Phytochemical evaluation and development of polyherb formulation for hepatoprotective activity

Liver is considered to be one of the most vital organs that functions as a centre of metabolism of nutrients such as carbohydrates, proteins and lipids and excretion of waste metabolites. Additionally, it is also handling the metabolism and excretion of drugs and other xenobiotics from the body thereby providing protection against foreign substances by detoxifying and eliminating them. The liver, a major organ of metabolism and excretion, is susceptible to a number of pathologies, classified as cirrhosis, acute chronic hepatitis and hepatitis. The liver is a major target organ for toxicity of xenobiotics and drugs, because most of the orally ingested chemicals and drugs first go to liver where they are metabolized into toxic intermediates. A large number of xenobiotics are reported to be potentially hepatotoxic (Ajith et al., 2007). Hepatocytes, which make up the majority of the liver structure, are very active in the metabolism of exogenous chemicals, and this is one of the major reasons why the liver is a target for toxic substances (Timbrell, 2001). During the detoxification of xenobiotics, reactive oxygen species (ROS) are generated which cause oxidative stress (Kohen and Nyska, 2002) which leads to the hepatic damage.

Liver cell injury caused by various toxicants such as certain chemotherapeutic agents, carbon tetrachloride, thioacetamide etc., chronic alcohol consumption and microbes is well-studied. Enhanced lipid peroxidation during metabolism of ethanol may result in development of hepatitis leading to cirrhosis. In recent times lots of interest has been generated to find out a natural remedy for hepatic disorders caused by toxins like alcohol and hepatitis virus. The agent should protect against such damage, especially of one which facilitates regeneration by proliferation of parenchymal cells after damage and arrest growth of fibrous tissue. There is no remedy for liver diseases which are so prevalent in the population. The treatment is mainly symptomatic. (Regeet al., 1984)

Liver disease is one of the major causes of morbidity and mortality in public, affecting humans of all ages. About 20,000 deaths occur every year due to liver disorders. Scientists and some industrialists deliberated on various prospective plant remedies for ailments of
liver disorder management Indian Council of Medical Research, New Delhi, in its revived research on traditional medicine, had adopted liver diseases as one among six thrust areas and for multidisciplinary study Hepatitis continues to be a major health problem in urban areas in India

Since time immemorial, mankind has made the use of plants in the treatment of various ailments. The Indian Traditional Medicine like Ayurveda, Siddha and Unani are predominantly based on the use of plant materials. Indian medicinal plants have been recognized and are extremely valued all over the world as a prosperous source of bioactives for the prevention and treatment of various ailments. Herbal medicines are being used globally of the world population primarily in the developing countries for primary health care. They have stood the test of time for their safety, efficacy, cultural acceptability and minimal side effects. Conventional and synthetic drugs used in the treatment of liver diseases are sometimes inadequate and can have serious adverse effects.

Steroids, vaccines, and antiviral drugs, have been used as therapies for liver pathologies, have potential adverse side-effects, especially if administered chronically or sub-chronically. Current medical treatments for these liver diseases are often ineffective, and therefore efforts are being made to seek new effective medications (Seeff et al., 2001). Developing pharmacologically effective agents from natural products has become a new trend by virtue of their little toxicity or few side effects. There are few plant derived drugs in the market which are used for the liver disorders

In spite of the tremendous advances in modern medicine, no effective drugs are available, which stimulate liver functions and/or offers protection to the liver from damage or help to regenerate hepatic cells (Chatterjee, 2000). In the absence of reliable liver protective drugs in modern medicine, there exists a challenge for pharmaceutical scientists to explore the potential of hepatoprotective activity of plants based on traditional use (Witte et al., 1983). A large number of medicinal preparations are recommended for the treatment of liver disorders (Chatterjee, 2000) and quite often claimed to offer significant relief. Study of many traditional plants used for liver problems led to the discovery of active compounds yet developed to successful drugs. Silymarin (Morazzoni & Bombardelli,
1995), schisandrin B (C Yong et al., 2000), phyllanthin, hypophyllanthin, picroside I and kutkoside (Ram, 2001) are examples of natural antihepatotoxic compounds derived from traditional herbs. About 600 commercial preparations with claimed liver protecting activity are available all over the world. About 100 Indian medicinal plants belonging to 40 families are components of liver herbal formulation (Handa et) however we do not have satisfactory remedy for serious liver diseases. So the search for effective hepatoprotective formulation continues.

Despite the significant popularity of several herbal medicines in general, and for liver diseases in particular, they are still unacceptable treatment modalities for liver diseases. The limiting factors that contribute to this eventuality are:

a) Lack of standardization of the herbal drugs
b) Lack of identification of active ingredient(s)/principles(s)
c) Lack of randomized controlled clinical trials (RCTs)
d) Lack of toxicological evaluation

The aim of the present is to develop and evaluate a hepatoprotective formulation using the selected medicinal plants having hepatoprotective activity and can be used in acute as well as chronic hepatic damage.