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Mikania Scandens Leaves Possess Potent & Prolong Antidiabetic Effect in Alloxan Induced Diabetes Mice

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Abstract

Mikania scandens (M. scandens) has been proposed to have several medicinal values for different ailments. This study evaluated the ethanolic extract of *M. scandens* leaves for its phyto-constituents, hypoglycemic, hypolipidemic and hepatoprotective effects in Alloxan Induced Diabetic Mice (AIDM). Phytochemical analysis was conducted using standard procedures while the anti-diabetic and hepatoprotective effects were determined using AIDM. The results of the phytochemical screening indicated the presence of steroids, alkaloids, phytosterol, flavonoids, phenolic compound, fatty acids and glycosides. The percentage reduction of blood glucose level was 33.18%, 33.19%, 54.77%, 75.29% & 80.93% in 4, 8, 12, 16 and 20 hours respectively. In case of HDL lowering activity, it showed similar reduction (33.83%) level of HDL compared metformin (32.29%), while 85.08% reduction was observed in case of LDL. The extract also significantly decreased (74.08%, $p<0.001$) the TG level while it lessened 69.7% of total cholesterol compared to metformin (76.70%). In addition to that comparative hepatoprotective activity revealed the significant reduction in sGPT (83.66%) and sGOT (76.14%) level which almost similar to metformin activity. Taken together, this study revealed that ethanolic extract of *M. scandens* leaves contain bioactive constituents with antidiabetic potentials, which goes to support its acclaimed traditional medical use of the plant in the management of diabetes.

Keywords: *Mikania Scandens*; Diabetes; Asteraceae; Antidiabetic; Hepatoprotective; Hypolipideamic; Traditional medicine

Introduction

Diabetes mellitus (DM) is one of the major global health complications demanding preventive and new therapeutic interventions. DM is a metabolic disorder categorized by chronic hyperglycemia with abnormal carbohydrate, fat, and protein metabolism due to defects in insulin secretion, insulin action, or both. The estimated number of people aged between 20 and 79 years with diabetes worldwide in 2017 was 425 million. The global dominance of DM is expected to rise to 552 million by 2030 [1]. Approximately 14% of the global health expenditure was estimated to be spent on diabetes in 2017 [2]. Diabetes mellitus can directly affect serum lipid levels causing diabetic dyslipidemia which is one of its complications [3]. Diabetic dyslipidemia is mainly characterized by higher serum levels of triglyceride (TG), lower high density lipoprotein cholesterol (HDL-C), and high small dense LDL levels [4].

Developing new antidiabetic medications from plant derived compounds which are easily accessible seems highly attractive research area as currently available medications have limitations in terms of safety, efficacy, and cost [5]. Many plants have been so far tested for their antidiabetic potentials [6-10]. One of the plant of Asteraceae family *M. scandens* have been traditionally used in Southeast Indian subcontinent with potential analgesic [11], antidiarrheal [12], antinoceptive, muscle relaxant, locomotor depressant and sedative potentiating [13], anti-inflammatory [14] and ulcerprotective activities [15]. This plant extract is being traditionally used for diabetes management. However, the antidiabetic activity of this medicinal plant is not scientifically validated.

Studies have found that flavonoids originated from foods could improve glucose metabolism, lipid profile, regulating the hormones and enzymes in human body, further protecting human being from diseases like obesity, diabetes and their complications [16]. Preliminary studies revealed that this plant contain several antidiabetic potential constituents including flavonoids, alkaloids, saponins proposing it to be a potential antidiabetic candidate for scientific verification [11]. This study investigated the hypoglycemic activity of this plant along with lipid lowering activity and hepatotoxicity in alloxan induced diabetic mice in order to fully ascertain the ability of *M. scandens* as a potential source of new, cheap and safe anti-diabetic drugs.

Materials and Methods

Plant material collection and preparation

Fresh leaves of *M. scandens* were collected from medicinal plant garden of Jessore University of Science and Technology, Jashore, Bangladesh. The leaves were dried completely under the mild sun and ground with an electric grinder into coarse powder and used for cold extraction. Then coarse powders were extracted using 70% ethanol for 7 days at room temperature with occasional shaking and stirring. The extract were filtered through cotton and filter paper. Then evaporated to dryness in a rotary evaporator and the final brown-coloured, powdery crude extract was stored in air-tight container until used.

Chemicals and drug collection

The standard antidiabetic agent, metformin hydrochloride was the generous gift samples from Square Pharmaceuticals Ltd. Bangladesh. Alloxan was purchased from Sisco Research Laboratories Ltd., Mumbai, India. Tween-80 was obtained from BDH Chemicals, UK and saline solution was collected from Beximco Infusion Ltd. Dhaka, ALTI

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FlexR reagent cartridge (cat.no.-DF143) for SGPT & AST FlexR reagent cartridge (Cat.No.DF41A) for SGOT; CHOL FlexR reagent cartridge (cat.No.-DF27) for TG & TC; ALDL FlexR reagent cartridge (cat.No-DF131) for LDL & AHDL FlexR reagent cartridge (Cat.No.DF48B) purchased from Siemens Healthcare Diagnostics Ltd, Camberley, UK. All the chemicals used were of analytical grade.

Phytochemical screening

Standard screening tests for the extract were carried out for various constituents like alkaloids, saponins, flavonoids, phytosterol, steroids, tannins, proteins, glycosides and volatile oils using standard procedures [17].

Induction of diabetes

Diabetes was induced in mice by single intraperitoneal injection of Alloxan monohydrate (150 mg/kg body weight in normal saline) into group II-V. After 48 hours their blood glucose content was measured by a Glucometer (SAFE TOUCH Glucometer, HMD BioMedical Inc., Taiwan Technology of USA). Mice with blood glucose levels above 11.1 mmol/L were selected for the study [18]. Their base line blood glucose level was also measured just prior to the administration of alloxan.

Experimental design of mice model

Mice were divided into 4 groups contain 5 animals in each group.

Group 1 (Normal Control): Normal mice + saline 1 ml/kg

Group 2 (Diabetic Control): Diabetic Mice + distilled Water

Group 3 (Positive Control): Diabetic mice + Metformin hydrochloride120 mg/kg

Group 4 (MSL 200): Diabetic mice + *M. scandens* 200 mg/kg body weight

Ethanol diluted plant extract was administered by intraperitoneal injection.

Biochemical analysis

Blood samples were withdrawn from tail-tip cutting of the mice on the 0, 4, 8, 12, 16, 20 and 24th hours of the day for estimating blood glucose. At the end of treatment, the animals were sacrificed and the levels of SGOT, SGPT, HDL, LDL, TG and TC were determined using commercial kits following the manufacturer's standard protocols in a semi-auto analyzer.

Statistical analysis

Data were expressed as mean ± standard error of mean (SEM). Statistical comparisons were performed by two-way and one way (ANOVA) for blood glucose, lipid profile and hepatotoxicity analysis. Results were considered to be significant when p values were less than 0.05 ($p<0.05$) by Tukey's multiple comparison tests using Graph Pad Prism 5.03 (Graph Pad Software, San Diego, CA, USA).

Results

Phytochemical screening of the extract of *M. scandens* revealed the presence of steroid, alkaloids, phytosterol, flavonoids, phenolic compound and tannin, amino acid, fixed oil and glycosides Table 1.

M. Scandens posseess significant hypoglyceamic effect in AIDM

In case of AIDM, Metformin Figure 1 reduced blood glucose level to

Phytochemicals	Test method	Inference
Steroid	Liebermann-burchard test	+
Saponin	Foam Test	-
Alkaloids	Wagners Test	+
Phytosterol	Salkowski's test	+
Carbohydrate	Benedicts Test	-
Flavonoids	Ferric chloride test	+
Phenolic Compound & Tannin	Ferric chloride test	+
Proteins	Biuret test	+
Amino acids	Ninhydrin test	+
Fixed oils & Fatty Acid	Spot test	+
Glycosides	Keller-Killani Test	+

Table 1: Phytochemical properties of ethanolic extract of *Mikania scandens* leaves. +ve & -ve mention the presence & absence of compound in the extract accordingly.

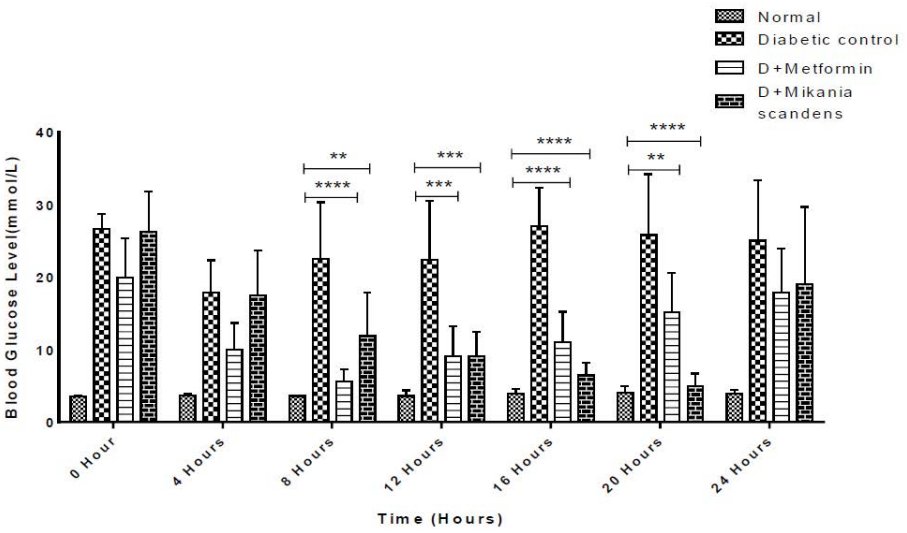

Figure 1: Hypoglycemic effect of ethanolic *M. scandens* leaves extract in alloxan induced diabetic mice (AIDM). Significant ($p<0.005$) to ($p<0.0001$) reduction was observed compared with diabetic control group from 8 to 20 hour. Data were analysed by ANOVA followed by Scheffe's post-hoc tests.

50.35% and 72.78% at 4th and 8th hour respectively, whereas *M. scandens* extract reduced blood glucose level to 33.18%, 33.19%, 54.77%, 75.29% & 80.93% at 4th,8th, 12th,16th & 20th hours respectively suggesting that *M. scandens* have prolong and potential hypoglycemic effect up to 20 hours copare to metformin. Maximum reduction of Blood glucose level was observed by *M. scandens* extract to 80.93% at 20th hour of the experiment.

Lipid lowering properties of M. scandens leaves in AIDM

Comparison of HDL levels: *M. scandens* rescued the HDL level in AIDM after successful diabetic induction Figure 2.

Comparison of LDL level: Metformin and *M. scandens* extracts reduced significant amount of LDL level to 88.50% and 85.08% respectively Figure 3.

Comparison of TG levels: *M. scandens* extract also reduced TG levels to 74.08% compared to diabetic control group Figure 4.

Comparison of Total Cholesterol (TC) level: Metformin is highly lipid lowering drug, *M. scandens* reduced TC level in AIDM to 69.7% which is very close to metformin (76.70%) Figure 5.

M. scandens possess significant hepatoprotective Effect in Alloxan Induced Diabetes Mice (AIDM).

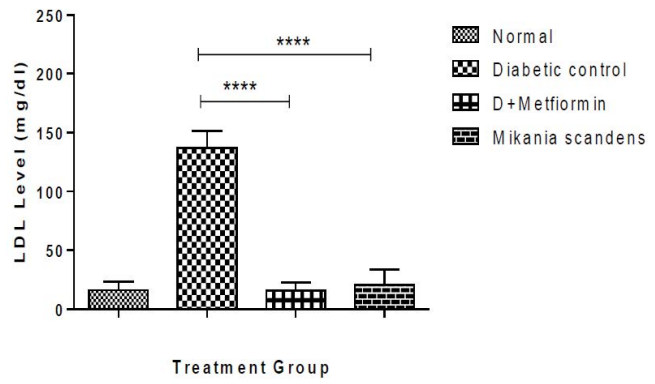

Figure 2: Comparing HDL activities among Metformin, *M. scandens* and diabetics control Mice. Significantly different (p<0.001) form the treatment at 24 hour .Data were analysed by ANOVA followed by Scheffe's post-hoc tests.

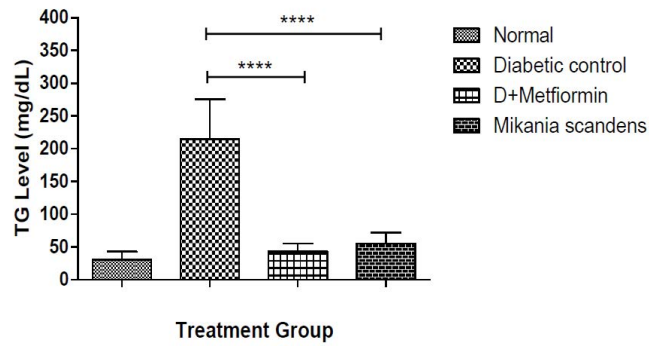

Figure 3: Comparison of LDL activities among metformin, *M. scandens* and Diabetic control Mice. Significant (p<0. 0001) reduction was observed form the diabetic control group at 24 hour. Data were analysed by ANOVA followed by Scheffe's post hoc tests.

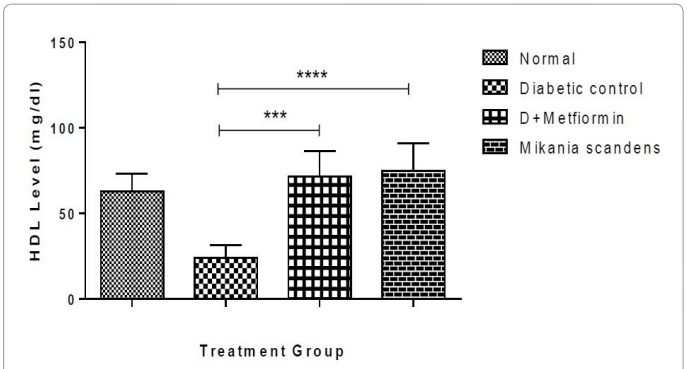

Figure 4: Comparison of TG levels among Metformin, *M. scandens* and diabetic control mice. Significant (p<0. 001) reduction from the treatment at 24 hour. Data were analysed by ANOVA followed by Scheffe's post-hoc tests.

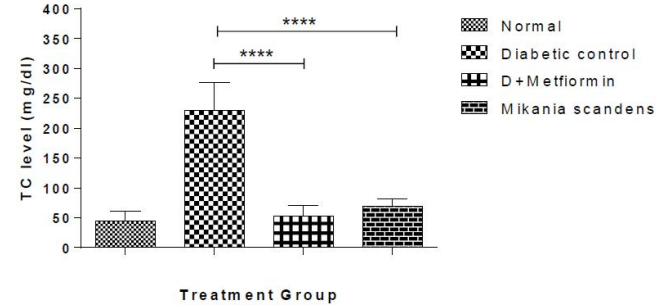

Figure 5: Comparison of TC levels among metformin, *M. scandens* and diabetics control mice. Significant (p<0. 001) reduction was observed from the diabetic group at 24th hour. Data were analysed by ANOVA followed by Scheffe's post-hoc tests.

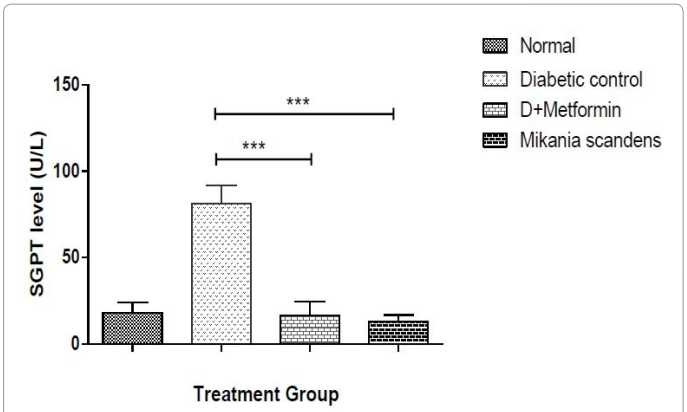

Figure 6: Comparison of sGPT enzyme level among Metformin, *M. scandens* and Diabetic control mice. Significant reduction (p<0. 0001) form the diabetic control group treatment at 24th hour. Data were analysed by ANOVA followed by Scheffe's post-hoc tests.

Comparison of sGPT level: *M. scandens* extract and metformin HCl decreased serum glutamic pyruvate transaminase (sGPT) to 83.66 % &79.59% respectively Figure 6.

Comparison of sGOT level: *M. scandens* extract and metformin HCl normalized the serum glutamic oxalate transaminase (sGOT) Figure 7.

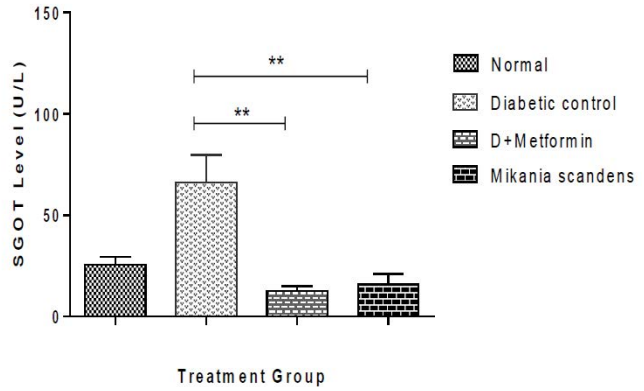

Figure 7: Comparison of sGOT levels among metformin, *M. scandens* and diabetic control group mice. Significant reduction ($p<0.005$) of sGOT level was observed form the treatment at 24th hour. Data were analysed by ANOVA followed by Scheffe's post-hoc tests.

Discussion

There is considerable attention for phytochemist to identify the therapeutic agents contained in plants in order to establish the basis for their uses in traditional medical practice. The phytochemical screening of the ethanolic extract of *M. scandens* revealed that alkaloids, flavonoids, phytosterol, phenolic compounds, tannins and glycosides were present. Alkaloids are generally inhibit α–glucosidase and decrease glucose transport through the intestinal epithelium [19]. Both flavonoids and tannins regenerate damage pancreatic islets cell, stimulate calcium and glucose uptake [20]. More recently, phenolic compounds and tannins have been reported as active principles and as being involved in glucose metabolism regulation [21]. The results from hypoglycemic studies suggests that the plant has better glucose lowering capacity than metformin hydrochloride. In addition to that glucose lowering capacity was longer and potential for the plant extract up to 20 hrs experimental paradigm.

The present investigation showed that the ethanolic fraction of *M. scandens* when administered by intraperitoneal injection in normoglycemic and alloxan induced diabetic mice induced hyperglycemic mice for a day long experiment produced hypoglycemia in different extent like other plant preparations such as, *Catharanthus roseus* [6], *Coccinia cordifolia* [7], *Bombax ceiba* [8], Cucumber and white pumpkin [9] have been reported to produce both hypoglycemia and hypolipidemia in alloxan induced-diabetic mice, but only after chronic/sub-chronic oral administration.

Most of the patients with type 2 diabetes show a dysliplidemia characterized by higher level of triglycerides, low HDL and the primeness of small-dense LDL particles [22]. Flavonoids prevent the oxidation of LDL, lower the blood levels of cholesterol and TG which deduct the risk for the development of atherosclerosis [23]. We focused on the effect of plant extract on lipid profile and our results revealed that HDL level rescued after diabetic induction by alloxan induced diabetic mice which are a beneficial impact in diabetes management. In addition to that LDL level was significantly decreased after diabetes induction.

Next we focused on hepatoprotective effect of the plant extract, because detoxification of a variety of drugs and xenobiotics occurs in liver. Most of the hepatotoxic chemicals/drugs damage liver cells mainly by inducing lipid peroxidation and other oxidative damages in liver resulting in elevation liver enzymes termed as sGPT and sGOT. We measured here the hepatoprotective activity of the plant extract on diabetic mice. The results suggest that *M. scandens* have hepatoprotective effect on diabetic mice at 24th hour experimental paradigm. Ethanolic extract of *M. scandens* possess flavanoids, tannins, and phenolic compounds, which are natural antioxidants. They can scavenge off free radicals. So, the anti-oxidant principles may be involved in the hepatoprotective activity.

Conclusion

In conclusion, the ethanolic extract of *M. scandens* possess bio-active constituents with antidiabetic, lipid lowering and hepatoprotective potentials and further the ethno medical claim of the use of the plant in the management of diabetes. This medicinal plant could be considered as a potential, prolong active and alternative for the management of diabetes. However, further screening of potential compound(s) with hypoglycemic activity is warranted to clarify the mechanism of action

Conflict of Interest

None

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