parts. The chemical makeup and physical characteristics of honey can vary widely depending on factors such as the floral source, environmental conditions like temperature, sunlight and water availability, as well as the geographical region where it is harvested. (Harif Fadzilah *et al*., 2017; Lavinas *et al*., 2019) [5, 6]

Harvesting and Characterization of Stingless Bee Pollen

Stingless bees produce pollen by collecting plant pollen as their primary resource. The distance these bees travel during foraging varies based on species, bee size, and food availability, with an average flight range of approximately 712 meters. For instance, Heterotrigona itama, a species of stingless bee, prefers to forage on plants located near their hive, showing a particular affinity for flowers that are white or cream-colored and contain nectar with a high sugar concentration. (Mohd & Zin, 2020; Badrulhisham *et al*., 2020) [7, 8]

Bees collect pollen using their salivary enzymes, such as amylase and glucosidase, along with honey to moisten and bind the pollen grains together. They then pack this mixture into specialized structures called pollen baskets located on their hind legs. Once combined with nectar, this transformed substance is known as bee pollen. Forager bees transport the bee pollen back to the hive for storage and use. The honeybee Apis is commonly used by beekeepers to harvest bee pollen. Typically, pollen is collected by placing a pollen trap at the hive entrance, which forces bees to pass through a narrow opening, gently removing some of the pollen carried on their legs without harming the bees. (Chauhan, 2020) [9]

Therapeutic Applications

Anticarcinogenic Activity

Several studies have shown that bee pollen possesses antimutagenic properties against certain cancer types. Its anticancer effects are believed to come from its antioxidant activity, which inhibits the formation and promotes the removal or inactivation of reactive oxygen species (ROS) (Arung *et al*., 2021) [10]. Additionally, stingless bee pollen has been linked to the induction of apoptosis and stimulation of tumor necrosis factor-alpha (TNF-α) release (Al-Hatamleh *et al*., 2019; Waheed *et al*., 2019) [11, 12]. This suggests that stingless bee pollen may exert cytotoxic effects by inhibiting cancer cell growth.

Research on stingless bee pollen from seven species in East Kalimantan, Indonesia, showed cytotoxicity against several cancer cell lines, including MCF-7, HeLa, and Caco-2. Among these, pollen from Heterotrigona fimbriata exhibited the highest cytotoxicity (Arung *et al*., 2021) [13]. Bee pollen extracts from Tetragonula incisa and Timia apicalis showed the strongest and weakest cytotoxic activities, respectively, with the HepG2 cell line broadly sensitive to the extracts. Among pure compounds tested, doxorubicin was the most cytotoxic, while propolis compounds were the least. The ChaGo-I cell line was sensitive to kaempferol, KATO-III to both kaempferol and apigenin, and all pure compounds were effective against the BT474 cell line (Kustiawan *et al*., 2014) [14]. The inhibition of cancer cell lines treated with stingless bee pollen extracts is likely related to their antioxidant potential (Belina-Aldemita *et al*., 2020) [15].

Anti-Inflammatory Effect

Stingless bee pollen extracts have shown significant anti-inflammatory effects in animal models, reducing inflammation similarly to indomethacin and cyproheptadine (Jorge *et al*., 2020) [16]. These effects are mainly due to phenolic compounds that inhibit histamine release and reduce prostaglandin synthesis. Polyphenols and flavonoids in the pollen regulate immune cells, aiding in the control of inflammation (Urcan *et al*., 2018) [17]. Quercetin, a major flavonoid, suppresses arachidonic acid metabolism, leading to lower levels of pro-inflammatory prostaglandins, resulting in analgesic and anti-platelet effects (Arulselvan *et al*., 2016; Biluca *et al*., 2017] [18, 19].

Moreover, bee pollen bioactive compounds modulate protein phosphorylation, thereby influencing cell signaling and proliferation (Ismail *et al*., 2018) [20]. Components like anethole inhibit the TNF-induced NF-κB pathway, which reduces expression of pro-inflammatory genes Fatty acids and phytosterols in stingless bee pollen also contribute to its anti-inflammatory activity, especially in cardiovascular and renal inflammation. Overall, its effects are comparable to NSAIDs such as naproxen and indomethacin (Roy *et al*., 2017) [21].

Antioxidant Properties of Stingless Bee Pollen

Barbara *et al*. demonstrated that extracts of stingless bee pollen possess valuable nutritional qualities, rich in polyphenols, flavonoids, and fatty acids, which contribute to its notable antioxidant activity (Barbara *et al*., 2015) [22]. The abundant presence of these bioactive compounds, especially polyphenols and flavonoids, underlies the strong antioxidant potential of stingless bee pollen (Badrulhisham *et al*., 2020) [23].

Oxidative stress occurs when reactive oxygen species (ROS) accumulate in cells beyond normal levels. These ROS can originate from both internal metabolic processes and external environmental sources (Comert & Gokmen, 2018) [24]. Elevated ROS levels can damage cellular membranes and DNA, triggering chronic inflammation and playing a critical role in the development of numerous diseases, including cardiovascular disorders, diabetes, neurodegenerative diseases like Parkinson’s and Alzheimer’s, as well as various cancers (Al-Hatamleh *et al*., 2017) [25].

The antioxidant effects of stingless bee pollen likely result from a combination of antioxidant enzymes and secondary plant metabolites such as phenolic compounds, carotenoids, vitamins C and E, and glutathione. Among these, flavonoids are the most prevalent and widely researched low-molecular-weight polyphenols. Stingless bee pollen contains several key flavonoids, including quercetin, caffeic acid and its phenethyl ester (CAPE), rutin, pinocembrin, apigenin, chrysin, galangin, kaempferol, and isorhamnetin (Arung *et al*., 2021) [26]

Antidiabetic Activity

Obesity is a major global health issue, with over 1.9 billion adults overweight and 650 million classified as obese worldwide in 2020 (Cole & Florez, 2020) [27]. Natural products, including stingless bee pollen, have been explored for their anti-obesity effects (Atanasov *et al*., 2021) [28]. One study demonstrated that Heterotrigona itama bee pollen significantly reduced obesity markers in high-fat diet (HFD)-induced obese rats. It lowered the Lee obesity index, total cholesterol (TC), low-density lipoprotein (LDL), fatty acid synthase (FAS) activity, atherogenic index, oxidized LDL (oxLDL), malondialdehyde (MDA), and improved antioxidant enzyme activities such as superoxide dismutase (SOD) and glutathione peroxidase (GPx). Histological analysis of the aorta showed smaller fat cells and absence of atherosclerotic plaques in treated rats (Othman *et al*., 2020) [29].

Another study investigated the protective effects of stingless bee pollen on obesity-related kidney damage. Administration of 0.5 g/kg H. itama pollen reduced oxidative stress, downregulated inflammatory markers, and suppressed bax-mediated apoptosis in the kidneys of obese rats (Eleazu *et al*., 2022) [30].

The antidiabetic effect is attributed to the pollen’s antioxidant properties, which neutralize free radicals and aid cellular regeneration. Additional research showed that stingless bee pollen reduced liver enzymes SGOT and SGPT and improved liver histopathology in high-fat diet-induced Wistar rats (Prahastuti *et al*., 2020) [31].

Antimicrobial Activity

Stingless bee pollen has gained attention for its potent antimicrobial effects, largely due to its phenolic content. These bioactive compounds show promising activity against bacteria, fungi, and even parasites, highlighting the therapeutic potential of bee pollen extracts. For instance, pollen extract from Melipona compressipes manaosensis demonstrated antimicrobial and larvicidal activity, significantly inhibiting the growth of Pseudomonas aeruginosa, Mycobacterium smegmatis, and Candida albicans, as well as Culex quinquefasciatus larvae in a dose-dependent manner (Carneiro *et al*., 2019) [32].

In another study, ethanol and hexane extracts of Heterotrigona itama pollen were tested against Bacillus cereus, Staphylococcus aureus, Escherichia coli, and Salmonella species. Gram-positive bacteria exhibited higher sensitivity, and ethanol extracts showed greater antibacterial potential than hexane extracts (Akhir *et al*., 2017) [33].

Further antimicrobial screening was conducted on bee pollen from Austroplebeia australis, Tetragonula carbonaria, and Tetragonula hockingsi in Australia. Ethanolic and methanolic extracts inhibited both Gram-positive (Staphylococcus aureus, Bacillus subtilis) and Gram-negative bacteria (Enterobacter cloacae, Escherichia coli, Pseudomonas aeruginosa). Ethanol extracts demonstrated the strongest effects, particularly from Tetragonula hockingsi (Perez-Pérez *et al*., 2018) [34].

Additionally, glycolic bee pollen extracts from Frieseomelitta, Melipona, and Tetragonisca species in Venezuela showed antibacterial activity against Bacillus subtilis, Staphylococcus aureus, Enterobacter cloacae, and Pseudomonas aeruginosa. However, no activity was observed against E. coli. These effects were strongly linked to the phenolic content in the extracts (Sulbarán-Mora & Pérez-Pérez, 2018) [35].

Anti-Allergenic Effect

Stingless bee pollen has demonstrated promising anti-allergenic effects, largely due to its content of flavonoids, steroids, and volatile oil compounds, which are known to modulate immune responses and inhibit allergic reactions (Denisow & Denisow-Pietrzyk, 2016) [36]. One of the primary mechanisms involves preventing the binding of immunoglobulin E (IgE) to its receptors, thereby inhibiting histamine release, which is central to allergic symptoms.

A study by De Farias *et al*. (2014) [37] evaluated the effects of stingless bee pollen in a mouse model of asthma. Treatment with stingless bee pollen extract resulted in a marked reduction in bronchoalveolar inflammation, total inflammatory cell count, and polymorphonuclear cell infiltration. These outcomes were comparable to those seen with dexamethasone, a standard anti-inflammatory medication used in allergy treatment.

Additionally, stingless bee pollen was shown to reduce levels of pro-inflammatory cytokines, particularly interleukin-1β (IL-1β) and tumor necrosis factor-alpha (TNF-α), both of which are central to the inflammatory cascade in allergic conditions (Franchin *et al*., 2012) [38]. Supporting this, a study on inflamed rat dental pulp tissues reported that bee pollen from Trigona species significantly decreased IL-6 expression, further confirming its cytokine-mediated anti-allergic properties (Sabir & Sumidarti, 2017) [39].

Other Promising Properties of SBH

Stingless bee honey (SBH) has demonstrated potential neuroprotective and metabolic benefits. Research has shown that SBH reduces anxiety and improves memory performance, while also lowering triglyceride and low-density lipoprotein (LDL) levels and normalizing blood glucose in rats with metabolic syndrome (Arshad *et al*., 2020) [40]

Due to its high antioxidant content, SBH has also been studied as an anti-ageing agent for skin. In an *in vitro* study using human dermal fibroblast cells, SBH treatment upregulated collagen expression in both ageing and senescent cells, while downregulating matrix metalloproteinases (MMPs) involved in collagen degradation. These findings suggest that SBH could be a promising natural treatment for skin ageing (Abdul Malik *et al*., 2019) [41]

Conclusion

This review underscores the significant health benefits of bee products, which are rich sources of bioactive compounds such as flavonoids, phenolic acids, and enzymes. These natural substances contribute to disease prevention and the promotion of overall health. Traditionally utilized in various medical systems, bee-derived products—including honey, propolis, royal jelly, and bee pollen—are now gaining increasing scientific attention for their therapeutic potential. Current research highlights their antioxidant, antimicrobial, anti-inflammatory, and anticancer properties. However, despite encouraging findings from *in vitro* and animal studies, more rigorous and well-designed human clinical trials are necessary to substantiate these effects and assess their safety and efficacy. To harness the full therapeutic potential of bee products, future studies should aim to standardize the identification and quantification of their active constituents. Moreover, a deeper understanding of their pharmacological mechanisms will be essential for the development of novel natural health products and integrative treatments. In summary, bee products represent promising natural agents with diverse functional and medicinal applications. Continued research is vital to validate their benefits and support their integration into evidence-based medical practice.

Conflict of interest

Authors declare there is no conflict of interest.

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