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A Review on Therapeutic Potential of *Piper nigrum* L. (Black Pepper): The King of Spices

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Abstract

Medicinal plants are very popular in different traditional systems of medicines due to their diverse pharmacological potentials and lesser side effects in biological systems. *Piper nigrum* L. (Family Piperaceae) is a well known spice considered as *"The King of spices"* among various spices. It contains a pungent alkaloid "piperine" which is known to possess many pharmacological actions. Piperine increases bioavailability of many drugs and nutrients by inhibiting various metabolising enzymes. *Piper nigrum* L and its active constituent "Piperine"exhibits diverse pharmacological activities like antihypertensive, antiplatelet, antioxidant, antitumor, anti-asthmatics, analgesic, anti-inflammatory, anti-diarrheal, antispasmodic, antidepressants, immunomodulatory, anticonvulsant, anti-thyroids, antibacterial, antifungal, hepato-protective, insecticidal and larvicidal activities etc. The current review article is aimed to provide an updated literature review on recent advancement of pharmacognosy, chemistry and pharmacological activities of *Piper nigrum* L.

Keywords: *Piper nigrum;* Black pepper; Piperaceae; Piperine; Bioavailability; Antioxidant

Introduction

Piper nigrum (family Piperaceae) is a valuable medicinal plant. It is one of the most commonly used spices and considered as "The King of spices" among various spices. Black pepper is grown in many tropical regions like Brazil, Indonesia and India. *Piper nigrum* is commonly known as Kali Mirch in Urdu and Hindi, Pippali in Sanskrit, Milagu in Tamil and Peppercorn, White pepper, Green pepper, Black pepper, Madagascar pepper in English. Hot and pungent peppercorns are obtained from Black pepper which is the most famous and one of the commonly used spices throughout the world. Black pepper is used as medicinal agent, a preservative, and in perfumery. Whole Peppercorn of *Piper nigrum* or its active components are being used in different types of foods and as medicine. Pepper is used worldwide in different types of sauces and dishes like meat dishes. It contains major pungent alkaloid Piperine (1-peperoyl piperidine, Figure 1) which is known to possess many interesting pharmacological actions. It is widely used in different traditional systems of medicine like Ayurvedic and Unani System of medicines [1, 2]. Piperine exhibits diverse pharmacological activities like antihypertensive and antiplatelets [3], antioxidant, antitumor[4], anti-asthmatics [5], antipyretic, analgesic, anti-inflammatory, anti-diarrheal, antispasmodic, anxiolytic, antidepressants [6], hepato-protective[7], immuno-modulatory, antibacterial, antifungal, anti-thyroids, anti-apoptotic, anti-metastatic, antimutagenic, anti-spermatogenic, anti-Colon toxin, insecticidal and larvicidal activities etc. Piperine has been found to enhance the therapeutic efficacy of many drugs, vaccines and nutrients by increasing oral bioavailability by inhibiting various metabolising enzymes [8]. It is also known to enhance cognitive action and Fertility [9]. Piperine also found to stimulate the pancreatic and intestinal enzymes which aid to digestion. Many therapeutic activities of this spice are attributed to the presence of piperine apart from other chemical constituents. The fruits of *Piper nigrum* are used to produce white and green peppers. *Piper nigrum* is also used as a flavoring agent [1].

In recent pasts, different therapeutic potentials of *Piper nigrum,* its extracts, or its important active chemical constituent "piperine" have been published in different international research journals. The current review is aimed to provide an updated literature review on recent research advancement of pharmacognosy, chemistry and pharmacological activities of *Piper nigrum* L. We have compiled a review on therapeutic potential of *Piper nigrum* by collecting updated scientific research informations from internet using Google search engine and Pubmed.

Pharmacognosy of the *Piper nigrum*

Taxonomical Classification of *Piper nigrum*:

Kingdom: Plantae

Class: Equisetopsida

Sub class: Magnoliidae

Super order: Magnolianae

Order: Piperales

Family: Piperaceae

Genus: *Piper*

Species: *nigrum*

Pharmacognostical Characteristics

Piper nigrum (Black pepper) plant is a flowering woody perennial climbing vine that belongs to Piperaceae family. Pepper plants easily grow in the shade on supporting trees, trellises or poles up to maximum height of 13 feets or 4 meters and roots may come out from leaf nodes if vine touch to the ground. The plants have heart shape

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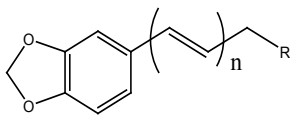
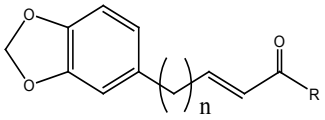


1-Piperine



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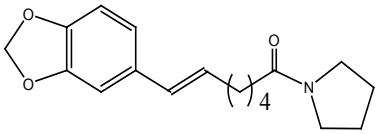

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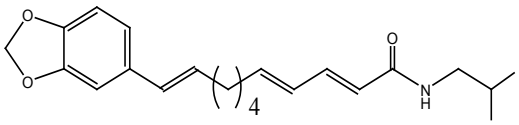
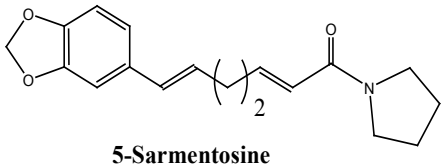
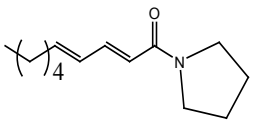


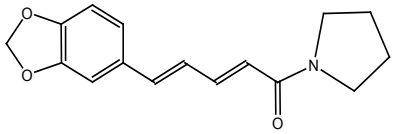
4-Pipericide



5-Sarmentosine



6-Sarmentine



7-Trichosta

Figure 1: Important chemical constituents of *P. nigrum*.

alternate leaves with typically large size of 5-10 cm in length and 3-6 cm across, with 5 to 7 prominent palmate veins. The flowers are small, monoecious with separate male and female flowers but may be polygamous which contain both male and female flowers. The small flowers are borne on pendulous spikes at the leaf nodes that are nearly as long as the leaves. The length of spikes goes up to 7-15 cm. The black pepper's fruits are small (3 to 4 mm in diameter) called a drupe and the dried unripe fruits of *Piper nigrum* are known as a peppercorn. The fully mature fruits are dark red in color and approximately 5 mm in diameter. A fruit contains a single seed. The plants bear fruits from 4th or 5th year, and continue to bear fruits up to seven years. A single stem contains 20-30 spikes of fruits. The collected spikes are sun dried to separate the peppercorns from the spikes. The fresh harvested unripe green fruits may freeze-dry to make green pepper. The fresh harvested unripe green fruits may sun-dried to make black pepper. The red skin of the ripen fruits is removed and the stony seeds are sun-dried to make white pepper [10].

Chemical Composition of *Piper nigrum*

The phytochemical investigations of *P. nigrum* revealed that it contains variety of phytochemicals. Piperine was the first pharmacologically active compound isolated from different members of Piperaceae family. Many investigators isolated different types of compounds viz Phenolics, flavonoids, alkaloids, amides and steroids, lignans, neolignans, terpenes, chalcones etc and many other compounds. Some of the compounds are Brachyamide B**,** Dihydro-pipericide, (2E,4E)-N-Eicosadienoyl-pereridine, N-trans-Feruloyltryamine, N-Formylpiperidine, Guineensine**,** pentadienoyl as piperidine, (2E,4E)-Nisobuty- ldecadienamid, isobutyl-eicosadienamide, Tricholein, Trichostachine, isobutyl-eicosatrienamide, Isobutyl-octadienamide, Piperamide, Piperamine, Piperettine, Pipericide, Piperine, Piperolein B, Sarmentine, Sarmentosine, Retrofractamide A Figure 1. The different pharmacological activities were reported due to the presence of these phytochemicals. Piperine reported to have four isomers viz; Piperine, Isopiperine, Chavicine and Isochavicine. Among all isolated compounds isolated from *P. nigrum.* Piperine, pipene, piperamide and piperamine were found to possess diverse pharmacological activities [1,11].

Evidence Based Pharmacological Activities

An attempt has been made to collect updated research information on *Piper nigrum* from the internet using Google search engine and PubMed. Many researchers carried out their researches on *Piper nigrum* & its active constituent ''piperine" using latest sophisticated scientific technologies and Important Pharmacological activities of *Piper nigrum* and piperine are summarized in Table 1. Some of the pharmacological

S. No.	Activities	References
1	Antihypertensive activity	3
2	Anti-asthmatic activity	5
3	Cognitive action and Fertility activity	9
4	Antimicrobial activity	12, 13
5	Antioxidant activity	14, 16, 17, 18, 25
6	Anti-cancer activity	4, 15,16,19,20, 21,26
7	Anti-inflammatory activity	22
8	Hepatoprotective activity	7, 23
9	Anti-diarrheal activity	24
10	Digestive activity	25,26,27,28, 29
11	Antidepressant activity	6, 30
12	Immunomodulatory activity	31,32
13	Anticonvulsant activity	33, 34
14	Analgesic activity	34
15	Effect of piperine on metabolism	2, 8

Table 1: Pharmacological activities of *Piper nigrum* L (Black Pepper)

activities of *Piper nigrum* are discussed below.

Antimicrobial activity of black pepper

Khan and Siddiqui in 2007 evaluated the antibacterial potential of aqueous decoction of *Piper nigrum* L. (black pepper), *Laurus nobilis* L. (bay leaf), *Pimpinella anisum* L. (aniseed), and *Coriandum sativum* L. (coriander) against different bacterial isolates from oral cavity of two hundred individual volunteers. Black pepper (aqueous decoction) showed strongest antibacterial activity comparable to aqueous decoction of *Laurus nobilis* and *Pimpinella anisum* at the concentration of 10µL/disc [12]. In a recent study, the silver nano-particles 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 [13].

Antioxidant activity of black pepper

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. 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. 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*. *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 memory-enhancing 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 (1-42) were investigated in Alzheimer's disease model in rats [14-16]. 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. 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 [17]. 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 [18].

Anti-cancer activity of black pepper:

Piper nigrum had been reported to inhibit tumors formation in different experimental models. Many studied revealed the antitumor activity of *P. nigrum* or Piperine by the oral administration. The alcoholic extract of peppercorn and piperine exhibited effective immunomodulatory and antitumor activities. Piperine is also reported to reduce the lung cancer by altering lipid peroxidation and by antioxidative protection enzymes activation [1,15-16]. Piperine has distinct pharmacological activities along with Anti-cancer activity. Piperine was reported to inhibit G1/S transition and the proliferation of human umbilical vein endothelial cells (HUVECs), migration of HUVECs and *in vitro* formation of tubule and angiogenesis induced by collagen and breast cancer cell in chick embryos. Piperine also inhibits the phosphorylation of Thr 308 residues of Akt of protein kinase B as well as Ser 473. Since phosphorylation of these is an essential controller of angiogenesis and function of endothelial cells. Therefore, Piperine may beused as an inhibitor of the angiogenesis for the treatment of cancer as angiogenesis plays a key role in the progression of tumor [19]. Docetaxel (a cytotoxic chemotherapeutic agent) is a FDA approved drug for the treatment for castration-resistant prostate cancer. The metabolism of docetaxel occurs in the liver by hepaticCYP3A4, and piperine is reported to inhibit the hepatic CYP3A4 enzymatic activity. Therefore, the administration of docetaxel in combination with piperine was investigated for both *in vitro* and *in vivo* pharmacokinetic activity of docetaxel. It was also reported that nutritional use of piperine increased the efficacy of docetaxel in a xenograft model devoid of any side effects on the mice [20].

The anticancer activity of piperine against many cancer cell lines has been reported earlier. Therefore, the mechanisms of anticancer activity of piperine against both androgen independent and dependent cells of prostate cancer were investigated. The proliferation of LNCaP, 22RV1, PC-3, and DU-145 prostate cancer cells was found to be dose dependently inhibited by piperine. Piperine treatment was also found to induce apoptosis, by the activation of caspase-3 and by the cleavage of PARP-1 proteins in different prostate cancer cells like PC-3, DU-145 & LNCaP prostate cancer cells. Treatment with piperine also found to disrupt the androgen receptor expression in LNCaP prostate cancer cells and cause significant diminutionin the level of Prostate Specific Antigen in LNCaP cells. The expression of phosphorylated STAT-3 and Nuclear factor-κB transcription factors were reduced in LNCaP, PC-3 and DU-145 prostate cancer cells after treatment of with piperine. These results suggested that there was a significant reduction in the androgen dependent and independent growth of tumor in naked mice model of xeno-transplanted with prostate cancer cells after treatment of piperine [21]. Piperine is non-genotoxic and found to possess anti-mutagenic and anti-tumor influences.

Anti-inflammatory activity of black pepper:

The piperine was evaluated for the anti-inflammatory, analgesic, and anti-arthritic activities. The *in vitro* anti-inflammatory activities were evaluated on interleukin 1β stimulated fibroblast like synoviocytes obtained from rheumatoid arthritis, while anti-arthritic including analgesic activities were evaluated on carrageen an induced acute paw model of pain and arthritis in rats. The prostaglandin E_2, cyclooxygenase 2, interleukin 6 and matrix metallo-proteinase levels were evaluated by ELISA and RT-PCR methods of analysis. Piperine treated groups were found to reduce the synthesis of prostaglandin E_2 in

a dose dependant comportment at the concentrations of 10-100 µg/mL. It significantly inhibited the synthesis of prostaglandin E_2 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 [22].

Hepatoprotective activity of black pepper:

It was found that piperine inhibited the increased level of serum GPT and GOT in dose-dependent manner in a hepato-toxicity model of mice caused by D-galactosamine. The hepatoprotective activity of methanolic extract of *Piper nigrum* fruits was evaluated in ethanol-CCl_4 induced hepatic damage in Wistar rats. Ethanol-$CCl_4$was used to induce hepatotoxicity in the rats. Prophylactic treatment with methanolic extract of *Piper nigrum* at a dose of 100 and 200 mg/kg body weight, p.o. and pre-treatment with piperine at a dose of 50 mg/kg body weight, p.o. for 15 days with Ethanol-CCl_4 treatment rats showed significant liver protection as evidenced from the triglycerides levels, Alanine transaminase, Aspartate transaminase, alkaline phosphatase, bilirubin and superoxide dismutase, Catalase, Glutathione reductase and Lipid peroxidation levels to assess the liver functions. In this study, administration of Ethanol-CCl_4 exhibited significant boost in triglycerides, Alanine transaminase, Aspartate transaminase, alkaline phosphatase, and bilirubin levels while there was significant decrease in the superoxide dismutase, catalase, and glutathione reductase levels which were restored to normal level after pre-treatment of methanolic extract of *Piper nigrum* and Piperine. Lipid peroxidations were also significantly decreased after pretreatment with methanolic extract of *Piper nigrum* and Piperine at given doses. The results were similar to that of reference standard-Liv52 at a dose of 1 mL/kg, p.o. for 15 days. The Morphological and histopathological studies of liver were also supportive of the biochemical parameters. Thus it is concluded that *Piper nigrum* possesses potential hepato-protective activity due to the presence of piperine alkaloids and have great therapeutic potential in treatment of liver ailments [23].

Anti-diarrheal activity of black pepper:

Aqueous back pepper extract (ABPE) at a dose of 75, 150, 300 mg/kg, po was evaluated for anti-diarrheal, anti-motility and anti-secretory activity in mice. The castor oil and magnesium sulphate were used to induce diarrhea for the evaluation of anti-diarrheal activity and gastrointestinal motility was assessed by charcoal meal, while castor oil was used for the evaluation of anti-motility and anti-secretory activities. ABPE showed a significant and dose dependent anti-diarrheal, anti-motility and anti-secretary effect. Anti-motility and anti-secretory activities of *Piper nigrum* might be due to the presence of carbohydrates and alkaloids, and anti-diarrheal activity of ABPE may be due to its anti-motility and anti-secretory activities [24].

Digestive activity of black pepper

Many spices are known for their digestive stimulant action. Dietary piperine enhances digestion by stimulation of the pancreatic enzymes and considerably decreases the food transit time of gastrointestinal tract. Piperine have been reported to increases the saliva production and gastric secretions, and increases the production and activation of salivary amylase. The orally administration of piperine or *P. nigrum* stimulate the liver to the secrete bile acids which in turn play key role in the absorption and digestion of fats. The oral administration of active compounds like piperine, pipene, piperamines and piperamides significantly increases the activities of enzymes like pancreatic amylase activity, protease activity, lipase activity and chymotrypsin activation [25,26]. An influence on digestive enzymes of intestinal mucosa were examined in experimental rats by Platel K and Srinivasan. The animals were fed with piperine (20 mg%) which significantly increased the activity of intestinal lipase, disaccharidases sucrase and maltase enzymes [27]. In another study, Platel K and Srinivasan evaluated the influence of piperine (20 mg%) on digestive enzymes of pancreas in experimental rats. Dietary piperine (20 mg%) significantly stimulated the activities of pancreatic lipase, amylase, trypsin and chymotrypsin [28]. The influence of some spices included in the diet, on food transit time was examine in adult female Wistar rats. Animals were maintained for 6 weeks on diets containing piperine (0.02 g%). The ferric oxide (0.5%) was included in the diet as an un-absorbable marker to monitor the food transit time. Time of excretion of colored stool was noted to follow the time of consumption of the diet with the marker. The piperine (0.02 g%) significantly shortened the food transit time [29].

Antidepressant activity of black pepper

The antidepressant-like effect of piperine and its possible mechanisms was evaluated in corticosterone-induced model of depression in mice. Depression-like behavior in mice was developed after 3 weeks corticosterone injections. The depression was revealed by the significant reduction in sucrose utilization and augmentation in immobility time in the forced swim test and tail suspension test. Further, the brain-derived neurotrophic factor protein and mRNA levels in the hippocampus were also significantly decreased in corticosterone-treated mice. Corticosterone induced the behavioral and biochemical changes were significantly diminished after treatment to animals with Piperine. These results showed that piperine produces an antidepressant-like effect in corticosterone-induced model of depression in mice [30].

Immuno-modulatory activity of black pepper

Immuno-modulatory and antitumor activity of piperine was evaluated. Piperine (250 µg/mL)was reported to be cytotoxic to Ehrlich ascites carcinoma cells and Dalton's lymphoma ascites. Piperine at a concentration of 50 µg/mL showed cytotoxicity to L929 cells in culture. Piperine administration also causes an increase in the total WBC counts in Bal b/c mice. Administrations of piperine were also increase the bone marrow cellularity and alpha-esterase positive cells [31]. *In vitro* immunomodulatory activity of piperine was evaluated to enhance the efficacy of rifampicin in a murine model of *Mycobacterium tuberculosis* infection. Mouse splenocytes were used to evaluate *in-vitro* immunomodulation of piperine for cytokine production, macrophage activation and lymphocyte proliferation. Piperine treated mouse splenocytes demonstrated an increase in the secretion of Th-1 cytokines (IFN-γ and IL-2), increased macrophage activation and proliferation of T and B cell. Protective efficacy of piperine and rifampicin (1 mg/kg) combination against *Mycobacterium tuberculosis* was reported due to immuno-modulatory activity [32].

Anticonvulsant activity of black pepper

The Anticonvulsant activity of piperine in maximal electroshock (MES) and pentylenetetrazol (PTZ) models of convulsions in mice was examined and further participation of transient receptor potential cation channel subfamily V member 1 (TRPV1) receptor was acknowledged in the inhibition of convulsion caused by pentylenetetrazol and maximal electroshock models. A significant

delay in the onset of myoclonic jerks and generalized clonic seizures was observed after administration of Piperine at doses of 40 and 80 mg/kg and Piperine also diminish the seizure stage and mortality as compare to the animals treated with 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 data reveals the anti-convulsant activity of piperine [33]. In another study, *in vivo* anticonvulsant activity of piperine was evaluated in pentylenetetrazole (PTZ) and picrotoxin (PIC)-induced seizures models of epilepsy in mice. A significant ($P<0.01$) delayedin the onset of PTZ-and PIC-induced seizures was observed after intra-peritonial injection of piperine at a dose 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 in mice. These results revealed the anticonvulsant effects of piperine which possibly mediated via GABA-ergic pathways [34].

Analgesic activity of black pepper

In vivo analgesic activity of piperine in mice was evaluated. The acetic acid-induced writhing and tail flick assay models in mice were used to evaluate the analgesic activity of piperine. There was a significant ($P<0.01$) inhibition in the acetic acid-induced writhing in mice after intra-peritoneal (i.p.) administration of piperine at a dose of 30, 50 and 70 mg/kg as compared with in domethacin at a dose of 20 mg/kg (i.p.). Intra-peritoneal injection of piperine at dose of 30 and 50 mg/kg and intra-peritoneal injection of morphine at dose of 5 mg/kg significantly ($P<0.01$) increase in the reaction time of mice in the tail flick assay. 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 [34].

Effect of Piperine on metabolism: a bioavailability enhancer

Piperine has shown bioavailability enhancing effects on many therapeutically important drugs and nutrients. Piperine increases the absorption of many drugs and nutrients from the gastrointestinal tract by various mechanisms. It alters the membrane dynamics and increases permeability at site of absorption. Piperine increases the serum half lives of some substances like beta-carotene and coenzyme Q10 and decreases metabolism of many drugs by inhibiting various metabolizing enzymes like cytochrome BS, CYP3A4, NADPH cytochrome, UDP-glucuronyl transferase, UDP-glucose dehydrogenase (UDP-GDH), and aryl hydrocarbon hydroxylase (AAH). These enzymatic inhibition by piperine resulted in increased bioavailability of many drugs and nutrients e.g. amoxicillin, ampicillin, acefotaxime, carbamazepine, ciprofloxacin, norfloxacin, metronidazole, oxytetracyclin, nimesulide, pentobarbitone, phenytoin, resveratrol, beta-carotene, curcumin, gallic acid, tiferron, nevirapine, and sparteine by different types of mechanisms. Therefore, piperine is known as bioavailability enhancer and a potent drug's metabolism inhibitor [2].

Other pharmacological activities

Piper nigrum (Black Pepper) or pure compound "Piperine" exhibits many more Pharmacological activities like antihypertensive, antiplatelets, antipyretic, antispasmodic, antifungal, anti-apoptotic, anti-metastatic, antimutagenic, anti-spermatogenic, anti-Colon toxin, anti-asthmatics, anti-anxiety, antithyroids, antifungal, insecticidal and larvicidal activities etc [1-5].

Conclusion

Many original research articles on the pharmacological potential of *Piper nigrum* (Black Pepper) or "Piperine" had been published so far. It was revealed from these articles that Black Pepper possesses significant *in vitro* and *in vivo* pharmacological potential for the treatment of different ailments and diseases and found to be safe. Piperine has also been found to increase the absorption of many drugs and shown bioavailability enhancing activity of many drugs and nutrients. This important property of piperine may be very helpful to enhance the therapeutic efficacy of many therapeutically important drugs. It is therefore concluded that Black pepper and its bioactive compound Piperine exhibited wide spectrum therapeutic potential and also emerged as an excellent adjuvant to enhance the therapeutic efficacy of the concurrently administered drugs and nutrients. Further detailed research studies are needed to obtain more scientific data on this miraculous King of spices.

References

1. Ahmad N, Fazal H, Abbasi BH, Farooq S, Ali M, et al. (2012) Biological role of Piper nigrum L. (Black pepper): A review. Asian Pacific J Trop Biomed: S1945-S1953
2. Acharya SG, Momin AH and Gajjar AV (2012) Review of Piperine as A Bio-Enhancer. Am J Pharm Tech Res 2:32-44
3. Taqvi SI, Shah AJ, Gilani AH (2008) Blood pressure lowering and vasomodulator effects of piperine. See comment in PubMed Commons below J CardiovascPharmacol 52: 452-458.
4. Manoharan S, Balakrishnan S, Menon V, Alias L, Reena A (2009) Chemopreventive efficacy of curcumin and piperine during 7,12-dimethylbenz[a] anthracene-induced hamster buccal pouch carcinogenesis. Singapore Med J 50:139-46.
5. Parganiha R, Verma S, Chandrakar S, Pal S, Sawarkar HA, Kashyap P (2011) In vitro anti- asthmatic activity of fruit extract of Piper nigrum (Piperaceae). Inter J Herbal Drug Res 1:15-18.
6. Li S, Wang C, Wang M, Li W, Matsumoto K, et al. (2007) Antidepressant like effects of piperine in chronic mild stress treated mice and its possible mechanisms. See comment in PubMed Commons below Life Sci 80: 1373-1381.
7. Matsuda H, Ninomiya K, Morikawa T, Yasuda D, Yamaguchi I, et al. (2008) Protective effects of amide constituents from the fruit of Piper chaba on D-galactosamine/TNF-alpha-induced cell death in mouse hepatocytes. See comment in PubMed Commons below Bioorg Med Chem Lett 18: 2038-2042.
8. Johnson JJ, Nihal M, Siddiqui IA, Scarlett CO, Bailey HH, et al. (2011) Enhancing the bioavailability of resveratrol by combining it with piperine. See comment in PubMed Commons below MolNutr Food Res 55: 1169-1176.
9. Wattanathorn J, Chonpathompikunlert P, Muchimapura S, Priprem A, Tankamnerdthai O (2008) Piperine, the potential functional food for mood and cognitive disorders. See comment in PubMed Commons below Food ChemToxicol 46: 3106-3110.
10. Black pepper
11. Parmar VS, Jain SC, Bisht KS, Jain R, Taneja P, Jha A, et al.(1997) Phytochemistry of the genus Piper. Phytochemistry46:597-673.
12. Khan M, Siddiqui M (2007) Antimicrobial activity of Piper fruits. Nat prod Rad 6:111-113.
13. Kumar KP, Gnanajobitha G, Vanaja M, Kumar SR, Malarkodi C, Pandian K, et al.(2014) Piper nigrum Leaf and Stem Assisted Green Synthesis of Silver Nanoparticles and Evaluation of its Antibacterial Activity against Agricultural Plant Pathogens. Scientific World Journal: 829894.
14. Vijayakumar RS, Surya D, Nalini N (2004) Antioxidant efficacy of black pepper (Piper nigrum L.) and piperine in rats with high fat diet induced oxidative stress. See comment in PubMed Commons below Redox Rep 9: 105-110.

15. Selvendiran K, Sakthisekaran D (2004) Chemopreventive effect of piperine on modulating lipid peroxidation and membrane bound enzymes in benzo(a) pyrene induced lung carcinogenesis. See comment in PubMed Commons below Biomed Pharmacother 58: 264-267.

16. Ahmad N, Fazal H, Abbasi BH, Rashid M, Mahmood T, Fatima N (2010) Efficient regeneration and antioxidant potential in regenerated tissues of Piper nigrum L. Plant Cell, Tissue and Organ Culture. Plarma Res 102:129-134.

17. Hritcu L, Noumedem JA, Cioanca O, Hancianu M, Kuete V, et al. (2014) Methanolic extract of Piper nigrum fruits improves memory impairment by decreasing brain oxidative stress in amyloid beta(1-42) rat model of Alzheimer's disease. See comment in PubMed Commons below Cell MolNeurobiol 34: 437-449.

18. Agbor GA, Akinfiresoye L2, Sortino J2, Johnson R2, Vinson JA2 (2012) Piper species protect cardiac, hepatic and renal antioxidant status of atherogenic diet fed hamsters. See comment in PubMed Commons below Food Chem 134: 1354-1359.

19. Doucette CD, Hilchie AL, Liwski R, Hoskin DW (2013) Piperine, a dietary phytochemical, inhibits angiogenesis. See comment in PubMed Commons below J NutrBiochem 24: 231-239.

20. Makhov P, Golovine K, Canter D, Kutikov A, Simhan J, et al. (2012) Co-administration of piperine and docetaxel results in improved anti-tumor efficacy via inhibition of CYP3A4 activity. See comment in PubMed Commons below Prostate 72: 661-667.

21. Samykutty A, Shetty AV, Dakshinamoorthy G, Bartik MM, Johnson GL, Webb B, et al.(2013) Piperine, a Bioactive Component of Pepper Spice Exerts Therapeutic Effects on Androgen Dependent and Androgen Independent Prostate Cancer Cells. PLoS One 8: e65889.

22. Bang JS, Oh da H, Choi HM, Sur BJ, Lim SJ, et al. (2009) Anti-inflammatory and antiarthritic effects of piperine in human interleukin 1beta-stimulated fibroblast-like synoviocytes and in rat arthritis models. See comment in PubMed Commons below Arthritis Res Ther 11: R49.

23. NirwaneA M, Bapat A R (2012) Effect of methanolic extract of Piper nigrum fruits in Ethanol-CCl4 induced hepatotoxicity in Wistar rats. Der Pharmacia Lettre 4:795-802

24. Shamkuwar PB, Shahi SR, Jadhav ST (2012) Evaluation of antidiarrhoeal effect of Black pepper (Piper nigrum L). Asian Journal of Plant Science and Research 2:48-53

25. Hussain A, Naz S, Nazir H, Shinwari ZK (2011)Tissue culture of Black pepper (Piper nigrum L.) in Pakistan. Pak J Bot 43: 1069-1078.

26. Srinivasan K (2007) Black pepper and its pungent principle-piperine: a review of diverse physiological effects. See comment in PubMed Commons below Crit Rev Food SciNutr 47: 735-748.

27. Platel K, Srinivasan K (1996) Influence of dietary spices or their active principles on digestive enzymes of small intestinal mucosa in rats. See comment in PubMed Commons below Int J Food SciNutr 47: 55-59.

28. Platel K, Srinivasan K (2000) Influence of dietary spices and their active principles on pancreatic digestive enzymes in albino rats. See comment in PubMed Commons below Nahrung 44: 42-46.

29. Platel K and Srinivasan K (2001)Studies on the influence of dietary spices on food transit time in experimental rats. Nutr Res 21:1309-14.

30. Mao QQ, Huang Z2, Zhong XM2, Xian YF3, Ip SP4 (2014) Piperine reverses the effects of corticosterone on behavior and hippocampal BDNF expression in mice. See comment in PubMed Commons below NeurochemInt 74: 36-41.

31. Sunila ES, Kuttan G (2004) Immunomodulatory and antitumor activity of Piper longum Linn. andpiperine. See comment in PubMed Commons below J Ethnopharmacol 90: 339-346.

32. Sharma S, Kalia NP1, Suden P2, Chauhan PS2, Kumar M1, et al. (2014) Protective efficacy of piperine against Mycobacterium tuberculosis. See comment in PubMed Commons below Tuberculosis (Edinb) 94: 389-396.

33. Chen CY, Li W, Qu KP, Chen CR (2013) Piperine exerts anti-seizure effects via the TRPV1 receptor in mice. See comment in PubMed Commons below Eur J Pharmacol 714: 288-294.

34. Bukhari IA, Pivac N, Alhumayyd MS, Mahesar AL, Gilani AH (2013) The analgesic and anticonvulsant effects of piperine in mice. See comment in PubMed Commons below J PhysiolPharmacol 64: 789-794.

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