Review Article

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Biomedical Applications of Black Pepper, the King of Spices: A Review

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ABSTRACT

Piper nigrum L. is known worldwide as the king of spices because it contains extremely important medicinal component of piperine and adds flavours to every food. *Piper nigrum* belongs to the family Piperaceae and is commonly known and consumed as black pepper throughout the world. Historically, it has been used since 50,000 B.C. by humans as aroma enhancer to food and attracted the attention of ancient emperors and voyagers who fought several wars and invented sea routes for India. The attraction of Indian spices trade was the major objective of the foundation of British East India Company in 1600 and black pepper as food additive, taste enhancer with great medicinal value was commonly referred as "king of spices" and the black gold in international trade. Black pepper is a fruit part of the plant known as Peppercorn, when dried peppercorn is almost mature pepper berry. *Piper nigrum* contains phytochemicals that includes alkaloids, flavonoids, phenolics, and capsaicinoids. Black pepper also contains secondary metabolic active compounds that are used in various medicine formulations, and as food preservative.

Piper nigrum is used in the treatment of various microbial diseases, cancer, diabetic, skin diseases, tooth ache, urinary tract infections, toxic mega-colon, auto-immune disorders, asthma, bronchitis, cough, sinus infection, measles, scabies, thyroid, obesity, gastrointestinal diseases, neurological, cardiovascular, and inflammatory diseases as well as pesticides, bactericides, insecticides and microbicide. In India people are using black pepper as home remedies for cough, throat pain, and indigestion of food. Black pepper is a useful spice having medicinal qualities that can be used in the making a number of foods with medical significance and also make food tasty, better and spicy. It showed antimicrobial activities which help in detoxification of the body.

Keywords: *Piper Nigrum;* Black Pepper; Piperine; Alkaloids; Flavonoids; Phenolics; Capsaicinoids

Introduction

Spices are excellent natural herbal food additives for treatment of numerous diseases because of their various medicinal characteristics and that too without any side effects. Ayurveda says that spices maintain a proper pH balance in the body, and they possess excellent antimicrobial properties and prolong food storage [1]. Different spices add different flavour, colour, and aroma to the food items and enhance their taste. In fact, these spices also help to protect the spleen and pancreas, protect from cough, sneezing, and sore throat, and improve digestion. Spices contains essential nutrients, minerals, and phytochemicals including phenolics, tannins, flavonoids, alkaloids, phenolic and antioxidant [1,2]. *Piper nigrum* (black pepper) is derived from Sanskrit word of "long pepper" or "pippali". In the ancient world, black pepper was so highly prized that traders referred to it as «black gold». The worldwide popularity of black pepper increased after the rise of the Roman Empire [3]. *Piper nigrum* is well

known as 'king of spices' because of its distinctive characteristics [4]. Archaeologists estimate that spices were used by humans 50,000 B.C. for their special qualities of aroma in various food preparations and black pepper has been used in Indian cuisine since then, eventually it was widely traded throughout Asia [5]. The cost of black pepper, cinnamon, cloves, and other spices was high that they were valued as silver and gold. Primitive man used sweet-smelling spices to enhance the taste of food, offered to their Gods and used them for healing of wounds. Trade in ancient world used caravans with as many as 4,000 camels that carried spices to Babylon, Carthage, Alexandria and Rome through Calicut, Goa, and the Orient. For hundreds of years, the traders also used ships that sailed along Indian coast, past the Persian Gulf, along the coast of South Arabia and finally through the red sea into Egypt.

South Arabia was the great emporium of antiquity. There are several stories and trade secrets of Arabians about their dominance in the trade of spices. In 1498, Vasco da Gama discovered an alternate route for India and the international trade in spices increased. Pepper, ginger, cloves, nutmeg, mace, cinnamon, saffron, anise, zedoary and cumin were considered as valuable spices in Europe and were mainly reserved for the tables of rich people, but the poor class of people used black pepper which they could get and afford easily. Despite their high costs, sacks of spices were used in for royal banquets and weddings and in 15th century, the household of Duke of Buckingham in England was using 900 gram (2 Pounds) of spices every day, mostly pepper and ginger. By 1511, Portuguese were in the control of spice trade through Malabar Coast of India and Ceylon and until the end of 16th century, they dominated and black pepper was a major part of spice trade and was considered as valuable as gold. By 1580, the dominance of Portugal in black pepper trade declined as Venice emerged a new trade market for bulk import of spices from India. With waning power of Portuguese, Dutch and English saw huge opportunities for their trade in spices as they were the major powers on marine routes [3]. The British East India Company was established in 1600 by Queen Elizabeth I with a major objective to get spice cargoes and they worked strategically to gain power away from Dutch and finally in 1780, England and Holland started a war that severely weakened Dutch power in India. By 1800s, everything that once belonged to Portugal and Holland was controlled by British and they ruled for 200 years and exploited Indian resources to their huge benefit, but they left behind the benefits of English language, transportation, communication, architecture, and construction while they took a lot away from us and also left several political geographical questions unresolved. One of the most significant things, they took home were India spices and till date they decorate European cuisine, especially black pepper is found in every European home and restaurant.

Piper nigrum L belonged from Piperaceae family [6,7]. Piperaceae family consist of 5 genera that are Piper, Peperomia, Zippelia, Manekia, and Verhuellia, essentially divided into two major important genera: Piper contained around 2,000 species and Peperomia contained around 1,600 species [8]. Black pepper is a tropical plant that survives in humid environments and requires frequent rainfall [9]. It is cultivated in the warm and moist atmosphere of sub-mountainous regions of the Western Ghats [10]. Black pepper contains several bioactive compounds that help to treat various diseases like tumors, asthma, diarrhea, thyroids, arthritis, obesity, dermatitis, acute liver failure, autoimmune disease, hypertension, and cardiovascular disease [11] and several health benefits of black pepper are depicted in (Figure 1). Black pepper is used to treat fever, tooth ache, inflammation, muscle cramps, anxiety, and depression [12]. It is also used as an antibacterial, antifungal, antiviral, antioxidant, anti-cancerous, insecticidal, and larvicidal characteristic [13]. Black pepper was recently discovered to help in healing wounds and provide nutrients for the body [14]. It has been shown to improve fertility and neurological functions [15]. Peppercorn also helps to secrete both pancreatic and intestinal enzymes, which help in digestion [16]. Piperine is a major phytochemical present in black pepper [2]. It also provides flavor, aroma, and color to food preparations [17].

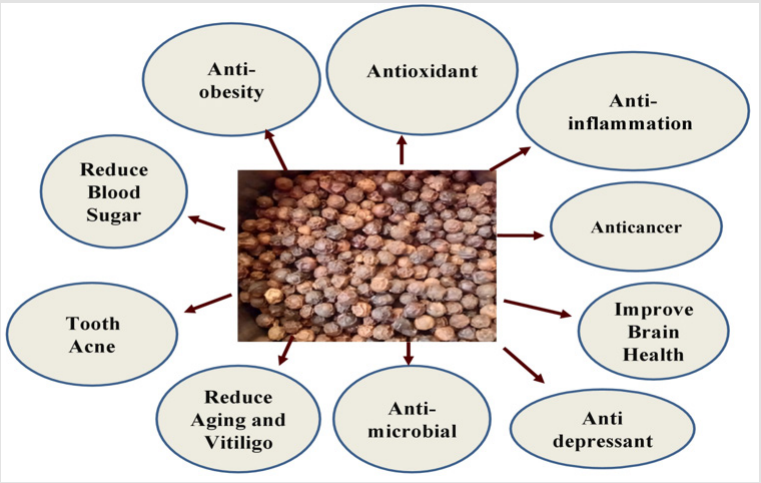

Figure 1: Major Health Benefits of Black Pepper.

Chemical Composition

Piper nigrum (black pepper) was the first scientifically medicinal product found in the Piperaceae family [6]. It has been demonstrated to be an excellent variety of bioactive compounds utilised in conventional medicinal therapy and reveal excellent effects; therefore, they are suggested in clinical therapies [18]. Numerous researchers identified that black pepper contained several phytochemical compounds like alkaloids, flavonoids, steroids, phenols, terpenes, tannins, and amides [1,19] that have numerous benefits. Black pepper is a good source of nutrients, vitamins, minerals, carbohydrates, proteins, and secondary metabolites [20]. The biochemical constituents of black pepper are piperine 2.1-8.9%, oleoresin 2.31-12%, essential oil 0.4-6.9%, starch 28-51%, and fatty acids 1.8-15%. The most prevalent bioactive chemical in black pepper includes are β-caryophyllene 30%, limonene 13.4%, β-pinene 8%, α-pinene 4.6% , sabinene 6%, caryophyllene oxide 9%, 3-carene 30%, and camphene 11% (Figure 2) [21-23]. There were a few phytochemicals discovered, including hydroxytyrosol 4-O-glucoside, 6-hydroxyluteolin 7-O-rhamnoside,2-hydroxybenzoic acid, apigenin 6,8-di-C-glucoside, scopoletin, rhoifolin, sesamin, and hydroxytyrosol [24,25].

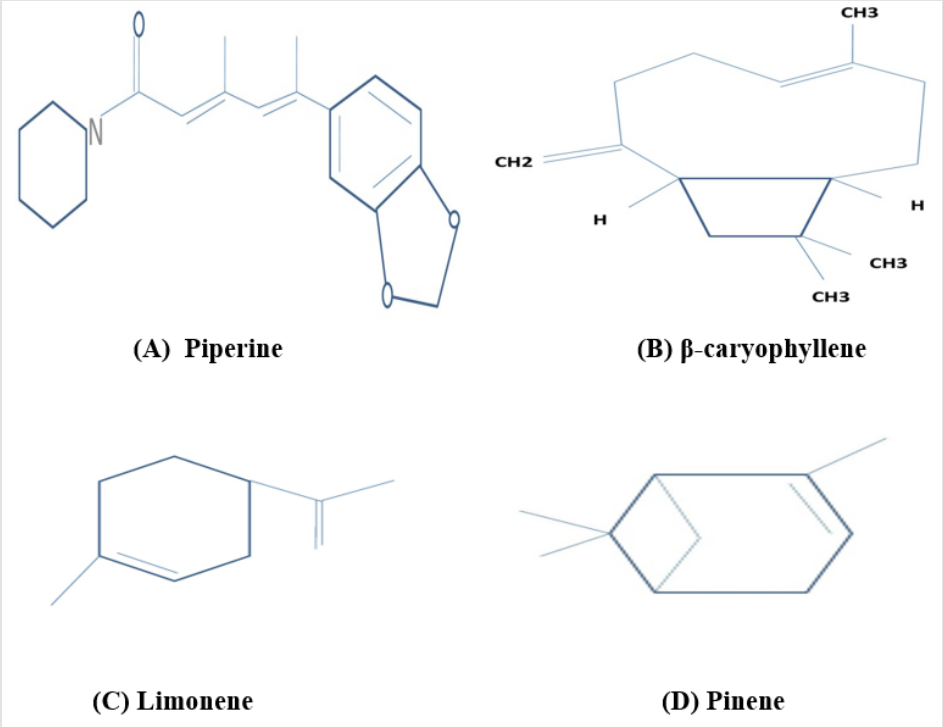

Figure 2: Biochemical compounds black pepper.
(A) Piperine
(B) β-caryophyllene
(C) Limonene
(D) Pinene

Nutrients Present in Black Pepper

Peppercorn (black pepper) is an excellent source of magnesium, which helps in blood clotting, the formation of bones and muscles, and anti-inflammation [26]. Black pepper contains antioxidants, alkaloids, flavonoids, steroids, essential oils, and phenolic substances that help boost the immune system, improve digestion, and protect tissues [27]. Black pepper is an excellent source of vitamin A, vitamin K, vitamin E, vitamin B1, vitamin B2, vitamin B5, and Vitamin B6 [28]. It also contains minerals including copper, iron, calcium, phosphorus, potassium, sodium, niacin, folate, fluoride, selenium, zinc, and chromium [29]. Due to the presence of antioxidants, nutrients, and bioactive chemicals in black pepper, it's worked as an antimicrobial activity [30,2], boost immunity, control cholesterol levels, and help to increase the shelf life of food [31]. Various nutrients, their amounts and applications are summarized in (Table 1 & Figure 3).

Table 1: Nutrients present in black pepper, their amounts, and their applications.

Sr. No	Nutrients	Application	Amount
1.	Calcium	Bones and teeth formation	11 mg
2.	Iron	Hemoglobin formation	1.2 mg
3.	Magnesium	Maintain function of nerve and muscles	4 mg
4.	Phosphorus	Maintain and repair tissues and cell	3.8mg
5.	Potassium	Helps contraction of muscles, movement of nutrients into cells and waste product out	31mg
6.	Sodium	Help nerve impulse, maintain the level of water and mineral	1.2mg
7.	Zinc	Boost immune system, help in cell division, and cell growth	0.27mg
8.	Manganese	Help in blood clotting, connective tissue, and sex hormones	1.29 mg
9.	Selenium	Formation of DNA, protect cell damage and infections	1.13 µg
10.	Fluoride	Prevent tooth decay and build strong teeth and bones	1.6 µg
11.	Niacin	Helps in digestive system and skin healthy	0.126mg
12.	Folate	Formation of DNA, other genetic material, and cell division	1.3 µg
13.	Betaine	Helps in liver function, cellular reproduction, and formation of carnitine.	1.205mg
14.	Beta-carotene	Help in vision, healthy skin, and mucous membrane	8 µg
15.	Lutein	Antioxidant properties, prevent eye disease	10.8 µg
16.	Zeaxanthin	Protecting eye tissue from sun light damage	11 µg
17.	Vitamin E	Strong antioxidant and anti-inflammatory agent for skin	0.98µg
18.	Vitamin A	Help in vision, immune system, reproduction, growth, and development	13 µg
19.	Vitamin K	Help in blood clotting and bone metabolism	4.1 µg
20.	Carbohydrates	Provide glucose and convert into energy	32 gm
21	Protein	Formation of tissue, allow metabolic reaction and maintain pH. of body	10 gm
22.	Sugar	Supply glucose to brain and provide energy to cells.	0.09 gm
23.	Fiber	Improve digestion, and cholesterol	1.5 gm
24	Energy	Helps in physical activity, growth, and repair tissue	6 calories

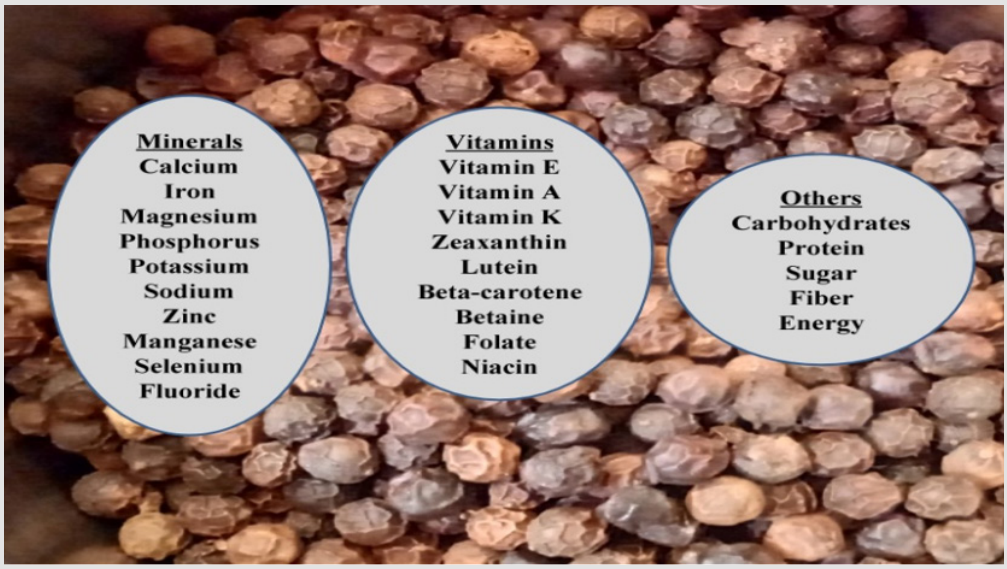

Figure 3: Major nutrients present in black pepper.

Medicinal Uses of Black Pepper

Black pepper contains piperine, which reveals a variety of additional pharmaceutical characteristics, including anticolon toxin, antimicrobial, anticancerous, antiobesity, antiviral, antiparastic, antibacterial, antifungal, antitumors, anti-asthmatics, anti-apoptotic, antispasmodic, antiplatelets, antithyroids, antidepressant, antimutagenic, antipyretic, antispermatogenic, antihypertensive, anti-metastatic, pesticides, and insecticides characteristics [32-35].

Anti-Obesity

Obesity is a major issue around the world due to a health issue that is stigmatised in society. US population is worst affected and accounts for 40% of population suffering from obesity. World Health Organization has referred it as a lifestyle disorder that paves the way for several diseases. Uses of *Piper nigrum* (black pepper) as a natural remedy and other nonclinical ways to control obesity include yoga, cardio exercise, a keto diet, meditation, and so on [36]. There are also many herbs and spices that possess anti-obesity properties [37].

Carminative Activity

Black pepper provides significant amounts of activating and carminative qualities, activating saliva for reflex flow, and enhancing the stomach for the synthesis of digestive juice that is pepsin, rennin, gastric lipase, gastric amylase, urease, and gelatinase, as well as enhanced appetite [38]. Gastro-intestinal motions have increased, which leads to gas eructation as well as colic relief [39]. In appropriate dosages, black pepper enlarges the skin's superficial vessels, causes a warm feeling, and causes hyperhidrosis as well as temperature reduction [40]. Several such characteristics make them frequently used as spices, particularly in warm countries. Black pepper has been suggested as a treatment against haemorrhoids (piles), prevents bloating, and reduces the level of prostaglandins because of reducing cramps [28,41]. Acetone extract of black pepper forms oleoresin, which is used in perfume formation, soap, and the cosmetic industry, as well as in the food industry for flavouring and colouring food [7,42].

Antipyretic Activity

In traditional medicine, including Ayurveda, Unani, Siddha, and Naturopathy, black pepper (*P. nigrum*) is used to formulate medicines for treating cough, cold, fever, teeth-acne, pain, sore throat, inflammation, acute sinusitis, asthma, and bronchitis [43]. Black pepper is also used as an anti-malarial medicine due to the presence of bioactive components. As a result, it also possesses analgesic and antipyretic qualities. Researchers investigated that piperine showed analgesic and antipyretic properties and observed potent antipyretic activity [44]. It is used in winter as an additive to the preparation of tea along with ginger and Ocimum sanctum leaves that keeps the cough and cold away from people.

Cholesterol Lowering and Immune Enhancer Activity

Black pepper contains piperine, which is used to decrease the absorption of cholesterol and improve the movement of cholesterol carrier proteins [45]. It improves the metabolism mechanism by supporting quicker emulsification of fat particles into comfortably digestible simple particles and protecting the developing body's fat. Black pepper showed an immunomodulatory effect on human beings [46]. *Piper nigrum* (black pepper) is utilised to increase piperine in diets that are high in fat (42 mg/kg), which beneficially decreases fatty acid, cholesterol levels, lipid (triglycerides), low-density lipoprotein (bad cholesterol), very-low-density lipoprotein, and body mass; additionally, it also raises high-density lipoprotein (good cholesterol) without changing [47]. The consumption of black pepper (*P. nigrum*) decreases the chance of arteriosclerosis, inhibits atherogenesis, and has hypolipidemic effects [48].

Antioxidant Activity

A significant component of naturally occurring antioxidants is found in black pepper, which is used for its several medicinal properties, food additives, and to increase shelf life of foods [2,31]. Recently, dietary supplements derived from plants have been utilised as antioxidants. The main primary function of antioxidants is to protect tissues from harmful free radicals, which may cause cardiovascular disease, tumours, and various other disorders [49]. These have a significant impact on the potency of lipid metabolism as an anti-diabetic. The beneficial uses of antioxidants protect biological function and protect from diseases like cirrhosis, chronic renal disease, gastropathy, tumours, diabetes, and cardiovascular disease [15].

Digestive Activity

The bioactive components of *P. nigrum* particularly piperine, increases the saliva production, secretion of salivary amylase enzymes, and secretion of gastric juices [8]. Through the consumption of *P. nigrum* synthesis digestive enzymes, perhaps the liver is stimulated to produce bile, which helps in food digestion [50]. Consumption of black pepper increases digestion through the secretion of pancreatic enzymes including lipase, protease, and amylase, while significantly reducing the bowel transit time of the GI tract [12]. The dietary consumption of *Piper nigrum* (black pepper) activates the liver for the synthesis of bile acids, which help in the absorption of fat and the emulsification of fats [51].

Antidiarrheal Effect

Piper nigrum is significant because of its strong piperine compounds. Many researchers reported that black pepper showed antidiarrheal properties. Additionally, black pepper showed antimicrobial properties against certain microbes that cause diarrhoea (1). Other studies indicate its tremendous effectiveness in preventing diarrhoea [52]. Fascinatingly, among most developing

nations, naturopathy and the pharmaceutical industry produce peppercorns specifically for diarrhoea in individuals of every age [53]. Additionally, the bioactive compound piperine in black pepper reduced the antidiarrheal action, leading to the supplementation of several biochemical stimulants and experiments using oil on animals. Aqueous extract of peppercorn with doses of about 76, 151, and 299 mg/kg provides strong dosage-dependent antisecretory agent, antimotility agent, and antidiarrheal activities [30].

Anti-Mutagenic, Antitumor and Anticancer Activity and Immunomodulatory Activity

Piper nigrum showed immunomodulatory and antitumor properties. Black pepper involves immunomodulatory drugs and anticancerous properties, and therefore the presence of bioactive compounds in black pepper works as a natural agent that can help boost the immune system. Due to the presence of piperine, it helps in immunomodulation, which involves the production of cytokines, the activation of macrophages, and the proliferation of lymphocytes [54]. *P. nigrum* and its biologically active compounds, especially black pepper extract, have been shown to suppress the growth of tumours in clinical trials. While lowered anticancer properties through oral administration had been investigated [55]. The solvent extract of black pepper was useful for Dalton's lymphoma, anti-cancerous properties, and immunomodulatory. It also possesses effective antimetastatic properties. Additionally, *Piper nigrum* contained piperine which helps in decreasing lung cancer through modulating lipid peroxidation and the synthesis of antioxidative protection enzymes [56].

Antimicrobial Activity

Numerous studies have demonstrated that black pepper has the capability of having antimicrobial characteristics in the form of oil or solvent extracts as well as aqueous extracts [57]. Black pepper contained antimicrobial properties that inhibited microbial growth and killed microbes. The antimicrobials can be classified into different groups depending on their primary function; they include antibacterial, antifungal, antiviral, anti-parasite, anti-insectide, etc. [58]. Antimicrobial effects were examined in both gram positive and gram-negative stain bacteria. The use of black pepper inhibits the growth of Pseudomonas aeruginosa, Bacillus subtilis, Shigella flexneri, Cronobacter sakazakii, Escherichia coli, Staphylococcus aureus, Salmonella enteric, and Vibrio cholera, various medicinal diagnostics beneficial to enhancing cell morphology, capsule processing, and lowering urease activity [2,59]. This property was attributed to piperine. The presence of limonene, pinene, β-caryophyllene attributed to the presence of several minor components, can possess the antimicrobial properties of black pepper. Black pepper showed anti-bacterial, anti-fungal properties, as well as inhibiting foodborne pathogens such as yeast, aflatoxins, and mycotoxin [2,30,60].

Conclusions

Black pepper is used as traditional medicinal remedies as well as for proving flavours, aroma, colour, and for increasing the shelf life of food products. It has numerous health advantages; protects from various diseases like cold, cough, throat infection, fever, thyroid, obesity, and diarrhea. It is also used as anti-cancer, anti-tumour, anti-mutagenic, antioxidant, anti-microbial, and antipyretic activities. Additionally, black pepper offers a wide range of medicinal benefits, including its capacity to enhance and maintain good health, reduce respiratory symptoms, enhance digestion, and improve the immune system. It is commonly used throughout the world and known as "king of spices". In ancient times, it was major attraction of trade and was valued as "black gold". It led to the discovery of alternate sea routes and the establishment of British East India Company in 1600.

Conflict of Interest

The authors declare no conflict of interest.

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