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Effects of Crabapple (*Malus sylvestris)* on Blood Glucose and Lipid Levels in Diabetic Rats

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Abstract We aimed to investigate the impact of crabapple on blood glucose and lipids levels in the streptozotocin (STZ)-induced diabetic rats. Rats were divided into 3 groups. The first group was control; the second group was diabetic rats while the third group was diabetic rats fed with crabapple (2 g/day). Diabetes was induced by STZ. After 6 weeks of experimental period blood samples were collected from the abdominal aorta under anaesthesia and lipid parameters were measured with auto-analyzer. However, there was significant increase both in blood glucose and lipid levels of untreated diabetes group. Likewise, blood triglyceride levels were found to be significantly reduced in the diabetic group fed with crabapple compared with untreated diabetic animals. This is the first study that approves blood glucose and triglyceride lowering effects of crabapple after six weeks supplementation. However, the underlying mechanisms of this action remain to be investigated later.

Keywords: *crabapple, diabetes mellitus, glucose, triglyceride*

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1. Introduction

The World Health Organization has acknowledged the existence of disease curative and preventive plants varieties and defined them as the likely precursors of pharmaceutical synthesis [13]. Since the importance of nutrition and natural medicine in the world has been increasing in recent years, molecules present in naturally grown nutrient and suggested to be effective in terms of health has becoming a subject of many research [3]. Nutraceuticals are non-toxic foods proven scientifically to be beneficial for health and utilized for treating or preventing diseases. Such foods have been shown to contain molecules that are generating effects on the body and thus likely to be useful in the treatment of certain diseases. Consistently the contribution of these compounds as supportive nutrients of medical treatment has been also concerned. Current findings show that use of phytonutrients by humans for this purpose has been increased 50% in recent years [12].

Crabapple (*Malus sylvestris*) is a kind of apple growing in a natural environment in western and middle Europe including Turkey and is considered to be the ancestor of the apple we know. It is a fruit of a member of the Rosaceae species that grows in the forests [2]. The fruits are small and have quite a sour taste. The leaves of some cultivars, such as Malus are often used as tea, and the fruits are consumed and utilized in the production of fruit beverages due to the fact that they are rich in antioxidant flavonoids [16]. Although most crabapple fruits are edible, very little has been reported on their biological activities in human [15]. In terms of the content it is very rich in polyphenols and malic acid. Malic acid is a natural compound that is found commonly in fruits and vegetables, including apples. Moreover it is also known as apple acid. Malic acid present in crabapple has been shown to exert medicinal effects [5]. Malic acid is not only required for energy production, but it was also found to play role in detoxification and removal of poisons from the body [1]. There are protective properties of crabapple from the toxic effects of metals such as aluminum and strontium. In a study conducted in the United States, malic acid along with magnesium has been found to be very useful for the treatment of muscle cramps and muscle pain [11]. In clinical trials performed in Spain it has been shown to be beneficial when used as a spray for the treatment of dry mouth as a comprising side effect of certain medications (including antidepressants) [4]. In addition, in a clinical study conducted in recent years malic acid has been shown to have positive effects in the treatment of kidney stones [10]. Moreover, boiled roots of crabapple are known to have sedative, hypnotic and headache relieving effects in traditional medicine.

Abnormal blood glucose and lipid levels are common health problems which are quite often in many diseases, especially diabetes and metabolic syndrome. In particular, glucose and lipid level abnormalities are preparing ground for the precipitation of cardiovascular disease in diabetes. Therefore, keeping these values within normal limits is very important in terms of protective and preventive medicine. Accordingly, the potential effects of various

molecules on regulation of blood glucose and lipid levels are being studied in certain disease models. Although it has been known since ancient times, crabapple has been studied rarely and only very little information has been published about the potential medical effects of this fruit. From this point of view this natural plant is remained to be investigated extensively. Therefore, in this study, we aimed to investigate the impact of crabapple on blood glucose and lipids levels in the STZ-induced diabetic rats.

2. Materials and Methods

Ten-weeks old female Wistar albino rats weighing 150-200 grams were used in this study. The rats were placed in cages randomly. Throughout the study, animals were fed freely with standard rat chow and tap water was available *ad libitum* and kept in a room adjusted for 12- hour light 12-hour dark cycle and humidity at 30–40%. All experiments were reviewed and approved by the Animal Research Ethics Committee of the Akdeniz University Faculty of Medicine.

Rats used in the experiments were divided into 3 groups. The first group was control; the second group was diabetic rats while the third group was diabetic rats fed with crabapple (2 g/day). Diabetes was induced by intraperitoneal injection of 50 mg/kg of STZ. Onset of diabetes was identified by polydipsia, polyuria, and blood glucose levels >300 mg/dL. Control animals were injected with citrate buffer containing no STZ. Three days after injection of STZ blood glucose levels of rats were measured and those with blood glucose higher than 300 mg/dl were considered diabetic and used in the following procedure. To prevent hypoglycaemic attack that may occur in the STZ-injected rats, solution containing 2% sucrose was added to drink water for the next two days. Blood glucose levels of rats were measured by using glucometer (Bayer Diagnostics).

After 6 weeks of experimental period blood samples were collected from the abdominal aorta under anesthesia and lipid parameters were measured with auto-analyzer (Beckman Coulter AU5800) in all groups. At the beginning and the end of experimental period body weight of animals were recorded.

3. Drugs

All drugs and chemicals were purchased from Sigma-Aldrich Chemical Company (St Louis, MI, USA). Crabapple was obtained from Nesil food product. STZ was dissolved immediately prior to its injection in 0,1 mol/l citrate buffer (pH4,5).

4. Analysis of Results

Blood glucose and lipid levels measured for groups were analyzed by Student's t-test. P values smaller than 0.05 were accepted significant. All values expressed as mean ± SEM.

5. Results

Body weights of control and diabetic animals were similar between the groups at the beginning and after 6 weeks of experimental period (Table 1). In control rats neither body weight nor blood glucose and lipid levels were changed significantly at the end of 6th week compared to the initial value. However, there was a significant increase both in blood glucose and lipid levels of untreated diabetes group (Table 2). On the other hand, diabetic animals fed with crabapple had lower blood glucose levels when compared to diabetic group supplemented with standard rat chow (Figure 1, Table 2). A remarkable decrease in blood glucose levels was detected at the 4th week and it was further decreased at the end of 6th week which implicates a regular and consistent reduction as a result of crabapple supplementation. Likewise, blood triglyceride levels were found to be statistically significantly reduced in the diabetic group fed with crabapple compared with untreated diabetic animals (Figure 2). But there was no significant change in the level of blood cholesterol (HDL and LDL).

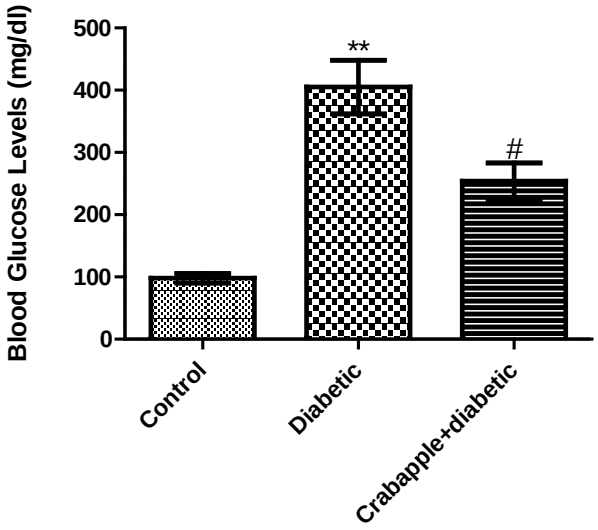

Figure 1. Blood glucose levels. ** P<0.001 vs control group, # P<0.05 vs diabetic group.

Table 1. Animal body weight, (n=10)

	Body weight (g)	
GROUPS	**Before**	**6 weeks later**
Control	158 ± 6.2	182 ± 4.1
Diabetic	160 ± 5.1	179 ± 7.8
Diabetic +Crabapple	157 ± 4.3	175 ± 6.2

Table 2. Blood glucose and lipid levels

GROUPS	Blood glucose (mg/dl)	Total cholesterol (mmol/l)	HDL	LDL	Triglyceride (mmol/l)
Control	98.0±7,7	66.1±3,0	49.0±2.2	12.0±0.8	61.3±9.2
Diabetic	462.3±34,5*	81.1±3,8	44.1±3,0	10.6±0,7	279.5±36,9*
Diabetic +Crabapple	216.1±18,1**	64.1±3,5	39.2±2,7	22.3±1,5	96.1±16,5**

* P<0.05 vs control group, (n=10), **P<0.05 vs diabetic group,.

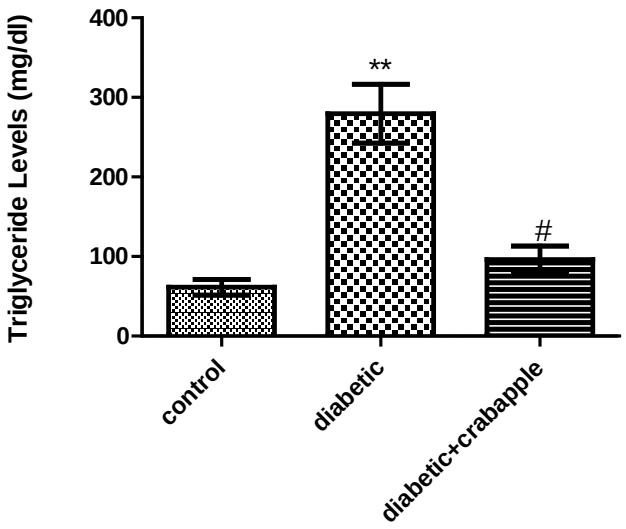

Figure 2. Blood triglyceride levels ** P<0.001 vs control group, # P<0.05 vs diabetic group

6. Discussion

Diabetes is a chronic disease of the endocrine system basically characterized by lack of insulin. It is a very common disease in the world and the number of suffered people is increasing continuously with each passing day. According to data of the World Diabetes Federation in 2013 the prevalence of diabetes has been reported to be 13% between the ages of 20-79 worldwide [6]. The permanent rise in the level of blood glucose in particularly type 2 diabetic patients is mostly associated with abnormal blood lipid levels and then provides basis for many diseases, including cardiovascular complications [7]. Therefore, since the prevalence of diabetes is increasing consistently worldwide, effective new therapies addressing these complications are still under investigation [14]. In recent years many plants used in traditional medicine for the treatment of diabetes are suggested to be useful as alternative therapies [9].

Malnutrition is one of the major underlying reasons of this disease. Therefore, consumption of healthy food and regulation of diet increasingly become important for society. When we look from this perspective, it is important to determine the healthy substances present in nutraceuticals to figure out their positive effects in details and eventually promoting consumption of them chronically. Consistent with this, we aimed to investigate whether crabapple has positive effects also on diabetes since it has been used for alternative medicine in earlier works. Indeed, crabapple is a fruit that attracts the attention of medical world due to its rich content and native characteristics. In this study blood glucose levels and triglyceride levels were found to be statistically reduced when experimentally induced diabetic rats supplied with crabapple for 6 weeks. However, there was no significant reduction in blood cholesterol levels. Thus, this is the first study that approves blood glucose and triglyceride lowering effects of crabapple after six weeks supplementation. This study has evaluated the impact of crabapple in subacute phase. In next step the substances or molecules by which the crabapple exerts these beneficial effects should be examined. Similarly, the molecular mechanism of this significant decrease in blood glucose and lipid levels also remains to be elucidated. Therefore this study is provided as a precursor of progressive new studies. Lack of significant decrease in blood cholesterol levels is another hallmark of this study and this might be ascribed to duration of experimental procedure and thus inadequate supplementation of crabapple. Experimental procedure which consists longer administration period may be required to observe cholesterol mitigating effect of crabapple in diabetic conditions.

As a result, we believe in diabetes which is a chronic disease, the crabapple can be consumed as a nutraceutical to support medical treatment due to its blood glucose and triglyceride lowering effects, particularly in case of long-term administration. However, the underlying mechanisms of this action and the molecules that play role in regulation of these physiological indexes are matters remain to be investigated later.

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