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KING OF SPICES: PIPER NIGRUM (BLACK PEPPER)

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ABSTRACT:-

Black pepper, the King of spices(Piper nigrum L.), is a widely used spice, known for its pungent odour. From time immemorial, plant sources were used in traditional systems of medicine and day-to-day common use, such as in meal preparation and cosmetic purposes. This is due to their vast pharmacological potential with minimum side effects. Among the various species of the Piperaceae family, black pepper is one of the most popular due to its principle pharmacological component, piperine. Which is an alkaloid that has diverse pharmacological activities like antioxidant, antiobesity,antitumor,antipyretic,anticonvulsant,antithyroid,antifungal,antibacterial,insecticidal,hepatoprotective,antiasthmatic,larvicidal,antihypertensive,anti-inflammatory,antidiabetic,antidiarrheal, bioavailability enhancer, immunomodulator, antiepileptic, antifertility, GI stimulant, lipid metabolism accelerator, anticancer, CNS stimulant, diuretic, aphrodisiac, blood purifier and antiplatelet activities, etc. Due to some religious value of black pepper, its being popular from ancient time to modern generation. This review is aimed to provide a literature review on recent advancement of chemistry, pharmacognosy, pharmacological activities, new piperine based formulations and other general use of Piper nigrum.

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 spicesamong 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 pepper corns 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], antiasthmatics [5], antipyretic, analgesic, anti-inflammatory, anti-diarrheal, antispasmodic, anxiolytic,antidepressants [6], hepato-protective[7], immuno-modulatory, antibacterial, antifungal, anti-thyroids, antiapoptotic, anti-metastatic, antimutagenic, anti-spermatogenic, antiColon 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 piperinehave 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. .

KEY WORDs:-

Introduction,Botanical description, Taxonomic Classification, Chemical constituents.,Pharmacological Activity.

BOTANICAL DESCRIPTION:-

The pepper plant is a perennial woody vine growing up to 4 m (13 ft) in height on supporting trees, poles, or trellises. It is a spreading vine, rooting readily where trailing stems touch the ground. The leaves are alternate, entire, 5 to 10 cm (2.0 to 3.9 in) long and 3 to 6 cm (1.2 to 2.4 in) across. The flowers are small, produced on pendulous spikes 4 to 8 cm (1.6 to 3.1 in) long at the leaf nodes, the spikes lengthening up to 7 to 15 cm (2.8 to 5.9 in) as the fruit matures.[9] Pepper can be grown in soil that is neither too dry nor susceptible to flooding, moist, well-drained and rich in organic matter (the vines do not do too well over an altitude of 900 m (3,000 ft) above sea level). The plants are propagated by cuttings about 40 to 50 cm (16 to 20 in) long, tied up to neighbouring trees or climbing frames at distances of about 2 m (6 ft 7 in) apart; trees with rough bark are favoured over those with smooth bark, as the pepper plants climb rough bark more readily. Competing plants are cleared away, leaving only sufficient trees to provide shade and permit free ventilation. The roots are covered in leaf mulch and manure, and the shoots are trimmed twice a year. 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. The cuttings are usually cultivars, selected both for yield and quality of fruit.A single stem bears 20 to 30 fruiting spikes. 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 the spikes.[10]Black pepper is native either to Southeast Asia[11] or South Asia.[12] Within the genus Piper, it is most closely related to other Asian species such as P. caninum.[11]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).[13] However, deforestation resulted in wild pepper growing in more limited forest patches from Goa to Kerala, with the wild source gradually decreasing as the quality and yield of the cultivated variety improved. No successful grafting of commercial pepper on wild pepper has been achieved to date.[13]

Fig: Flower, fruit and Leaf of black pepper

TAXONOMY OF PEPPER NIGRUM:-

Kingdome	Plantae
Class	Equisetopsida
Sub class	Magnolinidae
Super order	Magnolianae
Order	Piperales
Family	Piperales
Genus	Piper
Species	Nigrum

CHEMICAL CONSTITUENTS:-

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-pyridine,N-trans-FeruloylTyramine,N-Formylpiperidine, Guineensine, pentadienyl as piperidine,(2E,4E)-Nisobuty-ldecadienamid,isobutyl-eicosadienoic,Tricholein, Trichostachine,isobutyl-eicosatrienamide,Isobutyl-octadienamide, Piperamide, Piperamine, Piperettine, Pipericide, Piperine, Piperolein B, Sarmentine, Sarmentosine, RetrofractamideAThe 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 [14].One tablespoon (6 grams) of ground black pepper contains moderate amounts of vitamin K (13% of the daily value or DV), iron (10% DV) and manganese (18% DV), with trace amounts of other essential nutrients, protein, and dietary fibre.[15]

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AROMATIC AND VOLATILE COMPOUNDS PRESENT IN P.NIGRUM[16],[17]:-

Monoterpene	Sesquiterpenes	Others
Sabinene	Caryophyllene oxide	Cinnamic acid
Limonene	alpha-cis-Bergamotene	Benzaldehyde
Camphene	alpha-trans-Bergamotene	Eugenol
Terpinolene	alpha-cubebene	m-methyl acetophenone
alpha-phellandrene	gamma-cadinene	p-methyl acetophenone
1,8-cineole	alpha-selinene	Acetophenone
gamma-Terpinene	curcumene	safrole trans-Anethole

PHARMACOLOGICAL ACTIVITY:-

Antioxidant activity:-

Free radicals are responsible for causing many diseases. Different kinds of free radicals can attack the cell membrane, and cause or alter membrane permeability, membrane damage, oxidation of lipids, loss of different enzymatic activities, and ultimately disrupt proper cell function and body physiology, which may cause cancer. There are many antioxidants in our body to scavenge the free radical generated normally during metabolism. However, it can be insufficient sometimes. When there is imbalance between the free radical generation and antioxidant activity, oxidative stress is induced; which is harmful to our body, causing many side effects from simple health problems to cancer. Antioxidant activity of our body system includes enzymes like catalase, ascorbate, peroxidase, and superoxide dismutase, which are responsible for scavenging both free radicals and related oxygen species. Plants are a potent source of antioxidant activity from ethnomedicinal practices to todays finding. Many scientific findings prove its great antioxidant potency [18],[19] Piperine and P. nigrum maintain superoxide dismutase, glutathione peroxidase, catalase, glutathione-s-transferase, glutathione levels and reduce high fat diet induced oxidative stress [18]. Many screenings, using different solvent system for extraction of P. nigrum constituents, prove this potency [22]. The ethanolic extract of P. nigrum shows high antioxidant potency with 74.61± 0.02% with IC50 value 14.15 ± 0.02 µg/mgThe methanolic extract of P. nigrum fruits showing memory enhancing and antioxidant potency at a dose of 50 and 100 mg/kg, orally for 21 days in amloid-β (1-42) were investigated in rat model of

alzheimer's disease [22],[19] Research in Piper species viz. P. nigrum, P. guineense and P. umbellatum shows effects such as protecting cardiac, hepatic, and renal antioxidant status of atherogenic diet fed hamster at a dose of 1g/kg and 0.25g/kg for 12 weeks. The significant inhibition of atherogenic diet induced increased lipid profile and alteration in antioxidant enzyme activities; showed a great antioxidant protective role of the piper

extract against atherogenic diet generated oxidative stress in cardiac, hepatic, and renal tissues [21]. Thus, it will have important role in scavenging free radicals and delay aging process. As reported, P. nigrum has antioxidant potency that may be due to preseantioxi flavonoids and phenolic contents [22],[20]

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 ethanolCCl4 induced hepatic damage in Wistar rats. Ethanol-CCl4was 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-CCl4 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-CCl4 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]

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.). Intraperitoneal 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 [24]

Anticonvulsant Effects:

The mice model for anticonvulsant activity of piperine was evaluated by inducing seizure with pentylenetetrazol (PTZ)-and picrotoxin (PIC) in mice. On administering piperine (30, 50 and 70 mg/kg, i.p.) and reference standard drugs, valproic acid (200 mg/kg, i.p.), diazepam (1 mg/kg, i.p.) and carbamazepine (30mg/kg, i.p.) which showed significantly ($P<0.01$) delayed onset of PTZ-and PIC-induced seizures in mice. Which indicate that piperine exhibits anticonvulsant effects possibly mediated via GABA-ergic pathways 63Another experiment on anticonvulsant activity of piperine in pentylenetetrazol (PTC) and maximal electroshock (MES) model of convulsion in mice showed a delay in onset of generalized chronic seizure and myoclonic jerks with administering piperine (40- 80 mg/kg) and a significant reduction of PTZ-induced Fos immune reactivity in dentata gyrus and MES-induced tonic hind limb extension after piperine administration. The capsazepine, a selective TRPV1 antagonist blocked the antiseizure effect of piperine These findings reveal the potent anti-convulsant activity of piperine.[25]

Antitussive and Bronchodilator:

Many traditional practices prove it as well. 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[26]-5

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Antidiarrhoeal Effect:

Along with above described antimicrobial activity of black pepper, against some bacteria which are also responsible for causing diarrhea. Other research signifies its great potency in controlling diarrhea. As we know, diarrhea is a leading cause of morbidity and mortality globally, especially among the children in developing countries. Aqueous extract of black pepper at a dose of 75, 150, 300 mg/kg, produces a significant dosedependent antimotility, anti-secretory and antidiarrheal effects. The author concluded that this effect is due to the presence of lalkaloids in black pepper [27].

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 Daltons 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 werealso increase the bone marrow cellularity and alpha-esterase positive cells [28]. 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 immunomodulatory 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 [29]

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, UDPglucuronyl 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, cefotaxime, carbamazepine, ciprofloxacin, norfloxacin, metronidazole, oxytetracycline, 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 drugs metabolism inhibitor [2]

CONCLUSION:-

Many original research articles on the pharmacological potential of Piper nigrum (Black Pepper) or Piperinehad been published so far. It was revealed from thesearticles 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.

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