Aims & Objectives
2. AIMS AND OBJECTIVES

In third world country like India, liver diseases are most common. Acute hepatitis and viral hepatitis are most frequent, caused by infectious agents, particularly viruses, toxins and drugs. Patients with liver disease often present with characteristic symptoms and signs, but the clinical features may be non-specific and in some patients, liver disease is discovered incidentally. Alcoholic liver disease continuous to be the most serious liver disorder throughout the world and in India, chronic over indulgence in alcohol is a common cause of hepatic cirrhosis, which may produce fatty liver to hepatitis.\(^{12}\)

Management involves support of vital function and correction of metabolic imbalances. Respiratory failure, may necessitate artificial ventilation and haemodialysis may be necessary if renal failure occurs. Artificial hepatic support has little to offer and hepatic transplantation are being considered in severe liver diseases.\(^{12}\) As with cirrhosis, the advent of liver transplantation as treatment for fulminant hepatic failure has been highlighted, but donor organs are scarce and careful patient selection is vital. Following surgery, the major complications are immediate non-function, infection and rejection. Moreover, the expenses involved in the treatment is so high, that most of the individuals are unable to afford it.

As there is no confirmed remedy to this dangerous situation which is often irreversible and fatal, the present study has undertaken a systematic search to identify the active principle, in the aqueous extract of the leaves of *Cajanus indicus*. As mentioned earlier, in Ayurvedic system of medicine, the plant *Cajanus indicus* is used in the treatment of various types of liver disorders.\(^{49-51}\) Studies has been made to isolate, purify and characterise the active principle, responsible for hepatoprotection from the above plant.

Drug induced liver damage may have toxic effects when used in therapeutic doses; this response (idiiosyncratic hepatotoxicity)\(^{12}\) is unpredictable and is independent of the dose of the drug administered. Some idiosyncratic reactions to drug, such as halothane-induced liver damage, have an immunological basis, the binding of a metabolite to a liver cell protein alters its antigenicity and provokes an immune response.

Moreover, Tumor necrosis factor-alpha (TNF-\(\alpha\)) is elevated in the sera of rats administered with non-lethal doses of carbon tetrachloride followed by endotoxin.\(^{124,125}\) Elevated TNF-\(\alpha\) levels are correlated with the increased release of hepatic enzymes indicating hepatic damage. Under these conditions, nitric oxide (NO) was also produced in the liver as
evidenced by the formation of nitrosyl complexes. TNF-α and NO are induced following CCl₄, β-galactosamine and other hepatotoxins and lipopolysaccharide (LPS) exposure. TNF and NO may be important regulators in the hepatotoxicity of the liver injury model.

Therefore, it is necessary to see if this herbal extract or the active principle of the above plant directly or indirectly affect the TNF production from the Kupffer cells of the liver or not. Moreover, it is reported that in acute and chronic viral hepatitis, prolonged use of antibiotics suppress the function of both T and B cell mediated immunity and attempts are being made to immunomodulate immunosuppressed conditions. As T cells play a very crucial role in our immune surveillance system, a suppression in its activity might precipitate in wide variety of diseases. The present study thus critically evaluates the effects of *Cajanus indicus* on some non-specific and specific aspects of immunity in mice and rats.

The following programme of research has been carried out for this study:

(i) Isolation and identification of the active principle from the said plant.
(ii) Purification and characterization of the active principle.
(iii) Comparative study of liver damage induced by different hepatotoxins, namely CCl₄, acetaminophen or paracetamol, β-galactosamine HCl, ethanol and evaluation of the protective role of the active principle in each case.
(iv) Histopathology and electron microscopy of liver to study the comparative effects of the hepatotoxicants induced liver damage at ultrastructural level.
(v) Isolation of rat hepatocytes and assay of hepatoprotective activity.
(vi) Role of the active principle in cell-mediated and humoral immunity.