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Review

Escalation of liver malfunctioning: A step toward Herbal Awareness

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ABSTRACT

Ethnopharmacological relevance: About 2–5% of the world's population is suffering from liver toxicity including Pakistan with the second highest rate of hepatitis prevalence. Liver is a vital body organ which not only performs metabolic activities but also aids in detoxification, storage and digestion of food. Now a day's malnutrition, alcohol consumption and drug addiction are major causes of liver diseases throughout the world. In fact, there is no possible outcome to compensate liver malfunction for long term, and transplantation of liver is the only option left after the irretrievable injury of hepatic function. Subsequently, natural based therapeutic approaches are in the process of scrupulous testing as strong hepatoprotective mediator. In this regard plants are well thought hepatoprotective agents having multiple active components. In this review, based on species' pharmacology and safety we have compiled some plants which show strong hepatoprotective activity, main phytoconstituents with biological activities and few commercially used herbal formulations.

Materials and methods: Ethnopharmacological information was gathered by an extensive literature survey like WHO monographs on selected herbal medicinal plants (Vol 1-Vol 4); Principles and Practice of Phytotherapy, Mills S and Bone K, Churchill Livingstone, London, UK; Herbal Drugs and Phytopharmaceuticals, Wichtl M Medpharm Press, Stuttgart 3rd edn; Pharmacology and Applications of Chinese Materia Medica Vols 1 and 2, Chang H-M and But P P-H World Scientific, Singapore; British Herbal Compendium Vol. 2, Bradley P British Herbal Medicine Association, Bournemouth, UK; ESCOP Monographs 2nd edn. Thieme, Stuttgart, Germany; as well as by using electronic databases such as Pubchem, Chemspider, http://www.herbal-ahp.org; http://www.ahpa.org; http://whqlibdoc.who.int/publications/2003/9241546271.pdf; http://www.escop.com, Pubmed, HubMed and Scopus.

Results: Data for more about 29 plants have been accomplished for their bioactive constituent(s), biological activities and medicinal uses. Some of the plants have been identified as strong hepato-modulator. Such knowledge about traditional medicinal plants can be globally applied for safe and evidence based use in pharmacological applications.

Conclusion: With the rise in liver risks a meek struggle has been made to draw attention toward herbal therapy. Hepatoprotective constituents of said plants are expressed with chemical structures. However, for certain plants active constituents are not still isolated/purified but overall plant extract was found effective in providing protection against hepatic injury. As a future perspective, there is need to purify plant active constituents for ethnomedical rationale.

1. Introduction

In our body detoxification of various poisonous components is accomplished by liver. While detoxifying these compounds, it undergoes stress leading to malfunctioning of metabolic processes ending in liver failure and other severe health problems and even death (Marina, 2006). Oxidative stress due to over production of reactive oxygen species (ROS) is also considered as an imperative contributory factor of many diseases including liver damage. Moreover, liver diseases are also linked with viral infections (hepatitis A, B, C, D) and other microbial infections.

Hepatocytes constitute about 70% of all liver cells. Any alteration in hepatocytes can result into acute and chronic liver dysfunctions. Hepatocytes play their function at three different levels: (1) they

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prevent necrosis, steatosis and inflammation; (2) stimulate regeneration process; (3) inhibit fibrosis and cirrhosis. Hepatoprotective/anti-necrotic agents occupy central position because necrosis is a main liver laceration and if it remains untreated it results into fibrosis. Consequently, major goal of hepatic therapy is to control necrosis. Intensive research has been conducted for anti-necrotic agents and it is established that anti-necrotic agents especially plant flavonoids give a vital respite to hepatocytes. Flavonoids act by shielding membranes or by reducing their absorbency to bind with hepatotoxic substances (Gyr and Meier, 1991).

A significant number of individuals world-wide has been reported with severe state of hepatopathy induced by drug abuses, alcohol and other various viral infections (NIH Publication No. 94–1447, NIDDK, 1994). Therefore, protection and treatment of the liver is a major concern of today's medical science. Tremendous advancements which are made in the world of medicine until now, have failed to develop such a drug that vivify liver activity, inhibit liver degeneration, or stimulate rejuvenation of liver cells (Chattopadhyay, 2003). Moreover, most of them are immunosuppressive. Consequently, search for innovative approaches based on natural sources are under the process of meticulous testing (Gerbes et al., 2006). In this regard plants are well thought as strong hepatoprotective mediator having multiple active components. In the proceeding sections, some valuable information about hepatoprotective potential of some medicinal plants is given that will be highly beneficial for readers and pharmaceutical industry as well.

2. Medicinal plants having hepatoprotective activity

2.1. Acanthaceae

2.1.1. Andrographis paniculata

In traditional systems of medication *Andrographis paniculata* (Burm.f.) Nees (Acanthaceae) is well reported for its potential application to cure hepatitis. Dried aerial parts of *A. paniculata* are potentially used for medicinal purposes. Besides its hepatoprotective activity, this plant has also been traditionally used to cure vaginitis, chicken pox, burns and eczema owing to antimalarial, antidiarrheal, antivenom and antipyretic properties (Chang and But, 1986; Leelarasamee, 1990) (Table 1).

The chief constituent of *A. paniculata* is 'andrographolide' which is a diterpenoid lactone. The hepatoprotective role of andrographolide is ascribed to its ability to inhibit hepatic microsomal aniline hydroxylase, scavenge free radical and prevent lipid peroxidation (Maiti et al., 2010). Hepa-10 is valuable herbal product of *A. paniculata* recommended by practitioners to hepatic patients (Table 2).

In clinical testing rats with CCl_4 induced hepatic injury were orally treated with water extract of *Andrographis paniculata* (Burm.f.) Nees at 500 mg/kg p.o. A significant decline in the levels of ALP, SGOT and SGPT was observed, which might be due to its radical scavenging action, inhibition of lipid peroxidation and arresting the activities of hepatic microsomal enzymes (Nasir et al., 2013).

In an ulcer protective study, rats with pre-induced ulcer were administrated with different concentrations of andrographolide (1, 3 and 5 mg/kg) for 30 days. Ulcer sore found to be significantly reduced with 3 mg of andrographolide/kg b.w. The enzyme activities elevated in response to ulcer were also significantly minimized. This ulcer protective efficiency of andrographolide might be due to its cytoprotective, antioxidant and antiacid secretory effects (Saranya et al., 2011) (Figs. 1–27).

The recommended posology of crude drug is 1–3 g twice daily or 3–9 g as single dose after meal (Table 1). Its uses is inhibited during pregnancy, mild gastric discomfort and vomiting are reported side effects of *A. paniculata* extract hypersensitivity (Table 1)

2.1.2. Hygrophila auriculata

Hygrophila auriculata (Schumach.) Heine (Acanthaceae) is an herbal plant commonly grown on moist places. Medicinal system makes its use to treat a number of liver disorders (Vijayakumar et al., 2006). Roots and seeds have special application in medicines for jaundice and other hepatic obstruction. This plant is also popular for its anti-diabetes, antitumor, hypoglycaemic, antibacterial and radical scavenging activities. Unlike other herbal plants, this plant does not pose side effects or still no toxicity has been reported using this plant (Table 1). The important constituents of this plant are flavonoids, terpenoids, lupeol, butelin and fatty acids (Hussain et al., 2009).

Intake of *H. auriculata* extract at 100–250 mg/kg b.w for three weeks lowers TBARS (thiobarbituric acid reactive substances), blood glucose and hydroperoxide in diabetic rats. This antihyperglycemic activity might be attributed to the radical scavenging activity of *H. auriculata* (Vijayakumar et al., 2006).

2.2. Amaranthaceae

2.2.1. Amaranthus spinosus

Amaranthus spinosus L. (Amaranthaceae) traditionally known as Chaulai is an annual herb throughout the globe. Medicinally important part of *A. spinosus* is its leaves (Table 1). It is used to avert swelling around stomach and to cure jaundice and other hepatic disorders (Hema et al., 2006). It is also used as source of antiviral, anti-inflammatory, antidiuretic, antimalarial, antimicrobial, and antibacterial agents (Olajide et al., 2004). *A. spinosus* encompasses a number of bioactive components like kaempferol glycosides, quercetin isoamaranthine, hydroxycinnamates and amaranthine of antioxidant potential. Stigmasterol is the active ingredient responsible for hepatoprotective function of this plant (Srinivasan et al., 2005; Stintzing et al., 2004; Hilou et al., 2006). It also contains coumaroyl adenosine, amaranthoside, stigmasterol glycoside and betaine like trigonelline and glycinebetaine (Azhar-ul-Haq et al., 2006).

Albino rats with artificially induced oxidative stress and diabetes (streptozotocin-nicotinamide) were treated with *A. spinosus* leaf extract (ASEt) by administrating 250–500 mg/kg bw/day, i.p for twenty-one days. Biochemical and histological examination show diminution of blood glucose and ameliorate the enzymatic and non- enzymatic antioxidants. Moreover, administration of leaf extract also minimized the degenerative changes of pancreatic cells when compared to normal morphology (Mishra et al., 2012). Not any literature is available concerning *A. spinosus* extract sensitivity (Table 1).

2.3. Asteraceae

2.3.1. Artemisia gmelinii

Artemisia gmelinii Weber ex Stechm. (Asteraceae) is a perennial subshrubby plant. Aerial part and dried flowering tops has excellent hepatoprotective effect and used in chronic and acute hepatitis as a strong remedy (Table 1) (Li et al., 2004; Piao and Quan, 2007). Protective effects are credited to the presence of number of phytoconstituents like isofraxidin, esculetin, chlorosacroratin (Zhang, 2006) 2,5-dihydroxycinnamic acid, O-hydroxycinnamic acid, (Zhang, 2002) and scopoletin, which is a key component involved in hepatic protection (Fan et al., 2007). In herbal market, a number of commercial products made from plants of this family like livomap derived from *A. gmelinii* are accessible to patients with liver disorders (Table 2).

In randomized clinical trials alcoholic extract of *A. gmelinii* with dosage range of 10, 50 and 100 mg/kg/day shows its strong hepatoprotective effect by reducing oxidative stress in rat plasma (Mohammadian et al., 2016). Aside from hepatoprotective, extracts of this plant have also been used to treat patients with loss of appetite and suffering from gastrointestinal discomfort (Rauchensteiner et al., 2004). Tea infusion containing 4.5–3.0 g cut flowers are recommended for healthful effects. Duodenal and gastric ulcer are reported side effects of