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Review Article

Physiological changes due to hepatotoxicity and the protective role of some medicinal plants

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ABSTRACT

The liver is the largest, important organ and the site for essential biochemical reactions in the human body. It has the function to detoxify toxic substances and synthesize useful biomolecules. Therefore, damage to the liver leads to grave consequences. This damage resulted from chronic alcoholic abuse, viral hepatitis or inherited metabolic disease. Liver damage is associated with cellular necrosis, fibrosis, and increase in tissue lipid peroxidation and depletion in tissue glutathione level. Most of the hepatotoxic chemicals damage liver cells mainly by inducing lipid peroxidation and other oxidative damages in the liver. Natural antioxidants are found in many compounds classified as secondary plant metabolites, e.g. polyphenols (phenolic acids and flavonoids) and terpenoids (carotenoids), and the consumption of foods that contain these compounds in large quantities seems to play an important role in prophylaxis against many diseases. Herbal medicines derived from plant extracts are being increasingly utilized to treat a wide variety of clinical disease. More attention has been paid to the protective effects of natural antioxidants against drug induced toxicities especially whenever free radical generation is involved. Popularity of herbal remedies is increasing and at least one quarter of patients with liver disease use botanicals. The World Health Organization (WHO) estimates that 80 percent of the population of some Asian and African countries presently use herbal medicine for some aspect of primary health care. Some medicinal herbs have proven hepatoprotective potential. *Silybum marianum* (milk thistle) has been used to treat liver diseases since the 16th century. Its major constituents are the flavonoids silibinin, silydianin, silychristin, and isosilibinin, of which silibinin is the biologically most active compound and used for standardization of pharmaceutical products.

1. Introduction

The liver is one of the largest organs in the human body and the chief site for intense metabolism and excretion (Ahsan et al., 2009). It plays a major role in detoxification and excretion of many endogenous and exogenous compounds; any injury to it or impairment of its functions may lead to many implications on one's health (Subramaniam et al., 2015). Hepatic damage is associated with distortion of these metabolic

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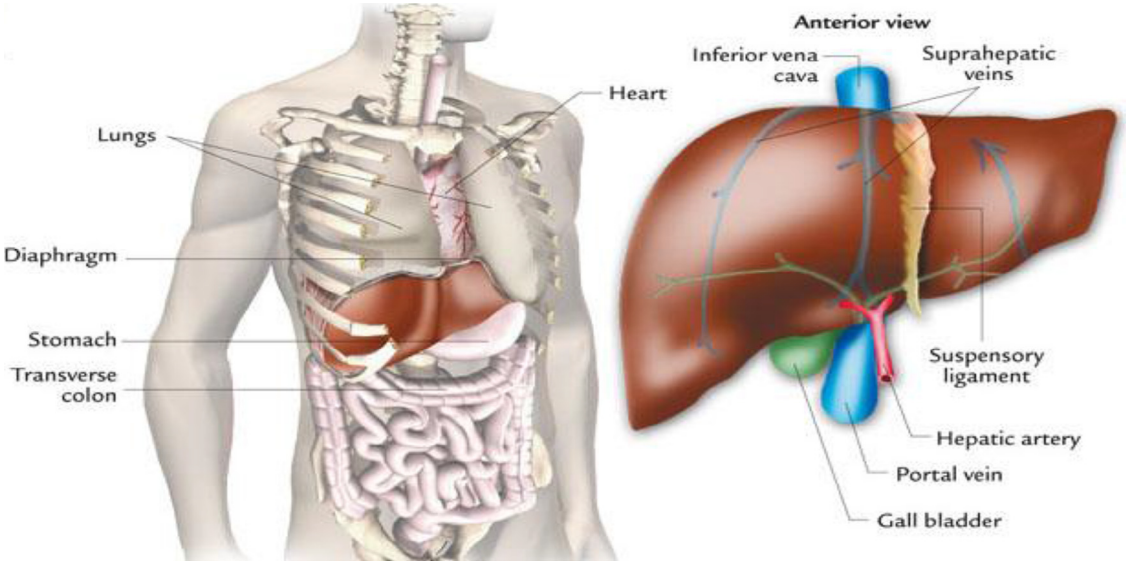

Fig. 1 – The liver (Polaxa, 2015).

functions. Liver damage is associated with cellular necrosis, increase in tissue lipid peroxidation and depletion of reduced glutathione levels. In addition, serum levels of many biochemical markers like transaminases, alkaline phosphatase, bilirubin, triglycerides and cholesterol are elevated in liver disease (Subramaniam et al., 2015). Liver diseases pose a serious challenge to international public health (Ahsan et al., 2009).

The liver plays a central role in transforming and clearing chemicals and is susceptible to the toxicity from these agents. Certain medicinal agents, when taken in overdoses and sometimes even when introduced within therapeutic ranges, may injure the organ. Chemicals that cause liver injury are called hepatotoxins (Friedman et al., 2003).

Hepatotoxicity is one of the main reasons behind withdrawal of a drug from the market. Fifty percent of all acute liver failures and 5% of all hospital admissions are associated with drug-induced hepatotoxicity (Dey et al., 2013).

A number of plants have been shown to possess hepatoprotective property by improving antioxidant status. Thus, the efficacy of the drug would be preventive and passive for defending against damages. Traditional medicines are effective in certain disorders and are based on experience in the use of plant products in amelioration of common diseases. Several Indian medicinal plants have in recent times been explored and the hepatoprotective effects of these plants have been established (Kumar et al., 2009; Abdel-Salam et al., 2014[1]).

Plant drugs are known to play a major role in the management of liver diseases. There are many plants and their extracts that have been shown to possess hepatoprotective activities (Girish and Pradhan, 2012).

Treatment options for common liver diseases are limited, and therapy with modern medicine may lack in efficacy. The effectiveness of treatments such as those using corticosteroids and interferons is inconsistent, carries the risk of adverse events, and is often too costly (Stickel and Schuppan, 2007). So, there is a need for effective therapeutic agents with a low incidence of side effects. The natural antioxidants, more recently, have attracted considerable attention of users and researchers largely on account of adverse toxicological reports on some synthetic antioxidants and growing awareness among consumers (Ramalakshmi et al., 2007). In fact, a single plant may have diversity of phytochemicals ranging from bitter compounds that stimulate digestive system, phenolic compounds for antioxidant and many other pharmacological properties, including antibacterial and antifungal, tannins that work as natural antibiotics, diuretic substances, and alkaloids. (Miguel, 2010).

2. The liver

The liver is the largest solid organ in the body, weighing about 1.5 kg in an adult. It lies in the right upper quadrant of the abdomen completely protected by the thoracic rib cage (Fig. 1). The liver is connected to two large blood vessels, one called hepatic artery and the other called the portal vein. The hepatic artery carries blood from the aorta whereas the portal vein carries blood containing digested food from the small intestine. The basic functional unit of the liver is the liver lobule; the human liver contains 50,000 to 100,000 individual lobules (Adi and Alturkmani, 2013).

2.1. *Hepatic physiology*

The liver is the center of metabolic homeostasis (Adi and Alturkmani, 2013; Sherwood, 1997). It serves as:

1. Vascular functions: for storage and filtration of blood.
   a. The liver can store 200–400 ml of blood in liver sinusoids (useful in hemorrhage).

[1] Underline (Abdel-Salam et al., 2014) means that this is Egyptian research.