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Name of Research Scholar: Archana M Navale

Place : Vadodara
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Name of Supervisor: Dr. Archana Paranjape

Place: Vadodara
**NAVALE, ARCHANA M. and PARANJAPE, ARCHANA N.. "ROLE OF INFLAMMATION IN DEVELOPMENT OF DIABETIC COMPLICATIONS AND COMMONLY USED INFLAMMATORY MARKERS WITH RESPECT TO DIABETIC COMPLICATIONS", International Journal of Pharmacy & Pharmaceutical Sciences, 2013.**
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ABSTRACT

Objective

To evaluate the effect of methanolic extracts of *Anogeissus acuminata* (AA) in Diabetes mellitus and its complications like diabetic neuropathy, nephropathy and cardiovascular complications.

Methods

Type 1 DM was induced by injecting Streptozotocin (STZ), 50 mg/kg, i.p. in 6 hour fasted rats. Rats with DM were treated with methanolic extracts of AA for 8 weeks at doses 100 and 300 mg/kg, orally. Human NPH Insulin (4 IU/kg, s.c.) was used as standard treatment. Plasma glucose levels (at 1, 2, 4, 8 weeks) and oxidative stress parameters (at 2 and 4 weeks) were assessed. Effect on diabetic nephropathy was evaluated by recording kidney weights, serum creatinine, blood urea nitrogen (BUN) levels (at 8 weeks). Effect on neuropathy was evaluated by hot plate test (at 4 weeks), formalin test (at 6 weeks), intestinal charcoal meal test and sciatic nerve conduction velocity (at 8 weeks).

Type 2 diabetes mellitus was induced in fructose fed rats by injection of STZ 40 mg/kg, i.p. in 6 hr fasted rats. Glibenclamide 5 mg/kg, p.o. was used as standard drug. Plasma glucose levels (at 2, 4, 8 and 11 weeks), insulin levels (at 11 weeks), glycated Hb (at 11 weeks), lipid levels (at 2 and 12 weeks) and oxidative stress parameters (at 2 and 12 weeks) were evaluated at specified time points. At the end of 12 weeks of treatment, mean blood pressure was determined by carotid artery cannulation, heart rate and force of contraction of isolated heart was determined using Langendorff heart technique. Heart weight, left ventricular weight and Serum CK-MB and LDH levels were measured. Insulin resistance and β cell function was determined using Homeostatic Assessment method. Preliminary phytochemical screening of both extracts was done as per standard protocol. Quantification of tannins and flavonoids was done in extracts by AOAC official method and spectrophotometry respectively. HPTLC fingerprinting was performed using quercetin and gallic acid as marker compounds. *In vitro* anti-oxidant activity of the extracts was assessed by DPPH assay, Reducing power assay and Thiobarbituric acid method. *In vitro* PTP 1B inhibitory activity of the extracts was measured using *in vitro* ELISA kit.
Results

Methanolic extracts of AA produced statistically significant (p< 0.05) hypoglycemic and antioxidant effect in animals with T1DM as well as T2DM. AA treatment could prevent elevations of serum creatinine and blood urea nitrogen levels in a dose dependent manner. Kidney hypertrophy could be attenuated remarkably as reflected by significantly lower kidney weight/100 gm body weight ratio (p< 0.05). AA treated rats exhibited beneficial effect on markers of neuropathy like, thermal and chemical hyperalgesia, charcoal meal transit and nerve conduction velocity as compared to diabetic rats (p< 0.05). Treatment with AA extracts also resulted in significant reduction in plasma glucose, HbA1C, lipid levels and oxidative stress parameters in Fructose fed STZ injected rats type 2 DM rats. DC rats had high levels of insulin resistance and reduced β cell function as assessed by HOMA method, while AA treated rats demonstrated significantly lower insulin resistance and improved β cell function. It could also prevent remarkably the development of cardiomyopathy as evaluated at 12 weeks. AA treatment resulted in improvement in cardiac and left ventricular hypertrophy as reflected by lower cardiac and left ventricular hypertrophy index. It could successfully improve the levels of cardiac enzyme markers like LDH and creatine kinase levels in a dose dependent manner. AA treatment could efficiently prevent abnormalities of haemodynamic parameters like mean blood pressure and heart rate in diabetic animals. Phytochemical investigation of AA extracts revealed the presence of abundant tannins and flavonoids in addition to several other secondary metabolites. Leaf extract was found to have 24.57% and 14.5% w/w tannins and flavonoids respectively, while bark showed presence of 13.63% and 57% w/w tannins and flavonoids respectively. HPTLC fingerprinting demonstrated several peaks, out of which one peak of leaf extract corresponded with that of gallic acid and one peak of bark extract matched with quercetin peak. Both extracts of AA also exhibited potent antioxidant activity in in vitro antioxidant assays. The in vivo beneficial effect of AA extracts on insulin resistance was confirmed by their ability to inhibit PTP1B activity.

Conclusion

The results suggest that methanolic extracts of AA exerted hypoglycemic and antioxidant effect on diabetic rats, which was comparable to that of standard. The treatment was also
able to attenuate development of diabetic complications like nephropathy, neuropathy and cardiovascular complications.

Keywords

Anogeissus acuminata, Diabetes mellitus, Diabetic nephropathy, Diabetic neuropathy, Cardiovascular complications.