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Hypoglycemic property of *Telosma procumbens* (Blanco) Merr. (Apocynaceae) in normal and alloxan-induced diabetic juvenile mice (*Mus musculus*)

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Abstract

The incidence of diabetes is alarmingly fast in both developed and developing countries. In Third World countries, medicinal plants have always played a significant role in the maintenance of health and management of diseases. In the Philippines, there are many plants with reported antidiabetic property, but are not scientifically tested yet including *Telosma procumbens* (Blanco) Merr. Using male mice as model organism, ethanolic leaf extract of the plant was tested for hypoglycemic activity in both normoglycemic and alloxan-induced diabetic mice. Results obtained proved the blood glucose reducing effect of the extract in a dose-dependent manner. *T. procumbens* extract (TPE) when given at a dose of 100 mg/kg BW produced a significant reduction in BGLs both in normal ($P<0.001$) and diabetic ($P<0.001$) mice. In diabetic mice, the maximum decrease in glycemia using the high dose of the plant extract was obtained 1 hr (59%) after treatment which is quite comparable to the effect of insulin (65%). These evidences clearly indicate that the ethanolic extract of *T. procumbens* exhibited antidiabetic potential. Further characterization of the active components of the plant is warranted to understand the mechanism of its hypoglycemic action.

Keywords: Alloxan, Antidiabetic, Hypoglycemic, Normoglycemic, *Telosma procumbens*.

Introduction

Diabetes is a metabolic disorder that leads to a number of chronic complications such as retinopathy, heart disease, and renal failure when not properly controlled.[1-5] The incidence of diabetes mellitus is rising all over the world, especially in Asia.[6] In order to prevent this alarming health problem, the development of research into new hypoglycemic and potentially antidiabetic agents is an urgent necessity. The researches conducted over the last decade have shown that many plants (176 species belonging to 84 families) have high potential to treat and control diabetes.[7] This finding poses another possibility that herbal plants might offer a natural key to unlock diabetic complications.

The Apocynaceae or dogbane family is a family of flowering plants, including trees, shrubs, herbs, or lianas with representative genera reported to possess hypoglycemic property. Many of these plants have milky sap; often showy flowers; many are sources of drugs and many species are poisonous if ingested.[8] The family, as currently recognized, includes some 1500 species divided in about 424 genera[9], including *Telosma procumbens* (Blanco) Merr. The plant (formerly under family Asclepiadaceae)

is popular for its flowers that are referred to as flower vegetables which are noted for its antimicrobial property.[10] The leaves are good source of essential oils as well as exhibit many medicinal properties; an infusion or decoction is used to cleanse the wounds, scabies, and ulcers; and as cataplast on the forehead for headache.[11] However, as to the plants hypoglycemic activity, no report has been made so far. The study was therefore conducted to evaluate scientifically if ethanolic leaf extracts of Telosma procumbens (Blanco) Merr. possess hypoglycemic property as exhibited by other members from the same family i.e. *Vinca rosea* L.[12], *Rhazya stricta*[13] and *Picralima nitida*[14] low and high concentrations. Mice are convenient model for this study because they can be easily induced to develop the disease; they share a high degree of homology with humans and they are practical and easy to keep.

Materials and Methods

Plant material and preparation of extract

T. procumbens plant parts collected by the Aetas from Morong Bataan were botanically authenticated at the University of the Philippines-Diliman. Voucher specimens were deposited at the Institute of Biology Herbarium. The leaves were dried, powderized, dissolved in 95% ethanol in 1:2 ratio (w/v) and allowed to stand for 48 hrs. The mixture was filtered and evaporated to dryness using a rotary evaporator. The solid residue was weighted, giving final concentrations of 50 mg/ml. The ethanolic extract was kept at -20°C until use.

Animals

The use of animals in the study and the experimental protocol were in compliance to the guidelines set by the Animal Care and Use Committee of the University of the Philippines.

Thirty six (36) male ICR/Jcl mice weighing 20 ± 5 g (4-6 wks old) were used in the study. The mice were acclimatized for one week, maintained in plastic cages and 12 hrs light/dark cycle, with free access to food (Purina Bio 300) and tap water. Animals described as fasted were deprived of food overnight but had free access to water.

Experimental protocol

The animals were divided into two big groups. The first group of mice received deionized water (vehicle of alloxan and plant extracts), served as the normoglycemic group. The second group received a single intraperitoneal injection of alloxan monohydrate (150 mg/kg) in order to induce diabetis.[15] (Lenzen and Panten 1988). Group 1 was later subdivided into small groups and each subgroup (n=6) were given (i.p.) either: deionized water (DW); high (100 mg/kg) or low (50 mg/kg) ethanolic extract of Telosma procumbens (TPE).

In the second group, diabetes mellitus was confirmed after the 5th day of alloxan treatment by estimation of elevated fasting blood glucose (FBG) level using OneTouch Ultra 2® Glucometer. Only those mice with blood glucose level 120 > mg/dl were included in the study. The diabetic mice were also divided into subgroups, each receiving treatment (i.p.) of either: 2 iu/g insulin; high (100 mg/kg) or low (50 mg/kg) ethanolic extracts of TPE.

Measurements of the fasting blood glucose (FBG) were done at 0 hr on overnight fasted mice. Thereafter, the treatments were administered and blood glucose levels (BGLs) were closely monitored 1, 2, 3 & 24 hrs post-treatments.

Statistical Analysis

Results are presented as means±S.D. for a given number of observations (n). Data (BGLs) from each set of observations were compared with the pretreatment blood glucose level using paired Student's t-tests. For the Comparison among groups, One-way ANOVA was performed using SPSS v.13 software, followed by Tukey as a post hoc test. Differences were considered significant if $P<0.05$.

Results

Effects of ethanolic extracts on fasting blood glucose in normoglycemic mice

Table 1 shows that intraperitoneal administration of the plant extract to normal mice showed hypoglycemic activity. TPE- treated mice (at 100 mg/kg bw) produced a consistent and significant decreases after 1, 2, and 3 hrs ($P<0.001$) in BGL by 46%, 52%, and 59% compared to 17%, 45% and 44% reduction observed in mice given with TPE at 50 mg/kg BW post-treatment at 1hr, 2 hrs ($P<0.01$) and 3 hrs ($P<0.05$). Further, animals given only

with deionized water has no significant effect on the BGLs of normoglycemic mice. These results indicate a clear hypoglycemic impact of the extract especially when given at a dose of 100 mg/kg BW.

Table 1: Hypoglycemic effect of ethanolic extract of *T. procumbents* (TPE) in normal mice (mean±SD)

Experimental Animals	Treatment	Blood Glucose Levels (mg/dl^{-1})				
		Pre-treatment levels	Post-treatment levels			
		FBG	1h	2h	3h	24h
Control	Deionized Water	87.75± 14.75	82.75±6.7	78±1.41	73± 15	80.5± 2.89
TPE-treated	100 mg/kg^{-1}	98±5.47	52.25± 11.62***	46.5± 11***	39.5± 9.47***	111.7±10
TPE-treated	50 mg/kg^{-1}	87.2±19.3	72.5±24	47.7± 25.6**	48.75±16.8*	93±24

*P<0.05 as compared to pretreatment level, **P<0.01 as compared to pretreatment level , *** P<0.001 as compared to pretreatment level

Glycemic potential of ethanolic extracts on glucose tolerance test in diabetic mice

As shown in Table 2, *T. procumbens* extract (TPE) resulted in a significant reduction in blood glucose concentration in diabetic mice both with high (P<0.001) and low (P<0.01) concentrations. The maximum decrease in glycemia using the high dose of TPE was obtained 1 hr (59%) after treatment. Whereas, with the lower dose (50mg/kg) the fall was 29%, 27%, and 16%, 1, 2 and 3 hrs after administration of the extract, respectively. For insulin, the maximum fall was also observed after 1 hr (65%) which is comparable with the result obtained using the high dose of TPE (100 mg/kg). Moreover, TPE when given at 100 mg/kg/BW (P<0.001) is as potent as the effect of insulin (P<0.001). These findings corroborate the previous works on Apocynaceaens having high antidiabetic potential when given to mammals.[13, 14, 16]

Table 2: Hypoglycemic effect of ethanolic extract of *T. procumbens* (TPE) in alloxan-diabetic mice (mean±SD)

Experimental animals	Treatment	Blood Glucose Levels (mg/dl^{-1})				
		Pre-treatment levels	Post-treatment levels			
		FBG	1h	2h	3h	24h
Control	Insulin	258.75± 22.24	89.5± 29.27***	53± 5.09***	58±14.9***	232.75± 49.35
TPE-Treated	100mg/kg^{-1}	186±35.5	77± 13.73**	63± 12.4**	44.7± 9.74**	145±13.3
TPE-Treated	50mg/kg^{-1}	175±16.6	124.7±58.7	90.3±32**	75.7±36.6**	194.8±45

*P<0.05 as compared to pretreatment level, **P<0.01 as compared to pretreatment level, *** P<0.001 as compared to pretreatment level

Discussion

The results of the present work suggest that the products of *Telosma procumbens* (Blanco) Merr. may provide new therapeutic avenue against diabetes and diabetes-related complications. The available data proved the hypoglycemic potential of the plant which has an immediate effect in reducing blood glucose level in mice. A similar effect was observed using rats with the methanolic extract of Ipomea aquatica (Convolvulaceae)

producing a highly significant decrease in glycaemia within 2 hrs after treatment.[17] Further, the efficacy of *Telosma procumbens* as hypoglycemic agent when given to both normoglycemic and diabetic mice resembles that of insulin.

It is known that the phytochemicals with antidiabetic action are classified as alkaloids, flavonoids, glycosides/sterosids/terpenoids, polysaccharides, proteins, saponins, and miscellaneous other compounds.[18] These chemicals appear to exert differential effects in regulating the level of blood glucose depending on the methods used in the experiments, model animals, doses, and the degree of hypoglycaemia. Overall, the data indicate that molecules with insulin-like bioactivity are present in *Telosma procumbens*. The proposed mechanism of action is the increase in insulin sensitivity due to saponins. To date, there is a growing body of evidence that saponins, although active in several systems, are responsible for modulation of glucose disposal and insulin release. Several studies[16, 19, 20] on mice and rats confirmed the hypoglycemic and hypolipidemic effects of the crude saponin fractions isolated from *G. sylvestre* (Asclepiadaceae); *A. senticosus* (Araliaceae) and *T. foenum* graecum (Leguminosea). Previous works may include other possible actions such as ; improved glucose homeostasis (increase of peripheral utilization of glucose, increase of synthesis of hepatic glycogen and/or decrease of glycogenolysis acting on enzymes, inhibition of intestinal glucose absorption, reduction of glycaemic index of carbohydrates, and reduction of the effect of glutathione.[7] Since all of these may be responsible for the reduction and or elimination of diabetic complications, work such as this confirms the promising effect of herbal plants in the prevention of chronic diseases such as diabetis mellitus.

Conclusion

There is a plethora of explanations regarding the mechanism of action of the active components of antidiabetic plants. However, many other active agents obtained from plants have not been well characterized. Further characterizations of the active components of Telosma procumbens are also warranted to understand the mechanism of its hypoglycemic action. Although no adverse effects were observed in all the mice exposed to the high concentration of the plant ethanolic leaf extracts, more information is needed to fully assess the safety and efficacy of the plants in treating diabetes.

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