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Therapeutic Potential of Bioactive Compounds of *Piper nigrum* L. (Black Pepper): A Review

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

The present study highlights the Bio activities and Pharmacology of *Piper nigrum* L. (Black Pepper). *Piper nigrum L* is commonly known as Kali Mirch, Pippali, Milagu Peppercorn, White pepper, Green pepper, Black pepper, and Madagascar pepper longum plant is a deciduous slender aromatic climber. The major source of bioactive constituents in black pepper is present in the fruits. It contains major pungent alkaloid piperine (1-peperoyl piperidine) which is known to possess pharmacological actions. Antimicrobial activity of black pepper evaluated the antibacterial potential of aqueous decoction of *Piper nigrum* L. (black pepper), against different bacterial isolates from oral cavity of individual volunteers.

Keywords: Black pepper; pharmacology; aromatic climber; alkaloid; medicinal agent.

1. INTRODUCTION

Piper nigrum (Black pepper), is called as ''The King of spices' 'and is used as a common spice among various spices [1,2]. It is used as a medicinal agent, a preservative, and in perfumery [3]. Furthermore, researchers suggest that the consumption of black pepper, due to the presence of the numerous bioactive compounds, exhibit several pharmacological activities with human dietaries, medicine, preservative, and biocontrol agents [4,5]. "The major source of

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bioactive constituents in black pepper is present in the fruits" [6-8].

It contains major pungent alkaloid piperine (1-peperoyl piperidine) which is known to possess pharmacological actions [9] reported that this plant and its active components piperine when orally administered, it can kindle the digestive enzymes of pancreas and intestine and also increases biliary bile acid secretion". It is used as medicine for digestive disorders like large intestine toxins, different gastric problems, diarrhea, indigestion respiratory disorders including cold fever, and asthma [10-12].

"Piper nigrum L is commonly known as Kali Mirch, Pippali, Milagu Peppercorn, White pepper, Green pepper, Black pepper, and Madagascar pepper longum plant is a deciduous slender aromatic climber. Structurally, it has perennial woody roots or a perennial creeping shrub that belongs to the family Piperaceae. Structurally it is Erect, glabrous with swollen nodes, roots clasping at nodes which help it to attach to the host trees" [13-16]. Leaves are ovate shape, an arrangement is alternate, apex acute to acuminate with entire margin [17], while the Fruits have Spikes which are long cylindrical, oblong, berries red or black when ripe, globose with aromatic odor and pungent taste [18,19] (Chadha KL et al. 1987). The flowers are, biologically male or female and are born on different plants. "*Piper nigrum L* is grown in the tropical rain forests of India, Nepal, Indonesia, Malaysia, Sri Lanka, Timor, and the Philippines [20-23]. It also occurs in hotter parts of India, from the central Himalayas to Assam, Khasi and Mikir hills, lower hills of West Bengal, and evergreen forests of the Western Ghats from Konkan to Kerala and Nicobar Islands" [24].

2. BIOACTIVE CONSTITUENTS FROM *Piper nigrum*

The major bioactive compounds in pepper are Phenolics, various derivatives of lignans, terpenes, chalcones, flavonoids, alkaloids, and steroids [25]. The bioactive compounds were isolated from the P. nigrum fruits. The major constituents of seeds include Dihydropipericide [25], (2E, 4E)-N-Eicosadienoyl pereridine [26] Guineensine [27], pentadienoyl as piperidine, (2E, 4E)-Nisobutyldecadienamide, isobutyl-eicosadienamide [28], isobutyl-eicosatrienamide [29], isobutyloctadienamide [25], Piperamide Chonpathompikunlert P, et al. [29] Piperamine, [32], Piperettine [30], Pipericide, [31] Piperine [33], Piperolein B, Trichostachine, Sarmentine, Sarmentosine, Tricholein, Retrofractamide A, [34]. The active agent of piper species was the first compound isolated from different species in family Piperaceae [35].

Important structural aspects of the bioactives from *Piper nigrum L.*

3. PHARMACOLOGY

3.1 Antioxidant Activity

"Plants are an important source of antioxidants. Some in vitro studies revealed that Piperine is known to possess protective effects against oxidative damage due to the inhibition property of free radicals and reactive oxygen species" [36,37]. Many studies were done on *Piper nigrum* and "it was found to prevent oxidative stress by inhibiting lipid peroxidation, human lipoxygenase, and arresting hydroxyl and superoxide free radicals, decreasing carcinogenesis in animal studies. The memory enhancing and antioxidant proprieties of the methanolic extract of *Piper nigrum* L. fruits were investigated in Alzheimer's disease model in rats" [38,39]. "The amyloid beta (1-42)-treated rats showed the diminishing of spontaneous star variation percentage within Y-maze task and enhancement of work memory and reference memory errors within the radial arm-maze task by measuring the total content of reduced glutathione, malondialdehyde, and protein carbonyl levels in the hippocampus the antioxidant activity was evaluated by measuring activities of glutathione peroxidase, catalase, superoxide dismutase. Injecting the methanolic extract of *Piper nigrum* significantly improved memory performance and exhibited antioxidant potential. Many 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" [40].

3.2 Anticancer Activity

Various studies have shown that flavonoids may serve as a protective role in breast cancer prevention (Cooray, et al. 2004; Marchand et al. 2002; Rodgers, et al. 1998). "Ethanolic extract off peppercorn and piperine showed effective immunomodulatory and antitumor activity" [41]. Piperine has been found to hinder the proliferation and survival of various cancerous cell lines via modulating cell cycle development and showing anti-apoptotic activity. The piperine

Image 1. Black pepper (*Piper nigrum* L.)

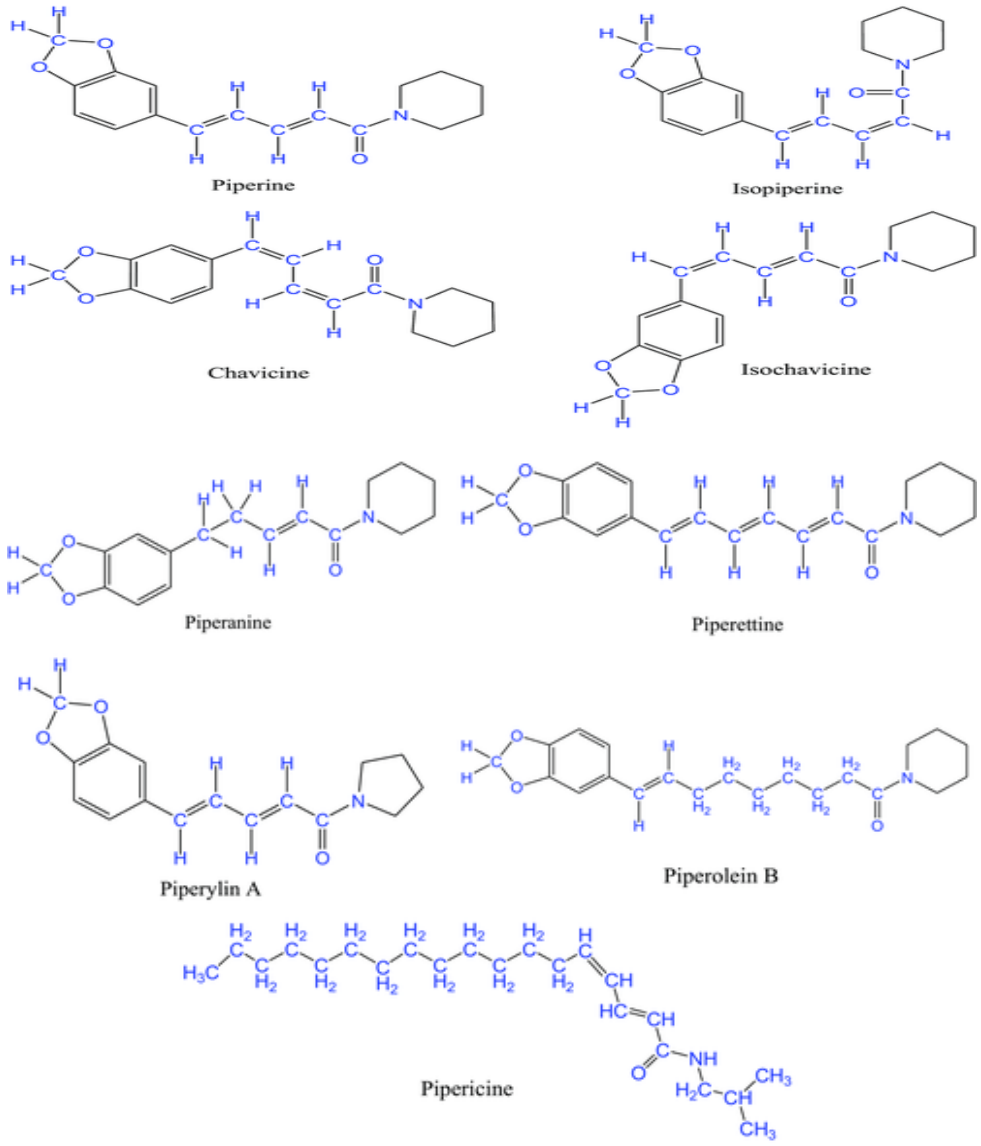

Fig. 1. Bioactive compounds from *Piper nigrum L*

can be considered as a worthy agent for controlling angiogenesis in the Prostate of men.

"Research has presented that piperine has good anticancer activity against prostate cancer cells

of both androgens dependent and independent. Piperine can modulate lipid peroxidation and activation of antioxidative protection enzyme, thus reducing lung cancer" [42].

3.3 Antimicrobial Activity

"Antimicrobial activity of black pepper Khan and Siddiqui in 2007 evaluated the antibacterial potential of aqueous decoction of *Piper nigrum* L. (black pepper), against different bacterial isolates from oral cavity of individual volunteers. The silver nanoparticles from leaf and stem extract of *Piper nigrum* showed excellent antibacterial activity against plant pathogens. The research findings showed the strongest antibacterial activity of Black pepper (aqueous decoction) at the concentration of 10µL/disc" [43]. In a recent study "antibacterial activity of the synthesized silver nanoparticles of *Piper nigrum* was evaluated against agricultural plant pathogens. Authors confirmed that the antibacterial activity of silver nanoparticles is a beneficial application in crop improvement and protection in agricultural nanotechnology" [44].

The aqueous seed extract of *Piper nigrum L* demonstrated an active antibacterial inhibitory effect against *Staphylococcus aureus, and Bacillus subtillis,* The research findings showed that the strongest antibacterial activity of Black pepper (aqueous decoction) at the concentration of 10µL/disc [43] on against agricultural plant pathogens. The silver nanoparticles from leaf and stem extract of *Piper nigrum* showed excellent antibacterial activity against plant pathogens [44].

3.4 Anti-inflammatory Activity

Piperine isolated from *P. nigrum* possesses potent anti-inflammatory analgesic and antipyretic activities. It inhibits the adhesion of endothelial monolayer to neutrophils and due to such inhibitory activity the tumor necrosis factor-alpha-induced expression of cell adhesion molecules was blocked i.e. intercellular adhesion molecule-1, vascular cell, and E-selectin. Vijayakumar RS et al. [38] also reported "another blocking system that piperine blocks the phosphorylation and degradation of IκBa alpha by attenuating tumor necrosis factor-alpha-induced IκB kinase activity". Singh and Duggal et al. [45] also documented that GM-CSF, IL-6, TNF-alpha, and IL-1 beta which was proinflammatory cytokines were dramatically reduced by the administration of piperine.

The in vitro anti-inflammatory activities were also evaluated on interleukin 1β stimulated fibroblast-like synoviocytes obtained from rheumatoid arthritis. The prostaglandin E2, cyclooxygenase 2, interleukin 6, and matrix metalloproteinase levels were evaluated by ELISA and RT-PCR methods of analysis. Piperine was found to reduce the synthesis of prostaglandin E2 comportment at concentrations of 10-100 µg/mL.

3.5 Hepatoprotective Activity

"Aqueous extract of fruits of P. longum and piperine were selected to study their hepatoprotective potential on administration with normal doses of anti-tubercular drugs" [46]. *P. longum* and piperine on administration with the anti-TB drugs lowered the rate of lipid peroxidation and also increased the reduced glutathione levels and thus exhibits the hepatoprotective effect.

"When experimental mice with D-galactosamine induced liver toxicity were exposed to dose-dependent piperine, it inhibited an increase in serum GPT and GOT levels and suggested that this inhibitory effect depended on the reduced sensitivity of hepatocytes to tumor necrosis factor" which is observed by Matsuda et al. [47].

3.6 Cosmoperine Activity

cosmoperine prepared from piperine used in cosmetics, [48] reported that a natural bio-enhancer improves the penetrability of active compounds through the skin. Cosmoperine activates and kindles the natural power of the skin to absorb nutrients [49,50]. Cosmoperine isolated from piperine is nonirritant, interacts with the skin quantitatively and qualitatively in various means, and also, cosmoperine is pain relieving and causes skin blushing due to vascular puffiness as well as a slight skin prickling sensation.

3.7 Antifertility Activities

Garg in 1981showed [51] at root extract of P. longum when used along with Embelia ribes seeds showed 100% anti-fertility activity in female albino rats. It is supposed that P. longum probably potentiates the contraceptive activity of other plant products, the probability of such a combination needs to be investigated further for the development of a contraceptive for the female without interfering with the activity of ovarian hormones on uterus [52] reported in

Ayurveda Garbhanivarana Aushadham which is used for both female and male.

3.8 Antidepressants Activities

"The aqueous extract of piperine was evaluated in a corticosterone-induced model of depression in mice.. The depression was observed by the significant decline in sucrose utilization and augmentation in immovability time in the Corticosterone-induced behavioral and biochemical changes were pointedly weakened after treatment to animals with Piperine. These results exhibited that piperine produces an antidepressant-like effect in a corticosterone-induced model of depression in mice [53].

3.9 Antidiabetic/ Anti-hyperglycemic Activity

In induced diabetic rats model, Piper longum root aqueous extract and its constituents, (PlrAqe) in streptozotocin (STZ) [54] suppresses insulin levels and liver glycogen. This study predicts that the plant extract is capable of managing hyperglycemia and complications of diabetes in STZ- induced diabetic rats. So the plant is considered as one of the possible sources for the isolation of new oral antihypoglycemic agents.

4. CONCLUSION

It is concluded that antimicrobial activity of black pepper evaluated the antibacterial potential of aqueous decoction of *Piper nigrum* L. (black pepper), against different bacterial isolates from oral cavity of individual volunteers.

COMPETING INTERESTS

Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.

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