INTRODUCTION
Liver, the key organ of metabolism, is continuously and variedly exposed to drugs and xenobiotics and plays an important role in the disposition of foreign substances. It is susceptible to first and persistent attack by the offending agents like viruses, chemicals, toxins, peroxides, drugs, environmental pollutants.

Liver diseases originate from toxins and drugs which gain access to the liver, in undesirable amounts and thus pose serious clinical concern. About 20000 deaths occur each year due to liver diseases. Although virus is the main cause of liver diseases, excessive drug therapy is another major cause.

Liver diseases are of very diverse nature with differing etiologies, which may be classified into acute or chronic hepatitis (inflammatory liver diseases) and hepatosis (non-inflammatory disorders). Hepatic fibrosis is a common response to chronic liver injury from many causes. Fibrosis is an accumulation of fibrous tissue resulting from an imbalance between several types of liver cells. As liver cell structure change, the function of the liver is altered. When the liver becomes permanently injured and scarred, the condition is called cirrhosis. This chronic disease results from slow deterioration of the liver.
The liver diseases appears to be common in lower socioeconomic strata due to malnutrition and exposure to toxins leading to recurrent infections. In India 90% of jaundice is due to infectious hepatitis. Lack of awareness among the people regarding its consequences, malnutrition, poor sanitation, exposure to air pollutants, industrial chemicals and pesticides aggravate the liver problems.

The Indian Council of Medical Research, New Delhi, in its revised research on traditional medicine has adopted liver disorders as one among six thrust areas for multidisciplinary study.

**Drug induced liver toxicity**

The amount of medicines consumed has increased greatly, resulting in dangers to the liver. As a result liver, the detoxifying factor in the body, has become an increasingly overworked organ.

Liver toxicity induced by the chemicals and drugs has been recognized as a toxicological problem for over 100 years. Liver injury is not a single entity; the lesion observed depends not only on the chemical agent involved, but also on the period of exposure. After acute exposure, one usually finds lipid accumulation in the hepatocytes, cellular necrosis, or hepatobiliary dysfunction, whereas
cirrhotic or neoplastic changes are usually considered to be the result of the chronic exposure. Different biochemical alterations may lead to the same endpoint; no single mechanism seems to govern the appearance of degenerative changes in the hepatocyte of alterations in its function.

Some forms of liver injury have been found to be reversible, while others result in a permanently deranged organ. The mortality associated with various forms of liver injury may vary. The incidence of injury can differ among species, and the presence of a dose-response relationship may not always be apparent.

Manifestations of hepatotoxicity produced by drugs are of extremely varied nature. There are agents which produce acute toxic hepatitis: Carbon tetrachloride, paracetamol, metals such as iron, cadmium, copper, lead, tetracycline, anaesthetic agents, frusemide etc. The manifestations are jaundice, periportal necrosis, fatty infiltration. There are certain drugs which cause less severe toxic hepatitis such as immunosuppressants, chlorambucil, methotrexate, salicylates, but their overuse causes hypersensitivity, necrosis and occasional fibrosis. Indisysncratic drug reactions (obstructive jaundice, cholestatic lesions, hepatic drug reactions) are caused by anabolic steroids, phenothiazines, anti-tubercular drugs,
chlorpromazine, methimazole, phenylbutazone, phenytoin, sulphonamides, hydralazine etc.

In certain cases a diffused type of hepatocellular damage also occurs by certain drugs such as antidepressants, anti-TB drugs, anti-convulsants, anti-inflammatory drugs, antibiotics, anti-bacterial drugs. There are numerous reports in the literature of liver damage (jaundice, cholestatic lesions) caused by anaesthetic agents, oral contraceptives, hypoglycaemic agents (Davies, 1999).

Drugs which are given for prolonged period of time and in high doses pose serious clinical concern.

One such category of drugs is anti-tuberculosis (anti-TB) drugs. Recently there has been a resurgence of tuberculosis (TB) in a number of countries including India. It has been revealed in a single large study that incidence of drug induced hepatotoxicity in indoor patients is caused almost all by anti-TB drugs (Kshirsagar, 1992).

It has been estimated that approximately one third of the world’s population is infected with *Mycobacterium tuberculosis*. This reservoir of infected persons results in 8 million new cases of TB and 2.9 million deaths annually.

The use of multidrug regimen for the treatment of TB with the combination of rifampicin (RIF), pyrazinamide (PZA) and isoniazid
(INH) is a highly effective therapy. However, it is offset by an increased incidence of drug-induced hepatitis which often necessitates the cessation or modification of treatment.

The reported risk factors for the development of anti-TB drug-induced hepatotoxicity include old age, high alcohol intake, malnutrition, chronic liver disease, and viral hepatitis. Chronic liver disease and viral hepatitis are also known to increase the risk of drug-induced liver injury. The relative risk of each individual category is not well defined.

There is no consensus as to which particular factors, whether alone or in combination are involved in the development of drug-induced liver injury (Wong et al, 2000).

Despite immense scientific advances made in the last 50 years, effective management of hepatotoxicity has remained elusive.

Modern drugs have very little to offer for the alleviation of drug-induced hepatic ailments. The currently available therapeutic agents are (a) steroids and other chemotherapeutic agents which have severe limitations (b) some vaccines have also been developed against the specific viral hepatitis but are expensive and beyond the reach of common man in this country.
In the absence of a reliable liver protecting agents, herbal medicines are receiving renewed attention worldwide. The traditional medicine all over the world is now a days revalued by an extensive activity of research on different plant species and their therapeutic principles. In the same context therapeutic antifibrotic drugs are also still at an experimental stage. The major problems in developing antifibrotics are toxicity owing to the need for chronic administration and lowered therapeutic effects, when agents are used clinically (Nan et al 2001). Numerous such medicinal plants and their formulations are used for liver disorders in ethnomedical practices as well as in traditional systems of medicine in India (Sharma et. al., 1993).

One of the most reputed of these is *Emblica officinalis* (Amla), which finds use in several polyherbal formulations. There are numerous reports showing its diverse pharmacological activities.

A Review of Literature of the last 20 years has been presented in succeeding section which reveals that *Emblica officinalis* (Amla) fruit, has not been subjected to systematic scientific evaluation to assess its hepatoprotective activity against toxicity caused by variety of chemicals and drugs especially the anti-TB drugs.

The objective of the present study has been to investigate the potential of *Emblica officinalis* (fruits) as (a) anti-fibrotic and (b)
hepatoprotective against chemical and drugs particularly in the reversal of toxicity caused by anti-TB drugs (RIF, PZA and INH), either alone or in combination.