ABSTRACT

The objective of the current study was to evaluate the protective effect of polyherbal formulation (PHF) in streptozotocin (STZ) induced diabetic rats, dexamethasone induced insulin resistance models and to investigate the relationship between hyperglycemia and cognitive impairment in selected in vitro and in vivo models.

Three plants roots of *Casearia elliptica* (Family- Flacourtiaceae), whole plant of *Cissus quadrangularis Linn* (Family- Vitaceae) and root tubers of *Cyperus rotundus* (Family- Cyperaceae) were selected for the study and screened for hypoglycemic and antidiabetic activity in oral glucose tolerance test and STZ (40 mg/kg, i.p) induced diabetic model. The parameters estimated were change in body weight, blood glucose, lipid profile, liver enzymes and histopathology of pancreas.

Polyherbal formulation was prepared from the EC50 values obtained from OGTT of three plant extracts in various doses. Antidiabetic effect of PHF was studied similar to that of individual plant extracts. Dexamethasone induced insulin resistance model was also employed to understand the effect of PHF on cognitive impairment by measuring insulin sensitivity, acetylcholinesterase levels (AchE), behavioural, and histopathology of brain. To explore the probable mechanism of action in vitro studies were performed with individual plant extracts and PHF to study their effect on α-glucosidase, α-amylase, total phenol and flavonoid content. MTT assay and hyperglycemia-induced ROS was also studied in SH-SY5Y neuronal cells using Carboxy-H$_2$DCFDA as marker dye.

The plant extracts individually exhibited hypoglycemic and antidiabetic effect by significantly reversing the STZ induced changes in body weight, lipid profile, liver enzymes, liver glycogen content and histological changes of pancreas.

PHF showed a significant synergistic effect in STZ induced diabetic rats and restored the parameters to normal. It also improved the insulin sensitivity, behavioural changes in dexamethasone treated rats and significantly ameliorated the cognitive impairment induced by dexamethasone by decreasing the levels of AchE in brain.

The in vitro findings of the study revealed that PHF showed significant synergistic effect in all the parameters compared to individual plant extracts. The PHF exhibited
significant inhibitory effect on α-glucosidase and α-amylase. It also showed protective role in central nervous system by markedly inhibiting the ROS generated by hyperglycemia, which was supported by histopathology findings in hippocampal region of rat brain. These results suggest that PHF has hypoglycemic and neuroprotective activity in diabetes induced cognitive impairment.

**Key words:** Antidiabetic activity, *Casearia elliptica, Cissus quadrangularis, Cyperus rotundus*, HOMA-IR, Insulin Resistance, Insulin Sensitivity, SH-SY5Y neuronal cells.