Miraculous effect of black pepper in Non-alcoholic fatty liver disease.

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Abstract: As everyone is aware, spices have always played a significant role in human meals and trade, particularly in India. Recent general acceptance of the connections between nutrition and health strengthens the significance of diet. It is a firm belief that plant therapy offers protection since it is risk-free and natural, offering an alternative to manmade medications. As the globe experiences a Renaissance, herbal treatments are once more on display. Numerous recent studies from the US and Europe have verified that within a few years, the use of herbal treatment for hepatic illnesses would soar by up to 65 percent. The reality is that regular use of hepato-protective medications is clearly insufficient, and in recent decades, research into the use of natural herbal remedies has increased. Due to their therapeutic potential for a variety of diseases, the bioactive components they contain are of great value. They frequently fall under the category of functional meals since they provide physiological advantages or prevent chronic illnesses in addition to providing basic nourishment. Due to its anti-oxidant, anti-microbial, and gastro-protective components, black pepper (Piper Nigrum L.) is a significant healthy food. Piperine, the active component in black pepper, is part of a complex phytochemistry that also contains volatile oil, oleoresins, and alkaloids.It may have a part to play in non-alcoholic fatty liver disease, according to several research. As it encompasses a range of liver abnormalities, from a simple non-alcoholic fatty liver (NAFL, simple fatty liver disease) to more advanced ones like non-alcoholic steatohepatitis (NASH), cirrhosis, and even liver cancer, NAFLD, the abnormal accumulation of fat in the liver in the absence of secondary causes of fatty liver, such as harmful alcohol use, viral hepatitis, or medications, is a serious health concern. The worldwide burden of NASH has more than quadrupled during the past 20 years. 94 lakh cases of compensated cirrhosis were caused by NASH globally in 2017, up from 40 lakh cases in 1990. In India, NAFLD is becoming a significant contributor to liver disease.
Key Words: Pepper, Spices, black pepper, hepatic properties, functional properties, nutraceutical

Introduction:

Black pepper (Piper nigrum L.), which is a common spice and is known as the "King of Spices," gives flavour to food on its own and improves the flavour of other ingredients. A perennial woody climber with a strong perfume, Piper nigrum may reach heights of 50 to 60 cm[(1)]. Black and white peppers are processed differently and are harvested at various times[(2)]. Black pepper includes the pulp because it is made by drying unripe fruit until a wrinkle develops, but white pepper is made by removing the pulp from mature fruit[3]. Both white and black pepper have a variety of uses, including as herbs, spices, preservatives, and pesticides[4]. India has the most historic accounts of P. nigrum in both human and veterinary medicine, particularly for gastrointestinal problems in animals and menstruation and ear-nose-throat illnesses in people. The most common ingredients were seeds and fruits, and the favoured methods of preparation were paste, pills, or tablets. It was also shown that Piper nigrum and the bioactive parts of it had important pharmacological properties. Antimicrobial effectiveness against a range of pathogens was achieved by inhibiting biofilm, bacterial efflux pumps, bacterial swarming, and swimming motilities[1].

Pepper:

Originally, only the western coastline area of India produced black pepper; from there, production of the spice spread to most tropical nations[5]. Pepper is presently grown in the tropical regions of the Asia-Pacific region, mainly in India, Indonesia, Malaysia, Sri Lanka, Thailand, China, Vietnam, and Cambodia. The crop is grown in around 26 nations outside of the Asia-Pacific area, including Brazil, Mexico, and Guatemala. The approximate four hundred thousand acres of land that is planted with pepper on a worldwide scale, generating 318 000 tonnes of pepper yearly[2]. Vietnam now holds the top spot for pepper output, while India has fallen to the fourth spot[6]. The EU nations are the next-largest importers of pepper after North America. In nations that produce pepper, like India, consumption is quite high, but not in others, like Vietnam, Thailand etc[7]. Large amounts of pepper are utilised in India's traditional medicine to create a wide variety of pharmaceutical compositions. In actuality, this industry consumes more than the food and spice industry. The pepper business is expanding, and pepper consumption is rising globally[8].

Composition: Two ingredients, piperine, which gives the pungency, and volatile oil, which is in charge of the scent and flavour, are what give pepper its character[9]. Oleoresin, piperine, and pepper oil are three items that are frequently created by industrial processing. Ground pepper is used to extract pepper oil using steam distillation, and the other two are extracted using solvents[10]. The main oleoresin found in black pepper is piperine. Black pepper also contains several related alkaloids that have been identified, including piperanine, piperettine, piperylin A, piperolein B, and pipericine. These piperine analogues have less pungency than piperine, though[11]. In addition to the piperine group of alkaloids stated above, the following alkaloids were listed: brachymide B, guineesine, retrofractamide A, sarmentine, sarmentosine, and tricholein[12]. Amberlite column chromatography was used to separate the fresh pepper scent, and GC and GC-MS were used to examine it. It was discovered that trans-linalool oxide and -terpeneol were the main substances. On the other hand, the main components in dried pepper oil were d-limonene, - and -pinene, and -caryophyllene. There is a noticeable shift in composition when oil is extracted during distillation. From 64.4% in the original fresh pepper scent to 17% in the distilled oil of dried black pepper, the quantity of oxygenated compounds decreased. This alteration explains why dried pepper and fresh pepper have different flavours and tastes[13].

Functional properties of black pepper

Ayurveda, Sidha, and Unani, three traditional Indian medical systems, all employ black pepper as a therapeutic agent for a variety of illnesses. Many of these conventional usages have been supported by pharmacological investigations[14]. The functional qualities of pepper include analgesic, antipyretic, antioxidant, and antibacterial effects[15].

Pepper's main component, piperine, has strong analgesic and antipyretic properties. In carrageenin-induced experiments, it was discovered that piperine at an oral dosage of 50 mg/kg body weight reduced inflammation[16]. Black pepper's anti-inflammatory properties can affect blood vessels, nerves, and subcutaneous tissues since they can be absorbed via the skin. It is possible that pepper has anticonvulsive and vasodilator properties based on how it affects the nervous system and sexual organs (priapism)[17]. Additionally, pepper affects breastfeeding by boosting milk production.Pepper oil stimulates circulation by warming the skin and drawing blood to the surface[18]. The bioavailability of medications, such as ampicillin and synthetic pharmaceuticals, is increased by pepper and piperine, and the absorption of amino acids from meals is also increased[19]. The market currently offers Bioperine, a commercially available patented product designed to increase the bioavailability of vitamin supplements (US Patent 5 536 506, Anon., 2011a, b) (2). The bioavailability of medications, such as ampicillin and synthetic pharmaceuticals, is increased by pepper and piperine, and the absorption of amino acids from meals is also increased[20]. Pepper is used in Ayurveda to cure epileptic seizures and promote sleep Penetrazole-induced seizures and electroshock seizures were both prevented by piperine[21]. Additionally, piperine has a potentiating impact on mouse hypnosis brought on by hexobarbital. It has been demonstrated that the peppery chemical 1-(3-benzodioxol-5yl)-1-oxo-2-propenyl piperidide, also known as anti-epilepsirine, has potent anti-epileptic effects. In Chinese hospitals, this is used to treat epilepsy[22]. Piperine and pepper both work to protect the liver. It was shown that piperine avoids the depletion of total thiols and GSH (gastric sulfhydryls) and lowers lipid peroxidation both in vitro and in vivo. This is a highly important characteristic because lipid peroxidation generates free radicals, which harm tissues[23]. The tocopherol and polyphenol content of pepper is responsible for its antioxidant properties. Supercritical CO_2 extracts of ground black pepper have been shown to be superior than solvent extracts at reducing lipid oxidation of cooked ground pork[24]. Black pepper's antioxidant properties can, at least in part, be attributed to the phenolic amides and glycosides of the flavonoids kaempferol, rhamnetin, and quercetin. All five of the pepper's phenolic amides were discovered to have excellent antioxidant properties, far superior to some synthetic antioxidants like butylated hydroxy toluene and butylated hydroxy anisole. Due to pepper's antibacterial characteristics, adding it to food improves keeping quality and prevents rotting[25].

The most significant property of piperine has been its suppressive effect on the liver's enzymatic drug-bio transforming response[26]. The process of biotransformation converts hydrophobic chemicals that enter the body into hydrophilic ones to speed up removal from the body. Typically, this procedure results in goods with little to no toxicological consequences. Hepatic and intestine aryl hydrocarbon hydroxylase as well as UDP-glucuronyl transferase are both severely inhibited. A key metabolic route that starts the transfer of glucuronic acid from uridine 5'-diphosphoglucuronic acid to endogenous and exogenous materials is catalysed by UDP-glucuronosyl transferases (UGTs). Bile acids, steroids, phenolic neurotransmitters, and bilirubin are examples of endogenous chemicals[(27)].

It has been discovered that piperine increases the bioavailability of a variety of medicinal medicines and phytochemicals. Because of this characteristic, piperine's capacity to boost bioavailability is also partially credited with facilitating more absorption due to its impact on the ultrastructure of the intestinal brush barrier[(28)]. The safety of black pepper and its primary ingredient, piperine, was subsequently confirmed by a number of animal experiments. At first, some disputed publications questioned its safety as a food additive, but none could provide any experimental proof[(29)]. Piperine is now recognised as having anti-mutagenic, anticancer, and non-genotoxic effects[(30)].

According to studies, pepper essential oil inhibits a variety of microorganisms, including Vibrio cholerae, Staphylococcus albus, Clostridium diphthereae, Streptomyces faecalis, several Bacillus species, Shigella dysenteriae, Pseudomanas auruginosa, etc. At a dosage of 0.2% to 1%, pepper oil inhibited Aspergillus parasite development and aflatoxin formation. Additionally, pepper leaf oil has antifungal properties[(31)].

Since oxidative breakdown of the lipids included in the food material is the primary cause of rapid food deterioration, the antioxidant property is crucial for the preservation of food materials (32). Utilizing spices like pepper, cardamom, and turmeric prevents or drastically delays oxidative degradation, greatly aiding in the preservation of food products[(33)].

Liver, Liver diseases and their global burden:

The liver is the chief and the most significant metabolic organ of the human body, It executes more than 500 significant functions such as conversion of food components to critical blood components, storage of vitamins and minerals, manufacture of many vital plasma proteins and minerals, maintenance of hormonal balance and metabolism, and detoxification of toxic wastes of the body. It secretes bile that helps in lipid digestion[(34)].

The liver is accountable for biotransformation of drugs and chemicals, thereby protecting the body against toxic foreign materials. In this mechanism, the liver is exposed to high con centration of toxic chemicals and their metabolites which may cause liver injury[(35)]. There are over hundreds of etiologies cause hepatic diseases. The majority of the hepatic diseases causing agents include microorganisms (hepatitis virus A, B, C; cytomegalovirus, Epstein-Barr virus, and yellow fever virus), metabolic diseases (obesity related fatty liver disease, hemochromatosis and Wilson’s disease), xenobiotics (alcohol, drugs, and chemicals), inherited related hepatic diseases, auto immune diseases (biliary cirrhosis, hepatitis and sclerosing cholangitis), and liver malignancies[(36)].

Hepatic diseases result in loss of workdays, reduced quality of life, decreased life span, and pose an economic burden to the individual as well as to the society (WHO, 2002).

Globally, hepatic diseases are dreaded disease cause greater morbidity and mortality. Among them, about 1.3 million populations die due to acute and chronic viral hepatitis. Over 350 million people are suffering chronically by HBV and 170 million people are infected with HCV[37]. Each year, HBV causes approximately 600,000 deaths and HBC cause 350,000 people deaths[38]. The recent statistics clearly show that the global burden of liver disease has increased over time with a huge impact on the overall world population[39].

It is proposed that compensated cirrhosis and liver cancer will reach more than 80 percent in the year 2020[40]. It was seen in the statistical analysis that decompensated cirrhosis will enhance more than 100 per cent and hepatic injury related deaths will enhance by 181 percent. Despite viral infections, increase rates of obesity and alcohol ingestion glob ally predict that the burden of hepatic diseases associated with alcohol and non-alcoholic diseases are set to two folds[41]. Moreover, those individuals having chronic hepatic diseases are more vulnerable to develop a severe illness like HIV infection and hepatic carcinoma (WHO, 2002). Non-Alcoholic Fatty Liver Disease (NAFLD) is closely associated with diabetes, metabolic syndrome, behavioural, and diet factors[42]. Globally, the prevalence of NAFLD ranges from 6% to 35%, with a median of 20% and in India, it ranges from 9% to 42%[43].

Non-Alcoholic Fatty Liver Disease (NAFLD)

Presently the definition of NAFLD as reported in most guidelines and recent publications is based on the presence of steatosis in more than 5% of hepatocytes in the absence of significant ongoing or recent alcohol consumption and other known causes of liver disease. NAFLD and liver fibrosis stages F3 or F4, the leading cause of death is cardiovascular disease[44]. Given the rapidly growing global burden of NAFLD and NASH, efforts must continue to find accurate non-invasive diagnostic and prognostic biomarkers, to develop effective treatments for individuals with advanced NASH and prevention methods for individuals at high risk of NAFLD and progressive liver disease[45].

NAFLD is a liver disease associated with obesity, insulin resistance, type 2 diabetes mellitus (T2DM), hypertension, hyperlipidaemia, and metabolic syndrome[46]. The subtype of NAFLD that is histologically categorised as non-alcoholic steatohepatitis (NASH) has a potentially progressive course leading to liver fibrosis, cirrhosis, hepatocellular carcinoma (HCC) and liver transplantation. All of these complications of NASH can pose significant health, economic, and patient-experience burdens to the patients, their families and the society[47]. NAFLD is also associated with extra-hepatic manifestations such as chronic kidney disease, cardiovascular disease and sleepapnoea[48]. NAFLD and NASH carry a large economic burden and create poor health-related quality of life[49].

Effect of pepper on liver disease:

Despite the burden of NAFLD, we are only beginning to understand its mechanisms of pathogenesis of NAFLD and the contribution of environmental and genetic factors to the risk of developing a progressive course of disease. Research is underway to identify appropriate non-invasive diagnostic methods and effective treatments and if the prevalence rates of T2DM and obesity are any indication, these countries will soon have a high burden of NAFLD[50]. Although the risk of liver-related mortality is increased in patients with Non-Alcoholic Fatty Liver Disease. Neither pepper nor piperine produces any hepatic toxicity[51]. For black pepper or piperine to be widely applicable in current medical practice, as a combination therapy, the clinical significance of food–drug interactions caused by concurrent use of black pepper or piperine should be carefully assessed with consideration for many compounding factors affecting the clinical outcome of pharmacokinetic interactions (e.g., dose, dosing regimen, genetic variation and species). Furthermore, the effective formulation strategy for the optimization of the pharmacokinetic characteristics of dietary components is crucial to improve their in vivo[52]. Piperine acts as a chemo preventive agent by modifying enzymes[53]. Dalvi and Dalvi (1991) used blood enzymes and hepatic mixed function oxidases as precise indicators of hepatotoxicity to study the hepatotoxic effects of piperine on rats[54]. Twenty four hours after treatment, an intragastric dosage of 100 mg/kg body weight resulted in an increase in hepatic microsomal enzymes (NADPH-cytochrome C reductase, cytochrome p-450, cytochrome-b5, benzphetamine N-demethylase, aminopyrine N-demethylase and aniline hydroxylase were estimated). A 10 mg/kg intraperitonial dosage, however, had no effect on the activity of the enzymes responsible for drug metabolism. The levels of the enzymes significantly decreased at greater doses of 800 mg/kg (intragastric) and 100 mg/kg (intraperitonial). However, these therapies had no effect on those specific markers of liver toxicity in the serum enzymes[51]. Significant protection from chemically induced hepatotoxicity is provided by piperine. A study that evaluated piperine's hepatoprotective activity to that of a recognised hepatoprotective medication, silymarin, as a reference chemical revealed that piperine has slightly less activity. In a feeding experiment study, Swiss albino mice were fed diets containing 1%, 2%, and 5% black pepper (w/w) for 10 and 20 days, and levels of the hepatic biotransformation enzymes (glutathione-s-transferase, cytochrome p-450, cytochrome b-5, acid soluble sulfohydril-SH) increased in a dose-dependent manner[55]. In a 1993 in vitro investigation, Reen et al. discovered that UDP-glucose dehydrogenase inhibition reduced the amount of glucuronidation[56].

According to research on the hypoglycaemic effects of several plants, pepper fruits had no discernible hypoglycaemic effects on rabbits. Dogs' blood pressure increased moderately after receiving 10–20 mg/kg of the aqueous extract of pepper plants. According to reports, both piperine and AE (antiepilepsirine) have detoxifying properties that may increase the absorption of other medications, changing the pharmokinetic parameter of the epileptic patient[58].

Mutagenic and Carcinogenic Effects

Investigations into the mutagenic and carcinogenic activities of pepper gave encouraging results on its beneficial effects. It was found to be non-mutagenic by Ames test[59]. The xenobiotic biotransformation enzymes are stimulated by pepper, which inhibits chemical carcinogenesis. The anti-oxidant qualities of piperine and related unsaturated amides inhibit the development of cancer [60]. Natural antioxidants in the diet may play a significant role in the body's defence mechanism against the deteriorating effects of mutagens. Additionally, the components of essential oils prevent xenobiotics from forming DNA adducts[61]. This finding demonstrates pepper's ability to prevent cancer. Research using pepper extracts, however, revealed a rise in the frequency of tumours in mice and a high amount of DNA damage brought on by piperine in studies using cell culture. Ames assay was used to determine the mutagenicity of pepper extracts in hexane, water, and alcohol on Salmonella typhimurium strains TA 98 and TA 100. The results showed that the extracts had no detectable mutagenic effects[51].

A large amount of antioxidant activity is elicited by the phenolic amides. Antioxidants are known to have a preventative effect on the development of cancer[62]. When the modifying properties of pepper essential oil were investigated, it was discovered that this oil also possessed an inhibitory activity. Aflatoxin B1 and the volatile oil's components prevent the development of DNA adducts. By means of the microsomal enzymes, this action was controlled. When mice were fed a diet containing 1.66% w/w of powdered pepper, no effect on carcinogenesis was seen; however, when mice were fed and painted with an extract of pepper for three months, the incidence of tumour-bearing mice increased. It was discovered that the powerful carcinogen methyl cholanthrene can be inhibited by the pepper terpene d-limonene. Safrole and tannic acid, two insignificant pepper components, are thought to have negligible carcinogenic potential. According to a tissue culture study employing the lung fibroblast cell line V-79, piperine treatment increased DNA damage in comparison to untreated cell lines[63]. The cytotoxic potential of the piperine was indicated by a decrease in the enzyme's glutathione-s-transferase and uridine diphosphate glucuronyl transferase activity after treatment. However, it may be deduced that the phenolic amide's conjugated unsaturated system substantially inhibits the oxidation of the amide nitrogen to n-nitroso compounds[58]. Additionally, pepper's essential oil components support its anti-carcinogenic potential by preventing DNA damage. Both carcinogenic and anticarcinogenic properties are revealed by investigations. Black pepper as a whole, however, displayed antimutagenic and anticarcinogenic properties. This is the form in which it is typically used as a spice and in many different Indian System medical preparations.

Antioxidant Activity

In a mammalian system, antioxidants scavenge free radicals and regulate lipid peroxidation. A continual supply of free radicals that start new peroxidations are produced by the chain reaction of lipid peroxidation[64]. In addition to causing food to degrade, this also damages tissue in vivo, this can lead to inflammatory illnesses, ageing, atherosclerosis, cancer etc. Studies have shown that pepper has strong antioxidant properties thanks to the phenolic amides it contains[65]. Tocopherol and vitamin C are two important natural antioxidants[66]. The antioxidant index of pepper is 6.1, while that of clove is 103.000, and that of turmeric is 29.6. In a study on various spices, it was discovered that pepper has antioxidant properties, which they attributed to the pepper's tocopherol concentration[58]. According to research on the Piperaceae family, P.

nigrum's five phenolic amides all have excellent antioxidant properties that outperform those of synthetic antioxidants like butylated hydroxy toluene and butylated hydroxy anisole(67).

Antimicrobial Activity

It was discovered that the pepper essential oil was effective against the penicillin-G resistant strain of Staphylococcus aureus. It has been documented that pepper oil has an inhibitory effect on a variety of bacteria, including Vibrio cholerae, Staphylococcus albus, Clostridium diphthereae, Shigella dysenteriae, Streptomyces faecalis, S. pyogenes, Bacillus pumilis, B. subtlis, Micrococcus sp., Pseudomonas pyogenes(68). Using cephazolin as a reference, the agar well diffusion technique was used to assess the antibacterial effect. At a dosage of 0.2% to 1%, pepper oil inhibited Aspergillus parasiticus' ability to grow its mycelium and produce aflatoxin. Both Candida albicans and Aspergillus flavus are susceptible to the antifungal properties of the leaf oil. Only isolated piperine demonstrated a growth-inhibiting effect at typical concentrations when pepper extract, essential oil, and sausage microflora (Lactobacillus plantrum, Micrococcus specialis, and Streptococcus faecalis) were tested in vitro for antibacterial activity(69). Only at high doses were pepper extract and powder active. It was discovered that an alcoholic extract worked well against the dangerous food-borne bacterium Clostridium botulinum(70). An experiment utilising pepper tincture revealed yet another potential activity. Nine Mycobacterium tuberculosis strains were investigated, and considerable antibacterial activity was discovered against each of the nine strains(71). The absorption of proteins and amino acids from diet as well as the bioavailability of medications are both increased by pepper. A study employing the ayurvedic remedy Trikatu, which contains the peppers Piper nigrum, Piper longum, and Zingiber officinale, discovered that formulations containing pepper increase the bioavailability of other medications(72). In an in vitro experiment utilising rat intestinal epithelial cells, piperine at a dose of 25–100 micromolar amount improved the absorption of L-leucine, L-isoleucine, and L-valine and accelerated lipid peroxidation. These findings imply that piperine and intestinal cell permeability may interact(73). According to one study, adding pepper and other typical Indian culinary spices at a level of roughly 1.5% of the diet improved the protein absorption from pulses(51).

Investigations on Human Subjects

There were very few research recorded that involved human beings. In a 1987 study, Mayore and his colleagues found that the stomach mucosal damage induced by pepper is only similar to that from aspirin at high doses. This result was reached in a study that administered pepper intra-gastrically to human volunteers under blind conditions. Healthy human participants were given meals containing 1.5 g of pepper; the positive and negative controls were aspirin (655 mg) and purified water(74). The long-term implications of consuming peppers on a daily basis are unknown. By assessing the orocaecal transit time using a lactulose hydrogen breath test on healthy human participants, the impact of intestinal peristalsis was investigated. They received 1.5 g of pepper in a gelatin capsule, and the OCTT was assessed over a number of days. It was discovered that pepper administration considerably lengthened orocecal transit time. This discovery is clinically significant for treating a variety of gastrointestinal problems. The effectiveness of pepper extract volatiles in the therapy of smoking cessation is revealed by yet another noteworthy study. According to Rose and Behmin's 1994 study on human participants, nicotine replacement products that contained volatile pepper compounds reduced the symptoms of smoking withdrawal. The positive findings from these two experiments on humans have the potential to be used for future medicinal purposes(75).

Discussion:

A very few studies using human subjects were reported. As reported before, Mayore and his collegues in the year 1987 showed that only in high doses, the gastric mucosal injury caused by pepper is comparable to that of aspirin. The majority of investigations have come to the conclusion that the allopathic system does not utilise pepper components' medicinal advantages. Since very early times, pepper has been used as a spice and culinary enhancer. No health risks or undesirable effects are likely to occur at the used concentrations. The total amounts of piperine and related phenolic amides are in the range of 7-9% w/w, while the volatile oil content is in the range of 2-4%. At this concentration, the actual doses of the various ingredients included in the pepper powder, oleoresin, or extractive employed will be insufficient to have any hazardous effects. Additionally, the flavour of the volatile oil ingredients and the piperine's strong flavour will function as a deterrent to the consumption of high doses. The Joint FAO/WHO Experts Committee on Food Additives has not established an acceptable daily intake (ADI) for volatile principles or piperine. At a dose of 1.5 g/kg meal, the stomach mucosal damage caused by pepper is the main adverse effect. Several reports have been made regarding piperine's ability to cause cancer. In mice, pepper extract increases the incidence of cancer and improves DNA adduct formation. According to a study, Egyptian toad forced-fed with a black pepper extract developed hepatocellular cancer, lymphosarcoma, and fibrosarcoma(76). However, large number of studies proves the anti-carcinogenic effects. Anyway, to establish the carcinogenicity or anti-carcinogenicity unequivocally, piperine must be subjected to further screening. The observation that it enhances the liver microsomalenzyme activity also must be investigated further. This is to ascertain whether constant use of pepper can produce any nonspecific enzyme induction.

Conclusion:

Pepper has been a part of many cultures and cuisines worldwide for time immemorable. Many traditional medicine practices have used pepper in treatment of various ailments. There are a large number of studies in animal models which have shown various promising effects of pepper on many physiological as well as pathological situations related to liver but very less data is available on human trials so there is dire need to experiment and study the effects of pepper on humans.

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