Chapter One

INTRODUCTION
Liver plays an astonishing array of vital functions in the maintenance and performance of the body. Some of these major functions include carbohydrate, protein and fat metabolism, detoxification and secretion of bile which among other things has an important role in digestion.

Liver diseases appear to be on increase in our society. Part of this increase may be due to our frequent contact with chemicals and other environmental pollutants. The amount of medicine consumed has increased greatly with resulting dangers to the liver. The liver, the detoxifying factory in the body, has become an increasingly overworked organ. While those who smoke, abuse alcohol and drugs and live in severely polluted environments are at great risk, we all suffer some threat of damage or disease to the liver (Scott 1998).

Though a strict delineation of various hepatic disorders is not possible yet from didactic point of view, liver disorders may be classified as Acute or Chronic Hepatitis, Hepatosis and Liver Cirrhosis (Morgan, 1985). The predominant type of liver disease varies according to country and may be influenced by local factors. For 1989 it was estimated that there were some 200 million chronic carriers of hepatitis B virus of which 40% were expected eventually to die of hepatocellular carcinoma and 15% of cirrhosis (Evans 1996).

In spite of the tremendous advances made in allopathic medicine, except for the use of the appropriate vaccine for the treatment of hepatitis caused by viral infection, there are few effective cures for liver diseases. A
considerable interest has therefore, developed in the examination of traditional plant remedies.

Herbal drugs have gained importance in recent years because of their efficacy and cost effectiveness (Subramonium, 1999). There are numerous plant and polyherbal formulations claimed to have hepatoprotective activities. About 600 commercial preparations with claimed hepatoprotective activity are available all over the world. Nearly 170 phytoconstituents from 110 plants belonging to 55 families have been claimed to possess liver protecting activity. In India more than 87 medicinal plants are used in different combinations in the preparation of 33 patented herbal formulations (Handa, 1986). Only a small portion of hepatoprotective plants as well as formulations used in traditional medicine stand pharmacologically evaluated for their efficacy.

*Cichorium intybus* and *Taraxacum officinale* have been claimed to possess hepatoprotective activity and *Cichorium intybus* is also a constituent of various Patent marketed Indian formulations for liver ailments.

*Cichorium intybus* Linn. (commonly known as Chicory or Kashni in Kashmir) is used in Indian medicine as a tonic. It is said to be useful in fevers, vomiting, diarrhoea and enlargement of spleen. Its root is reported as stomachic and diuretic. It has been reported to be useful in jaundice, liver enlargement, gout, and rheumatism. Roots are used as blood purifier, emmenagogue and asthma. Alcoholic extract is antimicrobial against micro-organisms causing gingival inflammation. Its seeds have been reported to be carminative, agglutinating and cholagogue (Chopra 1955, Kirtikar 1933, Wealth of India Vol 10)
In mice liver protection was observed at various doses of *Cichorium intybus* but optimum protection was seen with a dose of 75mg /kg given 30 minutes after Carbon tetrachloride intoxication (Kalantri and Rastmansh, 1997). Different fractions of alcoholic extract and one phenolic compound AB-IV of seeds of *Cichorium intybus* have been found to possess a potent antihepatotoxic activity comparable to standard drug Silymarin -Silybin-70 (Bahar et.al 2003).

Seven compounds have been isolated from the roots of *Cichorium intybus* and four of them identified as alpha-amyrin, taraxerone, baurenyl acetate and beta-sitosterol (Du, H et.al 1998). *Cichorium intybus* root callus extract has been reported to afford better protection against Carbon tetrachloride induced hepatocellular damage (Zafar .R, 1998).

*Taraxacum officinale* (Dandelion, Hand in Kashmir) is mainly used for kidney and liver disorders in the traditional system of medicine. Juice of the fresh plant is said to be effective against liver diseases, chronic hepatitis, visceral congestion, intermittent fever and hypochondria (Bhatacharya, 2001). Combined with other active remedies, it has been used in cases of dropsy and for induration of the liver (Chopra 1956). Its root has been reported to contain sesquiterpene lactones, triterpenes, carbohydrates, carotenoids, flavanoids, minerals etc.(Bradley1992). Root of *Taraxacum officinale* has also been indicated in Eczema, Jaundice, spleen, gall bladder and diabetes etc. (Wichtl & Bissett, 1994).
Different models are available for inducing liver cell damage in experimental animals.

**Carbon tetrachloride** intoxication in rodents is a commonly used model of both acute and chronic liver injury. Administration of carbon tetrachloride causes hepatocyte injury that is characterized by centrilobular necrosis followed by hepatic fibrosis (Chundong et.al 2002). It is an infrequent cause of accidental and occupational poisoning. It is used in home and in industry as component of cleaning fluids and degreasing agents. There is marked individual susceptibility to the level of exposure.

**Paracetamol** (acetaminophen) is widely used antipyretic and analgesic that seems safe when taken in therapeutic doses but larger amounts may cause fatal hepatic necrosis (Prescott et.al 1971). This necrosis is primarily centrilobular but may also extend through the midzonal area towards the periportal areas (Hinson 1980; Mitchell 1973a).

Liver injury will develop in all patients who ingest sufficient paracetamol becoming evident biochemically within 24-48 hrs after the time of ingestion. Typically such massive ingestion represents deliberate suicide attempts or accidental poisoning usually in children (Black 1980; James and Lesnam 1975).

Both *Cichorium intybus* and *Taraxacum officinale* are found abundantly in Kashmir which have been used by the practitioners of traditional system of medicine in treatment of liver disorders for pretty long time. However, no systematic study is available on the efficacy of *Taraxacum officinale* while some reports are available on *Cichorium intybus* for hepatoprotective activity.
With this background, the present work entitled "STUDY OF PROPHYLACTIC AND CURATIVE EFFECT OF CICHORIUM INTYBUS LINN. AND TARAXACUM OFFICINALE WEBER. AGAINST HEPATOCELLULAR DAMAGE INDUCED IN EXPERIMENTAL ANIMALS" was undertaken to screen Cichorium intybus and Taraxacum officinale for prophylactic and curative hepatoprotective activity using carbon tetrachloride and paracetamol as hepatotoxic agents in two animal species.