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Research Article

THE EFFECT OF ETHANOLIC EXTRACT OF *SOLANUM DUBIUM* IN GLUCOSE INTRAPERITONIALLY LOADED RATS (*IN VIVO*) AND GLUCOSE UPTAKE IN ISOLATED RAT HEMIDIAPHRAGM (*IN VITRO*)

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ABSTRACT

A total of 30 Wistar albino rats of either sexes weighing 120-250 g were divided into five groups to test three different doses of ethanolic extract of *Solanum dubium* for its blood glucose lowering activity in comparison with glibenclamide as a positive control and distilled water as a negative control group. Blood glucose in the rats was evaluated in the 1st, 2nd, and 4th hr. The 1st and 2nd hr the extract lowered blood glucose level potently to a decrement value of 25% in comparison to 17% decrement in the group administered glibenclamide. At the 4th hr, the extract showed no effect on blood glucose level, nevertheless, it start rising, the fact that reveals it as a short acting drug. Using rat hemidiaphragm to check the potential of *Solanum* extract in enhancing reuptake of glucose by tissues, it showed good synergistic activity when administered with insulin.

Keywords: *Solanum dubium*, Glibenclamide, Ethanolic, Hypoglycemic, Hemidiaphragm.

INTRODUCTION

Diabetes is a chronic, metabolic disease characterized by elevated levels of blood glucose (or blood sugar), which leads over time to serious damage to the heart, blood vessels, eyes, kidneys, and nerves. The most common is type 2 diabetes, usually in adults, which occurs when the body becomes resistant to insulin or doesnot make enough insulin. In the past three decades, the prevalence of type 2 diabetes has risen dramatically in countries of all income levels. Type 1 diabetes, once known as juvenile diabetes or insulin-dependent diabetes, is a chronic condition in which the pancreas produces little or no insulin by itself. For people living with diabetes, access to affordable treatment, including insulin, is critical to their survival. There is a globally agreed target to halt the rise in diabetes and obesity by 2025. It was reported that 1.5 million deaths are directly attributed to diabetes each year, 9% of adults in the world have diabetes and 90% of people with diabetes in the world have type 2 diabetes [1]. Many plants have been used for the treatment of diabetes mellitus in Indian system of medicine and in other ancient systems of the world. Out of these only a few have been evaluated as per modern system of medicine. Most of them seem to act directly on pancreas (pancreatic effect) and stimulate insulin level in blood. Some have extra pancreatic effect also by acting directly on tissues such as liver and muscle and alter favorably the activities of the regulatory enzymes of glycolysis, gluconeogenesis and other pathways. Since the plant products have less side effects, they have the potential as good hypoglycemic drugs. They may also provide clues for the development of new and better oral drugs for diabetes [2].

Family Solanaceae is a large family containing more than 2500 species of plants varying in their uses to cover the majority of life aspects. Tomato (*Solanum lycopersicum*) is cultivated as a food crops, tropical soda apple is grown as a source of steroids in some countries [3]. Many members of the Solanaceae are deadly poisonous. One type of phytochemical is anticholinergic poisons [4]. Members of the Solanaceae may also uptake excess nitrates [5]. Tobacco (*Nicotiana* spp.) contains a convulsant poison [4]. Tomato (*S. lycopersicum*), horse nettle (*Solanum carolinense*), and potato (*Symphytum tuberosum*) can cause contact dermatitis [4]. Steroidal saponins may also occur in the Solanaceae as well [6]. Several plants from the tomato family are considered invasive. Carolina horsenettle (*S. carolinense*) is native but a terribly invasive spiny toxic weed. Tropical soda apple (*Solanum viarum*) and aquatic soda apple (*Solanum tampicense*) are invasive in the South. Tropical soda apple spread from 25,000 acres to over 1 million acres between 1990 and 1996 [3]. Diabetes mellitus is a common and serious metabolic disorder throughout the world. Traditionally used medicinal plants play an important role as alternative medicine due to less toxic effects and cost. A total of eight *Solanum* species were reported in literature to have antidiabetic activity. Some of the plant species reported to modify different complications of diabetes like hyperlipidemia, oxidative stress in diseased animals. On the basis of antidiabetic and other related activities, plants of *Solanum* genus are the most promising plant species to develop as efficacious and safer medicines for diabetes and its complications. Considering the present status of this disease and potential of *Solanum* genus, there is much scope of studying this genus thoroughly, which may result in the development of affordable, efficacious and safer remedies against the silent killer disease [7]. The objective of the present study is to evaluate the hypoglycemic activity of the ethanolic extract of *Solanum dubium.*

METHODS

Experimental albino rats of both sexes weighing from 120 to 250 g were divided into five groups each of six rats and fasted for 18 hrs before the tests. All groups were loaded with glucose solution at a dose of 2 g/kg body weight. The first group was left as a negative control on distilled water at a dose of 10 ml/kg body weight, the 2nd group used as a positive control at a dose of 10 mg/kg glibenclamide using local factory (Blue Nile) produced tablets with batch number GLF2, production date January 2015 and expiry January 2018. 3rd, 4th, and 5th groups given *S. dubium* 80% ethanolic extracts in doses of 100, 200, and 400mg/kg body weight, respectively. The plasma glucose level was monitored at 0, 1st, 2nd, and 4th hr intervals [8-10].

Glucose uptake by isolated rat hemidiaphragm: Glucose uptake by rat hemidiaphragm was estimated by the methods described by Walaas and Walaas [11] and Chattopadhyay *et al.* [12] with some modification.

Table 1: The fluctuation of glucose according to time and doses of extract and standard drug glibenclamide

Groups	0 hr±SEM	1 hr±SEM	2 hr±SEM	4 hr±SEM
Control group	67.6±1.89	107.40±2.62	98.20±8.11	87.60±8.370
Glibenclamide 10 mg/kg	84.8±4.21	130.60±3.11	107.60±7.42	83.400±5.77
100 mg/kg	93.3333±2.66667	122.0000±5.91044	101.3333±3.81809	113.3333±4.58015
200 mg/kg	89.3333±3.37310	142.6667±6.42218	106.0000±3.05505	118.6667±4.34102
400 mg/kg	87.3333±3.48967	124.0000±3.86437	108.6667±4.31019	114.0000±4.47214

SEM: Standard error of means

Table 2: Uptake of glucose by rat hemidiaphragm showing maximum when insulin and *Solanum* extracts were administered together

Incubation medium	Glucose uptake (mg/g/30 minutes)±SEM
Tyrode solution with glucose (2 g%)	18.62±4.7
Tyrode solution with 2% glucose and regular insulin 0.4 unit/ml	19.87±4.5
Tyrode solution and 2% glucose and *Solanum* extract (100 mg/ml)	18.89±4.24
Tyrode solution with 2% glucose and regular insulin 0.4 units/ml and *Solanum* extract (200 mg/ml)	21.44±4.40

SEM: Standard error of means

Four sets containing six numbers of graduated test tubes (n=6) each were taken as follows: Group 1: 2 ml of tyrode solution with 2% glucose. Group 2: 2 ml of tyrode solution with 2% glucose and regular insulin (Nova Nordisk) 0.62 ml of 0.4 units per ml solution. Group 3: 2 ml of tyrode solution and 1.38 ml of *S. dubium* (200 mg/ml), Group 4: 2 ml of tyrode solution with 2% glucose and regular insulin 0.62 ml of 0.4 units per ml solution and 1.38 ml of *S. dubium* (200 mg/ml). Dose 200 mg/ml was used being the most effective dose in blood glucose lowering *in vivo*. The volumes of all the test tubes were made up to 4 ml with distilled water to match the volume of the test tubes of Group 4. 12 albino rats were fasted overnight and killed by decapitation. The diaphragms were dissected out quickly with minimal trauma and divided into two halves. Two diaphragms from the same animal were not used for the same set of experiment. Six numbers of diaphragms were used for each group. The hemidiaphragms were placed in test tubes and incubated for 30 minutes at 37°C in an atmosphere of 100% oxygen with shaking at 140 cycles/minutes. Glucose uptake per gram of tissue was calculated as the difference between the initial and final glucose content in the incubated medium.

Statistics

The data were analyzed using one-way ANOVA followed by Dunnett's test. The level of significance was set at $p \leq 0.05$.

RESULTS

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DISCUSSION

In Table 1, the reduction of glucose attained by dose of 10 mg/kg glibenclamide at the end of the 2nd hr was 17.69% while the reduction of glucose by doses of 100, 200, 400 mg/kg of *Solanum* extract at the 2nd hr was 17.21%, 25.35%, 12.9%, respectively. This mean that the ethanolic extract of *S. dubium* at dose of 200 mg/kg is more potent in blood glucose reduction than glibenclamide at the end of the 2nd hr. Dose of 100 mg/kg of *Solanum* extract showed an effect approximately same as that attained by glibenclamide at the end of 2nd hr. Blood samples detected in groups of rats which were administered *Solanum* extracts in different doses, showed rise in blood glucose at the end of the 4th hr while blood sugar reducing the effect of glibenclamide persisted in group administered glibenclamide. This could give proof of the fact that *Solanum* extract reduces blood sugar very effectively but for the duration of time shorter than effect produced by glibenclamide.

In the model of rat hemidiaphragm testing the ability of *Solanum* extract in enhancing uptake of glucose by tissues, the maximum uptake was shown (21.44 mg/g/30 minutes) when both insulin and the extract were administered together. Either insulin or the extract showed a lower potency of glucose uptake when administered separately with insulin being more potent than the extract alone. This could proof that *Solanum* extract works synergistically with insulin at the receptor site. More work should be done to investigate the ability of *Solanum* extract to work as insulin secretagogue at beta Langerhans cells.

CONCLUSION

S. dubium extract constitutes compounds which are powerful in reducing blood glucose with a short duration of action. The extracts contain insulin synergistic compounds and need to be further investigated for isolation and elucidation.

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