

Effect of Almond Oil on Lipid Profile in Male Rats Exposed to Thioacetamide

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Abstract: Currently, the exposure to chemical toxicants is increasing and causing many complex health problems. Generally, herbal medicine is considered as an integral part of dietary supplement. Herbal medicines encompass the combination of practices of indigenous systems of medicine and several therapeutic experiences of many previous generations. The present study was aimed to evaluate the effect of almond oil on lipid profile in Wistar male rats exposed to thioacetamide (TAA). Experimental rats were distributed into four groups. Rats of the first group were served as normal controls. Rats of the second group were exposed to TAA (300 mg/kg body weight). Rats of the third group were exposed to almond oil (800 mg/ kg body weight) and TAA. Rats of the fourth group were supplemented with almond oil. At the end of experimental period (six weeks), blood serum samples were analyzed to evaluate the levels of lipid profile in all groups. The levels of serum triglycerides, cholesterol, low density lipoprotein cholesterol (LDL-C), very low density lipoprotein cholesterol (VLDL-C), atherogenic index (AI) and cardiac risk ratio (CRR) were significantly increased, while the level of serum high density lipoprotein cholesterol (HDL-C) was statistically declined in rats of the second group which exposed to TAA. Treatment with almond oil improved the observed alterations of lipid profile induced by exposure to TAA in rats of the third group. These new data indicate that almond oil has potential therapeutics properties against TAA toxicity.

Key words: Almond oil • Thioacetamide • Lipid profile • Rats

INTRODUCTION

Environmental contamination by toxicants is a worldwide problem. Exposures to environmental toxicants are known causes of physiological and biochemical disorders. Fundamental in evaluating the safety of chemicals is an understanding of their intrinsic toxicological properties. Due to the rapid growth of the economy, environmental pollution has become a concern that imposes a severe risk to the health of human beings [1]. Thioacetamide (TAA) is an organosulfur, white crystalline compound having liver damaging and carcinogenic activity by causing cytomegaly [2]. TAA was first used to control the decay of oranges. It has been subsequently used as a fungicide [3]. The toxic effect of thioacetamide is due to its biological activity exerted through oxidase systems, particularly FAD mono

oxygenases and CYP2E1 [4]. TAA is a potent hepatotoxicant which requires metabolic activation by the mixed-function oxidases [5]. TAA is widely used to induce acute-toxic liver injury and specially causes membrane damage, oxidative stress and accumulation of lipid droplets in the hepatocyte cytoplasm to enhance inflammation and liver injury [6].

In recent years, interest has increased in using natural products for pharmacological purposes, as a form of complementary or replacement therapy. Nowadays, a lot of research has been conducted on the use of herbal products as natural antioxidants because of their fewer side effects, easy and cheap availability [8]. Many plants are known to have medicinal and therapeutic properties because of their phytochemicals and have tremendous applications in pharmaceutical industry [9]. The almond is the most important nut in the world in terms

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of commercial production. Taxonomically, the almond tree, *Prunus dulcis*, belongs to the *Amygdalus* subgenus inside the *Prunus* genus, the *Rosaceae* family and the order *Rosales* [10]. The almond contains as much as 50% oil [11]. Also, it contains proteins (12–22%) and carbohydrates (20%) [12, 13]. Almond oil has long been used in complementary medicine circles for its numerous health benefits, including anti-inflammatory, immunity-boosting and anti-hepatotoxicity effects. Accordingly, the purpose of this study was to investigate the protective effect of almond oil on lipid profile in male rats exposed to TAA.

MATERIALS AND METHODS

Animals: Male albino rats of the Wistar strain (*Rattus norvegicus*), weighing 110-139 g were used in the present study. The experimentations were conducted at the Experimental Animal Unit, Department of Biological Sciences, Faculty of Sciences, King Abdulaziz University, Jeddah, Saudi Arabia. The experimental treatments were conducted in accordance with ethical guidelines of the Animal Care and Use Committee of King Abdulaziz University. Rats were housed in standard plastic cages and maintained under controlled room conditions of humidity (65%), temperature (20±1°C) and 12:12 h light: dark cycle. Rats were fed *ad libitum* on normal commercial chow and had free access to water.

Experimental Treatments: About 40 rats were distributed into four experimental groups, ten of rats each. The experimental groups were treated as follows:

- Rats of the first group were served as controls and intraperitoneally injected with saline solution (0.9% NaCl), twice weekly for six weeks.
- Rats of the second group were given 300 mg/kg body weight of TAA (Sigma-Aldrich Corp., St. Louis, MO, USA) by intraperitoneal injection, twice weekly for six weeks.
- Rats of the third group were orally supplemented with almond oil at a dose of 800 mg/ kg body weight/ day for six weeks. Moreover, they were intraperitoneally injected with TAA at the same dose given to group 2.
- Rats of the fourth group were intraperitoneally injected with saline solution (0.9% NaCl), twice weekly and were orally supplemented with almond oil at a dose of 800 mg/ kg body weight/ day for six weeks.

Blood Serum Analyses: At the end of experimental period (six weeks), food was withdrawn from the rats and they were fasted for 8 hours but had free access to water and then anaesthetized with diethyl ether. Blood samples were collected from orbital venous plexus in non-heparinized tubes, centrifuged at 2500 rpm for 15 minutes and blood sera were then collected and stored at -80°C. Serum samples were used to determine the levels triglycerides, cholesterol, high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), very low density lipoprotein cholesterol (VLDL-C), atherogenic index (AI) and cardiac risk ratio (CRR). To estimate the triglycerides value, Fossati and Principi [14] method was used. The method of Richmond [15] was used to determine the level of cholesterol. The method of Warnick, *et al.* [16] was used to determine the value of HDL-C. The level of serum LDL-C was estimated according to the equation of Friedewald, *et al.* [17]. Serum VLDL-C was evaluated using the following equation:

$$\text{VLDL - C} = \text{Triglycerides}/2.175$$

AI values were determined following the method of Pandya, *et al.* [18].

$$\text{AI} = \frac{\text{LDL-C} + \text{VLDL-C}}{\text{HDL-C}}$$

CRR is calculated by dividing total cholesterol by HDL:

$$\text{CRR} = \frac{\text{Total cholesterol}}{\text{HDL-C}}$$

Statistical Analysis: The data were analyzed using the Statistical Package for Social Sciences (SPSS for windows, version 22.0). The experimental data were expressed the as mean ± standard deviation (S.D.). Data were analyzed using one-way analysis of variance (ANOVA) to determine differences between the mean values of experimental groups. Statistical probability of $P \leq 0.05$ was considered to be significant.

RESULTS

Figure 1 showed the level of serum triglycerides in all experimental groups. In comparison with control data of group 1, the level of serum triglycerides was significantly elevated in rats treated with TAA (+ 52.9%, $P \leq 0.000$) and almond oil plus TAA (+ 25.5%, $P \leq 0.01$). The level of serum triglycerides was statistically unchanged in rats

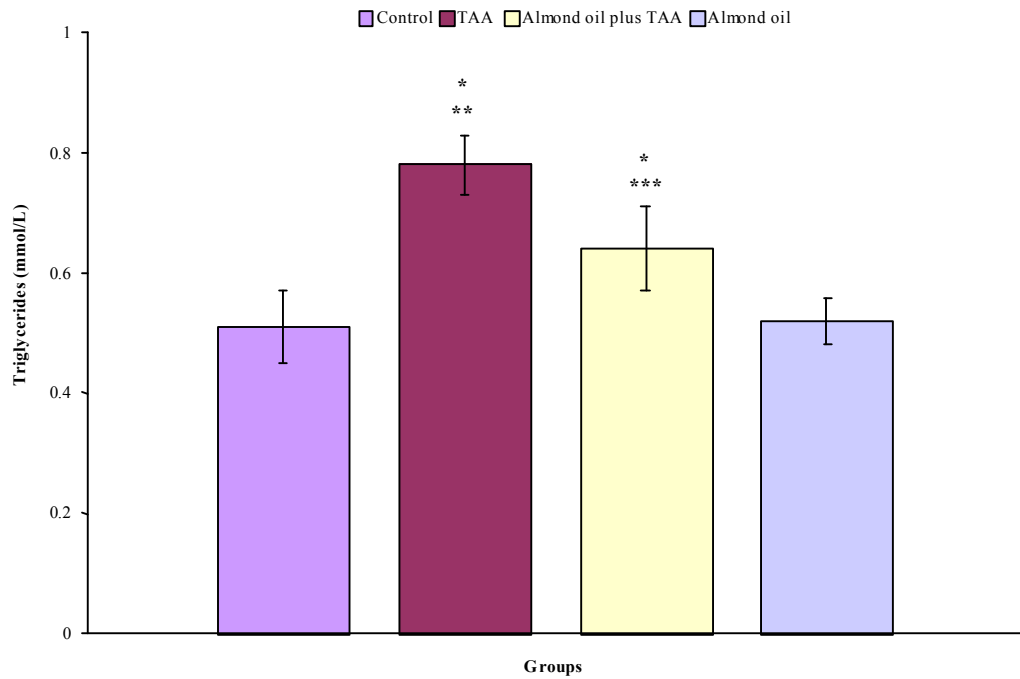


Fig. 1: Level of serum triglycerides in control, TAA, almond oil plus TAA and almond oil treated rats after six weeks. *Indicates a significant difference between control and treated groups. **Indicates a significant difference between rats treated with TAA and almond oil plus TAA and almond oil. ***Indicates a significant difference between rats treated with almond oil plus TAA and almond oil.

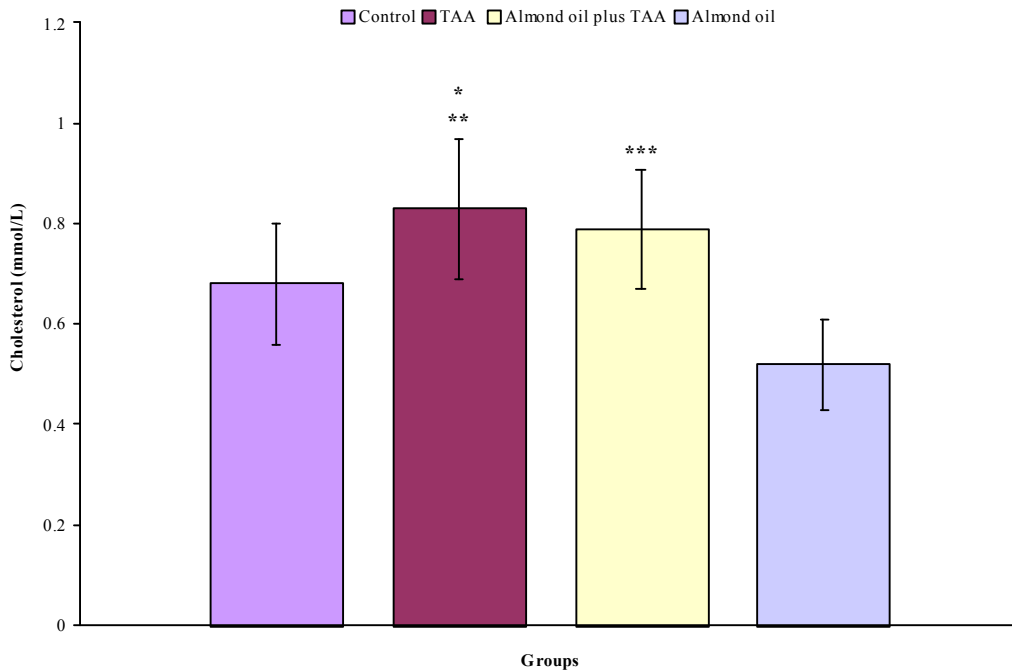


Fig. 2: Level of serum cholesterol in control, TAA, almond oil plus TAA and almond oil treated rats after six weeks. *Indicates a significant difference between control and treated groups. **Indicates a significant difference between rats treated with TAA and almond oil plus TAA and almond oil. ***Indicates a significant difference between rats treated with almond oil plus TAA and almond oil

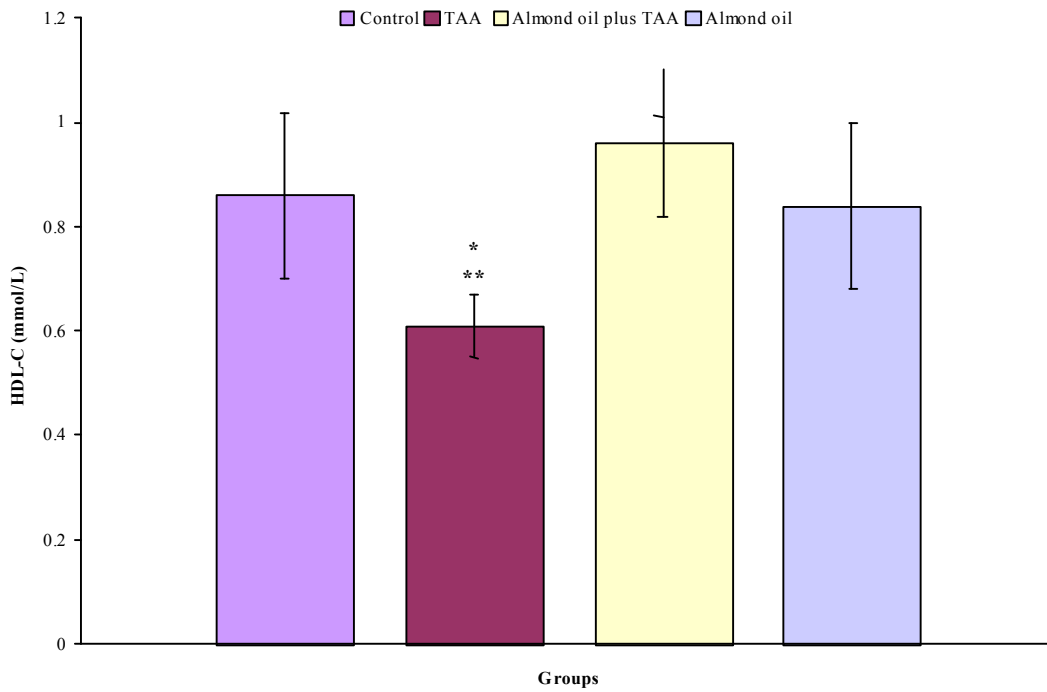


Fig. 3: Level of serum HDL-C in control, TAA, almond oil plus TAA and almond oil treated rats after six weeks. *Indicates a significant difference between control and treated groups. **Indicates a significant difference between rats treated with TAA and almond oil plus TAA and almond oil

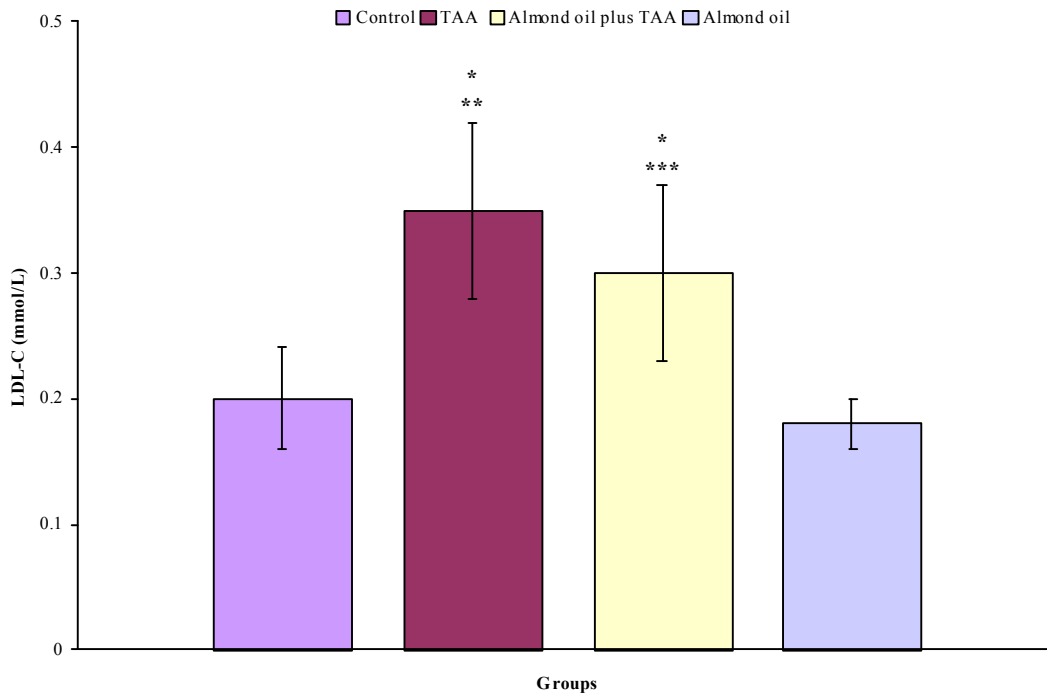


Fig. 4: Level of serum LDL-C in control, TAA, almond oil plus TAA and almond oil treated rats after six weeks. *Indicates a significant difference between control and treated groups. **Indicates a significant difference between rats treated with TAA and almond oil plus TAA and almond oil. ***Indicates a significant difference between rats treated with almond oil plus TAA and almond oil

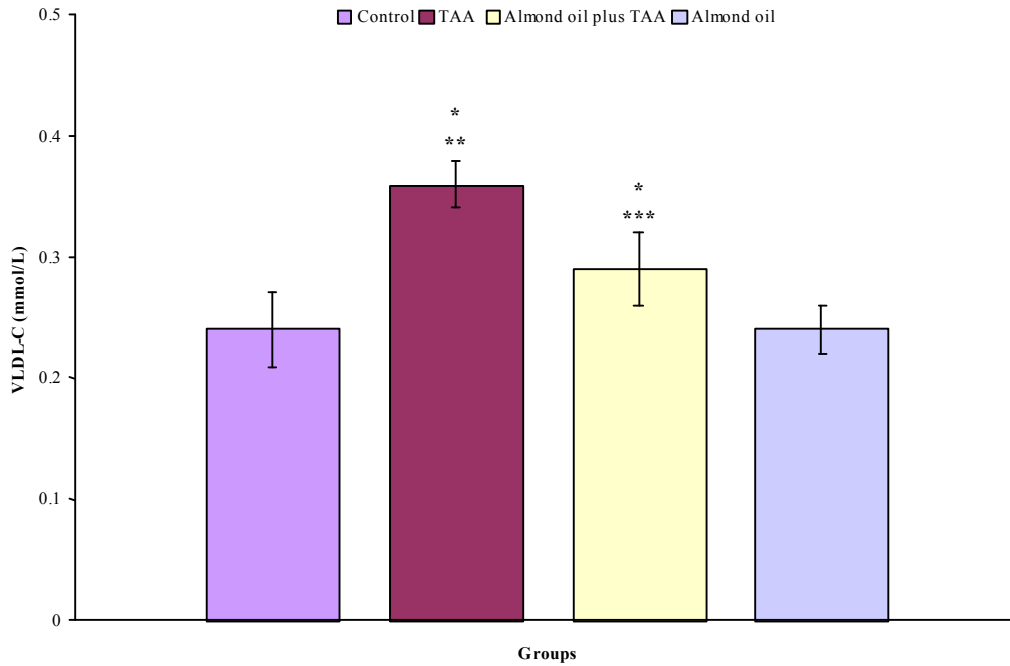


Fig. 5: Level of serum VLDL-C in control, TAA, almond oil plus TAA and almond oil treated rats after six weeks. *Indicates a significant difference between control and treated groups. **Indicates a significant difference between rats treated with TAA and almond oil plus TAA and almond oil. ***Indicates a significant difference between rats treated with almond oil plus TAA and almond oil

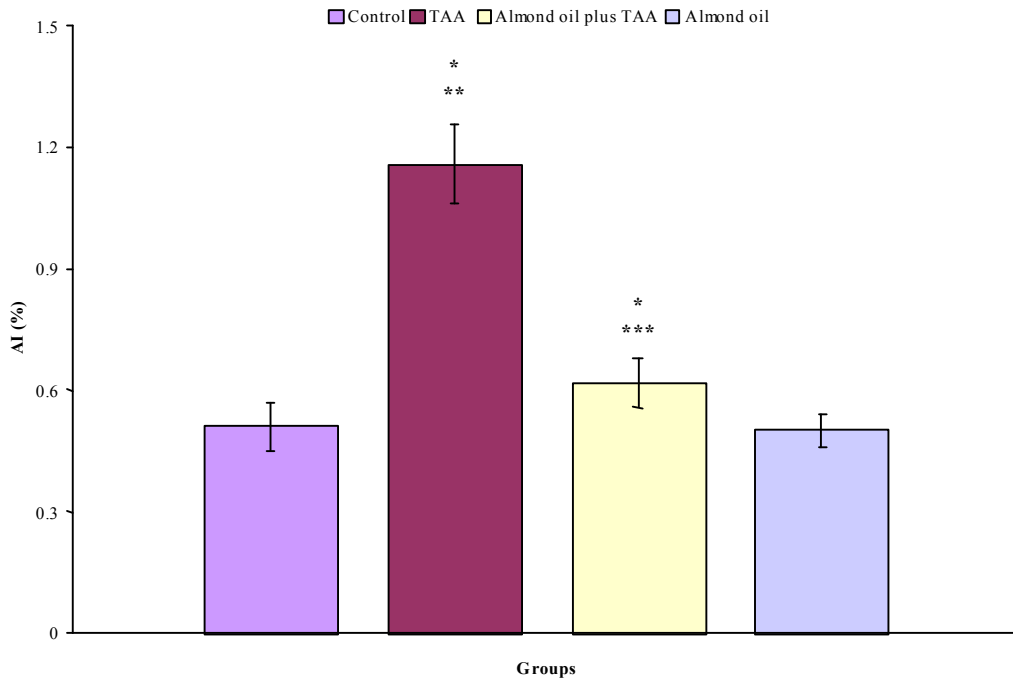


Fig. 6: Level of serum AI in control, TAA, almond oil plus TAA and almond oil treated rats after six weeks. *Indicates a significant difference between control and treated groups. **Indicates a significant difference between rats treated with TAA and almond oil plus TAA and almond oil. ***Indicates a significant difference between rats treated with almond oil plus TAA and almond oil

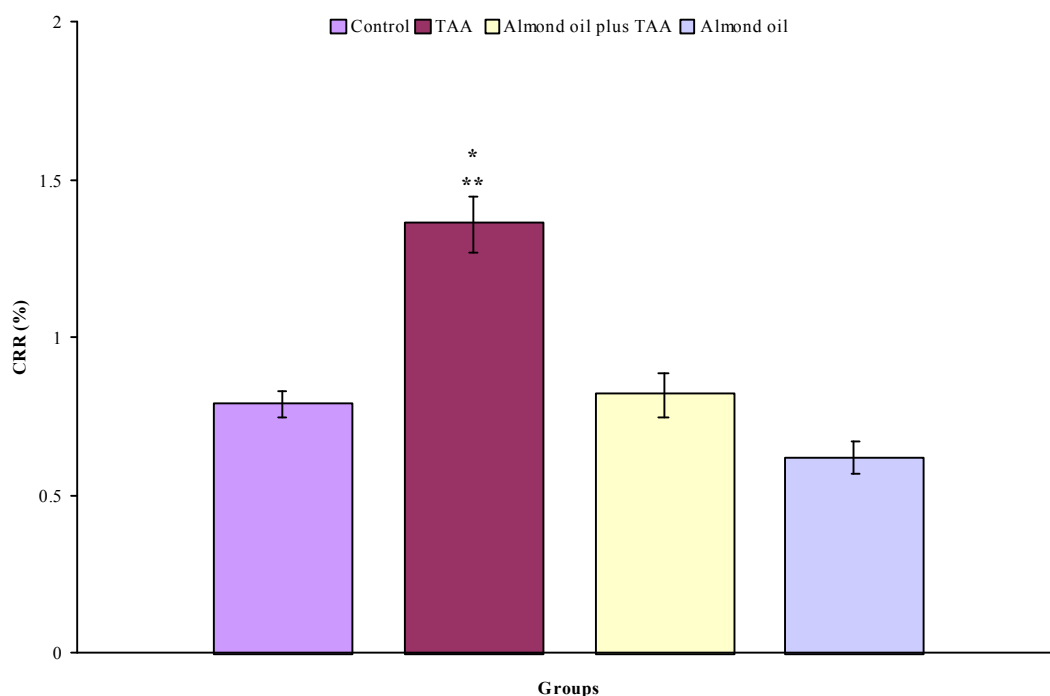


Fig. 7: Level of serum CRR in control, TAA, almond oil plus TAA and almond oil treated rats after six weeks. *Indicates a significant difference between control and treated groups. **Indicates a significant difference between rats treated with TAA and almond oil plus TAA and almond oil.

treated with almond oil (group 4) compared with control rats (Fig. 1). According to the data shown in Figure 2, significant elevation in the level of serum cholesterol was detected in rats treated with TAA (+ 22.1%, $P = 0.02$). No statistically significant differences were observed in the levels of serum cholesterol in rats of groups 3 and 4 as compared with control rats (Fig. 2). Relative to the control rats, the experimental rats exposed to TAA exhibited significantly decrease in the level of serum HDL-C (- 29.1%, $P \leq 0.02$). On the other hand, no statistically significant change was observed in the level of serum HDL-C in almond oil plus TAA and almond oil treated rats (Fig. 3).

Statistically, the treatment of rats with TAA (+ 75.2%, $P \leq 0.001$) and almond oil plus TAA (+ 50.3%, $P \leq 0.01$) showed an increase on the level of serum LDL-C compared with control rats. Treatment of rats with almond oil (group 4) did not cause any significant change in the level of serum LDL-C (Fig. 4). In comparison with control rats, the level of serum VLDL-C was statistically evoked in rats of groups 2 (+ 50.0%, $P \leq 0.000$) and 3 (+ 20.8%, $P \leq 0.01$). Specifically, there were no significant differences in the levels of serum VLDL-C in rats of group 4 (Fig. 5).

Figure 6 showed the level of serum AI in all experimental groups. There were significant increases in the level of serum AI in rats treated with TAA (+ 127.5%, $P \leq 0.000$) and almond oil plus TAA (+ 21.7%, $P \leq 0.05$) compared with control rats, while this parameter was statistically unchanged in almond oil treated rats (Fig. 6). Significant elevation in the level of serum CRR was observed in rats exposed to TAA (+ 72.2%, $P \leq 0.000$). Moreover, insignificant alterations in the level of serum CRR were observed in rats subjected to almond oil plus TAA and almond oil compared with control level (Fig. 7).

DISCUSSION

The data obtained in the present study revealed that the exposure to TAA caused significant increases in the levels of serum triglycerides, cholesterol, LDL-C, VLDL-C, AI and CRR, while the level of HDL-C was significantly decreased. Hyperlipidemia is one of the established major risk factors of coronary heart disease and cerebrovascular disease. Dyslipidemia is characterized by abnormally elevated plasma triacylglycerol and cholesterol concentrations, is an established risk factor in the development of coronary

heart disease (CHD) [19]. Dyslipidemia is characterized by elevated levels of blood triacylglycerol and total cholesterol associated with the increasing concentration LDL-C and VLDL and decreasing the concentration of HDL-C [20, 21]. Hyperlipidemia is modifiable risk factor for atherosclerosis and related cardiovascular diseases, including CHD, cerebral stroke, myocardial infarction and renal failure are becoming a major health problem in the world recently [22]. Hyperlipidemia is a heterogeneous group of disorders characterized by an excess of lipids in the blood stream, the term hyperlipidemia refers to increased concentrations of lipids (triglycerides, cholesterol, or both) in the blood [23-25]. Liver plays an essential role in lipid metabolism, several stages of lipid synthesis and transportation. Therefore, it is reasonable to expect an abnormal lipid profile in those with severe liver dysfunction [26]. The liver plays a central role in whole body lipid homeostasis and the triglyceride content of the liver has important physiological and metabolic functions [27].

Triglycerides are key metabolites through which energy can be stored in adipose tissue and transported throughout the organism for maintaining energy homeostasis. Triglycerides circulate in plasma incorporated in lipoproteins (preferably chylomicrons and VLDL) and are also found in fat globules inside of cells as energy stores. There are three fundamental organs that contain triglycerides: adipose tissue, muscle and the liver. These organs store triglycerides, hydrolyse them to release free fatty acids, export them and finally produce energy for cellular function. There is a continuous flow of free fatty acids between the three tissues via the blood [28]. The balance of lipogenesis and lipolysis is vital for maintaining triglycerides homeostasis [29]. Cholesterol homeostasis is regulated by the two mechanisms: cholesterol biosynthesis in which 3-hydroxy-3-methylglutaryl-coenzyme A (HMGCo-A) reductase catalyses rate limiting process and cholesterol absorption of both dietary cholesterol and cholesterol clearance from the liver through biliary secretion [30]. Hypertriglyceridemia is often observed as the result of lipid abnormality and frequently associated with other lipid and metabolic disorders. In addition, hypertriglyceridemia results from overproduction of triglyceride-rich lipoproteins. The metabolisms of triglyceride-rich lipoproteins are promoted by lipoprotein lipase and lipoprotein lipase activity is enhanced by insulin effect [31]. Hypertriglyceridemia could be attributed to: 1: the enhancement of hepatic synthesis and secretion of VLDL, which constitute the

main carrier molecule of triglycerides and 2: the inhibition of catabolism of VLDL associated with reduction of lipase activity. Hypercholesterolemia could be attributed to damage of hepatic parenchymal cells that lead to disturbance of lipid metabolism in liver [32]. Hypercholesterolaemia has been shown to be a major risk factor for atherosclerosis, associated with increasing oxidative stress and impaired endothelial function [33, 34].

Atherogenic indices are the ratios of such lipid profile parameters that have been studied as markers of lipid atherogenic risk [35]. Atherogenic indices (AI and CRR) have been described as powerful indicators of the risk of cardiovascular disease; the higher the value, the higher the risk of developing the disease and vice versa [36-38]. Traditionally, the atherogenic lipid profile is made up of increased triglycerides, cholesterol and LDL-C and decreased HDL-C [39]. AI indicates the deposition of foam cells or plaque or fatty infiltration or lipids in heart, coronaries, aorta, liver and kidney. The higher the AI, the higher is the risk of above organs for oxidative damage [40]. The higher the atherogenic indices are, the higher the risk of cardiac-related disease is as described by Ademuyiwa, *et al.* [41] and Shen [42]. However, the present increase of serum AI and CRR indicates that TAA caused cardiovascular damage. Generally, the present obtained results of serum lipid profile were in line with previous experimental studies, which investigated the association between liver fibrosis induced by TAA and alterations of lipid profile in mice and rats [43-49].

The present study showed that supplementation with almond oil was effective in improving serum lipid profile in rats exposed to TAA compared with control levels. The lipid profile indices are useful in monitoring health status of the cardiovascular system. Increased level of LDL-C has been associated with higher risk of atherosclerosis while elevated level of HDL-C is linked to reduced occurrences of cardiovascular disorder [50, 51]. Oxidative stress, defined as a disruption of the balance between oxidative and antioxidative processes, plays an important role in the pathogenesis of atherosclerosis [52]. Hyperlipidemia is a metabolic disorder associated with oxidative stress [53]. Since numerous studies have indicated that the effect of TAA contributes to oxidative stress, it has been suggested that the nutritional supplementation of antioxidants might reduce the oxidative stress and hence protect tissues from reactive oxygen species (ROS) damage. Previous studies showed that TAA induced excessive amounts of ROS eliciting oxidative stress damage that results in many

pathophysiological processes and disease development [54-58]. Fadlalla, *et al.* [59] and Torres, *et al.* [60] evaluated the hepatoprotective effects of almond oil on carbon tetrachloride (CCl₄)-induced liver injury in rats. They concluded that almond oil attenuated the CCl₄-induced alterations in serum and hepatic tissue in rats due to its antioxidant and anti-inflammatory properties. Al-Attar [7] investigated the therapeutic influence of almond oil against lead (Pb) toxicity in male rats. The treatment with almond oil notably improved the biochemical changes and showed antioxidative effect. The results disclosed the therapeutic influence of almond oil on the basis of its antioxidant effect against Pb toxicity. From the present study, it is not excluded that the effect of almond oil is due to its antioxidant properties. In conclusion, the present study showed that almond oil has protective effect on TAA-induced alterations of lipid profile. This study therefore suggests that almond oil may be a useful preventive factor against the effect of TAA at least partly due to its antioxidant properties. Further physiological and pharmacological investigations are needed to elucidate in detail the active principles and the real mechanism of action of almond oil against TAA toxicity.

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