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Original Research Article

Antidiabetic Efficacy of Aqueous Fruit Extract of Amla (*Emblica officinalis*, Gaertn) in Streptozotocin-Induced Diabetes Mellitus in Male Rats

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Abstract

Purpose: *To investigate the antidiabetic potential of Emblica officinalis, Gaertn on diabetic rats.*
Methods: *The study investigated the anti-hyperglycemic potential of the aqueous fruit extract of amla (E. officianalis, for eleven weeks in streptozotocin-induced diabetic obese rats. The study utilized forty eight rats divided into four groups as follows. Untreated diabetic control (group 1) received 2 % gum acacia as vehicle; groups 2 and 3 were diabetic rats administered the fruit extract in 400 and 200 mg/kg doses, respectively; while group 4 (diabetic rats) received metformin (600 mg/kg) as reference drug. The parameters assessed weekly were body weight, as well as fasting blood glucose, cholesterol and triglyceride levels in venous blood.*
Results: *Both plant extract-treated groups showed significant ($p \leq 0.001$) reduction in blood glucose levels in the fifth and sixth weeks compared to the metformin-treated group. Body weight significantly increased during the fourth, fifth and sixth weeks, being more pronounced in the extract-treated groups (272 ± 15.0 g and 227 ± 7.23 g for 200 and 400 mg/kg doses, respectively; the corresponding body weight for untreated diabetic control was 197 ± 9.83 g. Furthermore, both extract doses (200 and 400 mg/kg) produced significant decrease ($p \geq 0.05$) in serum glucose (186 ± 15.5 mg/L and 146 ± 15.1 mg/L), cholesterol (143.6 ± 0.86 mg/L and 151.0 ± 0.77mg/L) and triglyceride (82.6 ± 0.51mg/dl and 84.8 ± 0.84 m/dl) levels, respectively, similar to the metformin treated group.*
Conclusion: *The anti-diabetic activity of the aqueous extract of E. officianalis used showed a better potential than metformin.*

Keywords: *Antidiabetic, Emblica officianalis fruit, Obesity, Glucose, Cholesterol, Triglycerides*

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INTRODUCTION

Diabetes mellitus is a disease characterized by an altered glucose homeostasis and persistent hyperglycemia leading to many complications. Around 230 million people worldwide have been affected by diabetes and around 366 million people are expected to get affected by 2030 [1]. The pattern of prevalence has been the same in the Gulf including Saudi Arabia. Saudi Arabia has experienced an exponential socioeconomic growth over the past few decades which have led to a sedentary and affluent lifestyle of the people in the urban society. A recent follow up epidemiological study shows an alarming increase in the prevalence of diabetes during the past few years [2]. This has stimulated public

awareness of this endocrine disorder and the identification of risk factors associated with it.

Emblica officinalis, Gaertn commonly known as Indian gooseberry or amla in India, is a member of the small genus of Emblica (Euphorbiaceae). It is an important dietary source of vitamin C, minerals and amino acids, and also contains phenolic compounds [3]. The aqueous fruit extract of amla has been reported to exhibit hypolipidaemic [3], antidiabetic and anti-inflammatory activities. In the past decade, the aqueous fruit extract of amla has been tested for various pharmacological activities. Some of these activities includeantioxidant properties [4,5], and it has also been reported that the aqueous fruit extract of amla is a potent inhibitor of lipid peroxide formation and a scavenger of hydroxyl and superoxide radicals *in vitro* [6]. The present study includes a comparative assessment of the antihyperglycemic potential of the aqueous fruit extract of amla and a commonly used antidiabetic drug. Blood glucose, body weights and other related markers such as serum cholesterol and triglycerides associated with the progression of diabetes were studied in streptozotocin (STZ) induced diabetic rats.

EXPERIMENTAL

Materials

All chemicals and drugs were obtained commercially and of analytical grade. They include streptozotocin (Sigma Aldrich, USA) and metformin (Merck Serono, Middle East). Commercially available kits using Reflotron Assays (Roche) were used for the determination of serum glucose, cholesterol and trigycerides (United Diagnostic Company, Saudi Arabia).

Plant material and preparation of extract

Shade-dried amla fruits were obtained from the local market in Riyadh city, Saudi Arabia. The fruits also authenticated and found in the Botanical garden at King Saud University, were identified and authenticated by Dr Iram Siddique in the Department of Botany at King Saud University, Riyadh. A voucher specimen (voucher no. 2981) of the fruit was deposited in the herbarium of the Faculty of Science, King Saud University, Riyadh, Saudi Arabia.

For the preparation of the aqueous fruit extract, 100 g of the dried amla fruits were ground in an electrical grinder and soaked in 500 ml distilled water [7]. The mixture was left for 24 h with a magnetic stirrer at room temperature. Twenty four hours later, the mixture was strained out using a fine sieve and the crude extract air-evaporated for 3 days [8]. The aqueous fruit extract was then orally administered to the rats in the two extract treatment groups at doses of 200 and 400 mg/kg body weight, respectively.

Experimental animals and induction of diabetes

Male Wistar rats weighing 200 - 250 g were used. The animals were fed with standard laboratory chow obtained from the animal house at King Saud University and had free access to water under well ventilated conditions of 12 h day and dark cycles each. The animals were acclimatized to laboratory conditions prior to the experiment. The protocols were approved by the institution's National Committee for Medical and Bio-ethics. The animals were handled according to standard protocols for the use of laboratory animals [9].

Food was withdrawn 12 h prior to the induction of diabetes. Thereafter, they were injected with streptozotocin (70 mg/kg, i.p.) [8]. Five days after injection, the rats with fasting blood glucose higher than 200 mg/L were considered diabetic and used for the experiment [8]. Food was withdrawn 12 h prior to blood sampling.

Study groups

The forty eight rats were divided into the following groups and they were daily orally treated with the respective drugs as indicated for eleven weeks. Group 1; Untreated diabetic control (DC): diabetic rats administered 2 % gum acacia as vehicle, 2 and 3. Emblica officinalis aqueous fruit extract (400 and 200 mg/kg body weight) treated diabetic rats respectively, and group 4. Metformin injections for treated diabetic rats (600 mg/kg body weight) [8].

Blood sampling and biochemical analysis

Daily before and after administration of the aqueous plant extract of amla and metformin, rats were anaesthetized using carbon dioxide. Venous retro orbital blood samples were collected in the fasting state at specific intervals using a glass capillary and collected in polystyrene tubes without anticoagulant [10]. Serum was separated by centrifugation at 3000 rpm for 10 min after which it was tested for glucose. At the end of the experimental period, the blood samples collected were also tested for serum cholesterol and triglycerides. Samples were stored at -20 °C until assayed.

Statistical analysis

One-way analysis variance (ANOVA) was performed using GraphPad Prism statistical software. Tukey t-test was used for multiple comparisons. The values were considered significantly different at $p < 0.05$.

RESULTS

The basal serum fasting glucose levels of the rats from all the four experimental groups were comparable (94 - 100 mg/dL) and there was no significant difference between the groups. In the first week after the administration of STZ (70 mg/kg), the blood glucose level was increased in the diabetic group almost two-fold (120 - 280 mg/dL). Groups administered both doses of amla (200 and 400 mg/kg) showed no significant difference from the metformin group. The blood glucose level of rats from all the treated groups showed a significant ($p \leq 0.001$) decrease in compared to diabetic control; however, there was no significant difference observed between the amla-treated groups (Figure 1).

The mean basal body weight of all experimental groups ranged from 184 -199 g and no inter-group variation was observed. Post-administration of STZ (week 1) resulted in increase in body weight in all the experimental groups. The body weight of diabetic control group was not significantly different ($p < 0.05$) from those of the extract-treated groups. While the body weight of the rats from the group treated with the lower dose of the aqueous fruit extract of amla (200 mg/kg) ($p < 0.001$), it, however, significantly higher than that of the metformin-treated group, the higher dose (400 mg) of the aqueous fruit extract of amla group showed no significant difference in body weight. However, the body weight of rats in extract-treated groups were not significantly different from that of diabetic control. There was also no significant difference in body weight between the two extract-treated groups (Figure 2).

At the end of the experimental period, the level of serum cholesterol in diabetic control rats was significantly ($p < 0.05$) higher than in all the treated groups. On treatment with the plant extract a significant ($p < 0.001$) decrease in serum cholesterol level was observed for both extract doses (200 and 400 mg/kg) compared to diabetic control and metformin groups (Figure 3). There was a significant ($p < 0.05$) difference between the extract-treated groups.

At the end of the experimental period, the level of serum triglycerides in diabetic control rats was significantly ($p < 0.001$) than in all the treated diabetic groups. A significant ($p < 0.001$) decrease in triglyceride levels was observed for both the amla aqueous fruit extract treated groups when compared to the metformin (Figure 4).

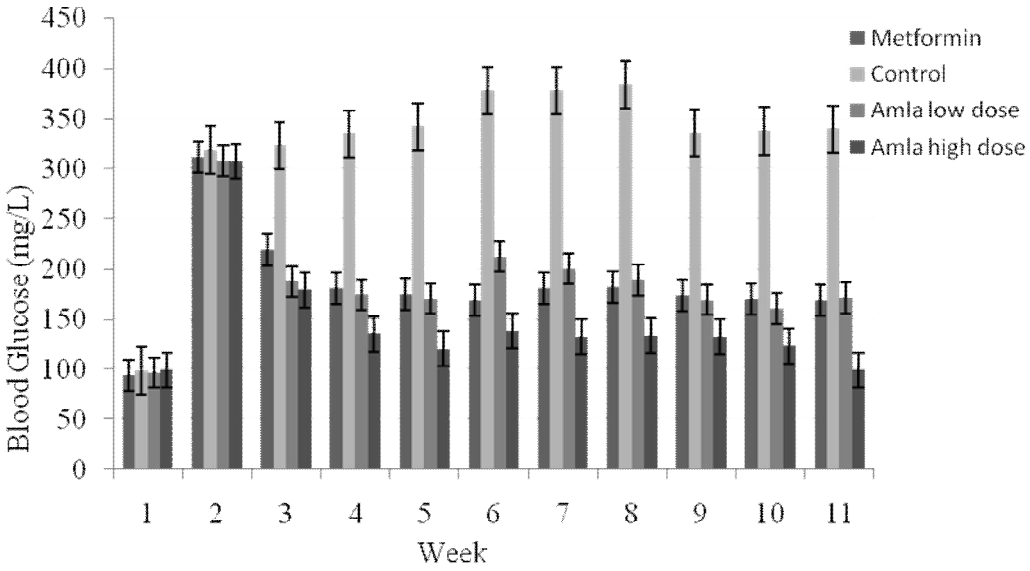

Figure 1: Effect of *Emblica officianalis* fruit extract on serum blood glucose level (mg/dL) of diabetic rats

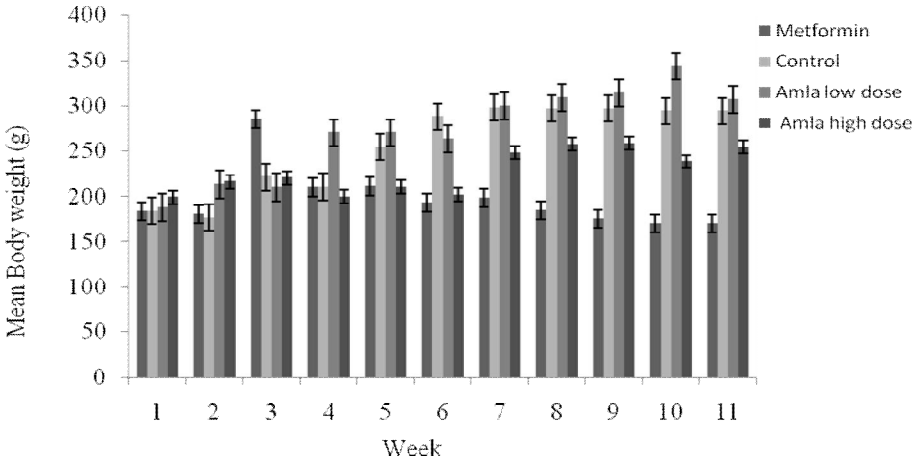

Figure 2: Effect of *Emblica officianalis* on body weight of diabetic rats

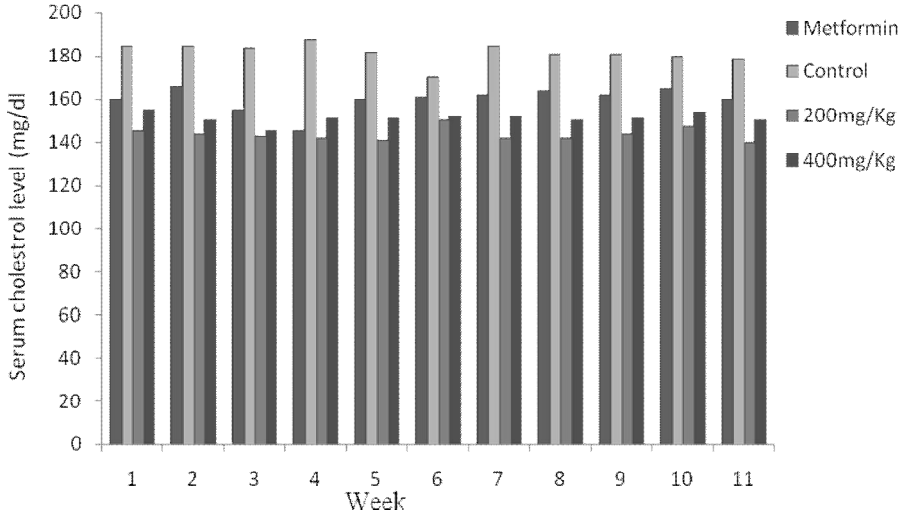

Figure 3: Effect of Emblica *officianalis* on serum cholesterol in diabetic rats

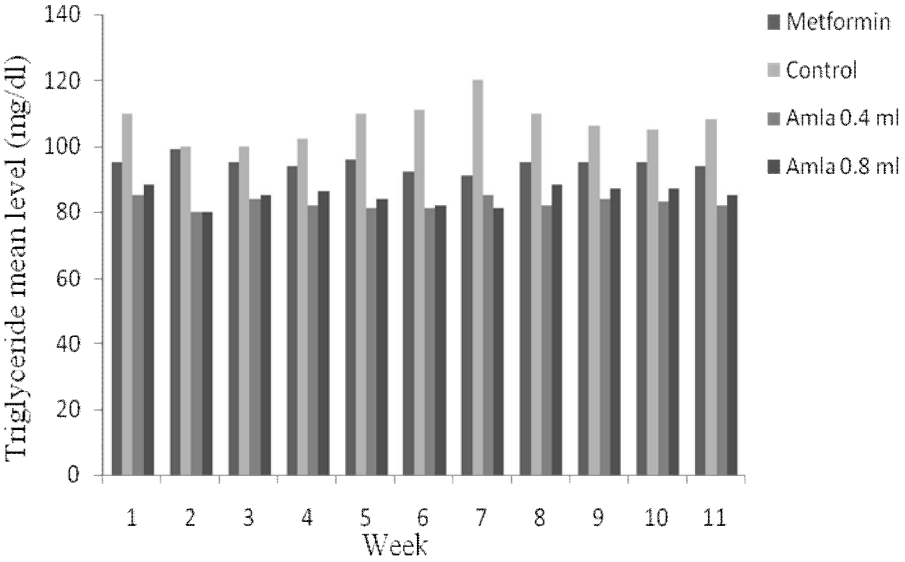

Figure 4: Effect of *Emblica officianalis* on serum triglyceride levels in diabetic rats

DISCUSSION

Phytotherapy has a promising future in the management of diabetes, considering its less toxicity and fewer side effects compared to the synthetic drugs used [11]. Also, they are important sources of antioxidant molecules and novelty. Phytocompounds have been proven to be safe and efficacious with fewer side effects in comparison to the synthetic antioxidants which could possibly be carcinogenic in nature [11].

Diabetes and obesity are chronic metabolic diseases that are associated with risk of hypertension, renal failure, coronary heart diseases, stroke, all being fatal [12,13]. The present study showed that treatment of STZ induced type I diabetic rats by amla aqueous fruit extract improved the antidiabetic effects.. Further, an experimental study on male wistar rats fed a high-fructose (65 %) diet for 1 week, and treated with an ethyl acetate (EtOAc) extract of amla, a polyphenol-rich fraction, at 10 or 20 mg/kg body weight per day, showed that the extract alleviated the dyslipidaemia caused due to the fructose – induced metabolic syndrome [14]. Similar findings were reported in another study [15] on diabetic rats treated with a plant extract, powdered rhizome of *Curcuma longa* (turmeric) and the dried fruits of *Emblica officinalis*. The treatment achieved significant lowering of plasma glucose and glycated haemoglobin in diabetic rats comparable to that of the glyburide, a sulfonylurea drug, treated group. Most phenolic and flavonoids compounds are described as having anti-oxidative action in living systems, as they act as scavengers of free radicals [16].

Thus there is a growing trend of using plant products in therapy as they are rich in these antioxidants. However, the non pharmacological management of type 2 diabetes should include an appropriate diet management. A myriad of foods like cereals, vegetables and spices have been assessed for their anti-hyperglycemic effect [17] in experimental as well as clinical studies. The present study showed that treatment of STZ rats with the extract improved insulin sensitivity. However, the plant extract had other effects such as anti-obesity although another study had reported no anti obesity effects [14].

The findings in the present study demonstrate an antihypercholesterolic and antihypertriacyl-glycerolaemic effect of the extract of amla at both doses used (200 and 400 mg/kg). Hypoglycemic herbs are widely used as nonprescription treatment for diabetes. However, few herbal medicines have been well characterized and demonstrated an efficacy in systematic clinical trials as those of synthetic drugs. Though these herbs may lower blood glucose, the test results are subject to several factors. For example, a plant may contain a myriad of components but only a few of which may be therapeutically effective. Therefore, phytochemical screening and clinical trials of this extract is necessary.

CONCLUSION

The use of phytonutrients to combat diabetes mellitus does offer a novel therapeutic approach to restore normal body functions. Findings from the present study indicate that the aqueous fruit extract of amla has a potential as an antidiabetic natural product. However, further pharmacological toxicological studies are required to determine its other effects and to elucidate its mechanisms of action.

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