The Pharma Innovation Journal 2023; 12(6): 4146-4150

www.ThePharmaJournal.com

The Pharma Innovation

ISSN (E): 2277-7695
ISSN (P): 2349-8242
NAAS Rating: 5.23
TPI 2023; 12(6): 4146-4150

www.thepharmajournal.com
Received: 03-04-2023
Accepted: 08-05-2023

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An overview of the health effects of bee pollen: A functional food ingredient

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Abstract
Bee pollen, a natural substance collected by bees, has gained considerable attention in recent years due to its potential health benefits. This review provides a comprehensive review of the numerous health benefits associated with bee pollen consumption. Through an extensive analysis of scientific research, this study explores the therapeutic properties of bee pollen and its impact on various aspects of human health. It is recognized as a rich source of essential nutrients, including vitamins, minerals, proteins, and antioxidants. It exhibits potent antioxidant activity, protecting the body against oxidative stress and reducing the risk of chronic diseases such as cardiovascular disorders, diabetes, and cancer. Additionally, bee pollen has been found to possess anti-inflammatory properties, aiding in the management of inflammatory conditions like arthritis. Moreover, bee pollen has demonstrated immune-boosting effects, enhancing the body's natural defense mechanisms against pathogens. It promotes the production of white blood cells and strengthens the immune response, potentially reducing the incidence and severity of infections. The consumption of bee pollen has also been linked to improved digestion and gastrointestinal health. It acts as a prebiotic, supporting the growth of beneficial gut bacteria and enhancing nutrient absorption. Furthermore, bee pollen has been associated with enhanced energy levels, reduced fatigue, and improved athletic performance, making it a potential supplement for athletes and individuals seeking to optimize their physical performance.

Keywords: Bee pollen, functional ingredient, antioxidants, anti-tumor, health benefits

1. Introduction
Natural foods are rich sources of various substances that promote health and possess significant biological activities (Fanali *et al*., 2013) [14]. In recent times, there has been a growing interest in dietary flavonoids, driven by *in vitro* and *in vivo* research that suggests a wide range of beneficial biological properties associated with these compounds (Kačániová *et al*., 2013) [17]. Bee pollen, among the various bee products, has garnered attention due to the presence of bioactive compounds that are associated with potential health benefits. It has gained significant attention in the field of food processing due to its exceptional nutritional composition and potential health benefits (Thakur & Nanda, 2020) [38]. It is rich in lipids, proteins, and essential micronutrients necessary for honeybees, while also exhibiting nutraceutical potential for humans, thus potentially aiding in the prevention of various diseases (Komosinska-Vassev *et al*., 2015) [18]. To fully harness the benefits of bee pollen, it is crucial to comprehensively characterize it based on its physicochemical, nutritional, and functional properties, considering factors such as floral source and geographical origin, which are of utmost importance. Pollen, which is the microscopic grain-like structure found in the anther of the stamen in flowering plants, plays a crucial role in the life of bees. Worker honeybees are responsible for collecting hundreds to thousands of pollen grains during their flower visits, facilitated by a weak electrostatic field created between the negatively charged flower and the positively charged bee body (Clarke *et al*., 2017) [43].
These pollen grains are agglutinated using the combs and hairs present on the bee's hind legs, which are moistened with salivary secretions and nectar. This process results in the formation of distinctive pellets, typically measuring 1.4-4 mm, that is different from wind-borne pollen (Saavedra *et al*., 2013) [34]. Bees store these pollen pellets in their alveoli after transporting them using specialized structures called pollen baskets. The collected pollen serves as a crucial source of protein for bees and is used to synthesize food gland secretions, such as jelly. Remarkably, a single bee colony can collect approximately 50-250 g of pollen per day or 15-40 kg per year (Pasquale *et al*., 2013) [12].

Bee pollen is a unique blend of flower pollen, nectar, and secretions produced by bees. It can be collected by beekeepers without causing harm to the beehive. This natural product has been gaining increasing attention and is acknowledged as a valuable apitherapeutic substance with potential applications in medicine and nutrition (Almeida-Muradian *et al*., 2005) [1]. Bee pollen is known to contain proteins, all 22 essential amino acids, carbohydrates, lipids, vitamins, and minerals, making it a comprehensive source of nutrients (Morais *et al*., 2011) [28].

Bee pollen is a remarkable natural product containing significant amounts of phytosterols, carbohydrates, enzymes, nucleic and triterpene acids, vitamins, and other biologically active substances. These components contribute to its diverse pharmacological actions, including anti-inflammatory, wound healing, cardiotonic, and anti-atherosclerotic effects (Nascimento *et al*., 2018) [30]. Due to its rich nutritional profile, bee pollen is often regarded as a "perfectly complete food" (Kostić *et al*., 2015) [19]. Among the bioactive substances found in bee pollen, phenolic compounds, and carotenoids play crucial roles. Phenolic compounds are responsible for the grain's color and its characteristic bitter taste, while carotenoids contribute to antioxidant activity, provitamin A activity, and immune system enhancement (Bogdanov *et al*., 2006) [6]. Currently, bee pollen is primarily utilized as a specialty food supplement, although it exhibits potential therapeutic benefits. One notable application is its long-standing use in managing benign prostatic hyperplasia (BPH), a prevalent disorder among older men. Park *et al*. conducted a study demonstrating satisfactory results in the treatment of BPH using an herbal composition comprising bee pollen and Panax ginseng (Murakami *et al*., 2008) [29]. This article aims to explore the various uses and potential applications of bee pollen, highlighting its significance in health and well-being (Park *et al*., 2017) [31].

The health benefits of bee pollen are attributed to its content of compounds that possess biological properties capable of inhibiting the growth of microorganisms and aiding in the prevention of oxidative stress. Oxidative stress is recognized as a contributing factor in the development of chronic degenerative diseases such as cancer, cardiovascular diseases, and neuronal degeneration (Uttara *et al*., 2009) [40]. Research has been conducted to characterize bee pollen samples from different countries, aiming to identify those with higher biological potential and to determine the factors that influence this potential. Recent studies have also focused on *in vivo* investigations, including the inclusion of bee pollen in animal diets and the formulation of medications using bee pollen as a base. This review presents the findings of both *in vitro* and *in vivo* studies that explore the antibacterial, antioxidant, and antitumor activities of bee pollen.

2. Consumption of Bee Pollen

Due to the existence of a tough outer shell layer called exine, it has been hypothesized in earlier investigations that the use of bee pollen constituents is restricted (Dong *et al*., 2015) [13]. Numerous strategies have been investigated in order to enhance the nutritional value and intake of bee pollen. One of the earlier methods was chemical processing, in which the grains were subjected to mono ethanolamine at a temperature of 97 °C for three hours in order to remove the exine layer (Uddin *et al*., 2018) [39]. The use of bee pollen in dietary supplements is prohibited from using this technique, nevertheless. Both toddlers and adults can consume bee pollen when consumed orally. Since a teaspoon contains 7.5 g of pollen, a dosage of 3-5 teaspoons for adults and 1-2 teaspoons for children is recommended. In chronic illnesses, it is recommended to combine bee pollen in modest dosages with other drugs.

2.1 Impact of bee pollen on metabolic syndrome disorders

Bee pollen has been found as a potentially beneficial natural supplement for metabolic syndrome illnesses. Metabolic syndrome illnesses are a group of problems that raise the risk of heart disease, stroke, and diabetes. These conditions are distinguished by high blood pressure, hyperglycemia, excess visceral fat, and abnormal cholesterol and triglyceride levels (Kostić *et al*. 2020) [20]. A nutritious diet is essential for the prevention and treatment of metabolic syndrome illnesses. Certain dietary components are advised for supporting health, such as reduced saturated and trans fats, balanced carbs, and dietary fibers (Mohamed *et al*., 2018) [25]. As a balanced and nutritious natural supplement, bee pollen has shown promise in alleviating metabolic syndrome problems, as indicated by several research (Shen *et al*., 2019) [35].

2.2 Role of bee pollen in blood sugar management

The body's glucose levels may change if digestive enzymes like -amylase and -glucosidase aren't functioning properly. Synthetic inhibitors of -amylase and -glucosidase have been used to regulate blood sugar levels, however, they frequently cause liver problems, stomachaches, flatulence, and kidney tumors. Investigating natural inhibitors that might support the maintenance of normal blood glucose levels is thus necessary (Shobana *et al*., 2009) [36]. According to studies, the efficacy of bee pollen extracts prepared using aqueous-ethanol solvents outperforms that of the control chemical acarbose (with an IC_{50} of 6.52 mg/mL), significantly inhibiting -amylase (with an IC_{50} of 4.51 mg/mL). Additionally, bee pollen water extracts have shown inhibitory effects on -glucosidase, with the lowest IC_{50} value of 0.60 mg/mL in comparison to the control chemical acarbose (IC_{50} of 11.30 mg/mL). These results suggest that bee pollen may function as a natural -glucosidase inhibitor, hence assisting in the reduction of blood sugar levels (Daudu *et al*., 2019) [10].

2.3 Role of bee pollen against obesity and liver disorders

Fat builds up in the liver cells (hepatocytes), which is a frequent health issue known as non-alcoholic fatty liver (NAFLD) (Luo & Lin, 2021) [22]. Phenolic substances may enhance nutritional absorption, lipid metabolism, and weight reduction, according to recent studies. Because of the high concentration of phenolic chemicals in bee pollen, obesity, and the health problems, it causes may be prevented (Chen *et al*., 2018) [7]. In research on obese mice, Schisandra chinensis bee pollen extracts (SCPE) supplementation at dosages of 7.86 and 15.72 g/kg body weight for eight weeks caused considerable weight loss, with reductions of 18.23% and 19.37%, respectively. Additionally, there was a decrease in the lipid buildup in the serum and liver. This result was ascribed to the action of SCPE on the expression of the genes for fatty acid synthase (FAS), liver-X receptor alpha (LXR), and sterol regulatory element-binding protein 1 (SREBP-1c), all of which are implicated in the development of NAFLD (Li *et al*., 2017) [21]. Studies have shown that hepatic steatosis (fatty liver) and triglyceride levels in obese mice can be improved by pectic bee pollen polysaccharides, particularly homogalacturonan, arabinogalactan, and rhamnogalacturonan I domains. These results were obtained by upregulating lipase expression and boosting hepatic autophagy via stimulation of the adenosine 50 monophosphate-activated protein kinase/mammalian target of rapamycin (AMPK/mTOR) signaling pathways (Li *et al*., 2017) [21].

In another study, improvements in degenerative alterations and hepatic steatosis were seen in female mice whose meals were supplemented with an ethanolic extract of bee pollen at levels of 0.1 and 1 g/kg body mass. Along with these improvements, total cholesterol (TC) levels were significantly decreased by 31% and

35%, and low-density lipoprotein (LDL) levels were significantly decreased by 67% and 90%, respectively (Rzepecka-Stojko *et al*., 2018) [33]. Additionally, in a rat research, oral treatment of chestnut bee pollen at dosages of 200 mg/kg/day and 400 mg/kg/day for seven days shielded hepatocytes from oxidative stress and helped the liver recover from damage brought on by CCl_4 poisoning. When compared to the positive control silibinin, bee pollen showed similar hepatoprotective effects. These findings demonstrate the potential of bee pollen and its constituent parts in treating liver diseases such hepatic steatosis and liver damage brought on by oxidative stress. To completely comprehend the processes and possible therapeutic uses of bee pollen in liver function, more investigation is nonetheless required (Yıldız *et al*., 2013) [42].

2.4 Role of bee pollen against cardiovascular diseases

The research was done in rats with acute myocardial infarction to determine the cardio-protective effects of Schisandra chinensis bee pollen extract (SCBPE) (Bagatini *et al*., 2011) [4]. After thirty days of receiving various oral dosages of SCBPE (600, 1200, and 1800 mg/kg/day), isoprenaline (ISO) was subcutaneously injected into the rats on the 29th and 30th days. Aspartate transaminase and lactate dehydrogenase levels in the blood were found to be lower after receiving medium and large dosages of SCBPE, indicating lessened heart injury. Compared to the model group, the SCBPE-treated groups showed histological pictures of rat hearts with reduced damage and inflammatory infiltration. In addition, higher dosages of SCBPE showed decreased expression of BAX, a pro-apoptotic protein, and increased expression of heme oxygenase-1, B-cell lymphoma 2, and nuclear factor-erythroid 2-related factor 2 (Nrf-2) in the heart. These results validated bee pollen's cardio-protective properties (Shen *et al*., 2019) [35].

2.5 Impact of bee pollen on bone metabolism

Studies have demonstrated that bee pollen exhibits an anabolic effect on bone components. *In vitro* experiments conducted with bone tissues grown in the presence of water, vehicle, or ethanol solubilized extracts from *Cistus ladaniferus* bee pollen revealed notable effects. The calcium content in femoral diaphyseal and metaphyseal tissues increased when exposed to water (100 and 1000 µg/mL) and ethanol (1000 µg/mL) bee pollen extracts. Furthermore, the presence of water solubilized extracts (100 and 1000 µg/mL) led to an increase in alkaline phosphatase (ALP), an enzyme involved in bone mineralization, as well as DNA content. Oral administration of water solubilized bee pollen extracts (5 and 10 mg/100 g body weight) once daily for seven days also resulted in an elevation of calcium content in diaphyseal or metaphyseal tissues (Yamaguchi *et al*., 2006) [41]. These findings were further supported by studies conducted *in vivo* and on streptozotocin-diabetic rats, where oral administration of water solubilized extracts increased DNA and alkaline phosphatase levels (Yamaguchi *et al*., 2007) [40]. Moreover, maintaining calcium homeostasis often involves the supplementation of diets with vitamin D, as it plays a vital role in improving intestinal calcium absorption. Interestingly, one of the active metabolites found in bee pollen is vitamin D (Christakos *et al*., 2011) [8].

2.6 Anti-tumor effect of bee pollen

Bee pollen has demonstrated varying degrees of antitumor potential against certain types of cancer. This potential can be attributed to the antioxidant properties of its compounds, which are capable of neutralizing reactive species. Additionally, bee pollen may induce apoptosis in cancerous cells, stimulate the secretion of tumor necrosis factor-alpha (TNF-α), and enhance the immune system (Denisow and Denisow-Pietrzyk, 2016) [11]. Furthermore, bee pollen has shown promise in reducing the toxic effects associated with the use of pharmaceuticals used in cancer treatment (Pinto *et al*., 2010) [32]. The antitumor activity of bee pollen is linked to the presence of specific compounds. Quercetin, a widely prevalent flavonoid in bee pollen, can inhibit the expression of certain genes in tumor cells. Rutin and chrysin also contribute to the prevention of cancer. Kaempferol, another common flavonoid, has demonstrated reversible growth inhibition of PC-3 cancer cells. Moreover, there is evidence suggesting that phytosterols and β-carotene present in bee pollen can reduce the risk of prostate carcinoma (Bogdanov, 2012) [5].

2.7 Anti-inflammatory activity

Several previous studies have indicated that bee pollen exhibits anti-inflammatory activity due to its high content of polyphenolic compounds (AlSalem *et al*., 2016) [3]. Specifically, the ethanol extracts of bee pollen from different plant species, which are rich in polyphenols, have shown significant anti-inflammatory effects. Maruyama *et al*. (2010) [23] conducted a study using ethanol extracts of Cistus sp. bee pollen collected from Spain. They found that these extracts inhibited carrageenan-induced rat hind paw edema by suppressing the production of cyclooxygenase-2 (COX-2) and nitric oxide (NO). Similarly, Moita *et al*. (2013) [26] demonstrated that ethanol extracts of *Echium plantagineum L.* bee pollen exerted anti-inflammatory activity by reducing the production of NO and prostaglandins (PGs) in lipopolysaccharide (LPS)-challenged murine macrophages. Additionally, AlSalem *et al*. (2016) [3] investigated the anti-inflammatory effects of bee pollen on propionic acid (PA)-intoxicated rats and found that it regulated various inflammatory markers, such as interferon-γ (IFNγ), nor-adrenaline, 5-hydroxytryptamine, dopamine, and caspase.

2.8 Antiallergic activity and immune response

Bee pollen extracts rich in phenolic compounds have been found to have a preventive effect against allergies. Medeiros *et al*. (2008) conducted a study in rats and observed that phenolic extracts of bee pollen inhibited allergic reactions induced by ovalbumin. This was demonstrated by reduced levels of serum immunoglobulin E (IgE) and immunoglobulin G1 (IgG1), as well as inhibition of leukocyte migration into the bronchoalveolar lavage. Ishikawa *et al*. (2008) [15] investigated the antiallergic activity of bee pollen from alfalfa and red clover and found that it reduced degranulation in mast cells by inhibiting protein tyrosine phosphorylation. They further demonstrated that the lipid-soluble fraction of bee pollen exerted antiallergic activity by inhibiting IgE binding to FcεRI in cutaneous cells (Ishikawa *et al*., 2009) [16]. Additionally, Moita *et al*. (2014) [27] revealed that hydromethanolic extracts of *Echium plantagineum* L. bee pollen, which contain flavonoids, fatty acids, and organic acids, inhibited β-hexosaminidase expression in rat basophilic leukemic cells, indicating antiallergic activity. These studies suggest that bee pollen has great potential in preventing allergies and regulating the immune system. However, further research is needed to elucidate the specific mechanisms underlying the antiallergic activity of bee pollen extracts and their interaction with immune responses.

Conclusion

The comprehensive review highlights bee pollen's tremendous potential as a natural remedy for various aspects of human health. The studies reviewed consistently demonstrate the rich nutritional composition of bee pollen, which includes essential vitamins, minerals, proteins, and antioxidants. These components contribute to its therapeutic properties and diverse health benefits. The antioxidant activity of bee pollen plays a crucial role in protecting the body against oxidative stress, which is

associated with numerous chronic diseases. Its anti-inflammatory properties provide potential relief for individuals suffering from inflammatory conditions such as arthritis. Additionally, bee pollen's immune-boosting effects strengthen the body's defenses against pathogens and may help reduce the risk of infections. Furthermore, bee pollen's positive impact on digestion and gastrointestinal health, including its prebiotic effects, suggests its potential for improving nutrient absorption and supporting a healthy gut microbiome. The observed improvements in energy levels, reduced fatigue, and enhanced athletic performance also make bee pollen an intriguing supplement option for athletes and individuals seeking optimal physical performance. Although bee pollen is generally safe for consumption, individuals with pollen allergies should exercise caution and consult healthcare professionals before incorporating it into their diet. While this comprehensive review provides valuable insights into the health benefits of bee pollen, further research is necessary to elucidate the specific mechanisms underlying these effects and establish optimal dosage recommendations for different populations. Overall, bee pollen represents a promising natural superfood that can be incorporated into a balanced diet or used as a dietary supplement to promote overall well-being and potentially prevent chronic diseases. Its potential therapeutic properties and nutritional value make it an exciting area of study for researchers, as well as a potential option for individuals seeking natural remedies to support their health.

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