Protective Effect of Red Grape Seed Proanthocyanidins against Induction of Diabetes By Alloxan in Rats

Amal J. Fatani, Amani A.E. Ahmed, Abir T. El-Alfy
Pharmacology Department, Faculty of Pharmacy, King Saud University, Riyadh 11495, Saudi Arabia

ABSTRACT

Diabetes is a chronic metabolic disorder that continues to present a major health problem in the world, especially developing countries. As a consequence of the metabolic derangements in diabetes, various complications develop. Recently, medicinal and natural products have been used as a major contributor to the pathogenesis of different diabetic complications. In order to find effective and safe therapies, the study of new potential therapeutic targets and their possible involvement in the development of diabetes is a major focus of research. The present study demonstrates that alloxan is an effective model for studying the effects of different therapeutic agents on the development of diabetes. The results showed that alloxan-induced diabetes was significantly reduced by the administration of red grape seed proanthocyanidins (GSP). The effects of GSP on blood glucose levels and pancreatic beta-cell mass were evaluated in diabetic rats. The results indicate that GSP significantly reduced blood glucose levels and increased pancreatic beta-cell mass. These findings suggest that GSP may have potential therapeutic effects in the management of diabetes.

INTRODUCTION

Diabetes is a chronic metabolic disorder that continues to present a major health problem in the world, especially developing countries. As a consequence of the metabolic derangements in diabetes, various complications develop. Recently, medicinal and natural products have been used as a major contributor to the pathogenesis of different diabetic complications. In order to find effective and safe therapies, the study of new potential therapeutic targets and their possible involvement in the development of diabetes is a major focus of research. The present study demonstrates that alloxan is an effective model for studying the effects of different therapeutic agents on the development of diabetes. The results showed that alloxan-induced diabetes was significantly reduced by the administration of red grape seed proanthocyanidins (GSP). The effects of GSP on blood glucose levels and pancreatic beta-cell mass were evaluated in diabetic rats. The results indicate that GSP significantly reduced blood glucose levels and increased pancreatic beta-cell mass. These findings suggest that GSP may have potential therapeutic effects in the management of diabetes.

MATERIALS AND METHODS

Animals

Male adult Wistar rats (180-200 g) were procured from the Animal House Faculty at King Saud University. The animals were housed in cages with 12/12-hour light/dark cycle at 37±1°C. The animals were given Purina rat chow and water ad libitum. The animals were kept under observation for one week prior to the start of treatment. All animal experiments were carried out in accordance with the Institutional Animal Care and Use Committee guidelines.

Chemicals

Grape Seed Proanthocyanidins (GSP; 95% purity) were purchased from Alphapharm (Egypt). All other chemicals were obtained from Sigma-Aldrich Chemical Co. (St. Louis, USA).

Induction of diabetes

The animals were fasted for 24 h prior to the induction of diabetes. Alloxan monohydrate, freshly prepared in normal saline, was intraperitoneally injected (150 mg/kg) through tail vein to induce diabetes. Groups treated with GSP were given one dose of the GSP one hour prior to alloxan injection. Diabetes development was monitored by commercially available glucose strips.

Experimental Procedure

A total of 96 rats were used and were divided into 8 groups of 12 rats each. Group 1: normal control rats; Group 2: diabetic control rats; Group 3: diabetic rats given 50 mg/kg BW GSP for 4 days; Group 4: diabetic rats given 100 mg/kg BW GSP for 4 days; Group 5: diabetic rats given 50 mg/kg BW GSP for 7 days; Group 6: diabetic rats given 100 mg/kg BW GSP for 7 days; Group 7: diabetic rats given 100 mg/kg BW GSP for 14 days; Group 8: diabetic rats given 200 mg/kg BW GSP for 14 days. The GSP was given in normal saline solution by oral gavage. At the end of the experimental period, the animals were killed overnight and then necropsied by decapitation. Blood collected, and the pancreas dissected out. The blood was centrifuged at 3000 g for 20 min and the clear serum collected. Dissected tissues and sera were kept at -4°C until further analysis.

Analytical Procedures

Blood glucose levels were estimated using a commercially available kit (HORIBA Ltd., TJA). Serum total cholesterol levels were determined with an enzymatic immunoassay (EIA) kit using rat as a model (Biomedica, London, Ontario, Canada). Total cholesterol levels were measured in pancreatic tissue homogenate by the reaction of the cholesterol/glyceride (CM) in the non-polar fractions of the homogenate with CM-C, and the absorbance at 340 nm was measured to determine the cholesterol level. The measurement was spectrophotometrically at 340 nm using the extinction coefficient of 0.023 cm-mg/ml.

The levels of interleukin-1β and tumor necrosis factor (IL-1b) in the serum were measured using a commercially available ELISA kit (Shanghai BestBio Technology Co., Ltd., China). Total cholesterol levels were estimated as an index of NO production, estimated using Griess reaction according to the procedures of a commercially available kit (Sigma, St. Louis, USA).

Statistical analysis

The results were analyzed using one-way ANOVA followed by Multiple Tukey test for comparison using GraphPad Prism software version 5.0.

REFERENCES


RESULTS & DISCUSSION

In summary, the results of the present study indicate that GSP possess potent anti-diabetic effects on the induction of diabetes by alloxan. The data provided suggest that the mechanism underlying such protection is mediated via suppression of pancreatic beta-cell destruction and prevention of pancreatic damage. Furthermore, the present study demonstrates that GSP may be a promising therapeutic agent for the prevention and treatment of diabetes. The data presented provide additional benefits of GSP administration and may offer a promising natural and safe new lead for the prevention or delay of diabetic complications.

CONCLUSION

Based on the observed stress hypothesis of diabetic action, it was considered as an adequate model for investigating the role of free radicals in the etiology of diabetes mellitus. The present study demonstrates that GSP, a potent antioxidant, can exert anti-diabetic effects by preserving pancreatic beta-cell function. The data presented suggest additional benefits of GSP administration and may offer a promising natural and safe new lead for the prevention or delay of diabetic complications.

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Fig. 1. Effect of red grape seeds proanthocyanidins (GSP) on fasting blood glucose level in alloxan-induced diabetic rats. Values are represented as means ± SD (n=15). Control diabetic animals were compared to normal group. *p<0.05; **p<0.01. GSP treated groups were compared with their respective diabetic controls. *p<0.05, **p<0.01.

Fig. 2. Effect of red grape seeds proanthocyanidins (GSP) on serum insulin level in alloxan-induced diabetic rats. Values are represented as means ± SD (n=15). Control diabetic animals were compared to normal group. *p<0.05, **p<0.01. GSP treated groups were compared with their respective diabetic controls. *p<0.05, **p<0.01.

Fig. 3. Effect of red grape seeds proanthocyanidins (GSP) on pancreatic glutathione level in alloxan-induced diabetic rats. Values are represented as means ± SD (n=15). Control diabetic animals were compared to normal group. *p<0.05, **p<0.01. GSP treated groups were compared with their respective diabetic controls. *p<0.05, **p<0.01.

Fig. 4. Effect of red grape seeds proanthocyanidins (GSP) on pancreatic malondialdehyde (MDA) level in alloxan-induced diabetic rats. Values are represented as means ± SD (n=15). Control diabetic animals were compared to normal group. *p<0.05, **p<0.01. GSP treated groups were compared with their respective diabetic controls. *p<0.01.

Fig. 5. Effect of red grape seeds proanthocyanidins (GSP) on pancreatic cytochrome c level in alloxan-induced diabetic rats. Values are represented as means ± SD (n=15). Control diabetic animals were compared to normal group. *p<0.05, **p<0.01. GSP treated groups were compared with their respective diabetic controls. *p<0.05, **p<0.01.

Fig. 6. Effect of red grape seeds proanthocyanidins (GSP) on pancreatic malondialdehyde (MDA) level in alloxan-induced diabetic rats. Values are represented as means ± SD (n=15). Control diabetic animals were compared to normal group. *p<0.05, **p<0.01. GSP treated groups were compared with their respective diabetic controls. *p<0.05, **p<0.01.