PREFACE

At present about 347 million people worldwide have diabetes. The prevalence of diabetes for all aged groups worldwide is estimated to be 4.4% in 2030. If this emerging global epidemic is not controlled, it will affect the humanity in a serious way.

Diabetes is described as one among the metabolic disorders characterized by chronic hyperglycaemia. As it is one among the noncommunicable diseases, making people aware about the cause and prevention can control the rapid increase in diabetic population.

In the presently used antidiabetic regimen, orally active antidiabetics and insulin therapy are followed. Better efficacy coupled with minimum side effects is always a much sought after dictum in chemical therapeutics. Plant sources have always been rich treasures of varied chemical entities which can provide the lead molecules required to achieve the above goal.

The sequence followed in the text is the identification of the plant followed by extract preparation from shade dried plants, phytochemical analysis, antioxidant studies, *in vitro* antidiabetic screening, *in vivo* antidiabetic studies, identification of active constituents, docking studies and evaluation of mechanism of action.
ABSTRACT

In the literature survey, it was found that many plants are utilized as antidiabetic agents, many of which have not been investigated for this purpose. The above claimed property of the plants *Chonemorpha macrophylla* and *Hemionitis arifolia* were evaluated in this study adopting scientific methods.

Phytochemical analysis of the hydroethanolic extract of both the plants revealed the presence of plant phenolics and flavonoids. Antioxidant studies of the extract of both the plants were performed using ABTS, DPPH, nitric oxide scavenging and lipid peroxidation inhibition methods and the results were promising.

In the next step, glucose uptake studies using L-6 muscle cell lines were performed and the values demonstrated by ME-CMRH (500 µg/ml) and standard drug metformin (100 µg/ml) were 68.5±7.33% and 115.8±3.4% uptake respectively over normal control. This active faction was tested for acute toxicity in female *Wistar albino* rats by following OECD 423 guidelines and the LD$_{50}$ was decided as 2000mg/kg body weight.

The above identified active fraction was used for animal studies in male *Wistar albino* rats. The percentage change in blood glucose level of diabetic animals treated with ME-CMRH (500 mg/ml) and standard drug Gliclazide (25 mg/kg) were 52.55±1.42 and 56.22±1.76 respectively.

*In vitro* screening methods were performed by enzyme inhibition methods and cell line studies. IC$_{50}$ values of CMRH in α-amylase inhibition studies and of ME-CMRH in α-glucosidase inhibition studies were greater than 1000 µg/ml and 249.50±2.35 µg/ml respectively. At 500 µg/ml concentration ME-CMRH showed 20.8% of DPP-IV inhibition. In the GLUT-4 translocation studies and PPARγ upregulation studies, ME-CMRH showed 0.31 and 0.3 fold upregulation compared to the standard drug metformin treated cells. The components identified in the active fraction of ME-CMRH were quercetin, rutin, and gallic acid.

The IC$_{50}$ value of defatted HALH in the α-amylase inhibition assay was found to be greater than 1000 µg/ml. In the DPP-IV inhibition studies, defatted HALH at a
concentration of 500 µg/ml demonstrated 15.83% inhibition compared to the standard Ile-Pro-Ile. In the GLUT-4 translocation studies performed, defatted HALH showed 0.15 fold upregulation compared to standard metformin. The components identified in defatted HALH were quercetin, rutin, apigenin and kaempferol.

Docking studies of all the above components were also performed and the glide score of all the molecules were found to be in the range of -6 to -11. The molecules were also found to obey the Lipinski’s rule of five.