Effect of Artichoke Extract on Hypercholesterolemic Status of Bile Duct Ligation Rat Model

Dr. Aisha I M Adawi

Ph.D. Student, Department of Anatomy, Institute of Health Sciences, Gazi University, Ankara, Turkey.

E-mail: aishaadawi@yahoo.com

Prof. Dr. Tuncay veysel PEKER

Prof. Doctor in Anatomy, Department of Anatomy, Faculty of Medicine, Gazi University, Ankara, Turkey.

E-mail: tpekeer@gazi.edu.tr

Abstract

Objective: Dietary plants have gained great attention, because they can play important role in enhancement of health and wellbeing. The purpose of our study was to look into the effect of artichoke extract on hypercholesterolemic status of bile duct ligation rat model.

Materials and Methods: In this study we used 21 Wistar albino rats. They randomly assigned into three groups; Group 1 (control group) underwent laparotomy alone and the common bile duct was only exposed and no drug was applied. Group 2 (BDL group) was subjected only to bile duct ligation (BDL) and no drug was applied. Group 3 (BDL +Ac) received a daily dose of 1.5 g/kg/per os of artichoke extract starting 24 hours after BDL. After 7 days of treatment, the animals were sacrificed, the blood samples were taken and total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) levels were analysed.

Results: TC decreased in BDL+ Ac group compared to BDL group (44.42±21.19, 61.2±11.3). The LDL-C decreased in BDL+ Ac group compared to BDL group (28,5±10,05, 38,4±3,91) with a statistical significance ($p<0,05$). HDL decreased in BDL group and in BDL+ Ac group compared to the control group; however, it indicated no statistically significant difference ($p>0,05$).

Conclusion: In this research, artichoke extract application may improve hypercholesterolemic status of bile duct ligation. Further studies with larger volume are required to support our promising results.

Keywords: Hypercholesterolemia, Artichoke, Cholestasis, Bile duct ligation, Rat.

1. Introduction

The risk of hyperlipidaemia in humans has increased in recent years as a result of stationary life with decrease in physical activity, and an increase in consumption of animal products. Hyperlipidaemia is a lipid metabolic disorder characterized by hypercholesterolemia, which may or may not be accompanied with elevated serum triglyceride levels (de Castro & Calder, 2018) (Linden et al., 2016)

The term hypercholesterolemia refers to an increase in cholesterol levels in the blood, and it is regarded as a major risk factor for the development of atherosclerosis and cardiovascular disease (Dongiovanni & Valenti, 2017). It can also cause a stroke and brain damage (Roger et al., 2011) (Clark, 1986). Hypercholesterolemia can result from a variety of causes, including both primary and secondary diseases. One of the secondary reasons is obstructive biliary cholestasis. Increased hepatic cholesterogenesis during cholestasis has been attributed to a variety of theories. Cholestasis may interfere with the cellular level negative feedback inhibition of cholesterol formation (Navi & Segal, 2009). On the other hand, Cholestatic hypercholesterolemia has been linked to a reduction in the supply of lymphatic lipoproteins rather than a failure of this feedback inhibition (Kattermann & Creutzfeldt, 1970).

Guidelines for hyperlipidaemia management recommend a treatment strategy that includes changes in lifestyle as well as medication based on the identification of groups at high, medium, or low risk of major cardiovascular events (Weis & Dietschy, 1971). There are also certain natural compounds, like artichoke leaf extract, which are traditionally used to lower cholesterol levels in the blood (Sabatine, 2016) (Urizar & Moore, 2003). The artichoke plant, it is a Mediterranean vegetable belongs to the Asteraceae family with incredible sensory characteristics and a high nutrient content. The artichoke's edible head (flower) is particularly high in bioactive phenolic components, fiber, minerals and inulin.

Furthermore, because artichoke leaves contain a considerable amount of phenolic compounds, they have traditionally used as a diuretic, liver-protecting, choleretic and fat-reducing agent (Lattanzio et al., 2009).

Various agents and different approaches have been previously studies for their effect on hypercholesterolemia. We aimed in this study is to investigate the effects of artichoke extract on hypercholesterolemia following bile duct ligation.

2. Materials and Methods

2.1. Animals

After obtaining the approval of Gazi University Animal Experiments Local Ethics Committee. This experimental study was carried out at Gazi University's Faculty of Pharmacy's Experimental Animal Care and Research Unit. All the procedures were performed according to accepted standards of Guide for the Care and Use of Laboratory Animals. In this study were used 21 healthy male Wistar Albino rats, 6-8 weeks old and weighing 250-300g. The animals were kept in a room with a temperature of 21-24°C, a humidity of 54-55%, 12 hours light/dark cycle, ad libitum feeding, and free access to water. Before the experimental model, all animals in this study were randomly divided into three groups, with seven rats in each group; control group (n=7, Group C), bile duct ligation group (n=7, Group BDL), and BDL+ artichoke extract group (n=7, Group BDL+ Ac).

2.2. Experimental Model and Treatment Protocol

The animals were anesthetized (with 10 mg/kg/ip xylazine and 50 mg/kg/ip ketamine). After that, they were placed in the supine position, and the abdominal wall was shaved and sterilized with povidone iodine. The bile duct was exposed by making an upper median incision of the abdomen, and two ligatures were performed with 3/0 polyglactin suture material, one from the proximal and the other from the distal region. The bile duct was then cut between these two ligatures. Group C (Control) underwent laparotomy alone and the bile duct was manipulated without ligation. After these procedures, muscle and skin were sutured with 3/0 polyglactin suture material and wound care of the incision site was performed. After 24h from the surgical procedures, control group and BDL group animals were given distilled water by gavage, and BDL + artichoke extract group

animals were given 1.5 g/kg/per os of artichoke extract by gavage after dissolving in distilled water.

After one week of treatment, the animals were sacrificed by taking intracardiac blood under the same anaesthesia protocol. The blood samples were centrifuged at 3000 rpm for 15 minutes, their serums were removed and total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) levels were analysed in the Biochemistry laboratories at Gazi University's Faculty of Medicine.

2.3. Statistical Analysis

For statistical analysis, the SPSS 24 program was utilized and $p<0.05$ was considered statistically significant. ANOVA variance analysis was used to evaluate the data. Duncan test was used to evaluate the variables with significance.

3. Results

The results of the study (table 1) indicated that all animals with bile duct ligation had jaundiced. The presentation of BDL led to a significant rise in the level of blood TC, LDL-C and reduction of the value of HDL-C in comparison with their parallel control animals. The treating of BDL group with artichoke extract showed a significant reduction in blood values of LDL-C in comparison with BDL rats, ($p=0,000<0,05$) (figure 2). TC were decreased in the BDL group treated with artichoke extract in comparison to BDL group, and HDL-C decreased in the BDL group treated with artichoke extract, but without statistically significant ($p>0,05$) (Figure 1, 3).

Table 1:

Levels of total bilirubin and of serum lipid profile parameters in Wistar rats

	Control grup	BDL grup	BDL+Ac grup
	X±ss	X±ss	X±ss
TC mg/dL	36,4±9,03	61,2±11,3	44,42±21,19
LDL mg/dL	8,75±1,78	38,4±3,91	28,5±10,05
HDL mg/dL	28±4,54	24,4±16,35	18,33±8,04
T-B mg/dL	0,14±0,06	8,78±1,68	3,91±1,77

TC: Total cholesterol, LDL-C: low-density lipoprotein cholesterol, HDL-C: high-density lipoprotein cholesterol, T-B: Total bilirubin

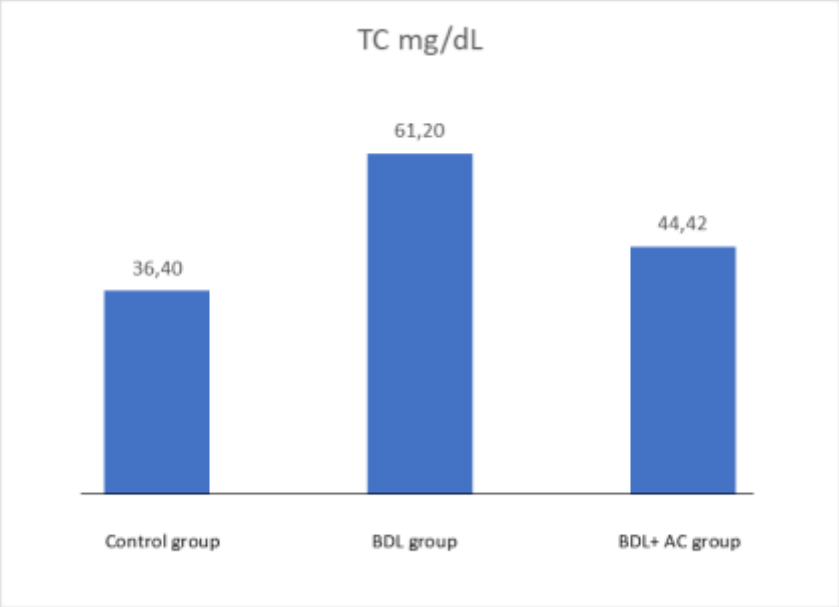

Figure 1: Serum total cholesterol (TC) values of control and experimental groups

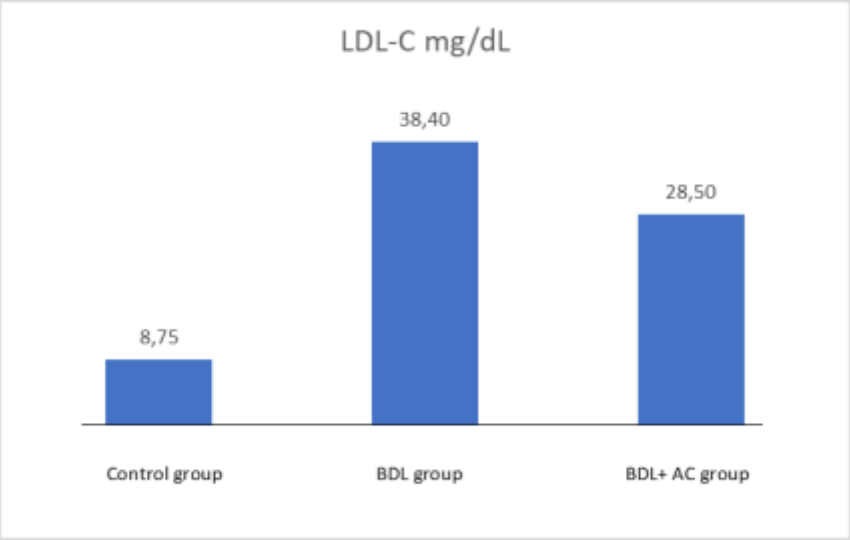

Figure 2: Serum low-density lipoprotein cholesterol (LDL-C) values of control and experimental groups

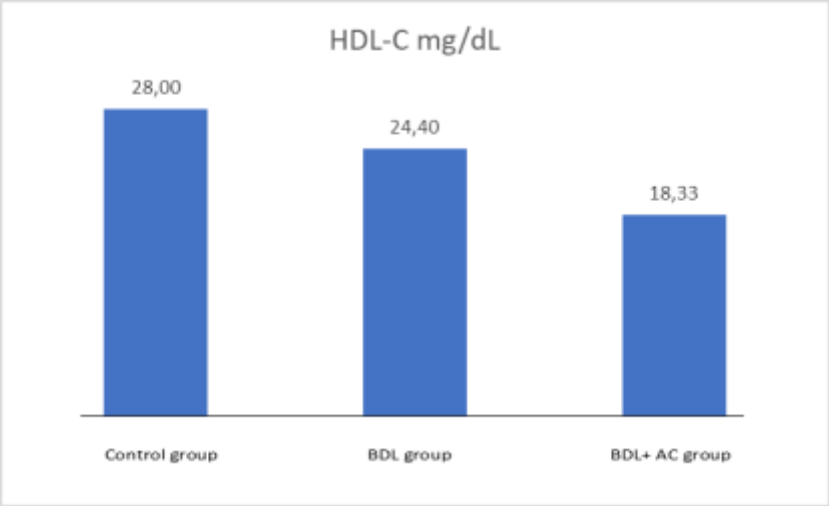

Figure 3: Serum high-density lipoprotein cholesterol (HDL-C) values of control and experimental groups

4. Discussion

Since hypercholesterolemia is one of the most important risk factors for the development of CHD, numerous animal experiments are carried out to better understand the relationship between cholesterol metabolism disorders and atherogenesis, as well as to evaluate potential treatments (Bersot, 2011). In experimental animals likes rats, pigs, and dogs, bile duct ligation induces cholestasis, results in the formation of an aberrant lipoprotein called LP-X in plasma. This lipoprotein is also found in people who have biliary stasis, but it goes away once the obstruction is relieved (Seidel et al., 1970). Many herbs contain antioxidant properties and can help to prevent the oxidation of low-density lipoproteins. Some phytosterols contained in plants can prevent cholesterol from being absorbed. Some polyphenols found in botanicals have the ability to inhibit cholesterol absorption. The artichoke appears to have 22 chemical components, 8 flavonoids and 11 caffeoylquinic acid (Schütz et al., 2004). Artichoke extract can have a substantial impact on hypercholesterolemia through a variety of methods, including suppression of cholesterol synthesis and LDL oxidation. The mono- and di-caffeoylquinic acids, as well as the cynarin concentration of artichoke, may be responsible for these therapeutic effects (Speroni et al., 2003) (Wittemer et al., 2005).

In the present research, we evaluated the effects of Artichoke extract on hypercholesterolemia in bile ligation rats. Animals from BDL treated with artichoke extract had normal growth and their serum were comparable to the control and BDL groups.

Interestingly, a one-week long period of supplementation with artichoke extract revealed a choleretic-protective aptitude, preventing the cholestasis-induced formation of hypercholesteremia in rats.

Serum cholesterol level are known to increase during the development of cholestatic liver injury in BDL rats (Cooper et al., 1974) (Dueland et al., 1991). It has been shown that administration of artichoke extract exerts an anti-hypercholesterolemic effect in rats with a diet high in cholesterol or with renal diseases (Mori et al., 1989) (Montilla et al., 1998). In the present study, rats with BDL had increased serum cholesterol concentration markedly. Artichoke extract given to rats with BDL, despite the decrease in cholesterol level, no significant differences were found compared to BDL group. The reason may be explained by the difference in the mechanism of hypercholesterolemia between extrahepatic cholestasis and feeding of a high cholesterol diet or renal diseases. Hypercholesterolemia in extrahepatic cholestasis is caused by the increases in hepatic cholesterol synthesis via increased 3-hydroxy-3-methylglutaryl-CoA reductase and cholesterol 7a-hydroxylase activities (Dueland et al., 1991), while hypercholesterolemia in feeding of a high cholesterol diet or renal diseases is brought about by the abnormal lipoprotein metabolism (Mahley & Holcombe, 1977) (Appel, 1991).

Artichoke leaves extract has been proposed to inhibit cholesterol biosynthesis in hepatocytes (Gebhardt, 1997), and to decrease the oxidation of LDL (Jimenez-Escrig et al., 2003). The study in (Kusku et al., 2010) recommend that artichoke leaf extract could be beneficial in preventing hypercholesterolemia-induced pro-oxidant states in the LDL+VLDL fraction as well as lowering elevated serum triglyceride and cholesterol levels. The authors of (Cervellati et al., 2002) (Lupattelli et al., 2004) showed that cynarine is utilized to mobilize and detoxify fatty deposits in the liver. Results of our study demonstrate that artichoke leaf extract can lower LDL-C levels of hypercholesterolemic rats. This finding is in agreement with study in (Englisch et al., 2000) which demonstrated, the using artichoke dry extract Lowering cholesterol and LDL-C levels.

Dyslipidaemia with abnormal lipoprotein levels is considered as a major risk factor for cardiovascular disease. However, HDL cholesterol has anti-inflammatory, antithrombogenic, anti-apoptotic and antioxidant properties to prevent atherosclerosis (Gylling et al., 2004).

In our study, there is no significant effect of artichoke on HDL-C level. This finding is in agreement with work in (Shahinfar et al., 2021) which demonstrated, that no significant effect of

artichoke on HDL-C level, and also with study in (Sahebkar et al., 2018) which reported that no significant alteration in plasma High Density Lipoprotein-Cholesterol by artichoke.

Over the last years, various pharmacological properties of artichoke extracts have been investigated. In a study by (Saenz Rodriguez et al., 2002) it has been proved to enhance bile flow and inhibit hepatocyte cholesterol biosynthesis in rats, and this is in agreement with authors of (Gebhardt et al., 2002) their results indicated importance of beta-glucosidase-dependent liberation of luteolin for the ability of artichoke extracts to inhibit hepatic cholesterol biosynthesis. The study reported in (Wider et al., 2013) have investigated the hypocholesterolemic effect of artichoke by humans, randomised controlled trials observed a moderate hypocholesterolemic impact. Compounds in artichoke leaves, such as cynarin and luteolin, may play an important role in inhibiting and reducing cholesterol synthesis (Englisch et al, 2000). In this context, Artichoke extract could be helpful as dietary supplement to reduce or prevent atherosclerosis which would help to maintain cardiovascular health.

The most herbal products and food supplements have antilipidemic effects supported by small-scale studies, their use in the treatment of dyslipidemia is limited (YAYLA & EU, K. (2016). The present results reinforce the idea that much more research regarding the potential and benefits of using the artichoke extracts as hypocholesterolemic agents is required.

5. Conclusion

As artichoke extract appears to positively modulate hypercholesterolemia, this study could contribute to the existing of evidence supporting the use of artichoke extract in the treatment of hyperlipidaemia.

6. Conflict of interest

No conflict of interest was declared by the authors.

7. Ethical statement

This experimental study was carried out after obtaining the approval of Gazi University Animal Experiments Local Ethics Committee (numbered G.Ü.ET-19.067).

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