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Hypoglycemic activities of ethanolic *Gynura procumbens* leaves extracts in rats

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Traditional medicinal plants including those with anti-hyperglycemic effect have been widely used in Myanmar. Indeed, hundreds of plants were used traditionally for management and/or control of both insulin-dependent (IDDM) and non-insulin-dependent (NIDDM) diabetes mellitus worldwide. There was no recorded evidence of *Gynura procumbens* leave for its anti-hyperglycemic effect in Myanmar. The present study aimed to evaluate the anti-hyperglycemic potential of *G. procumbens* leaves on adrenaline-induced hyperglycemic rats. It was a preclinical animal model, conducted during May, 2007 in DMR (Upper Myanmar). The extracts (different doses), glibenclamide and water were administered orally to different groups of adrenaline-induced hyperglycemic albino rats of both sexes (7 rats in each group). Oral administration of *G.procumbens* ethanol extracts (150 and 300 mg/kg) showed hypoglycemic effect in adrenaline-induced hyperglycemic rats. The efficacy was comparable with glibenclamide (0.5mg/ kg). *G. procumbens* ethanol extract (300 mg/kg orally) significantly inhibited hyperglycemia induced by adrenaline (0.2 ml/kg). *G procumbens* leaves extract with the dosage of 300 mg/kg was more potent than glibenclamide at the first 2 hours (1 hour and 2 hour) (P value = 0.0484, 0.0035), respectively. However, in 3 hour and 4 hour, there was no significant differences in tested extract and glibenclamide (P value = 0.4864, 0.4256), respectively. The results indicated that the ethanol extract of *G. procumbens* leaves possess anti-hyperglycemic activity.

INTRODUCTION

The World Health Organization's expert committee on diabetes mellitus estimated that about 150 million people worldwide suffered from diabetes mellitus in 1995; and predicted that this number will rise to an alarming figure of 300 million by the year 2025 [1]. Life expectancy can be halved by this disabling disease, particularly in developing countries of the world where its prevalence is increasing steadily, and adequate treatment regimens are often unavailable or economically unaffordable. In fact, phytotherapy has been widely used by the Myanmar population since time immemorial. There is a growing global interest in herbal and other forms of traditional medicine. Herb has long been an important source of effective drugs. Among WHO recommendations is the need for the investigation of local medicinal plants for their potential therapeutic efficacy [2]. This practice continues to be prevalent in the urban as well as in the rural environment because of the low cost and the easy availability of medicinal plants in the market all over the country. However, the efficacy study on antidiabetic plants used in Myanmar since 1991 has begun to evolve in the last few decades. Moreover, there is no extensive documentation of data on antidiabetic activities of this plant extract. *Gynura procumbens* Merr. belongs to the family Compositae. It is known in Myanmar as "Pyar Mee Swae". The leaves are edible.

Gynura procumbens is found in various parts of Southeast Asia. It has been used for the treatment of eruptive fevers, rash and kidney disease [3]. Medicinal uses of the species including treatment for kidney trouble, fever and rash have been reported [4]. It was used traditionally in Thailand as tropical anti-inflammatory, anti-allergic agents and recently it was reported to be effective against the herpes simplex virus [5]. Leaves extract of *G. procumbens* has also been reported to have hypotensive [6] and anti-inflammatory effects [7]. In Myanmar, by reviewing the current literature, there was no previous research on the pharmacological properties of this plant. Therefore, experiments were carried out to test the antidiabetic activities of this plant. The present study was undertaken to evaluate the possible hypoglycemic activity of the ethanolic extracts of *G. procumbens* leaves (which have been reported in Ayurveda to be useful in diabetes) in the adrenaline-induced hyperglycemic rats.

MATERIALS AND METHODS

Plant material and extract preparation

The leaves (*Gynura procumbens*) were collected from the herbal garden and identified by U Kyaw Nyan Linn (Research Officer), keeper of herbarium, DMR (Upper Myanmar). Fresh leaves were cut into small pieces (about 1 cm). The air dried *G. procumbens* leaves (100 g) were pulverized and then exhaustively extracted with ethanol. The extract was evaporated in vacuo and the yield was 5.37% (5.37 gm of ethanolic extracts were achieved by extraction of 100 grams of dry leaves).

Animals

Albino rats (180-250 gm) of both sexes were obtained from the Laboratory Animal Services Division, DMR (Upper Myanmar). These rats were randomly divided into 5 groups of 7 rats each.

Induction of hyperglycemia in rats

Screening of adrenaline-induced hyperglycemia in experimental animals was done one week before starting experiment. Diabetic rats (n=28) were induced by single intraperitoneal injection of freshly prepared adrenaline (MPF, Myanmar) (200 mcg/kg body weight) to overnight (18 hours) fasted rats. Negative controls (n = 7) were injected with sterile distilled water alone. Before induction, fasting blood glucose concentration was determined by Bayer's glucometer Elite. The ethanolic extracts of *G. procumbens* leaves in aqueous solution were administered orally at a concentration of 150 and 300 mg/ml body weight / rat.

Preparation of test solution

The aqueous solution of *G. procumbens* was prepared by mixing 5 grams of *G. procumbens* extracts with 25 ml of distilled water and was osterized until in a completely liquefied state. Resulting solution contained 200 mg of *G. procumbens* per 1ml aqueous solution.

Treatment schedules

The experimental rats were divided into 5 groups of 7 rats each. Group I and II were treated with 150 and 300 mg/kg body weight of extracts of *G. procumbens* leaves. In group III, the rats were treated with glibenclamide (0.5 mg/kg) (Braan Laboratories Ltd, Batch-42184 E, Expiry date– January 2008, India) and in group IV, the rats were treated with 2ml/kg body weight of distilled water. These groups III and IV were taken as positive controls. The rats in negative control group (group V) were given only distilled water.

Collection of blood samples

Blood samples (0.02ml) were collected from the tail vein at 0 hour, 1 hour, 2 hour, 3 hour and 4 hour post administration.

Statistical analysis

Data were checked and entered using Epi-info 3.1 software. All values were expressed as the mean ± SD values obtained from a number of experiments using one way ANOVA. The results were expressed in Table.

RESULTS

The effects of oral administration of different doses of the plant extract and the positive controls serum glucose levels of adrenaline-induced hyperglycemic rats are presented in Table 1.

Table 1. Effects of *G. procumbens* leaves on rats

Time of blood collection (hour)	Blood glucose level (mg/dl)				
	G-1	G-2	G-3	G-4	G-5
	G.pro-cumbens 150 mg/kg	*G. pro-cumbens* 300 mg/kg	Glibenclamide standard drug	Pc Dw only	Nc Dw
0	4.9	4.1	4.9	4.08	4.0
1	5.8	4.7	6.5	9.47	4.1
2	4.5	4.4	6.0	8.4	4.3
3	4.5	4.0	4.4	7.0	3.5
4	4.2	4.0	3.7	5.5	3.5

G=Group, Pc=positive control, Nc=Negative control
Dw= Distilled water
P value = 0.0484 at 1 hour , 0.0035 at 2 hour, 0.4864 at 3 hour, 0.4256 at 4 hour
n = 35 (7 rats per group for 5 groups)
Test = single ANOVA test

At 1 hour post-administration, serum glucose level of adrenaline-induced animals reached a peak but plant extracts treated groups and glibenclamide treated control group did not reach up to peak level. The high dose of extracts (300 mg/kg) produced significant decrease in serum glucose levels compared to glibenclamide treated group. This dose also produced a significant decrease in serum glucose at (1 & 2 hour) (p=0.0484, p=0.0035, respectively) compared to reference western drug (glibenclamide). Low dose extract (150 mg/dl) had significantly lowered the serum glucose level at 1st and 2nd hours. But 3 hours and 4 hours glibenclamide inhibition effects were more prominent than this low dose extract.

DISCUSSION

Although the morbidity and mortality associated with diabetes mellitus is primarily due to its complications, these longterm complications depend on a long-standing history of poor glycemic control. In the adult population worldwide, diabetes is the leading cause of end-stage renal disease, blindness, kidney failure, neuropathy, gangrene and amputation not resulting directly from accident or trauma. Although insulin still remains the main therapeutic agent for the management and control of type 1, juvenile-onset, IDDM, the major classes of synthetic oral hypoglycemic agents currently available for the management and/or adult-onset type 2 NIDDM include the sulphonylureas, biguanides, thiazolidinediones, alpha-glucosidase inhibitors, and so on. However, the use of these synthetic products is usually accompanied by some serious adverse effects. Therefore, there is an urgent need to find safe, cheap and effective pharmacological interventions for diabetes mellitus.

The hypoglycemic effect of ethanolic extract of *G. procumbens* was determined by evaluating its effects in adrenaline-induced hyperglycemic rats. As shown in Table1, the glucose levels of *G. procumbens* extract treated rats showed significant reduction in glucose level at 1st and 2nd hours compared to glibenclamide. *G. procumbens* leaves extract with the dosage of 300 mg/kg had more reduction level of glucose than glibenclamide at the first 2 hours (at 1 hour, p= 0.0484) and (2 hour, p= 0.0035). However, in 3 hour and 4 hour, there was no significant differences in tested extract and glibenclamide (P=0.4864, 0.4256, respectively). Zhang *et al.* [8] demonstrated that the ethanolic extracts of *G. procumbens* at 3 doses levels orally, significantly suppressed the glucose levels in diabetic rats. Rasadah MA [7] stated that methanol extract of *G. procumbens* leaves at the dose of 1 gm/kg presented a significant decrease in blood glucose level which was observed only at 60 minutes after administration of glucose as compared to vehicle (5% gum acacia).

In Myanmar, many plants have been reported to possess hypoglycemic activities. Indeed, hundreds of plants are now being used traditionally for the management and/or control of both insulin-dependent (IDDM) and non-insulin-dependent (NIDDM) diabetes mellitus worldwide. To date, however, only

a few of these plants have been subjected to scientific scrutiny either in laboratory animals or human subjects. In the present study, the hypoglycemic activity of the ethanol extract of *G. procumbens* was evaluated in the adrenaline-induced diabetic rats. Under the same conditions, glibenclamide produced a significant glucose reduction in adrenaline-induced diabetic rats. One study stated that the ethanolic extract of *G. procumbens* leaves had antihyperglycemic and antihyperlipidaemic activities in streptozotocin-induced rats [8]. It is well known that glibenclamide which is a derivative of sulfonylurea causes hypoglycemia by stimulating pancreatic β cells to release more insulin, and inhibiting glucagon secretion. As these effects require a functional pancreas, it can lower blood sugar levels in non-diabetic subjects [9]. The results showed that the ethanol extract of *G. procumbens* was assumed to stimulate insulin release in pancreatic β-cell lines. Therefore, extract of *G. procumbens* can represent a source of potential new hypoglycemic agent.

Conclusion

This study has confirmed the traditional uses of *G. procumbens* for treating diabetes. This plant possesses hypoglycemic activity in adrenaline-induced rats and also contains substances, which are able to stimulate insulin secretion, thus contributing to the anti-diabetic property of the plants. Therefore, *G. procumbens* has the potential to become a dietary adjunct for the treatment of diabetes and potential source for the discovery of new orally active agents for diabetes therapy.

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REFERENCES

1. Trinder P. Determination of glucose in blood using glucose oxidase with an alternative oxygen acceptor. *Annals of Clinical Biochemistry* 1969; 6: 24.
2. International meeting on the development of guidelines for national policy on traditional medicine. *EMR Drugs Digest* 1995; 10 (2): 3-12.
3. Perry LM. Medicinal plants of East and Southeast Asia: attributed properties and uses. England: The MIT Press. 1980; 94-5.
4. Burkill IH. A dictionary of the economic product of Malay Peninsular.Kuala Lumpur; Ministry of Agriculture and Co-operatives, Kuala Lumpur. 1966; 1(11): 24-44.
5. Jiratcharikul W, Jarikasem, Siritantikorn S, Somanabandhu A & Frahm AW. Antiherpes simplex viral compounds from *Gynura procumbens*, Merr. *Mahidol University Annual Research Abstracts* 2001; 28: 498.
6. Hoe SZ, Lam SK, & Ng LT. Hot water extraction releases unknown bradycardiac compounds from *Gynura procumbens*. Paper presented at 16th Scientific Meeting of Malaysian Society of Pharmacology and Physiology, 25-26 June, Kuala Lumpur, University Malaysia, 2001.
7. Rasadah.MA, Nik Musa'adah M, Muhajir H& Saufi MB. Anti-diabetes properties of *Gynura procumbens* (*Kecam Akar Journal*). 2004; 192-197.
8. Zhang XF & Tan BKH. Effects of an ethanolic extract of *G. procumbens* on serum glucose, cholesterol and triglyceride levels in normal and streptozotocin-induced diabetic rats. *Singapore Medical Journal* 2000; 41 (1): 1-7.
9. Karam JH. Pancreatic hormones and antidiabetic drugs. In: Katzung BG, editor. 7th ed. Stamford: Simon and Schuster Company. *Basic and Clinical Pharmacology* 1998; 684-705.