

# Piperine: A Remarkable Marker with Intense Biological Activity

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## Abstract

Piperine, the main active constituent obtained from the black pepper belongs to family Piperaceae used as medicinal herb along with the spices which named as a "king of spices". Piperine chemically carries formula of  $C_{17}H_{19}NO_3$  is a weak base and acquires a numerous medicinal properties. Principally, piperine showed intense biological activity as Antioxidant<sup>2</sup>, antitumor, antiasthmatics, antipyretic, analgesic, anti-inflammatory, antidiarrheal, anxiolytic, antidepressant, hepatoprotective, antibacterial, antifungal, anti-metastatic, anti-thyroid.

**Keywords:** *Piper nigrum*; *P. longum*; Piperine; Bioperine

## Introduction

Black pepper (*Piper nigrum*), originated in the tropical evergreen forests of the Western Ghats of India named as 'the king of spice' or 'black gold' belonging to family Piperaceae. World widely, the largest producer of the *Piper nigrum* of production area (1, 77,340 ha) with 55,000 t in the aspects of IPC (2004) [1]. Black pepper (*Piper nigrum*), named as per the area in numerous way as *Kalimirch* in Urdu & Hindi, *Pipali* in Sanskrit. *Milagu* in Tamil, Peppercorn, white pepper, Green Pepper Black pepper Madagascar pepper in English as reported. Traditionally, in biological systems numerous medicinal plants used due to its pharmaceutical potentials and lesser side effects. Along with medicinal properties black pepper can be used for various purposes such as various sauces & dishes like meat dishes as well as in perfumery due to pungent alkaloids piperine (5-9%) and volatile oils (1-2.5%)

Piperine, an active constituent found in *Piper nigrum* shows a numerous biological activity as Antioxidant, Antitumor, Antiasthmatics, Antipyretic, Analgesic, Anti-inflammatory, Antidiarrheal, Anxiolytic, Antidepressant, Hepatoprotective, Antibacterial, Antifungal, Anti-metastatic, Anti-thyroid [2-15].

## Pharmacognosy

Black pepper of Piperaceae obtained from dried unripe fruits is a perennial herb which climbs and contains not less than 2.5 % of piperine. Taxonomically, it can be classified in to

Kingdom - Plantae.  
Class - Equisetopsida.  
Subclass - Magnolidae.  
Super Order-Magnoliane.  
Order- Piperales.  
Family - Piperaceae  
Genus - Piper.  
Species - Nigrum [16].

For the first time, 45 species of Piper were studied and reported by Hooker in 1886 but 29 species were from Indian origin. Afterwards, Rama Rao (1914) also enlisted 14 species of Piper from Western Ghats in his 'Flowering plants of Travancore'. Subsequently in 1921 again six species reported by Fisher from Annamalai hills and Fyson (1932) also reported four species as *P. schmidtii* & *P. wightii* from Nilgiris & Pulney hills top. Later on, in 1940 from Assam three more species were reported by Kangilal, et al. and after that Duthie *P. longum*, *P. betle*, *P. mullesua*, *P. nepalense*, & *P. nigrum* from upper gangetic

plains and adjacent Siwalic & Sub Himalayan tracts which were reported in his flora in 1960. Recently Nirmal babu, et al. (1993), reported new five taxa of Piper from Kerala origin.

*P. silentvalleyensis*, *P. nigrum* var. *hirtellosum* *P. pseudonigrum* (Silent valley biosphere reserve) and *P. sugandhagiri*, *Psugandhi* var. *brevipillis* (Sugandhagiri Cardamomplantation, wynad, Kerala)

Cytologically, all species of Piper with chromosomal number  $2n=24$  from the polyploidy series was studied by the Raliman & Nair 1986 & Samuel 1986 and also with basic chromosomal number  $x=13$  from South India and Sri Lanka origin and from north India  $x=12$ . Single species as *P. cubeba* possess haploid number  $n=12$  as compared to previous chromosomal number  $x=13$  by Jose & Sharma, 1985 [17].

In pharmacognosy facet the unripe berries of size approx. 5mm of black pepper carries primarily as dietary fiber, calcium, magnesium, potassium, manganese, phosphorous and beta-carotene along with oleoresin and pepper oil. But basically, *Piper nigrum* species are rich of Vit A and K.

Piperine ( $C_{17}H_{19}O_3N$ ) (1-[5-(1-3, benzodioxal-5-yl)-1-oxo-2, 4-pentadienyl Piperidine]), obtained from *Piper nigrum* contains volatile oil, oleo resins & alkaloids. Amongst alkaloids (piperine, chavicine, piperidine & piperitine in majority) and starch (about 30%) in lesser extent. Terpenes, steroids, lignans, flavones & alkamides are the other primary constituents present in the *Piper* (Musenga, et al. 2007; murthy & Bhattacharya, 2008). Later on, in Piper species aroma due to essential oils present, taste due to oleoresin and pungency due to its alkaloidal content piperine.

## Chemistry

Piperine(1-[5-(1-3,benzodioxal-5-yl)-1-oxo-2,4-pentadienyl Piperidine]), confined first time by the Danish chemist Hans Christian or stedt in 1820 with molecular mass of 285.33 g/mol contains carbon (71.55%), nitrogen (4.91%), oxygen (16. 82%), Hydrogen (6.71%).

As per physicochemical studies, it attains a yellow crystalline substance with melting point (128-130°C) and insoluble in water physically. Chemically, Piperine is a weak base and exhibits hydrolysis nitric acid or aqueous alkali succumb to volatile base piperidine ( $C_5H_{11}N$ ) & exhibited 4 isomeric forms. Normally Piperine is a tasteless, out of 4 isomeric forms, three forms are weakly pungent only. Chavicine, a stereo isomer delivers property of pungency to Black pepper. Practically, due to it's highly sensitivity to light so direct exposure avoided. Piperidine & chavicine (a piperine &

its allied components) exhibits pungency to black pepper [18] (Figure 1).

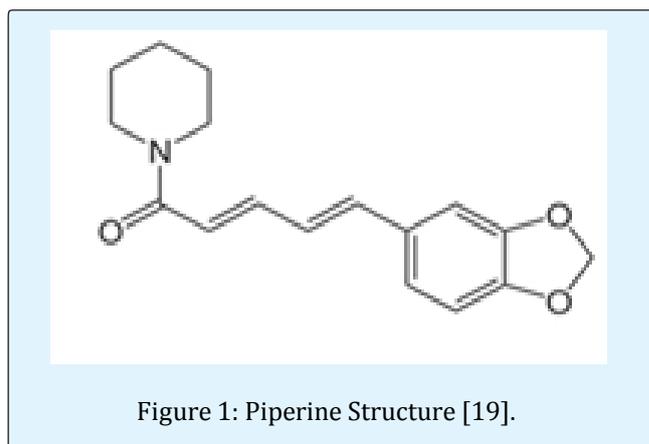


Figure 1: Piperine Structure [19].

Chemically, piperine having chemical formula  $C_{17}H_{19}NO_3$  a weak base which upon acid or alkali hydrolysis decomposed in to two compounds named as piperidine ( $C_5H_{11}N$ ) and piperic acid ( $C_{12}H_{10}O_4$ ). Structurally, piperine having trans-trans isomer while other isomers are cis-trans or trans-cis isomers and also others has no any pungency. In the pepper piperine gives pungent characteristic due to alkaloidal content in it.

## Pharmacological activities of Piperidine

Piperidine, isolated from the *Piper nigrum* showed a number of pharmacological activities. Principally, *Piper nigrum* exhibited some important activities as:

- Antioxidant
- Anti-diarrheal
- Antimutagenic & antitumor
- Anti-inflammatory
- Antiplatelet
- Analgesic
- Anti-hypertensive
- Hepatoprotective
- Anti-thyroid
- Antiasthmatic
- Cosmoperine
- Bioperine from *P. nigrum* [20]

## Anti-Oxidant Activity of Piper Nigrum

Oxidation is prerequisite step for the preservation of products. By the time gap, all products in the world whether they belong to natural & synthetic deteriorated due to several factors. Antioxidant prevents the deterioration of products categorized under oxidizable products as food, cosmetics & pharmaceuticals but efficacy, tendency and amount used varies as products. As concluded from 30years, spices reported many substances such as vitamins, flavonoids, terpenoids,

carotenoids (carrots), phytoestrogens & minerals found as active constituents in spices [20]. Gülçin İ, reported by comparing various extraction methods such as SOX, DPPH, ABTS & UE for activity. In this study, DPPH method becomes irrelevant and SOX & UE showed highest process yield [21]. Piper nigrum retards the induced stress (oxidative) by arresting the free radical production as well as inhibition of lipid peroxidation by considering enzymatically and nonenzymatically in rats as factor of oxidative stress in rats as reported by Vijayakumar, et al. [22].

### Anti-Diarrheal Activity

As traditional concept the prevalence of disease affects two ways primarily of therapeutic potential and efficacy of drug as per the WHO. As per the age of exploration, Ayurvedic medicine and their spices heals the disease naturally as they having the therapeutic potential. In the todays modern world, in developing countries the leading cause mortality and morbidity due to disease is diarrhea. The use of castor oil and magnesium sulphate in aqueous black pepper extract to treat diarrhea in mice through antimotility and antisecretory activity as reported by Prashant B. Sham Kumar, et al. [7].

### Anti-Tumor

From the primordial times also drugs related to the naturally derived compounds are used used to treat the tumours in various parts of the body as seen in Vinca, Piperidine, etc. By the refluxing the alkaloid piperidine purification done and showed 51.38% of inhibition of tumour at 5µg/ml concentration. In the ethanolic extract of *Piper nigrum* six alkaloidal bands reported and then purified by S.K. Reshmi, E. Sathya & P. Suganya Devi [23].

### Analgesic and epileptic

In traditional medicines, various drugs used but black pepper has been extensively used in various purposes as analgesic, anti-inflammatory as well as epileptics. Bukhari IA, et al. reported these effects in vivo in mice study by administering drug against standard (Valproic acid (200mg/kg), carbamazepine (30mg/kg) & diazepam (1mg/kg)) intraperitoneally (i.p.). In the study, they found piperine with significant delay on the onset of PTZ & PIC (Pentylene tetrazole & Picrotoxin) in mice and showed piperine exhibits pain as well as epilepsy properties [5].

### Hepatoprotective effect of *P. nigrum*

As a hepatoprotector Piper nigrum also reported after *Silybum marianum* experimentally, on animal models & in humans. Matsuda, et al. determined in mice treated with D-galactosamine that induced the liver toxicity profile in mice when exposed to the dose dependent

piperine. Which inhibited increase in serum GPT & GOT levels and further suggested the inhibitory effects that depended mainly on the reduced sensitivity of hepatocytes to TNF-α [24].

### Anti-asthmatics

Traditionally, Indian medicines and in pacific islands pepper from Piperaceae family Piper longum is slender climbing and glabrous plant carries piperine and piperlongumine as a major active constituent which shows antiasthmatic activity along with other activities. Many herbal practioners believed with the addition of black pepper in to the green tea (antioxidant, anticancer & soon) relieves the asthma as per literature review. Kim, et al. studied with different proportions the effects of piperine suppressed that infiltration of eosinophyl, hyper responsiveness also reduced and with the production of histamine, interlukin-5, IG-E & IL-4 significantly inflammation supressess [25].

### Anti-inflammatory Activity

Bang Jun Soo et al studied the inhibitory effects of piperine with reduction of IL6, MMP 13 and PGE production at different concentrations starting from 10 to 100 µg/ml but reduction in the production of PGE<sub>2</sub> at minimal dose. At some concentrations, activator protein 1(AP-1) migration also reduced due to the inhibitory activity if the piperine on clinical testing in rats and shown by the histological staining that piperine carries strong anti-inflammatory activity [6].

### Bioperine

Bioperine, natural black pepper extract containing more than 95% piperine the active constituent of the pepper to enhance the health and wellness after the standardization of the fruits of it [26]. Bioperine a specific product carries pure alkaloidal content obtained from the *Piper nigrum*. Presently, study conducted for the evaluation of the piperine potential by enhancing the serum response from the fat-soluble nutrients named as pro-vitamin beta-carotene [27].

### Conclusion

Black pepper is the “king of spices” and “real gold” used traditionally from the ayurvedic periods. The active constituent of the black pepper is the piperine along with alkaloids, olefins, fibers and other constituents. The content of piperine in the black pepper is more than 95 % by showing numerous biological activities and used in clinical purposes. Nowadays, present research carried out and extracted out a bioperine as a natural black pepper extract and having piperine as main active constituent in it as well as standardized out for the wellness of health.

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