

The anti-hyperglycemic effect of *Solenostemma argel* compared with Glibenclamide

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Abstract

The current study aimed to compare the anti-hyperglycemic effect of *Solenostemma argel*, which widely used for the treatment of diabetes mellitus in Sudan, with the antidiabetic drug (Glibenclamide). Twenty four albino rats were used in this experiment. Rats were assigned to 4 groups (N=6). All groups were fasted for 18 hrs. Group (1) was administered with glibenclamide (10 mg/kg b.w.) and served as control, groups (2, 3, and) were orally administered with aqueous extract of *Solenostemma argel* leaves and bark (200, 400, and 800 mg/kg b.w.), respectively, after loading with 5% glucose (2 mg/kg b.w). Blood samples were obtained to assess blood glucose, lipid profile and α -amylase concentrations. Sub chronic toxicity of *Solenostemma argel* has been evaluated which clearly demonstrated the non-toxic nature and safety profile. Obtained results indicated that *Solenostemma argel* aqueous extract significantly decreased blood glucose level in treated group received 800 mg/kg b.w. compared with glibenclamide treated group. At the dose of 200 mg/kg b.w. of *Solenostemma argel* aqueous extract, the activity of α -amylase decreased in comparison with that treated with glibenclamide and registered low concentrations of cholesterol and HDL as well. In conclusion, both blood glucose level and α -amylase activity can be ameliorated in diabetic rats by administration of *Solenostemma argel* aqueous extract. However, in prospective study more investigation has should to be carried out to explain the mechanism of *Solenostemma argel* in hypoglycemic animals.

Key words: Diabetes mellitus, *Solenostemma argel*, glibenclamide, antihyperglycemia, Hargel.

التأثير الخافض للسكر لنبات الحرجل بالمقارنة مع عقار Glibenclamide في الجرذان المصابة بداء السكري

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الخلاصة

هدفت الدراسة الحالية لمقارنة التأثير الخافض للسكر لنبات الحرجل مع عقار Glibenclamide. استحدثت داء السكري تجريبيا باستخدام التحميل بالكلوكوز 5% بجرعة 2 ملغم/كغم من وزن الجسم. تم توزيع 24 جرذا من كلا الجنسين بأعمار 60 يوما وأوزان تراوحت ما بين 135-150 غم على 4 مجموعات متساوية العدد. عوملت الأولى بعقار Glibenclamide (10 ملغم/كغم من وزن الجسم) وعدت مجموعة سيطرة وجرعت الثانية والثالثة والرابعة بالمستخلص المائي لنبات الحرجل بالجرعات 200 و400 و800 ملغم/كغم من وزن الجسم، على التوالي. تم سحب نماذج الدم لتقدير تركيز الكلوكوز والأميليز ألفا والكوليسترول والبروتينات الدهنية عالية الكثافة والكليسيريدات الثلاثية. أشارت النتائج الى انخفاض تركيز الكلوكوز في المجموعة الرابعة، المعاملة بجرعة 800 ملغم/كغم من وزن الجسم، بالمقارنة مع المجموعة

المعاملة بعقار Glibenclamide و انخفضت فعالية الأميليز ألفا في المجموعة الثانية المعاملة بجرعة 200 ملغم/كغم من وزن الجسم بالمقارنة مع المجموعة المعاملة بعقار Glibenclamide كما سجلت نفس المجموعة انخفاضا في تركيز الكوليسترول و البروتينات الدهنية عالية الكثافة . أوضحت الدراسة الحالية أن النبات المدروس غير سام وأمين عند استخدامه بالجرعات الحالية. يستنتج من الدراسة الحالية أن المستخلص المائي لنبات الحرجل يلطف مستوى السكر والأميليز ألفا في الجرذان المصابة بداء السكري.

الكلمات المفتاحية: مضاد ارتفاع السكر، مرض السكري ، *Solenostemma argel* ، glibenclamide ، الحرجل.

Introduction

Diabetes mellitus is one of the metabolic diseases characterized by hyperglycemia that result from defect in both insulin secretion and/or insulin action. The prevalence of diabetes worldwide will increase from 135 million people in 1995 to 300 million people by the year 2025 (1). Other studies proposed that the total number of people with diabetes will rise from 171 million in 2000 to 366 million in 2030 (2). The disease associate with a reduces quality of life and increase risk factors for the mortality and morbidity, the disease lead to the development of cardiovascular complications as well as neuropathy and cardiovascular disease (3). The control of blood glucose concentration to near normal range in patients is mainly based on the use of insulin or oral hypoglycemic agents, Glibenclamide drug. However, all of the hypoglycemic treatments have limited efficacy and are associate undesirable side effects such as gastrointestinal disturbances which had lead to an increasing interest in the use of medicinal plants as an alternative management for type2 diabetes mellitus. *Solenostemma argel* is one of the of traditional herbs which has been used in Sudan for treatment of diabetes it widely distributed in Egypt, Libya, Chad, Algeria, Saudi Arabia, Palestine, Central and Northern part of the Sudan, however, among these above mentioned countries, Sudan is regarded as the richest source of the Hargel plant which found between Barber and Abu Hammed area in north Sudan (4). It is used in traditional medicines for treatment of diabetes (5). The leaves and/or stem of *Solenostemma argel* contain phytates and phenolic compounds which have the active compounds (6). Glibenclamide is one of the Sulfonylurea; hypoglycemic agents which inhibiting the sulphonylurea receptor 1 (SUR1), the regulatory subunit of the ATP-sensitive potassium channels (K_{ATP}) in

pancreatic β cells which results in an increase in intracellular calcium in β cells and subsequent stimulation of insulin release (7). These drugs are in-effective in pancreatectomized animals or patients who having no endogenous insulin. Glibenclamide is used in the treatment of type 2 diabetes. It is one of only two oral antidiabetics in the World Health Organization Model List of Essential Medicines (8). The present study aimed to investigate the anti-hyperglycemic activity of *Solenostemma argel* extract in normal and 5% glucose induced diabetic rats compared with the antidiabetic drug (Glibenclamide). This study also investigates the toxicity effect of *Solenostemma argel*. Furthermore we investigate the effect of the extract on α -amylase activity.

Material and methods

Study area: Medicinal and Aromatic Plants Research Institute, National Center for Research, Khartoum, Sudan.

Plant materials: The plant was selected according to questionnaire (conducted after ethical consents in all diabetic centers in Khartoum by the researchers) which resulted in 57.1% of Sudanese diabetic patients used *Solenostemma argel*. The plant was purchased from local market at Omdurman, purified, ground to powder using mechanical grinder and preserved in air tight container and kept in dry bottles (9).

Preparation of aqueous extraction: Aqueous extracts were prepared according to the method described by Harborne (10); 300g of the plant powder was soaked in 2000 ml of hot distilled water, and left till cooled down with continuous stirring at room temperature. Extract was then filtered and freezes in a deep. Freeze extract was dried using Freeze drying apparatus till powdered extract obtain.

The powder residue was re-dissolved in drinking water before experiment.

Animals and induction of diabetes: Wistar albino rats of either sex (weighing 135-250 g and aged 60 days) were kept on a fixed diet so as to stabilize the fasting plasma glucose level at 70-110 mg/dl for 3 days, as an adaptation period. All groups were fasting for 18 hours then loaded with 5% glucose (2mg/kg b.w., po) (11) to induce diabetes mellitus. Rats with a FBG level higher than 120 mg/dl were included in the study as diabetic animals.

Experimental groups: Twenty four diabetic rats were assigned to 4 equal groups (6 each). Group (1) was administered with glibenclamide (10 mg/kg b.w.) and serve as control. Treated groups (G2, G3 and G4) were administered with *Solenostemma argel* aqueous extract (200, 400 and 800 mg/kg b.w., respectively). Blood samples (2 ml) were drawn out by capillary tubes in fluorinated test tubes from the orbital plexus of rats according to Khana *et al*, (12) and centrifuged at 3000 r.p.m for 5 minutes to separate plasma. The plasma prepared was used to assess: blood glucose, α -amylase, cholesterol, high density lipoprotein (HDL) and triglycerides concentrations. Blood glucose, cholesterol, HDL and triglycerides concentrations as well as α -amylase activity were determined by using Hitachi 902 analyzer using commercial kits (Biosystem Chemicals, Barcelona, Spain). Data were statistically analyzed by SPSS using ANOVA-1 and LSD (13).

Results

The effect of *S. argel* aqueous extract on blood glucose concentration in diabetic rats, cholesterol, HDL, triglycerides and α -amylase were determined in induced diabetic rats compared with the Glibenclamide, the drug used usually for the treatment of type 2 diabetes. As illustrated in Fig. (1), blood glucose level of diabetic rats was not affected by the administration of 200 mg/kg b.w. of *Solenostemma argel* aqueous extract. The level slightly decreased with 400 mg/kg b.w. but still significantly higher ($p < 0.05$) at zero and after two hours compared with Glibenclamide treated group (G1). Marked

decrease ($p < 0.05$) of blood glucose was observed when the diabetic rats have been administered with 800 mg/kg b.w. of the plant extract.

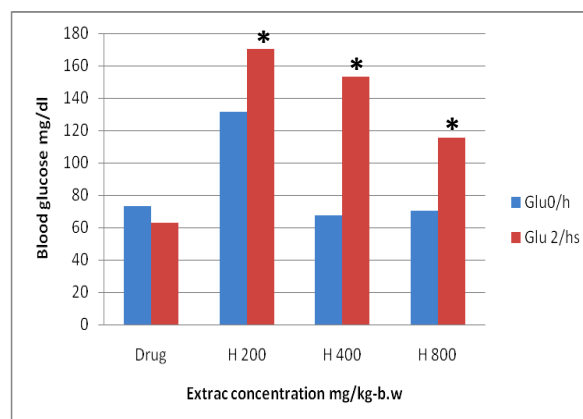


Fig. (1). Effect of administration of different doses of *Solenostemma argel* aqueous extract and Glibenclamide on blood glucose concentration (mg/dl) in diabetic rats. *represent significant compare with Glu 0h ($p < 0.05$).

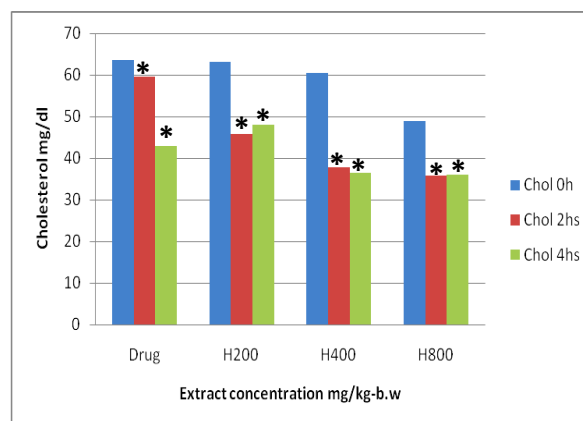


Fig. (2). Effect of administration of different doses of *Solenostemma argel* aqueous extract and Glibenclamide on blood cholesterol concentration (mg/dl) in diabetic rats. *represent significant compare with Chol 0h ($p < 0.05$).

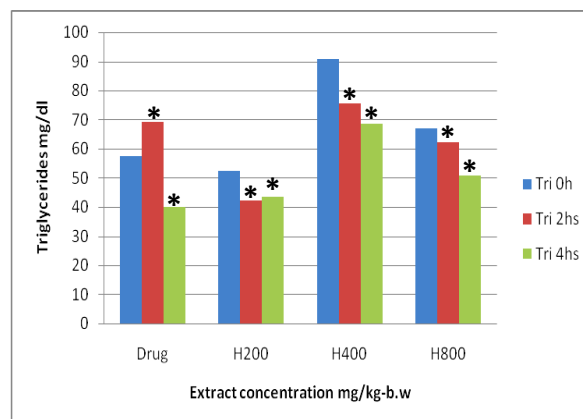


Fig. (3). Effect of administration of different doses of *Solenostemma argel* aqueous extract and Glibenclamide on blood triglycerides concentration (mg/dl) in diabetic rats. *represent significant compare with Tri 0h ($p < 0.05$).

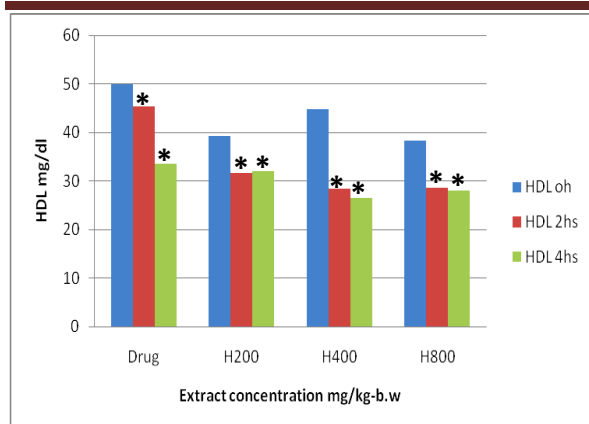


Fig. (4).Effect of administration of different doses of *Solenostemma argel* aqueous extract and Glibenclamide on blood HDL concentration (mg/dl) in diabetic rats.*represent significant compare with HDL 0h ($p<0.05$).

Concerning the comparative effect of *S. argel* aqueous extract and Glibenclamide on blood cholesterol, fig. (2) revealed significant decrease ($p<0.05$) of blood cholesterol concentrations in *S. argel* treated diabetic rats (at doses 200, 499, and 800 mg/kg b.w.) compared with Glibenclamide treated group (G1). The lowest concentration of cholesterol was observed in G4 which administered with 800 mg/kg b.w.) after 4 hrs. (fig. 2). Lower blood triglycerides were observed in *S. argel* treated diabetic rats at a dose of 200 mg/kg b.w after 2 hrs. However, similar effect has been observed after 4 hrs. when diabetic rats treated with same dose of *S. argel* aqueous extract compared to that treated with Glibenclamide. At higher concentration, when the diabetic rats (G3) have been administered with 400 mg/kg b.w.) of *S. argel*, blood triglycerides was significantly higher ($p<0.05$) than G1. Administration with 800 mg/kg b.w. slightly decreased blood triglycerides but still slightly higher than G1

Discussion

Medicinal plants are used in a wide range in order to normalize the hyperglycemia by induction of insulin secretion, improvement the utilization of glucose by body cells or by reduction of carbohydrates absorption by inhibition of α -amylase activity and reduction of gluconeogenesis. The current study resulted in hypoglycemic effect of *S. argel* when compared with the anti-

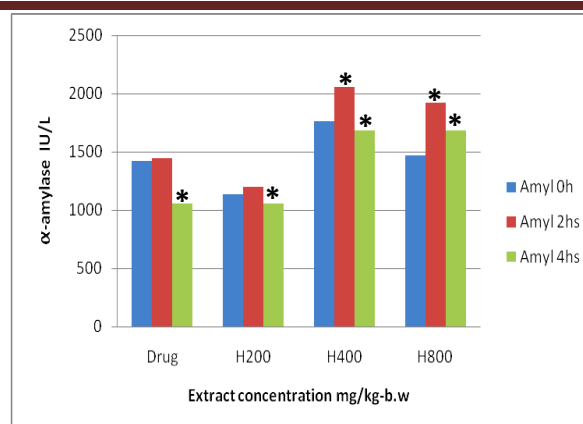


Fig. (5).Effect of administration of different doses of *Solenostemma argel* aqueous extract and Glibenclamide on blood α -amylase activity in diabetic rats. *represent significant compare with Amyl 0h ($p<0.05$).

diabetic drug (Glibenclamide). As it has been reported that *S. argel* is one of the traditional herbs which has been used in Sudan (4), different concentrations (200, 400 and 800 mg/kg b.w.) of *S. argel* aqueous extract have been used in the study. Our present investigation suggested that the aqueous extract of *S. argel* may has the capacity to affect α -amylase activity, the enzyme which is

responsible for hydrolysis of α -1,4-glucans such as starch and related polysaccharides to yield maltose and other oligosaccharides. As it has been illustrated from the present results, 800 mg/kg b.w. of *S. argel* aqueous extract decreased blood glucose to the normal level in comparison with the treatment with 10 mg/kg b.w. of glibenclamide. On the other hand the three doses (200, 400, and 800 mg/kg b.w.) of the plant extract gave a benefit results on lipid profile, by lowering concentrations of cholesterol, TGs and HDL. In addition, treatment with 200 mg/kg b.w. of *S. argel* aqueous extract significantly decreased α -amylase activity after 2 hrs. This result confirmed the results of

previous study which represented that phytic acid represents a complex class of naturally occurring organic form of phosphorus compounds that can significantly influence the functional and nutritional properties of foods (14). In conclusion, findings of this study indicate the anti-hyperglycemic effect of *S. argel* aqueous extract when used in diabetic rats at a concentration of 800 mg/kg b.w. The combined history human use of this plant and the data from the current study support the safe use of these plants. More studies on *S. argel* mechanism of action in hypoglycemic effect are needed to support its usage in diabetes treatment.

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