ABSTRACT

Background: Medicinal plants are well documented for treating diabetes mellitus however, their efficacy and safety after prolonged use is not scientifically established. *Abroma augusta* L. (Malvaceae) has been traditionally used to treat diabetes in India and Southestern Asia. The scientific evidence on antidiabetic activity of *A. augusta* from Malaysian origin has not been reported so far.

Objective: The objective of present study is to evaluate the antidiabetic potential of ethanolic extract of *Abroma augusta* in STZ induced type 2 diabetic Sprague Dawley rats.

Methods: Qualitative and quantitative phytochemical analysis were carried out using standard procedures. Antioxidant activity was determined by 2,2-Diphenyl-1-picryl-hydrazyl (DPPH) and ferric reducing antioxidant power (FRAP) assay. Polyphenols and ascorbic acid were identified using high performance liquid chromatography (HPLC). Initially, acute toxicity studies were carried out as per the guidelines of OECD. Based on the result of acute toxicity studies, the antidiabetic activity of ethanolic extract of *A. augusta* leaf was evaluated in streptozotocin induced diabetic rats orally administered at the dose of 120, 140 and 160 mg/kg body weight and glibenclamide (6 mg/kg) as standard drug daily for 28 days. The changes in body weight, food and water intake were monitored. Biochemical parameters (blood glucose, lipid profile and liver enzymes) and histopathology of pancreas, liver and kidney were also studied. Besides, specific glucose regulating gene expression (*Slc2a2* and *Pck1*) were studied by RT-PCR.

Results: Qualitative analysis of *A. augusta* leaf extract showed the presence of reducing sugar, tannins, alkaloids, phenols and flavonoids. Total phenolic and flavonoid content were found to be 15.76±0.16 mg GAE/g and 8.6±0.11 mg QE/g respectively. Antioxidant activity showed that the IC_{50} value was 790±3.6 µg/ml and 367.6±16.9 mg $FeSO_4E$/g by DPPH and FRAP assay respectively. The HPLC analysis of EEAAL indicated the presence of gallic acid,

quercetin and ascorbic acid. Acute toxicity study revealed that 1400 mg/kg body weight was found to be the safe dose. Water and food intake, fasting blood glucose, serum cholesterol, triglycerides, low density lipoproteins (LDL), very low density lipoproteins (VLDL), alanine aminotransferase (ALT), aspartate aminotransferase (AST), were significantly ($p<0.05$) decreased while, high density lipoproteins (HDL) and body weight were increased in ethanolic extract of *A. augusta* and glibenclamide treated group rats compared to diabetic control rats. Histopathological study of pancreas in *A. augusta* and glibenclamide treated rats showed significant regeneration of β cells of islets of Langarhans compared to diabetic control. The histopathological study of liver and kidney in experimental animals indicated that EEAAL was not toxic. Further, the *A. augusta* extract treated rats showed expression of glucose transporter 2 (*Slc2a2*) and phosphoenolpyruvate carboxykinase (*Pck1*) genes.

Conclusion: This study provided ample evidences for significant antidiabetic activity of *A. augusta* which may be attributed to prevention of oxidative stress and regeneration of β cells of islets of Langerhans leading to increased secretion of insulin which would have facilitated transport of glucose in to the cells. In addition the results conclusivey proved the role of *Abroma augusta* in activatiing *Slc2a2* (GLUT2) and *Pck1* genes. The future studies shall be directed towards identification of active biomolecule and elucidation of the molecular and biochemical mechanisms involved in the antidiabetic effect of *A. augusta* in providing a safe alternative treatment for diabetes.

Keywords: *A. augusta*, antidiabetic activity, type 2 diabetes, histopathology, gene expression.