

## Lipid Lowering Effects of Aqueous Saffron Extract in Diabetic Rats

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### Abstract

**Introduction:** Diabetes mellitus is one of the most common non-communicable and chronic diseases. The present study aimed to review the lipid lowering effects of aqueous saffron extract in diabetic rats.

**Methods:** Sixty diabetic rats with fasting blood glucose of over 300 mg/dl were selected as sample and divided in two groups of saffron extract and control. Group of saffron extract received 25 mg/kg daily aqueous saffron extract peritoneally for 4 weeks. Lipid profile was measured by enzymatic method with *zist shimi* commercial kits provided by *yasa teb* Company. For statistical analysis of data, Kalmogorov- Smirnov test and paired sample and independent sample t- tests ( $p \leq 0.05$ ) were used.

**Results:** Findings showed that 4 weeks saffron extract induces significant reduction in LDL, VLDL, TG and Cho of diabetic rats ( $p=0.001$ ); nevertheless, it has no significant effect on HDL ( $p=0.07$ ).

**Conclusion:** It is concluded that 4 weeks aqueous saffron extract has lipid lowering effect in diabetic rats.

**Keywords:** Saffron, Lipid Profile, Diabetes

### Introduction

Diabetes mellitus is one of the most common non-communicable and chronic diseases in most developing and developed countries (1), with existence of this disease increasing rapidly, so that it is reported that the number of people with diabetes in 2000 was estimated to be around 147 million and it seems to reach 320 million in 2025 (2). Diabetes mellitus is one of the chronic diseases that leads to increased levels of glucose, lipid profiles and metabolic disturbances due to reduced function or insulin levels (3). In the present world, the current prevalence of this disease has increased with the changing diet and lifestyle culture from traditional to industrial (1). In order to prevent short-term complications and to reduce the risks of long-term complications of diabetes, the diabetic patient should continuously be given care, support and required training; therefore,

lifestyle modification and dietary patterns are recommended for people with diabetes. Currently, the tendency of people to use more healthy, less complicated therapeutic methods and also the use of traditional medicine and herbs has been increased to treat diseases. In fact, the use of plants for the treatment of diabetes has a long history and, before exogenous insulin production, diabetes was controlled by these plants (4). Saffron is considered to be one of the most expensive spices, belonging to gladiola family, which has the scientific name of *crocus sativus* (4). The bitter taste of saffron is due to the presence of a substance called picrocrocine. During the processing of the new plant, picrocrocine is converted into an aromatic aldehyde called safranal, through thermal or enzymatic decomposition (5). Crocins, being glycosides consisted of carotenoid called crocins and sugars, are responsible for the color of saffron. Other carotenoids, such as beta-carotene,

lycopene and zeaxanthin, and vitamins, especially riboflavin and thiamine, are found in saffron. Crocin, crocetin and safranal are the main sources of saffron (5). Saffron is one of the medicinal plants known as health flower, king of spices and red gold. In traditional medicine, it is believed that cardiovascular health can be achieved by taking saffron (6). Recent studies have shown that saffron and crocin are effective in lipid and glycemic indices (7- 15). However, most studies have used doses that can be risky for humans. Taking a review of the research aspects of previous research, there is a lack of studies on the evaluation of safe doses of saffron on lipid profiles levels in diabetic patients. So, the main aim of this study is to investigate the effects of lipid reduction of saffron aqueous extract in diabetic rats.

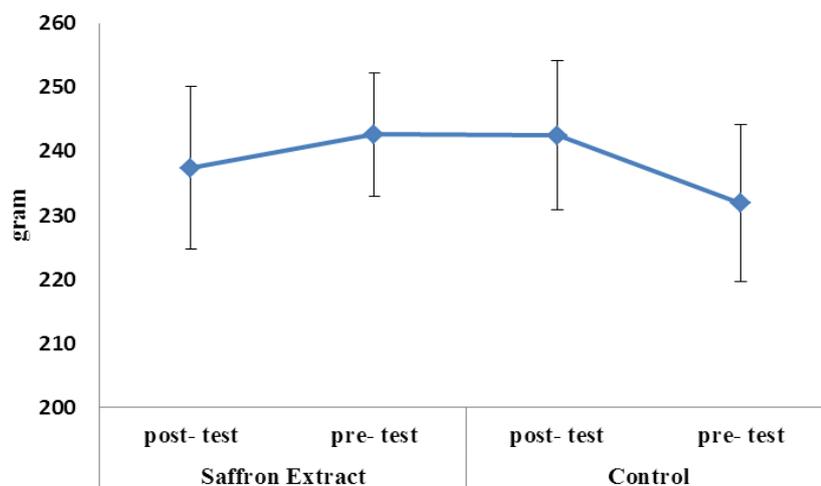
## Methods

In this experimental study, 20 male adult Sprague- Dawley rats with a weight range of 200- 260 g were purchased from the house of animals of the Islamic Azad University of Marvdasht Branch, and transferred to the university's Physiology Laboratory. After a week of adaptation to laboratory environment, rats were administered with intraperitoneal injection of 60 mg/ kg soluble streptozotocin, and were subjected to diabetes induction in citrate buffer. In the following, 4 days later, rats' fasting blood glucose was measured by glucometer to confirm the induction of diabetes mellitus, and 16 rats with fasting glucose up to 300 mg/ dl were selected as the statistical sample. To evaluate the effects of saffron extract for 4 weeks, rats were divided into two groups of saffron extract and control group based on fasting glucose. Then, saffron extract group received 25 mg/ kg of intraperitoneal aqueous extract of saffron for 4 weeks. During the research period, the access of rats groups of saffron extract and control to the food and water was unlimited and free. In relation to the dosage of 25 mg/ kg of saffron extract, it should be stated that based on a

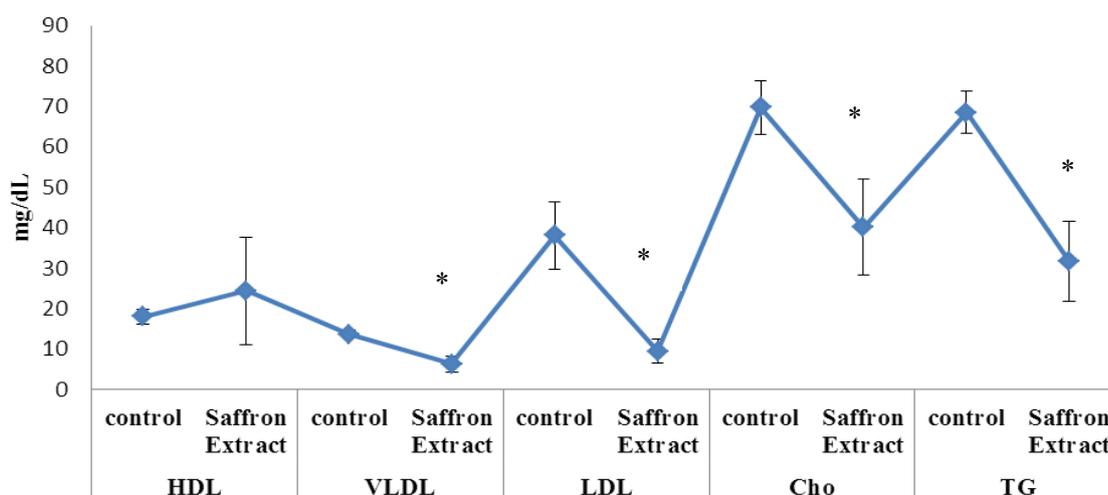
review study, studies have reported that researchers consider the dose to be safe for human consumption, and in fact, in vivo studies in animals, the toxicity of saffron and its components has been very low or zero (16). At the end of the study, rats were sacrificed using an appropriate easy-to-kill method. In fact, rats were anesthetized by ketamine and xylosine on blood sampling day. Blood samples were then taken directly from the left ventricle of the rats using chest opening. All the ethical aspects of this research were reviewed and approved by the Ethics Committee of the Islamic Azad University of Marvdasht University. To prepare the extract of saffron, 4 grams of dried crest of saffron, known as smooth saffron, were prepared. Then, 400 cc distilled water was added and the solution was placed in the shaker incubator for 72 hours. The sample was then strained and the extract was separated and powdered with a freeze-dryer machine (7). Measurement of lipid profiles was performed by enzymatic method using commercial biochemical kits prepared by *Yasa Teb*. To analyze the findings, Kolmogorov-Smirnov statistical tests were used for paired sample and independent sample t-tests ( $p \leq 0.05$ ).

## Results

Pre-test and post-test levels of weight and lipid profiles of rats are presented in Figures 1 and 2, respectively. The results of paired sample t-test showed that there was no significant difference in pre-test and post-test levels of rats in saffron extract ( $p = 0.44$ ) and control groups ( $p = 0.08$ ) (Figure 1). The results of independent sample t-test showed that the use of saffron extract for four weeks resulted in a significant decrease in LDL, VLDL, TG and Cho in diabetic rats ( $p = 0.001$ ), however, it has no significant effect on HDL ( $p = 0.07$ ) in diabetic rats (Figure 2).



**Figure 1.** Weight of rats in pre- test and post- test



**Figure 2.** Lipid profile levels in rats of saffron extract and control groups

\*Significant reduction than control group  $p=0.001$

## Discussion

In the current world population, the incidence of diabetes is increasing and due to the adverse effects of synthetic drugs, there is a clear need for the development of natural plant sources for anti- diabetic drugs (17). In fact, one of the economically efficient strategies to reduce complications, disorders, problems and mortality due to diabetes is the use of appropriate nutritional methods. Saffron, in addition to being a high-quality spice, has a

large pharmacological effect and is a strong drug (18, 19). As indicated, the results of this study showed that 4 weeks of daily consumption of 25 mg/ kg of aqueous extract of saffron resulted in a significant improvement in lipid profiles in diabetic rats. A significant decrease in the oxidation of lipoproteins can be attributed to the antioxidant potential of saffron (12). Contrary to the findings of the present study, the results of a study showed that although eight weeks of

saffron consumption at 40 mg/ kg dose decreased the LDL/ HDL ratio in obese rats with high fat diet, it had no significant effect on lipid profiles. Also, eight weeks use of 40 mg/ kg of crocin had no significant effect on the improvement of lipid profiles in obese rats with high fat diet; however, consuming 80 mg/ kg of crocin resulted in a significant reduction in TG and Cho. Consistent with the results of this study, saffron consumption did not have a significant effect on the weight of rats (20). Among the reasons for the above results not being in line with the results of this study can be kind of subjects, so that lipid profile disorders in diabetic rats are much higher than in obese rats. Although the duration of consumption of saffron and also the dose of saffron in this study was higher than the present study, these findings indicate the different responses of diabetic rats and obese rats to saffron extract. It was also reported that four weeks of taking 30 mg of saffron did not have a significant effect on lipid profiles in patients with depression (21), and eight weeks of use of 30 mg of crocin had no significant effect on lipid profiles in patients with metabolic syndrome (22). However, in a study by Sheng *et al.* (2006), the use of 25 to 100 mg of crocin per day for 10 days resulted in improved lipid profiles in rats. The researchers reported that Crocin inhibits pancreas and gastritis lipase, however, its mechanism is unknown (23). The reasons for the inconsistency of the results of the study include the type of subject, the dose, duration of use, and also the method of measuring the variables of the research. Concerning the beneficial effects of saffron consumption on the improvement of diabetes mellitus, Xi *et al.* (2007) showed that crocetin can be effective in treating insulin resistance and related diseases, and significant effects of the expression of leptin, adiponectin and TNF-  $\alpha$  in white fat tissue can be effective in improving insulin sensitivity induced by crocetin- fed rats (24). Saffron enhances high levels of glucose uptake and AMPK/ ACC (acetyl-CoA carboxylase/

AMP-activated protein kinase) and AMPK (mitogen-activated protein kinases) phosphorylation, however, it does not enhance the phosphorylation of PI3-kinase (Phosphatidylinositol 3-kinase). The interactive effects of insulin and saffron improve insulin sensitivity through insulin-dependent signaling pathways (AMPK/ ACC and MAPKs) and non-insulin dependent (PI 3-kinase/ Akt and mTOR). AMPK plays a major role in the effects of saffron on glucose uptake and insulin sensitivity in skeletal muscle cells (25).

### Conclusion

According to the findings of this study, it seems that the use of aqueous extract of saffron for four weeks has a lipid-lowering effect in diabetic rats.

### Ethical issues

Not applicable.

### Authors' contributions

All authors equally contributed to the writing and revision of this paper.

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