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Phytochemical Profile & Pharmacological Significance of *Piper nigrum* - King of spices

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ABSTRACT

Piper nigrum, commonly referred to as black pepper, has long been used to cure a wide range of illnesses, such as piles, fever, dyspnea, stomachaches, worms, and coughs and colds. Black pepper's metabolites, which include phenolic chemicals, alkaloids, flavonoids, carotenoids, terpenoids, etc., are responsible for its pharmacological potential. Given the diverse applications of black pepper dried seeds, both conventional and alternative medical viewpoints have identified a number of additional positive health benefits. Black pepper's primary chemical components—carbohydrates, proteins, calcium, magnesium, potassium, iron, vitamin C, tannins, flavonoids, and carotenoids—have been identified by phytochemical investigations.

Dried berries have a volatile oil concentration that varies from 0.4 to 7%. Sabinene, 3-carene, D-limonene, α-pinene, caryophyllene, β-phellandrene, α-phellandrene, α-thujene, and β-bisabolene are the main components of black pepper. Furthermore, piperine is the main bioactive alkaloid found naturally in black pepper and has been linked to a number of possible medical benefits, including improved nutrient absorption and cerebral brain function. Antioxidant, anti-inflammatory, anticancer, anti-obesity, antidepressant, antidiabetic, antibacterial, gastroprotective, and insecticidal properties are only a few of the biological functions of black pepper. The review's objectives are to go over black pepper's taxonomy, geographic range, phytochemical composition, and pharmacological characteristics.

KEY-WORDS: Diabetes, Inflammation, Black pepper, Flavonoids, Terpenoids

INTRODUCTION

Due to their many therapeutic properties and lack of adverse effects, spices are great natural herbal food additives for the treatment of a wide range of disorders.[1] According to Ayurveda, spices help the body maintain a healthy pH balance, have potent antibacterial qualities, and extend the shelf life of food. Different spices improve the flavor, color, and scent of food products while also improving their taste. [2] Indeed, these spices also aid in improving digestion, preventing coughing, sneezing, and sore throats, as well as protecting the pancreas and spleen. Essential minerals, nutrients, and phytochemicals such as flavonoids, phenolics, tannins, alkaloids, and antioxidants are found in spices. *Piper nigrum*, belonging to the Piperaceae family, is a useful medicinal herb. Known as "The King of spices" among other spices, this is one among the most often used spices. [3]Many tropical countries, including Brazil, Indonesia, and India, cultivate black pepper. Common names for Piper nigrum include Milagu in Tamil, Pippali in Sanskrit, Kali Mirch in Urdu &

Hindi, and Peppercorn, White, Green, Black, and Madagascar pepper in English. Black pepper, the most well-known and widely used spice in the world, is the source of hot and spicy peppercorns. Black pepper is utilized in fragrance, as a preservative, and as a therapeutic ingredient.[4-7] Whole Piper nigrum peppercorns or their active ingredients are utilized as medicine and in a variety of cuisines. Pepper is a common ingredient in many sauces and meals, including meat dishes, all around the world. Its main pungent alkaloid, piperine, is known to have a variety of intriguing pharmacological effects. It is extensively utilized in several conventional medical systems, including the Unani and Ayurvedic systems.[8] Numerous pharmacological properties of piperine include its antihypertensive and antiplatelet properties, as well as its antioxidant, antitumor, antiasthmatic, antipyretic, analgesic, anti-inflammatory, anti-diarrheal, antispasmodic, anxiolytic, antidepressant, hepato-protective, immuno-modulatory, antibacterial, antifungal, anti-thyroid, antiapoptotic, anti-mutagenic, anti-spermatogenic, antiColon toxin, insecticidal, and larvicidal properties, among others.[9-12] It has been shown that piperine increases oral bioavailability by blocking several metabolizing enzymes, hence improving the therapeutic efficiency of numerous medications, vaccines, and minerals. It is also known to improve fertility and cognitive function. It has also been discovered that piperine stimulates the intestinal and pancreatic enzymes that help in digestion. In addition to its chemical components, piperine is responsible for many of the spice's medicinal properties. Green and white peppers are made from the fruits of the Piper nigrum plant. Another usage for Piper nigrum can be as a flavoring.[13]

VERNACULAR NAMES[14-17]

English	Black pepper, pepper
Hindi	Habush, Kali mirch
Sanskrit	Dharmapattana, Katuka
Kashmir	Martz
Konkan	Miriam
Malayalam	Kolakam, Maricham
Marathi	Kalimirch
Persian	Filɓil-e-aswad, Filɓil-e-gard
Punjab	Golmirch
Russian	Peretz

Spanish	Pimienta negra
Tamil	Aguttam, Arisu, Kari
Telugu	Marichamu, Miremu
Urdu	Kalimirch
Bengal	Golmorich, Kolukung
Bombay	Kalamiri, Miri
Ceylon	Molavu
Chinese	Fou Tsiao, Hu Chiao
Deccan	Choca, Kali mirchingai
Italian	Pepe, pepe nero
German	Pfeffer
Greek	Peperi
Gujrati	Kalmari, Kalomirich

TAXONOMY[18]

Kingdom	*Plantae*
Sub-kingdom	Tracheobionta
Super-division	*Supermatophyta*
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	*Magnoliidae*
Order	Piperales
Family	Piperaceae
Genius	*Piper L.*
Species	*P. nigrum* L.

BOTANICAL DESCRIPTION

The pepper plant is a perennial wooden vine that may reach a height of 4 meters (13 feet) when it is supported by poles, trellises, or trees. It spreads easily and roots itself anywhere its trailing branches come into contact with the ground. Leaves: alternating, whole, ranging in length from 5 to 10 cm (2.0 to 3.9 in) and in width from 3 to 6 cm (1.2 to 2.4 in). The tiny flowers are produced on pendulous spikes that are 4 to 8 cm (1.6 to 3.1 in) long at the leaf nodes. As the fruit ages, the spikes can go as long as 7 to 15 cm (2.8 to 5.9 in).[19,20] Pepper may be cultivated in soil that is wet, well-drained, rich in organic matter, and neither excessively dry nor prone to floods (the vines do not fare so well over an altitude of 900 m (3,000 ft above sea level). About 2 meters (6 feet 7 inches) apart, climbing frames or nearby trees are used to rope up cuttings of the plants that are 40 to 50 centimeters (16 to 20 inches) long. Rough-barked trees are preferred since pepper plants can climb them more easily than smooth ones.[7] All competing vegetation is removed, leaving only enough trees to shade the area and allow for unrestricted airflow. Manure and leaf mulch are applied to the roots, and the sprouts are pruned.On dry soils, the young plants require watering every other day during the dry season for the first three years. The plants bear fruit from the fourth or fifth year, and then typically for seven years.[21] The cuttings are usually cultivars, selected both for yield and quality of fruit.A single stem bears 20 to 30 fruiting spikes.[22] The harvest begins as soon as one or two fruits at the base of the spikes begin to turn red, and before the fruit is fully mature, and still hard; if allowed to ripen completely, the fruit lose pungency, and ultimately fall off and are lost. The spikes are collected and spread out to dry in the sun, then the peppercorns are stripped off thespikes.[23] Black pepper is native either to Southeast Asia or South Asia. Within the genus Piper, it is most closely related to other Asian species such as P. caninum. Wild pepper grows in the Western Ghats region of India. Into the 19th century, the forests contained expansive wild pepper vines, as recorded by the Scottish physician Francis Buchanan (also a botanist and geographer) in his book A journey from Madras through the countries of Mysore, Canara and Malabar (Volume III). Deforestation, however, caused wild pepper to grow in smaller forest sections from Goa to Kerala; as the production and quality of the cultivated variety increased, the wild supply eventually decreased. To far, no commercial pepper has been successfully grafted onto wild pepper.[24-26]

Figure 1: Different parts of ***Piper nigrum***

GEOGRAPHICAL DISTRIBUTION

Many tropical countries, including Brazil, Indonesia, and India, cultivate black pepper. Geographically, it is limited to South India's Western Ghats. Nonetheless, there are also some reports of cultivation from the West Indies, Brazil, Malaysia, Indonesia, and Sri Lanka. P. nigrum was discovered in extensive alpine areas and had remarkable environmental adaptation, resulting in interspecies variety. The common term "black-pepper" refers to the peppercorn's color. Because of its trading on the global market, it is referred to as the "king of spices." [27-30]

PHYTOCHEMICAL PROFILE

Black pepper is a great source of vitamins, minerals, and nutrients. 100 g of black pepper seeds contain 66.5 g of carbohydrates, 10 g of protein, and 10.2 g of fat. They also contain a comparatively high amount of minerals, including calcium (400 mg), magnesium (235.8–249.8 mg), potassium (1200 mg), and phosphorus (160 mg), with

lower amounts of sodium, iron, and zinc.[31] These minerals are necessary components for human daily activities. In addition, a substantial concentration of vitamins, including C, B1, B2, and B3, is also present in black pepper. Tannin concentrations in nine Nigerian black pepper accessions ranged from 2.11 to 2.80 mg/100 g.. In a recent study on black pepper, researchers reported flavonoids such as catechin, quercetin and myricetin, and carotenoids, namely lutein and β-carotene was detected in significant concentration. [32]

Numerous investigators assessed the presence of essential oils (EO), oleoresin, and piperine in different components of black pepper. Black pepper berries and leaves have varying essential oil yields: 1.24 to 5.06 percent and 0.15–0.35 percent, respectively. But the kind, location, and age of the product, as well as the components and techniques employed, all affect the oil production. In 14 black pepper accessions, the researchers found variations in the volatile oil and oleoresin content, with values ranging from 2.7% to 5.1% and 7.6% to 9.4%, respectively. These researchers reported that volatile oil content was positively correlated with oleoresin and suggested concurrent improvement of these characters by simple selection programme is the best tool for improvement of quality traits in black pepper.[33-37] Researchers also reported classical hydro-distillation as a better method of volatile oil estimation compared to other techniques. The oleoresin content of black pepper ranged between 4.27 and 12.73 %, and the characteristic natural alkaloid of black pepper "piperine" ranged from 2.13 − 5.80 % and 0.12 − 20.86 %, in seeds and leaves correspondingly.[38]

Black pepper seeds from south India have a predominantly β-caryophyllene essential oil profile, with limonene, sabinene, α-pinene, β-bisabolene, α-copaene, α-cadinol, α-thujene, and α-humulene following closely behind. Pepper leaves were found to have a high nerolidol content, followed by α-pinene and β-caryophyllene [38, 41] (Table 3). Similarly, β-caryophyllene (18.39%), α-pinene (16.68%), limonene (16.16%), β-pinene (13.61%), δ -3-carene (9.23%), β-phellandrene (3.16%), copaene (3.13%), 1-napthalenol (3.0%), and β-myrcene (2.89 %) were found in seeds from Bangladesh. Major metabolites in the EO of seeds from Brazil, Malaysia, and Sri Lanka varied noticeably. The yield of minor EO of black pepper contained β-Elemene (1.74 %), δ-Elemene (0.60 %), α-Cubebene (0.99 %), α-Guaiene (0.36 %), α-Zingiberene (0.74 %), p-Cymene (0.70 %), Bicyclogermacrene (0.31 %), γ-Cadinene (0.65 %), γ-trans-Bisabolene (1.39 %), Hedycaryol (0.37 %), and Germacrene D (0.22 %).[39-42]

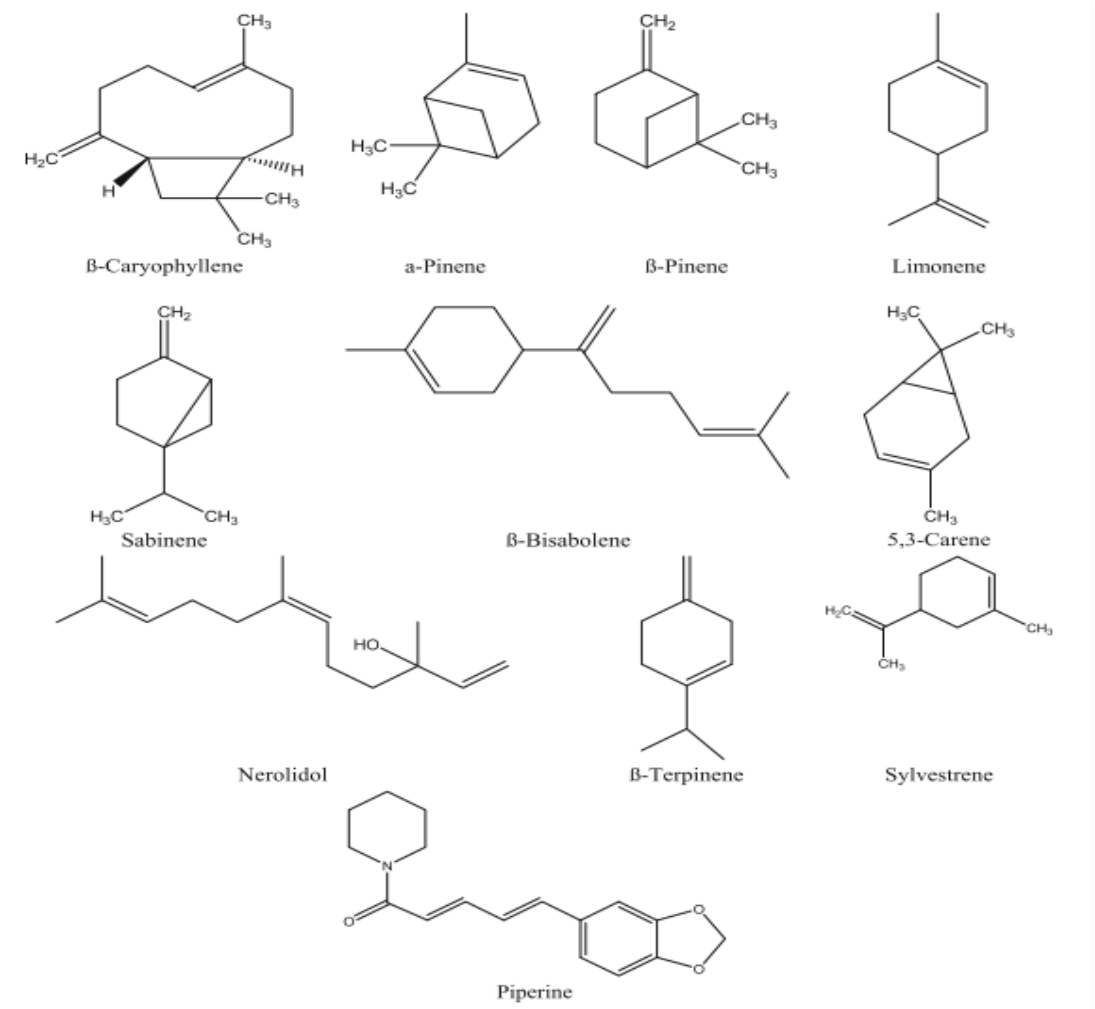

Figure 2: Different Constituents present in Black pepper

PHARMACOLOGICAL PROFILE

*1. **Anticonvulsant activity***

Piperine was found to have anticonvulsant properties in both the maximal electroshock (MES) and pentylenetetrazol (PTZ) models of convulsions in mice. Additionally, the transient receptor potential cation channel subfamily V member 1 (TRPV1) receptor was found to play a role in the inhibition of convulsions induced by both PTZ and PTZ models.[43] When piperine at dosages of 40 and 80 mg/kg was administered, there was a noticeable delay in the start of myoclonic jerks and generalized clonic seizures. Additionally, piperine reduced the mortality and seizure stage in comparison to animals treated with a vehicle. A significant reduction was also observed in the incidence of MES-induced tonic hind limb extension (THE) and PTZ-induced Fos immune reactivity in the dentate gyrus after of piperine administration. Capsazepine (TRPV1- selective antagonist) blocked the anti-seizure effects of piperine. These findings demonstrate piperine's anti-convulsant properties.[44] In a different investigation, mice with epilepsy models produced by picrotoxin (PIC) and

pentylenetetrazole (PTZ) were used to assess the in vivo anticonvulsant effect of piperine. Following intraperitonial injections of piperine at doses of 30, 50, and 70 mg/kg (i.p.), valproic acid at a dose of 200 mg/kg, carbamazepine at a dose of 30 mg/kg, and diazepam at a dose of 1 mg/kg, a substantial ($P<0.01$) delay in the start of PTZ- and PIC-induced seizures was noted in the mice. These findings demonstrated piperine's anticonvulsant properties, which may be mediated by GABAergic pathways.[45]

*2. **Anti-Obesity***

Because obesity is associated with a health problem that is stigmatized in society, it is a big global problem. The US population is the most severely impacted, with 40% of people there suffering from obesity.[46] According to the World Health Organization, it's a lifestyle problem that can lead to several illnesses. Black pepper, or Piper nigrum, is used as a natural cure. Other nonclinical methods of reducing obesity include yoga, aerobic activity, the ketogenic diet, meditation, and so on. Numerous herbs and spices have anti-obesity qualities as well.[47]

3. Antimicrobial activity

Aqueous decoctions of Piper nigrum L. (black pepper), Laurus nobilis L. (bay leaf), Pimpinella anisum L. (aniseed), and Coriandum sativum L. (coriander) were tested for their antibacterial properties against various bacterial isolates obtained from the oral cavities of two hundred individual volunteers.[48] At a concentration of 10µL/disc, the aqueous decoction of black pepper exhibited the greatest antibacterial activity, matching that of Laurus nobilis and Pimpinella anisum. In a recent study, the silver nanoparticles from leaf and stem extract of *Piper nigrum* were synthesized and then antibacterial activity of the synthesized silver nanoparticles of *Piper nigrum* was evaluated against agricultural plant pathogens. These silver nano-particles showed the excellent antibacterial activity against plant pathogens. Authors concluded that the antibacterial activity of silver nano-particles is a beneficial application in crop improvement and protection in agricultural nanotechnology.[49-51]

4. Anti-Cancer activity

It has been shown that Piper nigrum inhibits the genesis of cancers in a variety of experimental animals. According to researchers, piperine lowers the risk of lung cancer via modifying lipid peroxidation and activating enzymes that provide antioxidant defense. Piperine has unique pharmacological properties in addition to its anti-cancer properties. It has been shown that piperine inhibits the G1/S transition, HUVEC proliferation, migration, and in vitro tubule formation as well as angiogenesis in chick embryos induced by collagen and breast cancer cells.[52,53]

*5. **Antioxidant activity***

Free radicals cause many diseases. Different free radicals attack on membranes causing oxidation of lipids, loss of different enzyme activities and may cause cancer. Antioxidants completely stop or delay the process of oxidation.[14] Antioxidant protection system includes enzymes like Ascorbate, Catalase, Peroxidase and Superoxide dismutase which scavenge both radicals and related non radical oxygen species. Plants are important source of antioxidants. [54,2] Some *in vitro* studies revealed that Piperine inhibited free radicals and reactive oxygen species, therefore known to possess protective effects against oxidative damage. *Piper nigrum* or piperine also found to decrease lipid peroxidation *in vivo*. [55] *Piper nigrum* reported to possess antioxidant activity that might be due to the presence of flavonoids and phenolic contents. *Piper nigrum* was found to prevent the oxidative stress by inhibiting lipid peroxidation, human lipoxygenase and arresting hydroxyl and superoxide free radicals, decrease lung carcinogenesis in animal studies. The memoryenhancing and antioxidant proprieties of the methanolic extract of *Piper nigrum* L. fruits at a doses of 50 and 100 mg/kg, orally, for 21 days in amyloid beta were investigated in Alzheimer's disease model in rats. The memory-enhancing effects of the extract were studied by means of *in vivo* (Y-maze and radial arm-maze tasks) approaches. While, the antioxidant activity was evaluated by measuring activities of glutathione peroxidase, catalase, superoxide dismutase, and by measuring the total content of reduced glutathione, malondialdehyde, and protein carbonyl levels in the hippocampus. The amyloid beta (1-42)-treated rats showed the diminishing of spontaneous starvariation percentage within Y- maze task and enhancement of work memory and reference memory errors within radial arm-maze task.[56] Administration of the methanolic extract of *Piper nigrum* significantly improved memory performance and exhibited antioxidant potential. These studies suggest that methanolic extract of *Piper nigrum* ameliorates amyloid beta (1-42)-induced spatial memory deterioration by depletion of the oxidative stress in the hippocampus of rats . The antioxidant effect of three Piper species viz *P. nigrum, P. guineense* and *P. umbellatum* was evaluated for the protection of renal, cardiac, and hepatic antioxidant

status in atherogenic diet fed hamsters. Animals were fed atherogenic diet addition with different doses of Piper species viz *P. nigrum, P. guineense* and *P. umbellatum* at a dose of 1 g/kg and 0.25 g/kg for 12 weeks. Piper species significantly inhibited the atherogenic diet induced increased lipid profile and alteration in antioxidant enzymes activities. This study showed an antioxidant protective role of the extracts of Piper species against atherogenic diet induced oxidative stress in renal, cardiac and hepatic tissues. [57-62]

*6. **Antipyretic Activity***

Black pepper (Piper nigrum) is used in traditional medicine, such as Ayurveda, Unani, Siddha, and Naturopathy, to make remedies for cough, cold, fever, teeth-acne, discomfort, sore throat, inflammation, acute sinusitis, asthma, and bronchitis. Black

pepper's bioactive ingredients make it a useful anti-malarial medication as well. [63] Consequently, it also has analgesic and antipyretic properties. Researchers found that piperine has strong antipyretic efficacy and analgesic and antipyretic qualities. 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. Antitussive and Bronchodilator: Many traditional practices prove it as well.[64] P. nigrum is widely used in many herbal cough syrups due to its potent antitussive and bronchodilator properties 60. Many old people and herbal practitioners believed that the addition of little amounts of powered peppercorn in a green tea significantly reduces asthma The oral administration of piperine in different amount to mice reduced and suppressed the hyperresponsiveness, infiltration of eosinophils and inflammation possibly due to suppression of production of histamine, immunoglobulin E, interleukin -4 and interleukin. [65]

7. ***Anti-inflammatory activity***

The anti-inflammatory, analgesic, and anti-arthritic properties of piperine were assessed. The anti-inflammatory and anti-arthritic properties were assessed in vitro using fibroblast-like synoviocytes triggered by interleukin 1β from rheumatoid arthritis, and the analgesic properties were tested using a carrageen-induced acute paw model of pain and arthritis in rats. Using ELISA and RT-PCR techniques, the levels of prostaglandin E2, cyclooxygenase 2, interleukin 6, and matrix metallo-proteinase were assessed. Piperine treated groups were found to reduce the synthesis of prostaglandin E2 in a dose dependant comportment at the concentrations of 10-100 μg/mL.[66] It significantly inhibited the synthesis of prostaglandin E2 even at 10 μg/ mL. The expression of interleukin 6 and matrix metallo-proteinase 13 were also inhibited. The migration of activator protein1into the nucleus in interleukin 1β treated synoviocytes was inhibited by piperine while migration of nuclear factor κB was not affected by piperine. The pain and arthritic symptoms in rats were significantly reduced by piperine. It was concluded that piperine showed anti-inflammatory, analgesics and anti-arthritic activities in arthritis model of rats.[67,68]

8. ***Anti- Alzheimer activity***

Alzheimer's disease resulted due to the alteration in neural region on treatment with black-pepper fruit extract at a concentration of 35 μg/mL has demonstrated the ability to decrease the levels of phosphorylated forms of pro-apoptotic proteins. Pepper extract inhibits the working of acetylcholinesterase (AChE) and the aggregation of amyloid-beta (Aβ) in SHSY5Y cells produced by hydrogen peroxide (H2O2) . In AlCl3-induced AD rats, supplementation by black pepper orally reduced amyloidal plaque development and cholinesterase levels and improved memory performance. [69,70]

9. Anti Parkinson activity

Degeneration of dopaminergic neurons is the primary cause of Parkinson's disease (PD), which is strongly associated with the onset of motor impairments and cognitive decline in patients.[71] The results obtained from the in vitro trials suggest that piperine treatment both increases cell survival and reduces toxicity. Additionally, the therapy's administration showed a protective effect via activating the purinergic receptor P2X 4 (P2RX4) in SK-NSH cells that were suffering decreased autophagy flux due to SNCA expression. By improving autophagosome-lysosome membrane fusion, autophagy flux was stimulated, leading to the reported protective effects.[72]

10. ***Anti-diarrheal activity***

Mice were treated with aqueous back pepper extract (ABPE) at doses of 75, 150, and 300 mg/kg po to test its anti-secretory, anti-motility, and anti-diarrheal properties. In order to evaluate the anti-diarrheal activity, castor oil and magnesium sulphate were used to cause diarrhea, and charcoal meal was employed to measure gastrointestinal motility.[22] Castor oil was also utilized to evaluate the anti-motility and anti-secretory activities. Significant and dose-dependent anti-diarrheal, antimotility, and anti-secretary effects were demonstrated by ABPE. The anti-motility and anti-secretory properties of Piper nigrum may stem from the presence of alkaloids and carbohydrates, whereas the anti-diarrheal properties of ABPE may be attributed to these same properties.[73]

11. ***Carminative Activity***

Significant levels of carminative and activating properties are offered by black pepper. It also stimulates reflex saliva flow and the production of digestive juice, including pepsin, rennin, gastric lipase, gastric amylase, urease, and gelatinase, in the stomach. Finally, it increases hunger.[74] Increased gastrointestinal motility results in both gas eructation and alleviation from colic. When used in moderation, black pepper reduces body temperature, increases the size of the skin's superficial vessels, and gives the user a warm sensation.. Several such characteristics make them frequently used as spices, particularly in warm countries.[75] Black pepper has been suggested as a treatment against haemorrhoids (piles), prevents bloating, and reduces the level of prostaglandins because of reducing cramps. 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 .[76,77]

12. ***Antidepressant activity***

In a mouse model of depression caused by corticosterone, the potential mechanisms behind piperine's antidepressant-like activity were assessed. After receiving corticosterone injections for three weeks, mice began to exhibit depressive-like behaviors.[41] The depression was demonstrated in the forced swim test and tail

suspension test by a substantial decrease in sucrose consumption and an increase in immobility duration. Furthermore, corticosterone-treated animals also showed a substantial drop in the amounts of mRNA and brain-derived neurotrophic factor protein in the hippocampus. After treating rats with piperine, the behavioral and physiological alterations caused by corticosterone were greatly reduced. These findings demonstrated that piperine has an antidepressant-like effect in a mouse model of depression produced by corticosterone.[23]

13. ***Immunomodulatory Activity***

Piper nigrum exhibited anticancer and immunomodulatory effects. Due to its anticancerous qualities and involvement with immunomodulatory medications, black pepper's bioactive components function as a natural immune-stimulating agent. Piperine's presence aids in immunomodulation, a process that includes cytokine synthesis, macrophage activation, and lymphocyte proliferation. [78]

14. Analgesic activity

Piperine's in vivo analgesic efficacy in mice was assessed. The mice tail flick and writhing assay models generated by acetic acid were utilized to assess piperine's analgesic efficacy. When piperine at doses of 30, 50, and 70 mg/kg was administered intraperitoneally (i.p.) to mice, there was a substantial ($P<0.01$) reduction in the acetic acid-induced writhing in comparison to domethacin at a dose of 20 mg/kg (i.p.). The tail flick experiment demonstrated a substantial ($P<0.01$) increase in the response time of mice upon intraperitoneal administration of piperine at doses of 30 and 50 mg/kg and morphine at dose of 5 mg/kg.[79] The analgesic activities of both piperine and morphine in the tail flick assay were reversed on pre-treatment of animals with naloxone at dose of 5 mg/kg (i.p.). These results revealed the analgesic activity of piperine which possibly mediated via opioid pathway. [80]

15. ***Antiplatelet Activity***

According to research, piperine, a vital component of some piper species, is primarily in charge of a variety of functions. It has been found by several researches that piperine has anti-platelet properties. Researchers found that collagen and thrombin, two distinct substances that activate platelets, were responsible for the harmful effect of piperine on platelet aggressiveness in experimental rabbits. [81]

16. ***Hepatoprotective activity***

It was discovered that in a dose-dependent way, piperine reduced the elevated levels of serum GPT and GOT in a mouse hepatotoxicity model induced by D-galactosamine.[82] Wistar rats were used to test the hepatoprotective effects of a methanolic extract of Piper nigrum fruits after the rats' livers were damaged by ethanolCCl4. Rats were made hepatotoxic by using ethanol-CCl4. In rats treated with ethanol-CCl4, pre-treatment with piperine at a dose of 50 mg/kg body weight, p.o.

and prophylactic treatment with methanolic extract of Piper nigrum at doses of 100 and 200 mg/kg body weight, p.o. for 15 days demonstrated significant liver protection as measured by triglycerides, alanine transaminase, aspartate transaminase, alkaline phosphatase, bilirubin, superoxide dismutase, catalase, glutathione reductase, and lipid peroxidation levels. [83] In this investigation, the administration of ethanol-CCl4 resulted in a significant increase in triglycerides, aspartate transaminase, alanine transaminase, and bilirubin levels. On the other hand, superoxide dismutase, catalase, and glutathione reductase levels significantly decreased, but these levels were later returned to normal following pre-treatment with a methanolic extract of Piper nigrum and Piperine.[84] Following pretreatment with pipesr nigrum and piperine methanolic extract at specified concentrations, lipid peroxidations were likewise markedly reduced. At a dosage of 1 mL/kg, p.o. for 15 days, the outcomes were comparable to those of the reference standard, Liv52. The liver's morphological and histological investigations corroborated the biochemical values. Therefore, it can be said that Piper nigrum has significant medicinal potential and may have hepato-protective effects because of the presence of piperine alkaloids.[85-87]

CONCLUSION

Up to now, a large number of unique research studies on the pharmacological potential of Piper nigrum, often known as "Piperine," or black pepper, have been published. These publications demonstrated that black pepper has substantial pharmacological potential both in vitro and in vivo for the treatment of many illnesses and disorders, and that it is safe to use. Additionally, it has been shown that piperine increases the absorption of several medications and enhances the bioavailability of numerous medications and minerals. This significant piperine characteristic may significantly improve the therapeutic effectiveness of several therapeutically significant medications. Thus, it can be said that black pepper and its bioactive ingredient piperine have a broad range of therapeutic applications and may be used as a great adjuvant to increase the effectiveness of other medications being taken at the same time.To get additional scientific information about this amazing King of spices, more in-depth study investigations are required.

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