Chapter 2

Aims and Objectives

2.1 EVOLUTION OF THE PROJECT

In the treatment of T1DM, even today the best medicine is insulin and the route of administration is injection. In case of T2DM, many oral antidiabetic agents are available and most of them are synthetic API. An oral antidiabetic is found to be able to maintain normoglycaemia on chronic administration lasting only for 3 to 5 years. On long term therapy with oral antidiabetics, it is observed that a T2DM patient requires insulin injection for adequate control of glucose level. In addition to that, progressive development of dyslipidemia with increase in both circulating triglycerides and very low-density lipoproteins (VLDL) occurs. This increases morbidity and mortality due to cardiovascular complications in diabetic patients (Wincour P H et al. 1989). Thus the efficacy of currently used antidiabetic drugs is compromised in several ways.

In addition to that, these agents do not have the ability to improve insulin sensitivity, to prevent progressive damage of β-cell death or the ability for regeneration of β-cells of the pancreas. Any alternative medicine which could address the above points should be encouraged.

In the first decade of 21st century, WHO approved the use of traditional medicines as a part of their health programme. Now many neutraceuticals are available and are being consumed for perceived benefits in health care and improvement of the quality of life.

Two medicinal plants with acclaimed antidiabetic activity in the Indian system of medicine were selected for the study.

1. *Hemionitis arifolia* (Burm.f) T.Moore. (*Hemionitidaceae*)
2. *Chonemorpha macrophylla* (Moon) Alson. (*Apocyanaeaceae*)

Investigating these plants chemically and for the said activity was thought worthwhile.
2.2 OBJECTIVES OF THE PROPOSED STUDY

- Preliminary pharmacognostical studies.
- Preparation of 95% and 50% hydroethanolic extracts.
- Preliminary phytochemical studies.
- Chromatographic separation of the extract based on polarity.
- Separation of the API present in the lead fraction, characterization of the isolated components using melting point, UV $\lambda_{\text{max}}$, IR, NMR and LCMS studies.
- Quantification of API with HPLC and LCMS-MS methods.
- **Invitro** antioxidant studies to evaluate the antioxidant property of different extracts.

Good antioxidants are found to prevent degeneration of tissues; so they are expected to prevent deterioration of $\beta$-cells of the pancreas also. Many of the naturally occurring identified antidiabetics are found to possess antioxidant properties also.

- **Invitro** toxicity studies by MTT assay on L-6 muscle cell lines
- **Invitro** $\alpha$-amylase, $\alpha$-glucosidase and DPP-IV inhibition studies.

Alpha amylase inhibitors delay/prevent hydrolysis of polysaccharides to disaccharides. Similarly $\alpha$-glucosidase inhibitors will delay/prevent hydrolysis of disaccharides. So, they are good in preventing postprandial glucose shootup in diabetics. DPP-IV inhibition prevents the destruction of incretin hormones GLP and GIP. These two hormones present in the intestine facilitate glucose uptake in the intestine.

- **Invitro** glucose uptake studies using L-6 muscle cell lines for identification of plant, selection of plant, selection of extract and identification of lead fraction.
This method is followed to minimize the use of animals in the biological studies by following RRR concept.

- Glut-4 translocation studies and PPARγ studies for identification of the mechanism of action.
- Rat hemidiaphragm method for glucose uptake studies and confirmation of antidiabetic activity in male *Wistar albino* rats in the streptozotocin induced diabetic model.
- Histopathological evaluation of the efficacy of the extracts.