Anti-hyperglycaemic, anti-oxidant and anti-hyperlipidaemic effects of *Momordica charantia* L. on streptozotocin-induced diabetic rats

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The study was aimed to determine the effects of *Momordica charantia* (MC) on fasting blood glucose levels, oxidative stress and plasma lipid profile in streptozotocin (STZ)-induced diabetic rats. Diabetic rats were orally administered MC extract (200 mg/kg) and subcutaneous insulin (1 IU) for 21 days. MC and insulin treated groups showed a significant decrease in the fasting blood glucose levels from the 7th day (p < 0.001). There were no differences in HDL cholesterol and triglyceride levels. There was a decrease in the LDL and VLDL cholesterol levels (p < 0.05). Furthermore, treatment with MC and insulin reduced in the erythrocyte TOS levels (p < 0.05). However, there were no significant differences in plasma and erythrocyte TAS levels between the untreated diabetic group and MC group. The anti-hyperlipidaemic property of the MC extract was determined, while the more antioxidant and anti-hyperglycaemic features of the insulin was observed. Based on this information, it is considered that it will be more effective to use MC and exogenous insulin in combination for preventing complications such as oxidative stress and, hyperlipidaemia shaped by diabetes.

**Keywords:** Diabetes mellitus, *Momordica charantia*, Lipid profile, Oxidative stress

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In *Diabetes mellitus* which is one of the leading chronic metabolic diseases 1, oxidative stress occurs due to the increase in free oxygen radical formation after hyperglycaemia and the anti-oxidant defence mechanism becoming insufficient 2. Type1 diabetes also occurs due to the hormone-sensitive lipase activation because of insulin insufficiency 3, increases in LDL cholesterol and triglyceride levels and decreases in HDL cholesterol levels. It is known that hyperlipidaemia is one of the most important causes of cardiovascular disorders 4. Because there is no certain treatment for Type1 diabetes, the applied treatments cause various complications and are expensive. For this reason, researchers tend to find new sources for anti-diabetic compositions. Thus, it has become popular in Asian counties to study herbs such as *Momordica charantia* used as a traditional medicine for centuries 5.  

MC of the Cucurbitaceae family is an annual plant 6 that is commonly known as *Karela* or bitter melon 7. The plant originates in India and China, and is commonly cultivated in Asia, East Africa, Amazons and Caribbean 8. In Turkey, mature fruits of MC are used in traditional medicine for the treatment of peptic ulcer and rapid healing of wounds 8. There are some important phytochemicals isolated from MC; charantin, polypeptide P (insulin-like peptide), vicine, momorcharin, momordicin and oleanolic acid are the most important among the phytochemicals 9. It is considered that MC exerts its anti-hyperglycaemic effect by charantin 10, vicine 11 and polypeptide P 9, which is similar to bovine insulin and also identified as phytoinsulin. It is stated that MC exerts its hypoglycaemic effect both in human and animals and includes alloxan- and STZ-induced experimental diabetes mellitus 12 and Type1 and Type 2 diabetic patients 13.  

In this study, we aimed to determine the effects of administering oral MC extract and subcutaneous insulin for 21 days on fasting blood glucose levels, oxidative stress and plasma lipid profile in STZ-induced diabetic rats.

**Material and methods**

**Experimental animals and setup**

This study was conducted under the approval of Kafkas University Animal Experiments Local Ethics
Committee (2012/54). A total of 40 Sprague Dawley rats, aged 5–6 months, divided into 4 groups including 10 individuals, were used. The rats were fed under standard conditions ad libitum.

I. Control Group: The group received physiological saline solution intraperitoneally (i.p.).

II. Diabetes control group: This group received 50 mg/kg Streptozotocin (STZ) i.p. (50 ml citric acid + 40 ml disodium hydrogen phosphate buffer pH 4.5) + physiological saline solution.

III. Momordica charantia group: This group received 50 mg/kg STZ i.p. + 200 mg/kg Momordica charantia orally (Easy Pha-max Insupro Forte). It is stated that each capsule contains 200 IU plant derived insulin. The stock solution of Momordica charantia was dissolved in drinking water after that opened the capsules. Administered by oral gavage in dose volumes of 200 mg body weight daily from this stock solution for 21 days.

IV. Insulin group: The group received 50 mg/kg STZ i.p. + subcutaneous 1 IU insulin (Levemir Flexpen).

The rats were defined as diabetic if the blood fasting glucose levels were >200 mg/kg after 72 hrs of STZ administration. The rats received MC and insulin according to the procedure explained above for 21 days. At the end of the experiment, the blood samples were collected under 0.4 ml/kg pentobarbital sodium anaesthesia via the intra cardiac route. The blood samples were then centrifuged at 3000 rpm for 10 min at 4°C and the plasma samples were stored at −20°C until use.

Biochemical analysis
Blood glucose levels were determined by using a glucometer and strips after 8 hrs of fasting (Gluko Leader-Yasee brand). Total oxidant (TOS) and total antioxidant (TAS) levels in plasma and erythrocyte samples were detected by spectrophotometry using test kits (Rel-Assay Diagnostic Gaziantep-Turkey). In plasma samples, LDL, HDL, VLDL, total cholesterol and triglyceride levels were measured using an auto-analyser (Architect c16000 Abbott Diagnostics-USA model).

Statistical analysis
One-way ANOVA was used to determine the differences between the treated groups and the control group. Duncan’s multiple range test was used for detecting the alterations between the groups. Significance was considered at p < 0.05, p < 0.01 and p < 0.001. All statistical evaluations were made using SPSS 18.

Results
On the initial and 3rd day and after diabetes was induced on the 7th, 14th and 21st days, the blood glucose levels of all groups were measured and evaluated. Initially, the blood glucose levels of the groups were between 85 mg/dl and 106 mg/dl. It was detected that blood glucose levels increased significantly when the control and diabetic groups were compared after STZ application up to 72 h (p < 0.001); no statistical significance was found when the diabetic groups were compared between each other (p > 0.05). On the 7th, 14th and 21st days, a significant decrease in the blood glucose levels of the groups treated with MC and insulin (p < 0.001) occurred when compared to the diabetes control group. In addition, it was determined that the blood glucose levels decreased (p < 0.01) in the insulin group when compared with those of the MC and insulin groups on the 21st day (Table 1).

The erythrocyte TOS levels of the MC and insulin groups were decreased as compared to those of the diabetic group and the erythrocyte TOS levels of the insulin group were less than those of the MC group (p < 0.05). However, when the groups were compared in terms of erythrocyte TAS and plasma TOS levels, statistical significance was not found (p > 0.05). Plasma TAS levels of the diabetes control and MC groups were decreased as compared to the control group. In the insulin group, similar values with the control group were observed (p < 0.05) (Table 2).

Table 3 shows the decrease in plasma LDL cholesterol levels of the MC group as compared with the diabetic control group (p < 0.05). When LDL cholesterol and total cholesterol levels of the diabetic control group were compared with that of the control group, both cholesterol levels increased in the diabetic control group (p < 0.001 and p < 0.01, respectively). Although the MC and insulin groups showed a decrease in total cholesterol and triglyceride levels and an increase in the HDL cholesterol levels when compared to those of the diabetic control groups, no statistically significant difference was observed. Moreover, a decrease (p < 0.05) in the VLDL cholesterol levels of the MC and insulin groups was detected when compared with those of the control groups.

Discussion
In numerous studies14,15,16, it has been highlighted that increasing blood glucose levels, oxidative stress, total cholesterol, triglyceride, LDL and VLDL cholesterol in Type1 diabetes have significantly
important roles in the formation of chronic complications of diabetes (including nephropathy, neuropathy, retinopathy and arteriosclerosis).

In this study, anti-hyperglycaemic, anti-hyperlipidaemic and anti-oxidant effects of MC in STZ-induced diabetic rats were evaluated.

After the 7th day of the study, it was determined that there was a significant decrease in the fasting blood glucose levels of the rats that were administered MC and insulin when compared to those of the untreated diabetic rats (Table 1). Sekar et al. demonstrated that the MC extract decreased glycosylated haemoglobin and blood glucose levels significantly in diabetic rats. It is considered that the MC anti-hyperglycaemic effect is due to charantin, vicine and/or polypeptide P material that is also identified as phyto-insulin, which is similar to bovine insulin. Four different opinions are presented on the anti-hyperglycaemic mechanisms of MC; the first of these is to prevent the dying of partially blasted beta cells, the second is the stimulation of insulin excretion from beta cells in Langerhans islets, the third is stimulated insulin sensitivity and the intake of glucose into cells by increased insulin substrate tyrosine phosphorylation and GLUT4 translocation and the fourth is increased glycogen synthesis in liver.

Previous studies show that MC administration decrease total cholesterol, triglyceride, LDL and VLDL cholesterol levels and also increase the HDL cholesterol levels. It is considered that MC drives this effect on lipids by inhibiting cholesterol absorption in the intestines via sterols known to have hypocholesterolaemic effects. In addition, it provides controlled mobilization of serum cholesterol, triglyceride and phospholipids by stimulating lipoprotein lipase activity and inhibiting hormone-sensitive lipase enzyme. Fernandes et al. and Ahmed et al. stated that the MC extract has hypolipidaemic effects. In this study was obtained similar results some previous studies, and although decreases in the total cholesterol and triglyceride levels and an increase in HDL cholesterol levels were
observed in the MC group when compared to those of the untreated diabetic group, it was observed that there is no significance. In addition, it was found out that the MC extract significantly decreased LDL and VLDL cholesterol levels (Table 3).

Although there is no significance between plasma TOS levels in this study, a significant decrease in erythrocyte TOS levels was observed in the MC and insulin groups when compared to those of the untreated diabetic group. However, when plasma and erythrocyte TAS levels were compared, no statistical significance could be detected between the untreated diabetic group and MC group (Table 2). It is considered that the decrease caused by the MC extract on TOS levels is related to the scavenging effect of polyphenolic compounds (caffeic acid derivatives and flavonoids) in the structure of MC.

Wua et al. stated that the MC extract inhibits TBARS increase in plasma, liver, and brain tissues, and Tripathi et al. stated that MC extract decreases TBARS level and increases SOD, GST and CAT levels in the cardiac tissue.

**Significance of study**

According to the International Diabetes Federation, the number of people living with diabetes is expected to rise from 382 million in 2013 to 592 million by 2035. Diabetes is a serious disease that threatens human life. There is no certain treatment for type 1 diabetes, the applied treatments cause various complications and are expensive. For this reason, researchers tend to find new sources for antidiabetic compositions such as Trigonella foenum-graecum L. (Fenugreek), Momordica charantia L., Ganoderma lucidum, Mirabilis jalapa L. medicinal plants which are widely used in folk medicine. In our study determined that Momordica charantia have an effect of reducing known as diabetes complications on hyperglycaemia, oxidative stress and hyperlipidemia. We believe that our study is a step in this quest.

**Conclusion**

In this study was observed that increased fasting blood glucose, total cholesterol and LDL cholesterol levels in diabetic control group. However plasma TAS levels were showed a significant decreased in diabetic control group compared to control group. MC extract has been shown a significant decreased in the blood glucose levels on the 7th, 14th and 21st days, erythrocyte TOS levels, LDL cholesterol and VLDL cholesterol levels. The decreased in the blood glucose levels, erythrocyte TOS levels, LDL cholesterol and VLDL cholesterol levels may be due to charantin, vicine and polypeptide P found in the composition of MC. In addition, it was found that MC has greater anti-hyperlipidaemic characteristics, whereas insulin has greater antioxidant and anti-hyperglycaemic characteristics. Based on these results, it may be effective use of MC and exogenous insulin together to prevent complications such as oxidative stress, hyperglycaemia and hyperlipidaemia due to diabetes.

**References**

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