ABSTRACT

The main objective of the present study is the phytochemical and pharmacological evaluation of aerial parts of *Grewia serrulata* DC for its anti-diabetic activity in experimental animal models.

Initially shade dried plant material was powdered and evaluated for physicochemical properties and successive solvent extraction of plant powder was carried out using different solvents. The obtained extracts were subjected to phytochemical screening. Aqueous and ethanolic extracts of aerial parts of *Grewia serrulata* DC (AEGS & EEGS) were subjected to acute oral toxicity and sub-acute toxicity studies as per OECD guidelines 423 and 407. The doses 200mg/kg and 400mg/kg of aqueous and ethanolic extracts were selected for the evaluation of therapeutic efficacy based on their LD<sub>50</sub> values. These two extracts were then screened for anti-oxidant activity both *in vitro* and *in vivo* and also evaluated for hypoglycaemic activity on glucose induced hyperglycaemic and streptozotocin induced hyperglycaemic rats. EEGS was then screened for its anti-diabetic activity both *in vitro* and *in vivo*. Ethanolic extract was subjected to isolation of bioactive principle and the obtained compound was further screened for anti-diabetic potential.

Physicochemical studies reveals the percentage loss on drying as 3.26% (w/w), high water and alcohol soluble extractive value and the high extractive yield attained by ethanol solvent. Preliminary phytochemical evaluation report illustrates that EEGS showed the existence of glycosides, saponins, phytosterols, flavonoids, phenols,
steroids, terpenoids and AEGS showed the presence of carbohydrates, saponins, phytosterols, flavonoids, steroids and terpenoids as phytoconstituents. The extracts of petroleum ether, benzene, chloroform and acetone reveal the absence of many chemical constituents.

In acute toxicity study, both AEGS and EEGS at the dose of 2000mg/kg indexed neither visible signs of toxicity nor mortality and observations did not point out any proofs of substance related toxicity. During sub-acute toxicity both extracts did not show significant change in their body weight gain, food and water usage contrasted to that of control and did not revealed any variation in haematological and biochemical parameters except a minimum hypoglycaemia and hypolipidemia.

A marked amount of phenolics and flavonoids were found in AEGS and EEGS among which EEGS is of potent. The EEGS also showed marked total antioxidant activity and ferric reducing capabilities, supporting their antioxidant property. Furthermore the test extracts have significant scavenging activity against the DPPH, Superoxide, Peroxide, NO radicals in a concentration dependent manner and provide protection against oxidative damage induced by the biomolecules. The antioxidant potential of the test extracts was further studied by taking in-vivo parameters and found that the liver lipid peroxidation products were decreased while antioxidant enzyme levels were increased in a significant extent, which evidenced the in-
**vivo** antioxidant property of the extracts supporting their anti diabetic activity.

Anti diabetic evaluation studies of EEGS revealed that, both the tested dose levels, significantly reduce blood sugar in both normoglycemic and hyperglycemic rats, both on acute and sub-acute study, as well as in glucose loaded hyperglycemic rats. The glucose lowering activity of the extract may be due to the effect of the extract on pancreatic cells and/or on the extra pancreatic site. The extra pancreatic site of action of the extract is supported by glucose uptake study, in which both the extracts showed significant activity in the peripheral utilization of glucose, which is still evidenced by recovery of body weight of the animals in sub-acute test, with fact that increased utilization and decrease storage of protein responsible for reduction of body weight essentially by depletion of body proteins. The pancreatic action of the extracts is supported by the insulin secretagogue effect of EEGS as per the study report of determination of plasma insulin levels.

Since the test report embodied in the thesis evidenced that EEGS shows comparatively better activity, hence it enforced us to isolate the new compound present in the extract, and found a flavonoid derivative having molecular formula C$_{23}$H$_{24}$O$_{12}$, bearing the IUPAC nomenclature as: 2-((3,5-dihydroxyphenyl)-5,7-dimethoxy-3-((3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl)oxy)-4H-chromen-4-one in line with the characteristics details of FTIR,$^{13}$C-NMR,$^1$H-NMR and LC-MS spectra.
2-(3,5-dihydroxyphenyl)-5,7-dimethoxy-3-((3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl)oxy)-4H-chromen-4-one isolated from ethanolic extract of aerial parts of *Grewia serrulata* DC (EEGS-C1) has promising anti-diabetic effect, which potentially improved abnormalities of diabetic conditions in high fat diet fed – streptozotocin (HFD-STZ) induced diabetic rats. The probable hypoglycemic effect of EEGS-C1 may be attributed to increase in serum and pancreatic insulin levels and due to its antioxidant property.

**Key words:** Aerial parts of *Grewia serrulata* DC, Anti diabetic activity, Streptozotocin, Anti oxidant activity, Secretagogue, Hypoglycemic, Hypolipidemic, High fat diet fed-streptozotocin.