REVIEW ARTICLE

Hepatoprotective effect of Indian herbs and spices in alcohol-induced liver diseases

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Abstract

Alcoholic liver disease is the manifestation of liver due to chronic overconsumption of alcohol sequentially leading to alcoholic fatty liver, alcoholic hepatitis and then to alcoholic cirrhosis, which is the most fatal and is treatable only if the person undergoes liver transplantation. According to researches, 90% of the heavy alcohol drinkers or more develop fatty liver while only 20% of them show signs of alcoholic hepatitis and alcoholic cirrhosis. Women are more susceptible to liver damage through alcohol. India is a home of 50 different types of spices grown and traded internationally to more than 150 countries globally; There are many herbs and spices in our kitchen that have positive hepatoprotective actions against the alcohol-induced hepato-toxicity. The mechanism of the hepatoprotective role of these herbs can be associated with their free-radical scavenging properties, actions of decreasing lipid peroxidation and oxidative stress and increasing antioxidant properties.

Key words: Nutrition, Alcohol, Liver disorders

INTRODUCTION

Alcohol overconsumption is liver damaging, this damage is commonly known as "alcoholic liver disease (ALD)," was categorized into three sequential stages- alcoholic fatty liver, alcoholic hepatitis and alcoholic cirrhosis. Alcoholic fatty liver or steatosis can be termed as the "onset" of ALD. This is the very first stage of ALD, due to excess use of alcohol there is buildup of large fatty globules in the liver leading to fatty liver. It is an acute condition that can be reversed if treated with proper measures along with withdrawal of alcohol intake.[1,2]

Alcoholic hepatitis - fatty liver when left ignored progresses to the second stage, the liver cells get further inflamed leading to hepatocyte ballooning and dysfunction, due to excessive alcohol abuse.[3] This is the stage in which the person being affected is aware about the damage caused by alcohol to the liver. Alcoholic cirrhosis is the late stage of ALD, the most severe one as it has a high mortality rate. Many epidemiological studies stated that over a period of 5 years, minimum consumption of 50 g of alcohol/day for males and 30 g/day in females is enough to develop liver cirrhosis.[4] Continuous intake of alcohol despite progression of alcoholic hepatitis leads to permanent damage and even death of liver cells and is in most cases it is irreversible.[5]

Understanding the agents of alcohol-induced liver damage is a little controversial. There are a number of factors that aid to alcohol-induced liver damage and which are complex too. When the liver starts getting adversely affected by chronic alcohol use, cellular enzymes starts getting leaked into the plasma.[6] The presence of free radical can be categoried as one of the reasons influencing liver damage, high amount of free radical production along or due to impaired defense properties of antioxidants can lead to major harm or even death of the hepatocytes.[1] Free radicals also contribute to lipid peroxidation leading to its noxious effect on liver.[7]

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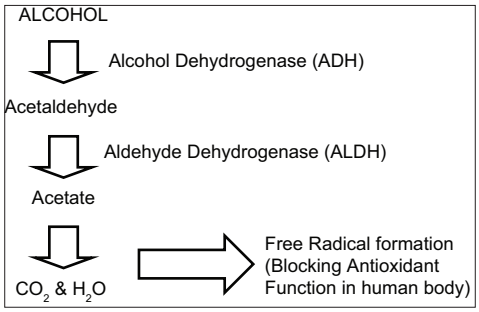
In humans, the organ that is most likely to get negatively affected by chronic alcohol abuse is liver. The alliance of heavy alcohol use and liver damage is well known as liver itself is the primary site of alcohol metabolism. The most common pathway of metabolism of alcohol is carried out with the help of enzymes alcohol dehydrogenase and aldehyde dehydrogenase, alcohol molecules are first broken down into acetaldehyde and then further to acetate by cooperation of these enzymes. Acetate is then metabolized to carbon dioxide and water for easy elimination from the body.[8] Acetaldehyde is the primary metabolic product and is a potent damager than alcohol itself.[9] Too much of alcohol intake leads to oxygen radical production which in turn causes dysfunction of body's antioxidant defence mechanism. Further, the elevation of plasma transaminases (aspartate and alanine aminotransferases [AST, ALT]), alkaline phosphatase (ALP), and gamma-glutamyl transferase is also remarkable.[10]

METABOLISM OF ALCOHOL



Alcohol is the most commonly available and freely consumed psychotic recreational substance allworldwide, and the most abused one also. As recommended by the Royal College of Physicians, safe alcohol intake weekly limit for men is 21 units and was lowered to 14 units for women.[11]

In 2014, WHO issued a Global Status Report on Alcohol and Health delineating that approximately 38.3% of the world population have a habit to pleasure themselves with alcohol daily. Even, the Economic Co-operation and Development reported that the use of alcohol grew by about 50% between the year 1992 and 2012.When talking about India only, it was stated by WHO (2014) that about 30% of the Indian subcontinent consumed alcohol on daily basis and even gave figures that each year 3.3 million deaths are occurring, alcohol being the direct or indirect cause.[12]

It is always said that "excess of everything is bad," same lies in the case of alcohol intake. Alcohol was picked out to be a liver-damaging or hepato-toxic substance in the 1960s, from the past few decades overuse of alcohol has become a matter of major health concern. In the race of being the most common preventable cause of deaths, alcohol abuse stands on the third position after smoking and hypertension being the first and second.[2]

The commonness of liver damaging effect of alcohol on women was more even in lesser quantities when compared to men.[2] The difference in absorption capability or liver response to injury caused by alcohol, can be the reasons behind the contrast between men and women susceptibility to hepatotoxic effect of alcohol.[11]

Diet has always played a crucial part in every disease's eruption as well as in its cure. Alcohol-induced liver diseases are also influenced very much by the food intakes, deficiencies of different nutrients, vitamins and minerals, intake of foods high in fats etc., are some of the factors that can affect the body adversely.[1]

India has always been known for its wide stretch of spices and herbs for decades. Fortunate enough to be supported by its agro-climatic zones, India is a home of 50 different types of spices grown and traded internationally to more than 150 countries across the globe, it is the largest producer, consumer, and exporter of spices.[13] Every Indian spice has its own uniqueness and backed with therapeutic values for our day to day health issues. Many of these spices and herbs are blessed with hepatoprotective and antihepato-toxic properties, some of which are discussed below.

PHYTOCHEMICAL PROPERTIES OF GINGER *(ZINGIBER OFFICINALE)*

Ginger or *Z. officinale* is one of the easily found and largely used spice and cooking ingredient in India. It belongs to the family of Zingiberaceae. The presence of a number of phytochemicals such as zingerone, shogaols, gingerols, pardols, β- phellandrene, curcumene, cineole, geranyl acetate, terphineol, terpenes, borneol, geraniol, limonene, β- elemene, zingiberol, linalool, αa-zingiberene, β-sesquiphellandrene, β-bisabolene, zingiberenol and α-farmesene, braces ginger with a number of medicinal and therapeutic values.[14]

These active constituents imparts it benefits of being anti-microbial, antiviral, gastroprotective, antidiabetic, antihypertensive, cardio-protective, anticancer, chemo-preventive, analgesic, anti-allergic, anti-aggregant, anticonvulsant, antidepressant, anti-edemic, anti-inflammatory, anti-lipidemic, antipyretic, hypotensive, anti-neoplastic, etc.[15]

Along with all above properties ginger was found laced with anti-alcoholic as well as hepatoprotective properties. A study done on mice concluded that the presence of 6- gingerol in ginger has shown to make better, the injuries caused due to alcohol to the liver and the brain, by lowering L-ϒ-glutamyl transpeptidase and butyrylcholinesterase.[16]

In another study done by Liu *et al*., when mice were fed with liquid diet containing alcohol their D-glucurono-6,3-lactone, glycerol-3-phosphate, pyruvic acid, lithocholic acid,

2-pyrocatechuic acid, and prostaglandin E1 were increased, but upon getting treated with essential oil and citral of ginger, the levels went down to normal, confirming ginger to be of antioxidant and hepatoprotective nature.[17] Thus, it could be said that ginger has the potential to rehabilitate the damage done to the liver by alcohol.

ANTIOXIDANT PROPERTIES OF GARLIC *(ALLIUM SATIVUM)*

A. sativum L. commonly known as garlic is one of the medicinal plants known for its therapeutic importance and culinary use for ages. Medicinal use of garlic goes back to 5000 years according to the Sanskrit evidences, while its use in Chinese medicines is at least 3000-year-old.[18]

The presence of not <33 sulfur compounds along with 17 amino acids and many enzymes and minerals make it a spice worth use.[18] Allicin, allin, alliase, S-allyl cysteine, diallyl disulfide and allyl methyl trisulfide are the main organosulfur compound present in garlic.[19]

Garlic was found to have a positive role in the treatment of various diseases, it possess properties of being antihypertensive, antidiabetic, anticancer, antifungal, anti-atherosclerosis, hypolipidemic, antimicrobial, immunomodulatory, antioxidant, anti-inflammatory, antihelmentic, anticoagulant, fibrinolytic, antiaggregant, antiarthritic, anti-bacterial, anti-pyretic, antirheumatic, antiseptic, antithyroid, antiulcer, vasodilator, gastronomic, cardiotonic, etc.[15] The bioactive compounds can be said to be the reason behind the success of Garlic being such a rich source for nursing many diseases.

Hepatoprotective role of garlic can be said to be more associated to its antioxidant activity and protection against the oxidative stressed caused. It protects the liver from tissue damage caused by elevated oxidative stress by increasing the antioxidant level through hunting reactive oxygen species (ROS), and lowering lipid peroxidation in the cells.[20] Hence, it can be said that along the above therapeutic properties, garlic was found effective for the treatment of ALD as well.

PHENOLIC CONTENT OF CLOVE *(SYZYGIUM AROMATICUM)*

Often referred to as "champion of spices," clove belongs to the family of Myrtaceae, has a pleasant fragrant of its own.[21] Cloves are available throughout the year. Dried flower buds of clove is a daily used Indian spice with rich amount of dietary phenols such as β-sitosterol, ascorbic acid, hydrostable tannins, ellagic acid, phenolic acids, gallic acid, flavonoids etc., laced with abundant therapeutic and medicinal values.[22,23] These impart clove with its property of being analgesic, anesthetic, antiaggregant, antiarthritic, antibacterial, anticancer, antidote, anti-inflammatory, antioxidant, antiseptic, antispasmodic, antiviral, carminative, digestive, vasodilator, etc.[15]

One of the main bioactive constituents present in clove is eugenol, which is an antioxidant and anti-inflammatory agent. Since oxidative stress along with inflammatory changes are pivotal role players in advancement of ALD, eugenol and its derivatives, safeguard the liver cells against the oxidative injury and tissue damage and even induce apoptosis to protect the hepatocytes against alcohol cause hepatotoxicity, which has the expertise to form complexes with reduced metal[24,25] and administration with eugenol rich fraction of clove helps to lower increased levels of ALP, γ-glutamyl transferase and other biochemical changes, it has the potential to reverse the liver back to its normal functioning.[26] Hence, it can be inferred that clove has the gift of being hepatoprotective against alcohol-induced liver damage.

TUPENOIDIC PROPERTY OF TURMERIC *(CURCUMA LONGA)*

C. longa or turmeric, is a perennial rhizomatous herb from the family Zingiberaceae, a daily used culinary ingredient in India. It is mainly used as a coloring and flavoring agent in the kitchen. However, apart from its use in the kitchen only, turmeric is a pack of which includes many pharmacological actions as of being analgesic, antacid, antiaggregant, antibacterial, anti-inflammatory, antileukemic, antioxidant, antipyretic, antiseptic, antiulcer, cardioprotective, decongestant, digestive, diuretic, hepatoprotective, hypotriglyceridemic, astringent, antitumor, antimutagenic, neuroprotective, and antidermophytic.[15] These properties can be due to the presence of 235 constituents especially phenols and terpenoids such as diarylheptanoids (including commonly known as curcuminoids), curcumin,diarylheptanoids, monoterpenes, sesquiterpenes, diterpenes, triterpenoids, alkaloid, and sterols.[27]

When talking about the efficacy of turmeric in liver diseases caused by chronic use of alcohol, curcumin was found with the potential to decrease the activities of plasma AST, ALT, lactate dehydrogenase and ALP, which when increase have hazardous effect on the liver functioning. It also helps to suppress fatty liver, by modulating the alcoholic metabolic enzymes activities and along with its properties to inhibit oxidative stress, lipid peroxidation and being antioxidant, it protects the liver from the damage of alcohol overuse.[28,29] Hence, it can be summarized that dietary treatment with turmeric can prove to ameliorate fatty liver, necrosis, and inflammation caused due to chronic alcohol abuse.

FLAVONOIDS CONTENT OF FENUGREEK *(TRIGONELLA FOENUM-GRAECUM)*

"*T. foenum-graecum*" in a layman's language is known as fenugreek or "methi" in Hindi, is one more of the oldest medicinal plant which has got its root from India and Northern Africa. It is a daily used condiment or flavoring agent, use of fenugreek has been traditionally as well as clinically reported to be safe and well tolerated.[30]

Fenugreek contains many phenolic compounds and nutrients in abundance, such as saponins, coumarin, fenugreekine, nicotinic acid, phytic acid, scopoletin, trigonelline, along with vitexin, tricin, naringenin, quercetin, and tricin-7-O-β-D-glucopyranoside.[31] These property of being polyphenol-rich imparts fenugreek to be antioxidant, chemopreventive, anticancer, antidiabetic,anti-inflammatory, antipyretic, gastroprotective, analgesic, anesthetic, antiatherosclerotic, antidiuretic, antiseptic, antitumor, cardiotonic, carminative, hypocholesterolemic, hypotensive, laxative etc.[15,32]

Dietary administration of fenugreek seeds were found to be potent to protect the liver against alcohol abuse as it neutralizes free radicals which are a responsible source of liver damage and enhance antioxidant apparatus.[33] The presence of flavonoids also helps the liver to cope against the cell injuries caused due to oxidative stress.[34]

POLYPHENOLIC PROPERTY OF GREEN TEA *(CAMELLIA SINENSIS)*

Tea is the most commonly consumed aromatic beverage worldwide. Eastern, Central, and Southern Africa, the Indian subcontinent, Malaysia, Indonesia, Vietnam, Papua New Guinea, China and some Latin American countries are the major cultivator countries of *C. sinensis*.[35] Green tea, black tea, oolong tea are some types of tea from *C. sinensis*. Tea also contains flavonoids, amino acids along with caffeine, chlorophyll, inorganic constituents, pectins and other enzymes. The main polyphenols present in tea are catechins, epicatechin (EC), epigallocatechin (EGC), EGC gallate, and EC gallate.[36] Tea consists of therapeutic potentials such as antioxidative, antimicrobial, analgesic, antialzheimeran, anticancer, antiatherosclerotic, antibacterial, antidepressant, antidiabetic, anti-inflammatory, antiviral, neurotonic, etc.[15,37]

Black tea was found to be hepatoprotective as it is rich in polyphenols which impart antioxidant abilities to the cell to fight against alcohol-induced injuries done to the liver.[38] Since it was seen that there was a decrease in the oxidative stress levels on administration of black tea extract, it can be summarized it prevents chronic ethanol toxicity caused due to ethanol consumption.[39]

ANTIOXIDANT PROPERTIES OF AMLA *(PHYLLANTHUS EMBLICA)*

Emblica officinalis/*P. emblica* or commonly known as Indian gooseberry or "Amla" is a part of family Phyllanthaceae, is considered as one of the "best rejuvenating herb" according to Ayurvedic literature.[40] Amla is rich inmany nutrients and phenolic constituents such as chebulinic acid, chebulagic acid, emblicanin A, emblicanin B, punigluconin, pedunculagin, citric acid, ellagotannin, trigallayl glucose, pectin, and isostrictiniin. It also contains flavonoids such as Quercetin.[41] There are accounts amla to be antimicrobial, antioxidant, anti-inflammatory, analgesic, antipyretic, antitumor, hepato-protective, antiulcerogenic, diuretic, antidiabetic, antidiarrheal, hypocholesterolemic, hypolipidemic, anticancer, antiproliferative, cardioprotective, antitussive, neuroprotective etc.[42]

Oxidative stress and ROS-induced toxicity are the main listed mechanism for alcoholic liver injury and dysfunction. Due to the presence of nitric oxide hunting compounds in amla fruit extract, protection is provided to the liver from alcohol-induced alterations by lowering the process of lipid peroxidation and increasing the antioxidant abilities of the enzymes.[43] The presence of radical scavenging abilities can be due to presence of tannoids and phenolic compounds as it can act as a protective mechanism for protection against oxidative stress which can result into hepatic damage.[44]

IMMUNOSUPPRESSIVE PROPERTIES OF CURRY LEAVES *(MURRAYA KOENIGI)*

In India, *M. koenigi* is known by the name of curry leaves, which is recognized for its distinct smell and use in kitchen. Alkaloid, volatile oil, alpha-selinene, beta-bisabolene, glycolozoline and xanthotoxin are present in good amount in curry leaves.[45] Curry leaves also comprises of sesquiterpenoid, turpentine, sesquiterpene, monoterpenoid, carbazole Alkaloid, terpene, indole alkaloid, dicarboxylic acid, etc.[46] Consumption of curry leaves impart with the properties of being antibacterial, antipyretic, antiseptic, antiulcer, antispasmodic, astringent, carminative, laxative, hypoglycemic, etc.[15]

The presence of phytoconstituents those of antioxidant nature and immunosuppressive properties in curry leaves can be counted as the reason behind the reduced inflammation of the hepatocytes which was caused due to chronic alcohol abuse. Even the tannins and the carbazole alkaloids provide excellent hepatoprotective action against alcohol-induced hepatotoxicity.[47]

RADICAL SCAVENGING ACTION OF MAKOI OR BLACK NIGHTSHADE *(SOLANUM NIGRUM)*

S. nigrum in India is usually known by the name of "Makoi," the plant contains two specific alkaloids which are solasodine and solasonine.[48] It is enriched with qualities of being analgesic, antipyretic, anticancer, hepatoprotective, antispasmodic, antiulcer, diuretic, hypotensive, laxative, sedative, tranquilizer, etc.[15] In India, *S. nigrum* is an crucial ingredient in liv 52, a herbal formula used for treatment of many liver diseases.[49]

Hepatoprotective role of makoi comes mainly from its ability to deal with the increased oxidative stress and its radical scavenging action against the free radicals in the liver cells, hence, preventing hepatic dysfunction from alcohol abuse.[48] Fruit of *S. nigrum* is also associated with the regeneration processes of liver and even detoxifies the body from the harmful toxins such as acetaldehyde, which again is due to its ability to hunt down-free radicals.[50] Hence, it can be concluded that fruits of makoi are hepatoprotective agents which work against alcohol-induced liver injuries.

ANTI-INFLAMMATORY PROPERTIES OF BLACK CUMIN *(NIGELLA SATIVA* [NS])

"Kalonji" or black cumin is the common Hindi name for NS; is an indigenous inhabitants of South and Southwest Asia from the family of Ranunculaceae. The role of NS in treatment of various disease and ailments is known for thousands of years. The main bioactive contents of kalonji include thymoquinone, *p*-cymene, carvacrol, thymohydroquinone, dihydro thymoquinone, *α*-thujene, thymol, *t*-anethole, *β*-pinene, *α*-pinene, and *γ*-terpinene, which have varied therapeutic as well as pharmacological values.[51] Kalonji is the most well-known herb in the Muslim world, Islamic Literature has proofs of kalonji as a "cure to all" spice. It is world known for its actions such as analgesic, anticancer, antidote, antiseptic, antioxidant, antispasmodic, antiviral, chemopreventive, hepatoprotective, antibacterial, antiviral, anti-schistosomiasis, antidiabetic, immunodulator, cardioprotective, gastroprotective, nephroprotective, anti-asthmatic, pulmonary protective, anticonvulsant etc.[15,52]

During the course of damage done due to the chronic use of alcohol the activities of liver enzymes AST, ALT, and ALP get increased, which can be lowered with treatment with NS seeds, as it possess ameliorative potential against ethanol-induced hepatotoxicity.[53]

The antioxidant and anti-inflammatory properties of NS mainly coming from thymoquinone are also responsible for healing liver injury. Kalonji has the abilities to cope up with the injuries done to the liver by high levels of free radicals due to the presence of radical scavenger properties and enhanced antioxidant defenses produced through its action in the body.[54]

CONCLUSION

Alcohol abuse can be counted as one of the preventable causes of human death, however, there are evidence of increased mortality and birth defects caused by ALD due to over-consumption of alcohol worldwide. India has always been a home of many dietary substances holding therapeutic importance, and proper use of them have its own aura in treatment and prevention of many diseases and ailments. There are many daily used herbs and spices in our kitchen that have positive hepatoprotective actions against the alcohol-induced hepato-toxicity. The properties responsible for their action are given above and using the above herbs and spices in our daily life can protect and increase the life of our liver.

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