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Hepatotoxicity and the Role of Some Herbal Hepatoprotective Plants in Present Scenario

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Abstract

Liver is the principal site for metabolism and excretion in body. The human liver metabolizes substances by various biochemical pathways including oxidation, reduction, hydration, condensation, hydrolysis, conjugation or isomerization. Disorder of any of the afore mentioned process may lead to liver cell injury, what we call as hepatotoxicity which in turn leads to many diseases. Such diseases are responsible for higher mortality rates worldwide. Hepatotoxicity can be due to medicines, chemicals, dietary disturbances or herb induced liver damage via hepatotoxins. A number of herbal and herbomineral preparations are available in the Ayurveda, the traditional Indian Medicine which have been investigated for their hepatoprotective potential to treat different types of liver disorders. The present review is focused on different herbal plants that have potential to cure the hepatotoxicity.

Keywords: Herbal plants; Hepatotoxicity; Liver disease; Herbal drugs; Indian; Herb; Phytochemical

supporting immune system [6]. Therefore, healthy liver is key to healthy individual.

Causes of liver diseases

Liver disorders are the most common health hazard found in developing countries due to dietary habits, alcohol ingestion, poor hygiene, unsupervised drug use and smoking etc. Liver diseases can be non-inflammatory, inflammatory and degenerative. High levels of plasma total cholesterol (LDL-C) and triacylglycerols (TGs) are associated with high risk of atherosclerosis and cardiovascular disease owing to the hepatic insufficiency [7,8]. Hepatotoxicity caused by many toxins carbon tetrachloride (CCl₄), thioacetamide, acute or chronic alcohol consumption, various infections like hepatitis A, B, C and drugs, in which drugs are most common offender. Free radical generations in the alcohol use result in development of hepatitis leading to cirrhosis [9].

Role of medicinal plants in hepatotoxicity

In Ayurveda, plant materials have been used to protect liver injury by various chemicals and dietary agents. Therefore, herbal drugs are safe and have potential to cure such diseases, so they have gained popularity in recent years. Long term uses of these medicines are very cost-effective too. So many medicinal plants, present in different parts of India have been mentioned as hepatoprotective drugs and these are extensively used to treat the liver disorders. Various plants and polyherbal formulations have hepatoprotective activity. Approximately 160 phytoconstituents and other phytochemicals have been claimed to possess hepatoprotective activity [10]. In India more than 87 plants are used, out of which 33 are patented and have proprietary multi-ingredient plant formulations [11]. To emphasize the importance of their use, we reviewed some popular herbal plants having hepatoprotective potential.

Introduction

The liver tolerates maximum insult in detoxifying the various toxins present in the food, drinks, drugs and environment. Many risk factors predispose an individual to hepatic drug injury such as pre-existing liver disease, aging, female sex, and genetics. Liver being a major site of metabolism plays a pivotal role in detoxification of various toxins ingested and or produced during absorption of the food material [1-3]. The liver usually filter all the blood from the digestive tract, before passing it to the rest of the body to avoid entering toxins in the other body system [4]. It utilizes different metabolic pathways for energy production, metabolism and reproduction to control almost all systems of the body [5]. Liver also synthesizes many complement systems and proteins for

Trigonella-foecum-graecum

Trigonella (Hindi: methi, English: fenugreek) belongs to the family Fabaceae. It is an annual herb which is widely grown in India, Pakistan, Egypt and Middle Eastern countries [12]. *Trigonella* has gained importance due to its strong aroma and medicinal properties to treat various diseases [13]. The leaf of *Trigonella* is a rich source of Calcium, Iron, β -carotene and other phytochemicals. Leaves and seeds are used for culinary dishes [14]. The main chemical constituents of *Trigonella* are flavonoids, polysaccharides, saponins, fibers, and some alkaloids like trigocoumarin, choline and trigonelline [15]. Singh et al. [16] suggested cytoprotective, antioxidant and hepatoprotective properties of *Trigonella* leaf extracts which may be used in the form of dietary components and also in formulations against liver diseases. Tripathi and Chandra [17] reported antioxidative potential of *Trigonella* protects liver tissue in against deltamethrin (DM) induced toxicity. DM induces oxidative stress in rat liver as evidenced by increased levels of LPO, GSH contents and lowered activities of antioxidants viz SOD, GST and catalase. The exposure with *Trigonella* resulted in significant recovery in altered levels of these parameters. On the basis of the above facts it may be suggested that the use of natural *Trigonella* is having antioxidative and antilipidemic properties. It is also beneficial in pesticide induced hepatotoxicity. *Trigonella* have potential properties as antiulcer, wound healing, CNS stimulant, immunomodulatory, antioxidant, antidiabetic, antineoplastic, anti-inflammatory and antipyretic drugs. The extract prepared from the dried seeds of *Trigonella* exhibits hepatoprotective potential against rat model induced liver cirrhosis by thioacetamide [18]. The methanol extract of *Trigonella* have significant hepatoprotective effect against CCl_4 induced hepatotoxicity [19].

Allium cepa

Allium cepa, a garden onion, belongs to the family Liliaceae. It is extensively cultivated in China, India and US. It contains good amount of carbohydrates, potassium, sodium and phosphorus. Traditionally, it is used to treat intestinal infections, ear ache, eye infections, headaches, drowsiness, urinary tract, burning ulcers and cough [20]. It has therapeutic effects as antiviral, antifungal, antibacterial, antiparasitic, and has antihypertensive, hypoglycemic, antithrombotic, antihyperlipidemic, antiinflammatory and antioxidant [21-23]. Ozougwu and Eyo [24] reported that *A. cepa* has hepatoprotective effects against paracetamol induced liver damage in rats. Aqueous bulb extract of *A. cepa* have hepatoprotective effects against hepatotoxicity in adult male albino wistar rats [25]. Ige et al. [26] reported hepatoprotective potential of *A. cepa* against cadmium induced hepatotoxicity in rats. Lee et al. [27] also reported the hepatoprotective effects of *A. cepa* extract on acetaminophen induced liver damage in mice.

Azadiracta indica

Azadiracta indica, commonly known as Nimba or Neem, is a very commonly grown tree. It belongs to the family Meliaceae and commonly known as neem. *A. indica* is native to India and Burma, growing in tropical and semi tropical regions. It is a fast growing tree that can reach a height of 15-20 meters rarely to 35-40 m. *A. indica* is reported to be useful in leprosy, intestinal worm, skin infections, constipation, epistaxis, biliary affliction, anorexia, blood morbidity and biliousness. Different parts of the plant possess bitter active principles [28]. It lowered the blood glucose level and attenuated gastric ulcerogenesis [29]. Patel et al. [30] reported the hepatoprotective activity of aqueous, alcoholic, ethyl acetate and petroleum ether extracts of *A. indica* leaves. The antioxidant and hepatoprotective activity of fresh juice of young stem bark of *A. indica*, were also evaluated against hepatic damage caused by CCl_4 [31]. The results suggested that antioxidant and hepatoprotective effect of fresh juice of neem is possible related to the free radical scavenging activity. Chattopadhyay et al. [32] also reported the hepatoprotective effect of *A. indica* leaves against hepatic damage induced by paracetamol in rats.

Boerhavia diffusa

The roots of *Boerhavia diffusa*, (Punarnava), are used for the treatment of various hepatic disorders due to their safety and efficacy. The word Punarnava means one which renews the body. Punarnava has an important place among Indian medicinal herbs from ancient time. *B. diffusa* (family Nyctaginaceae) is an important medicinal plant to cure the liver diseases in India, South America and African continents.

Different parts, especially roots have been used to treat different disorders such as gastrointestinal, hepato-protective and gynecological indications, immunomodulation, antifibrinolysis, anticancer activity, antidiabetic activity, anti-inflammation and diuresis. *B. diffusa* has been widely due to its phytochemical constituents and therapeutic activities. The root contains different compounds such as isoflavanoids (rotenoids), flavanoids, flavanoid glycosides, xanthenes, purine nucleoside, lignans, ecdysteroids and steroids [33]. *B. diffusa* is useful to treat the hepatotoxicity, induced by paracetamol and acetaminophen [34-37]. Punarnava is also important for the treatment of jaundice [38,39]. Shameela et al. [40] reported that the prior administration of *B. diffusa* at 150 mg/kg body weight/day for 45 days prevents the hepatitis in rats induced by proterenol. The hepatoprotective effects of *B. diffusa* may be due to its oxidant property, or by its membrane stabilizing action, or to its ability to maintain near to normal status the activities of free radical enzymes and the level of GSH, which protect hepatocellular membrane against oxidative damage by decreasing lipid protection.

Curcuma longa

Curcuma longa commonly known as turmeric (Hindi: Haridra or Haldi), is a rhizomatous perennial herb. It belongs to the family Zingiberaceae and native to South Asia. It is a popular ingredient for preparing different culinary dishes. Turmeric has

also been used in traditional medicine and it has therapeutic potential against jaundice and other disorders of liver, parasitic infections, ulcers, various skin diseases etc. The rhizome juice from *C. longa* is useful in the treatment of many diseases such as anthelmintic, asthma, gonorrhoea and urinary infections. Its essential oil is also used in the treatment of carminative, stomachic and tonic [41,42]. In traditional medicine, several herbal remedies have been used to treat liver disorders, including liver cirrhosis [43,44]. Different extracts of *C. longa* are reported to have hepatoprotective activity against CCl₄ and TAA induced toxicity [42-45].

Ocimum sanctum

It has a wide range of therapeutic potential. *Ocimum sanctum* is commonly known as tulsi (family Lamiaceae). *O. sanctum* is popular Ayurvedic remedy for common cold, headaches, stomach disorders, inflammation, heart disease, various forms of poisoning and malaria [46]. Different parts of this plant have been reported to exhibit several medicinal properties. Pharmacological properties like anabolic, hypotensive, cardiac depressant, smooth muscle relaxant, anti-fertility and anti-stress activity of this plant have been reported by several workers [47]. Hepatotoxic potential of *O. sanctum* against paracetamol, CCl₄, and lead induced liver damage, have been reported by several workers [11,46,48-51].

Conclusion

The commonest form of iatrogenic disease is drug and chemical induced hepatotoxicity. Chronic liver disease is characterized by variable degree of fibrosis, cirrhosis or neoplasia. According to the report of WHO, about 80% of the world's population adopt herbal medicines for their basic healthcare needs in developing countries. Modern medicine offers very limited range of drugs and therapies for the liver protection even from the drugs. Thus, use of herbal remedies is gaining popularity all over the world which is easy to procure and further easy to make formulation for the treatment of any type of hepatotoxicity. These therapies are fortunately very efficacious and cost-effective, therefore, attracting the research world for constant search of better drug, more potent active principles of the plant, and more palatable formulations. In this review article, every effort has been taken to collect and compile the details regarding a few hepatoprotective plants, which will be useful to the society to venture in to a field of alternative systems of medicine.

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