Review of literature
**REVIEW OF LITERATURE**

*Piper longum* (L) belongs to the family Piperaceae. The common name is Long Pepper. It is chiefly grown in Bengal, Bihar, Assam, Trivandrum, Nepal, Bhutan, Terai regions of Himalayas, Phillipines, Malaysia, Singapore, and Bangladesh. It is a creeper which spreads on the ground or climbs up nearby trees for support. Leaves are 5-6 cm long, resemble betel leaves and has five veins. They are bitter to taste. The flowers are unisexual. The fruits are long, red when ripe and turn black when dried. It flowers during rainy season and gives fruits during autumn.

*Piper longum* is commonly used in the Indian Ayurvedic system of medicine(Krishnamurthy.A., 1969). The dried fruit is extensively used in rural and tribal areas of the world as an alternative and tonic. It is administered in the form of a powder. The dose used in therapy is 5-10g (Vaidya Vishnu Mahadev Gogte ,2000) (Jain.S.K and Tarefdar .C.R 1970). The ripe fruit is widely used as popular medicine to treat diseases like tuberculosis and leprosy (Kirtikar.K.R *et al*., 1950). It is used as a rasaayana drug. Rasaayana drugs promote body’s resistance and immunity, increase vitality, improve mental acuity, memory and intelligence (S.S.Handa., 1996).
PHOTO 1

Fruits of *Piper longum*
The other uses of *Piper longum* are as follows.

**External use**

It increases blood flow when applied locally. Therefore it is used in swelling accompanied with pain. A compound preparation of *Piper longum* is also said to be a good remedy of leucoderma. (Prasad.B.N, 1966)

**Internal use**

(i) **Nervous system**—It is a brain tonic. The fruit is used as a sedative in insomnia and epilepsy. It is also present in snuffs used in coma and drowsiness.

(ii) **Digestive system**: It has digestive stimulating quality. It is an appetizer, carminative, analgesic and mild laxative. It helps in reducing hepatomegaly and splenomegaly. It acts as a vermicide. It is effective in cases of anorexia, loss of appetite, indigestion, colic, liver disorders, and ascites. The ripe fruit is anti diarrhoeic and antidysentric.

(iii) **Circulatory system**: It is used to treat anaemia and various blood disorders. It regulates the function of liver and spleen. It is used after child birth to check postpartum hemorrhage.
(iv) **Respiratory system:** It is an excellent medicine for asthma (Ashok.D.B.Vaidya.,1996). It strengthens the lungs. A decoction of the immature fruits and roots is used in chronic bronchitis, cough and cold.

(v) **Reproductive system:** It reduces seminal debility and acts as a rejuvenator. It is useful in dysmenorrhoea and painful labour.

(vi) **Thermoregulation:** It is the best medicine for typhoid and chronic fever. It is also effective in remittent fever.

(vii) **Antidote:** The fruits and root are used as an antidote for snake bite and scorpion sting.

Several studies have been carried out to isolate and characterise all the components of fruits of *Piper longum* [Shankaracharya,N.B., 1997, Desai,S.J., et al 1989, Koul.S.K and Taneja.S.C .,1988, Das.B et al ., 1998]. The results indicate that it is mainly composed of essential oils, starch, protein, saponin, carbohydrates, gum, fatty oil, organic matter, and alkaloids like piperine (1-2%), piper longumine and piper longuminine, polyphenols etc. Minor amides are isobutylamide, longamide etc.
Numerous studies have been carried out on *Piper longum* and mixture of herbs containing *Piper longum* in the recent years.

Studies have been carried out to assess the activity of *Piper longum* fruits against Entamoeba histolytica (Ghoshal *et al*., 1996). The anti-bacterial activity of isolates from *Piper longum* has been evaluated against six different species of gram positive and gram negative bacteria (P.Srinivasa Reddy., 2001).

The antigiardial property of *Piper longum* has also been evaluated (Tripathi.D.M.,1997)(Agarwal.A.K.,1997). The efficacy of Dehydropiperonaline, an amide possessing coronary vasodilating activity isolated from *Piper longum*, has been assessed (Shoji.N. *et al*.,1986). Effect of Ayurvedic medicines including *Piper longum* on beta glucuronidase activity of Brunner’s glands has been assessed (Nadar.T.S and Pillai. M.M., 1989).

The anti allergic activity of *Piper longum* has also been studied (Dahanukar.S.A. and Karandikar.S,M.,1984) and its role in treatment of childhood asthma has been evaluated (Dahanukar.S.A., *et al*., 1984). The hepatoprotective of *Piper longum* against carbon tetra chloride induced liver damage has been studied (Rege.N.,et al.,1984).
The role of Ayurvedic herbals including *Piper longum* as a bioavailability enhancer of drugs has been studied (Atal.C.K.et al., 1981). Toxicity studies of *Piper longum* in mice have also been carried out (Shah.AH.,et al., 1998). The pharmacodynamics of extracts of *Piper longum* has been studied(Prasad.B.N and Chowdhry.B.,1967).

Numerous studies have also been carried out on piperine, an alkaloid isolated from *Piper longum*. Stability of piperine in different solvents has been evaluated (Sowbhagya.H.B.,1990). Piperine was found to be active against *Staphylococcus aureus* (MIC 12.5µg/ml) but not active against *E.coli* (MIC160µg/ml) (P.Srinivasa Reddy., 2001). Piperine possesses leishmanicidal activity (Raay.B et al.,1999). The liver protective potential of piperine has been evaluated (Koul,I.B. and Kapil.A.,1993). The protective action of piperine against experimental gastric ulcer has also been studied (Bai.Y.F and H.Xu.,2000).

Piperine is believed to increase the bioavailability of not therapeutically diverse drugs. It is believed to increase the bioavailability of drugs by two mechanisms. (a) It is believed to increase the oral absorption of drugs (Khajuria,A., et al.,1998). It prevents the
inactivation of the drug by acting as a potent inhibitor of cytochrome P-450 enzymes (Rashmeet, K. Reen and Jaswant Singh., 1991).

Piperine not only increases the bioavailability of drugs but also of other nutritional substances like β carotene, curcumin, selenium, pyridoxine, glucose and amino acid. It is useful since many therapeutic treatments are also accompanied by loss of essential nutraceuticals in the course of therapy.

Toxicity studies of piperine have been carried out in animal models (Pawinee.P., et al., 1983). The LD 50 value is very high compared to the therapeutic index of piperine which means a high degree of safety for nutritional use of piperine.

Studies carried out on Piper longum and piperine in the context of treatment of tuberculosis are as follows:

As mentioned earlier, Piper longum is used as a tonic in tuberculosis as it strengthens the lungs in the ancient Ayurvedic system of medicine. It alleviates the fever associated with tuberculosis. Recently the Korean Institute of Chest diseases is carrying out studies on Piper longum.
The anti tubercular activity of essential oils of *Piper longum* and semi synthetic analogues of Piper amides has been studied (Bhargava and Chauhan., 1968) (Gupta *et al.*, 1980).

The hepato protective effect of *Piper longum* when administered with antitubercular drugs has also been studied but the antioxidant status has not been evaluated. Moreover the study has not been carried out with the normal doses of drugs administered. (Chaajeed.S., *et al.*, 991). Trikatu (*Piper longum, Piper nigum and Zingiber officinale*) is believed to reduce the bioavailability of isoniazid in rabbits (Karan.R.S , *et al.*, 1998).

It has been demonstrared that piperine acts as a bioenhancer of Rifampicin in *vitro*. (Veena Balakrishnan *et al.*, 2001). Piperine being a bio availability enhancer, in combination with piperine the dose of Rifampicin can be reduced by about 50% while retaining the therapeutic efficacy of the drug on par with standard dose(450mg). It is also believed to act as a bio availability enhancer of other anti TB drugs (Kapil.R.S *et al.*, 1995) (Qazi,Ghulam Nabi *et al.*, 2003 ).