ABSTRACT

*Andrographis lineata* Wall.ex.Nees an endemic medicinal plant of South India has been widely used as an ancient folklore medicine for the treatment of diabetes by the tribal’s of Kolli hills of Nammakal district, Tamilnadu, India. Till now there was no scientific documentation pertaining to the active principle for its antidiabetic effect.

Hence, an attempt was made to scientifically investigate the diabetic potentiality of this medicinal herb. To avoid batch to batch variation and to obtain uniform characteristic features of the plant material (phytochemicals), micropropagation techniques was employed. BAP (1.5 mg/l) supplemented with AdS (30 mg/l) produced maximum number of shoots with 25.7±0.11 shoots/explant in the shoot tip explants where as the nodal explants produced only 15.0±0.19 shoots/explant. The juvenile *in vitro* regenerated shoots were elongated in the MS medium containing GA3 (0.3 mg/l). The elongated *in vitro* shoots were rooted in IBA (1.0 mg/l). Later the plantlets were hardened and transferred to green house at 70% survival rate. The micropropagated plant was confirmed for its genetic stability using RAPD primers namely, OPA-7 and OPA-10.

The best solvent system for maximum extraction of phytochemicals was observed in ethanolic leaf extract (EtALL). The qualitative and quantitative analysis revealed the presence of potent phytochemicals for antioxidant and antidiabetic activities. The ethanolic leaf extract was subjected to *in vitro* antioxidant studies (DPPH, lipid peroxide, superoxide, nitric oxide and reducing power ability assays) which exhibited increased...
scavenging activity in dose dependent manner. There was a profound antidiabetic effect observed in in vitro model systems such as α-glucosidase, insulin mimicking and sensitization (3T3-L1 cell line).

Streptozotocin (40 mg/kg b.w.) was used to induce diabetes in rats. In vivo antidiabetic parameters such as (blood glucose, plasma insulin, glycosylated hemoglobin, carbohydrate metabolizing enzymes, lipid and protein profiles) and antioxidant parameters (SOD, CAT, TBARS, H$_2$O$_2$, ALT, ACP, LDH, AST, ALP, GSH and GPx) levels were determined. These biochemical parameters and histopathological analysis revealed the ameliorative effect of EtALL for antidiabetic activity.

Bioactivity based screening (lipogenesis) was performed in the isolated fractions (I to V) of the EtALL extract. The fraction IV (chloroform: methanol (70:30)) was found to possess significant lipogenic activity. The selected fraction (fraction IV) was further purified and subjected to spectral analysis. The bioactive compound for the antidiabetic principle was identified as Dimethyl 3, 3', 4, 4'-tetrahydroxy-δ-truxinate (DTδT).

Further evaluation of bioactive principle was carried out by gene expression profiling of PPAR-γ and C/EBP-α for adipocytes differentiation. The DTδT (active principle) decreased fat accumulation by inhibiting the expression of PPAR-γ and C/EBP-α at 25µg/ml. Molecular docking studies suggested that the DTδT was capable of binding with PPAR-γ and C/EBP-α, effectively than rosiglitazone (standard drug). Hence, DTδT may be considered as a lead molecule in developing target based antidiabetic drugs.