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Anti-Lipidimic and Anti-Hyperglycemic Properties of Methanolic Extract of Grape Seed in Diabetic rats

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Abstract: The aim of this study was to assess the effect of methanolic grape seed extract on the blood glucose and lipid profile in diabetic rats. For this research 30 male adult rats were randomly selected and divided into three groups as nondiabetic control; diabetic control; diabetic rats treated with methanolic extract of grape seed. In diabetic groups, alloxan monohydrate (120 mg/kg) was injected intraperitoneally to develop diabetes. Then the Test group received intraperitoneal injection of methanolic extract of grape seed (100 mg/kg). At last, glucose, cholesterol, triglyceride, HDL, VLDL, LDL and insulin contents of the rats' serum sample were determined. Diabetic rats treated with extract showed a significant decrease in blood glucose level ($P<0.05$). There was a significant decrease in serum contents of total cholesterol (TC), LDL, VLDL and TG, but a significant increase in insulin level and HDL of extract-treated group was observed in compare with diabetic group ($P<0.05$). These results show that the methanolic extract of Grape Seed may be effective in the treatment of diabetes. This effect may be due to the presence of flavonoides and antioxidant properties of grape seed.

Keywords: grape seed, blood sugar, lipid profile, insulin.

INTRODUCTION

Diabetes is the most common endocrine disease being characterized with increased blood sugar (hyperglycemia) and disorders in metabolizing carbohydrates, lipids, and proteins.(Jodeph, 2003). In diabetes mellitus, chronic hyperglycaemia produces multiple biochemical sequelae, and diabetes-induced oxidative stress could play a role in the symptoms and progression of the disease. Oxidative stress may result in overproduction of oxygen free-radical precursors and/or decreased efficiency of the antioxidant system. The oxygen free-radical generation is associated with auto-oxidation of glucose, impaired glutathione metabolism, alterations in the antioxidant enzymes and formation of lipid peroxides.3–5 There are various endogenous defence mechanisms against free radicals, such as the enzymes GSH, SOD, GPx and CAT, whose activities eliminate superoxide, hydrogen peroxideand hydroxyl radicals (Soto et al., 2003).

Use of medicinal plants in medicine is increasing because of their widespread use and for their curing various diseases. Grape seed is well known for its pharmaceutical properties including; anti-inflammatory (Shipochliev et al., 1981; Al-Hindawi et al., 1989), immunomodulatory activity (Uteshev et al., 1999), arcaricadal property (Macchioni et al., 2004), antipruritic effect (Kobayashi et al., 2009), treatment of gastrointestinal disorders (. Mahady et al., 2005), antimicrobial activity (Nogueira et al., 2008), treatment of stress and depression (Pinto et al., 2008), anti-allergic activity (Kobayashi et al., 2003), antisolar agent (Ramos et al., 1996). With regard to these properties, this study was undertaken to evaluate the antidiabetic activity of methanolic extract of grape seed, since up to now no pharmacological evaluation has been done on grape seed for its antidiabetic activity. This prompted us to pursue the activity and was examined for their efficacy and for determination of their possible mechanism of action.

MATERIALS AND METHODS

Plant material: From grapes the seeds were removed and dried in shadow according to drying process on January 2011, at department of biology, Science and Research Branch, Islamic Azad University, Fars, Iran. Then, the dried seeds were grinded to a uniform powder and weighed. The most important and essential part of extraction of plant material is the selection of a proper organic solvent which depends on the part and constituents of the plant. In this study, 500 g of the grape seed powder were extracted by maceration method in the methanol for three days. The extracted material was filtered and the filtrated material was concentrated under vacuum evaporator until dryness.

Animals: In present study, we used 30 male rats from Wistar race in weight range of 180 and 220 grams.

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Table. 1: Effect of methanolic extract of grape seed on level of serum glucose, Insulin, cholesterol, triglyceride, and lipoproteins in studied group of rats (mean ± standard deviation)

Experimental Groups (groups of 10 rats)			
Index	Control	Diabetic control	Treated by methanolic extract of grape seed
Glucose (mg/dl)	128±16.2	758±112.4	281±35.2
Triglyceride (mg/dl)	106±11.0	237±15	136±29
Cholesterol (mg/dl)	96.7±11.2	112.9±11.5	104.2±11.8
LDL (mg/dl)	25±5	42±12	23±9
HDL (mg/dl)	51±7	23±6	54±12
VLDL (mg/dl)	23±2	45±3	28±5
Insulin (μu/ml)	13.15±1.45	4.96±1.41	11.18±1.7

Mean glucose difference of treated group with diabetic control and control groups: meaningful ($p<0.05$)
Mean triglyceride difference of treated group with diabetic control group: meaningful ($p<0.05$)
Mean LDL difference of treated group with diabetic control group: meaningful ($p<0.05$)
Mean HDL difference of treated group with diabetic control group: meaningful ($p<0.05$)
Mean VLDL difference of treated group with diabetic control group: meaningful ($p<0.05$)
Mean insulin difference of treated group with diabetic control group: meaningful ($p<0.05$)

Animals were randomly divided to three groups of ten rats: 1) control group: healthy rats which received physiologic serum equal to the injected extract volume. This was done to equalize the shock resulted from injection; 2) diabetic control group: diabetic rats which were affected by single intraperitoneal injecting of 120 mg/kg monohydrate alloxan, and were treated with physiologic serum; 3) diabetic rats treated with grape seed extract: the rats which were affected as well as the second group. And 100 mg/kg methanolic extract of grape seed injection was performed for 10 successive days after assuring that rates were affected by diabetes.

48 hours after the last injection, the bleeding was performed from all groups and the resulted serum was used to determine blood glucose, cholesterol, triglyceride, and lipoproteins (LDL and HDL) with enzyme kits (from Zist-Shimi, Iran).

During the study, storage, injection of various materials, bleeding, and perishing animals were performed according to standard methods of working with laboratorial animals. In statistical survey of findings, the one-way ANOVA test was applied to compare average of each variable in test groups and then Tukey test was performed. Statistical analysis of findings was done with SPSS software and $p<0.05$ was treated meaningful.

RESULTS

Results of biochemical tests of glucose, Insulin, cholesterol, triglyceride, HDL, LDL, and VLDL is shown in table 1.

DISCUSSION

In present study, we examine the effect of methanolic extract of grape seeds on biochemical parameters of blood. Results from this study show that in treated group, blood glucose, triglyceride, cholesterol, LDL, HDL, and VLDL level had a meaningful decrease ($P<0.05$) compared to the diabetic control group and blood insulin and HDL level had a meaningful increase ($P<0.05$) compared to the diabetic control group.

According to several studies, specific toxicity of alloxan for Beta-cells of pancreas is due to quick absorption of alloxan by pancreatic Bata-cells and free radicals production by alloxan. Free radicals can cause reversible or irreversible damages to cellular compound of creatures (such as proteins, lipids, carbohydrates, nucleic acids, etc.) and thereby affect cellular activities such as function of membrane, metabolism, and gene expression. Therefore, some cells would lose their structure and activity. According researches, oxidative damage of free radicals is main cause of damage to cells and tissues in some diseases such as arthroscleroses, cancer, mellitus diabetes, etc (Szkudelski, 2001) Antioxidants are compounds that protect cellular membrane and various components of creatures against oxidants. Mechanism of action of these compounds is gathering free radicals, transferring electron to these electrons, and inactivation of them (Fukuda et al., 2004; Vaya and Aviram, 2002).

Researches in recent years by Yassa, Puiggros and saad also address to ability of grape seed extract to increase anti-oxidative defense and to control damages resulted from oxidative stresses. They point to presence of flavonoids as an essential factor in extract structure and suppose it probable that Proanthocyanidin compounds existing in grape seed extract are among effective factors in incidence of anti-oxidative properties (Yassa et al., 2008; Puiggròs et al., 2009; saad et al., 2009).

Irina et al (2009) and Atsushi (2007) pointed to decrease of Malondialdehyde and noted that 50 to 100 mg/kg of grape seed extract has an anti-oxidative characteristic and contribute to protect cells and control of their death.

According to results from this research, consumption of antioxidants existing in grape seed contributes to decrease damages to cells and, specially, accelerates restoration of pancreatic cells and subsequently increases insulin and decreases blood glucose.

In rats affected by diabetes with alloxan, increased blood glucose level can indirectly increase cholesterol, triglyceride, LDL, VLDL level of serum and decrease HDL level (Yanardag et al., 2002) Similarly, this accounts for to some extent undesirable changes serum lipids level in rats affected by diabetes in present study. According to the results, disorders in lipids metabolism resulted from diabetes would be obviated by controlling blood glucose with grape seed extract. Therefore, this would also decrease HDL in addition to decreasing blood glucose, triglyceride, LDL, and VLDL. This is in turn due to high level of anti-oxidative substances existing in extract of grape seed, which can induce desirable metabolic changes associated to hepatic enzymes as to improve undesirable changes blood glucose and lipid levels. According to this study, it can be concluded that one of mechanisms of methanolic extract of grape seed effect on diabetes in rats is restoration of Islets of Longerhans followed by increased insulin level.

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