Effect of Virgin Olive Oil on the lipid profile of Hyperlipidemic induced Rats

[1]Aghwider. A. A ,[2]AboRokia. M. A,[3]Tarhuni. A. H,[4]Estuty. N,[5]Najah. A, [6]Bakar. L

[1]Dep. of Public Health, Faculty of Medical Technology, University of Azzytuna
[2]Dep. of Basic Nursing, Faculty of Nursing, University of Tripoli
[3]Center for Agriculture, Ministry of Agriculture and Animal Wealth
[4]Libyan Authority for Scientific Research, Libyan Olive Tree Research Center
[5]Dep. of Physiology, , Faculty of Science, University of Azzytuna
[6]Faculty of Veterinary Medicine. University of Zawia

الملخص

يرتبط تناول نسبة عالية من زيت الزيتون بانخفاض كبير في الإصابة بأمراض القلب مقارنة بالنظام الغذائي العادي الذي يحتوي على دهون الهدف من هذه الدراسة هو ملاحظة تأثير زيت الزيتون البكر (VOO) ، جرعة منخفضة من زيت الزيتون البكر (LVOO) أو جرعة عالية من زيت الزيتون البكر (HVOO)على المظهر الدهني للفئران التي تعاني من فرط شحميات الد (HLD). أظهر انخفاضًا معنويًا ($P \leq 0.05$) في HDL-C ، والدهون الثلاثية (TG) ، والكوليسترول الكلي (TC) ، والبروتينات الدهنية منخفضة الكثاف (LDL–C) والبروتينات الدهنية منخفضة الكثافة جدًا (VLDL-C) في الفئران المكملة بـ (LVOO) أو (HVOO) مقارنة بمجموعتي التحكم (ND) و فرط شحميات الدم (HLD)، من ناحية أخرى ، تم تسجيل زيادة (P 0.05) في البروتين الدهني عالي الكثافة (HDLP) ، مقارنةً بمجموعتي التحكم (ND) و مجموعات فرط شحميات الد (HLD). لا يوجد فرق كبير بين LVOOو HVOO على بروتينات الملف الشخصي ،

الكلمات المفتاحية: فرط شحميات الدم ، الدهون ، البروتينات الدهنية ، زيت الزيتون

Abstract

High olive oil content is associated with a significant reduction in incidence of heart diseases in comparison with normal fat diet. The aim of this study is to observe the effect of Virgin Olive Oil (VOO), low dose of virgin olive oil (LVOO)or high dose of virgin olive oil (HVOO) on the lipid profile of hyperlipidemic (HLD) rats.The results

showed a significant decrease($P \leq 0.05$) in HDL-C, Triglycerides (TG), Total cholesterol(TC), low density lipoproteins (LDL-C) and very low density lipoproteins (VLDL-C) in rats supplemented with (LVOO) or (HVOO) as compared with both control (ND) and hyperlipidemic (HLD) groups, on other hand an increase ($P \leq 0.05$) in high density Lipoprotein (HDLP) was recorded, as compared with that of both control (ND) and hyperlipidemic (HLD) groups. No significant difference between the LVOO and HVOO on the profile proteins,

Key words Hyperlipidemia, lipid profile, lipoproteins, Olive oil

Introduction

High consumption of salt, saturated fats, and refined carbohydrates represents an important factor in causing of cardiac problems as a result of development of hyperlipidemia, atherosclerosis and ischemic heart disease (Lioyd-Jones, 2010).

Hyperlipidemia is known as lipoprotein metabolic disorder, with high serum low density lipoprotein (LDL-C), triglyceride (TG), and total blood cholesterol (TC), to be one of the most important risk factors in the initiation and development of atherosclerosis which leads to cardiovascular diseases (Festi *et al.,* 2004).

Many Studies have reported that the serum levels of TG, LDL-C, and HDL-C have been significantly affected by the consumption of phenolic compounds (Elias *et al*., 2017 and Khan *et al*., 2017).A regional differences with rates lower in Mediterranean countries than those in northern European ones, U.S.A, and Canada as the Mediterranean diet consisted of high olive oil content is related to significant decrease in incidence of heart diseases in comparison with normal fat diet from other nation (Moreno *et al.*, 2012).

Cholesterol and triglycerides are the major plasma lipids present in the body and are vital for human health (Russo *et al.,* 2005). Diet is the source of Cholesterol which in turn synthesized by hepatocytes and then absorbed through the intestine. Cholesterol is an essential component of cell membranes and serves as a precursor of bile acids and steroid hormones (Russo *et al.,* 2005). Lipids are not water-soluble and transported in the blood in specialized form, called lipoproteins that contain lipid and protein called (apolipoproteins). There are three major classes of lipoproteins are categorized in three major classes: low density lipoprotein (LDL), high density lipoproteins (HDL), and very low-density lipoproteins (VLDL). In addition to intermediate density lipoprotein (IDL), which falls somewhere between VLDL and LDL and is included in the (LDL) measurement (Otunola *et al.,* 2010).

The present study was designed to investigate the influence of low and high doses of virgin olive oil administration to normal and hyperlipidemic male albino rats on the lipid profile of hyperlipidemic rats.

Materials and methods

Materials:

Animals and Housing: The study was conducted in the Animal House of National Research Centre (NRC), Cairo, Egypt. From August to November 2016. Fifty males Sprague dawaly rats, (90-110 g), were randomly selected .All rats were active, apparently healthy and free from abnormalities and disease .The experimental animals were housed in commercial cages, equipped with automatic drinkers and feeders, they were supplied with food and water ad libitum under standard conditions of light (14-10) light dark cycle, humidity and temperature (22-25°C). All experimental procedures in this study were carried out according to the guidelines of Ethics Committee of (NRC), Cairo - Egypt

Feeding regimen: Basal and experimental diets were formulated to cover the requirements of growing rats as recommended in NRC (1977). Composition and proximal chemical analysis of formulated diets is shown in Table (1). Diets were subjected to chemical analysis according to AOAC (2012).

Olive Oil: Olive oil in the present study was obtained from olive (Olea europaea; family Oleaceae), a traditional tree crop of Tarhuna city farms, according to (ARC) Agriculture Research Centre – Tarhuna – Libya) Olive oil was administered in two doses:

- Low dose (1 ml / 100g B.W) olive oil.
- High dose (2 ml / 100g B.W) olive oil.

Table (1) The Composition of diet:

Ingredient (g/kg)	Basal diet	Exp. Diet
Corn	729.60	729.60
Casein	17.56	17.56
Fat	2.7	2.7g/100g
Butter oil	0.00	19g
Soy bean oil	0.00	1.00g
Mineral/vitamin mix	60.40	60.40

Table (2): Fatty acid composition of dietary olive oil (g/100 g)

Fatty acid	g/100g
Palmitic acid	10.28
Palmitoleic acid	0.77
Stearic acid	3.39
Oleic acid	1.80
Lenoleic acid	14.34
Lenolenic acid	0.64
Archidonic acid	0.74
Gadoleic acid	0.62
Behenic acid	2.84
SFA	17.28
MUFA	66.20
PUF	14.99
SFA: saturated fatty acids; MUFA: monounsaturated fatty acid; PUFA: polyunsaturated fatty acid	

Induction of hyperlipidaemia: Hyperlipidaemia was induced by feeding rats for three weeks with a mixture composed of 20g of fat/100g of diet (19g of butter oil and 1g of soybean oil) to provide essential fatty acids, added to basal diets, according to the method described by Woods *et al.* (2003). Serum samples were collected to confirm hyperlipidaemia in groups receiving fat in the diet

Methods

Experiment: The rats were equally and randomly divided into five groups (10 in each): The first group was considered as control group, received basal diet (ND) and supplemented with 1ml saline by gastric tube for 4 weeks. The second group was received diet-induced hyperlipidaemia (HLD), to the end of experiment (4 weeks). The third group, received diet-induced hyperlipidaemia and supplemented by low dose of virgin olive oil (1 ml/100g B.W) (HLD+LVOO), administered by gastric tube for 4 weeks. The fourth group received diet-induced hyperlipidemia and supplemented by high dose of virgin olive oil (2 ml/100g B.W) (HLD+HVOO), administered by gastric tube for 4 weeks. The fifth group after the received diet-induced hyperlipidemia, followed the basal diet (HLD +ND), to the end of experiment.

Blood samples: Were collected individually by orbital Venus plexus technique under mild ether inhalation anaesthesia. Samples were obtained at the early morning before access to feed and water at the end of every week. Blood samples was collected into plain tubes and allowed to coagulate at room temperature and centrifuged at 1000 g for 20 min to obtain sera. The clear, non-haemolysed supernatant sera was quickly

collected for each animal and stored at (-20C̊) until used for determination of biochemical assay.

Assays:

Determination of triglycerides (Tri-Gmg/dl): Triglyceride was determined in serum according to the method described by Fossati and Prencipe, (1982), using commercial kit obtained from Spectrum Diagnostic, Egypt.

Determination of Total cholesterol (TCmg/dl): Total cholesterol in serum was estimated according to the method of Allain *et al.* (1966)., using commercial kit obtained from Spectrum Diagnostic Egypt.

Determination of high Density Lipoprotein (HDL–cholesterol mg/dl): HDL–cholesterol concentration was estimated by HDL–cholesterol kit obtained from Spectrum Diagnostic Egypt. According to the method described by Lopez- Virella *et al.* (1977).

Determination of Low Density Lipoprotein (LDL- cholesterol) VLDL-cholesterol concentration was calculated from the total cholesterol concentration, HDL-cholesterol and triglycerides concentration according to Friedewald *et al.* (1972) using the following equation: Serum LDL-c = TC – (HDL-c + TGs.) / 5.

Determination of Very Low Density Lipoprotein (VLDL)- cholesterol: LDL-cholesterol concentration was calculated according to Satheesh and Pari (2008) using the following equation: Serum VLDL-c = TG/ 5

Statistical analysis: Data are presented as means ± S.E. and analyzed by two-way ANOVA using Costate computer program Costate version 6.400 (Copyright© 1998 – 2008 coHort software). Groups were compared by the least significant different test (LSD) at the at P value ≤ 0.05. Correlation studies between different treatments and measured parameters among different groups were adopted according to the method of Snedecor and Cochran (1980).

Results

Data showed that hyperlipidemia (HLD) significantly ($P \leq 0.05$) increase the values of TG levels (167.80± 3.11, 170.60± 2.30, 173.80±2.28, and 174.80±2.58 *mg/dl*) during 1st, 2nd, 3rd, and 4th weeks of the experimental periods, as compared with normal diet (ND) group (152.20±2.80, 154.80±3.27, 157.20±2.38, and 159.60±1.67 *mg/dl),* respectively Figure (1) .

The values for TC in hyperlipidemic diet (HLD) during 1st, 2nd, 3rd and 4th week of the experimental periods (138.00±2.23, 154.40±2.12, 166.40±2.70, and 175.40±3.36 *mg/dl*), revealed significant ($P \leq 0.05$) increase, as compared with normal diet (ND) group (78.65±3.33, 81.46±2.00, 83.83±2.77, and 85.86±3.98 *mg/dl),* respectively Figure (2)

Significant ($P \leq 0.05$) increase in the values of LDL-C in hyperlipidemic diet (HLD) during 1st, 2nd, 3rd and 4th week of the experimental periods (84.24±2.67, 101.88±2.74, 115.64±2.60, and 126.24±2.74*mg/dl)*, as compared with normal diet (ND) group (24.21±1.65, 22.90±1.97, 23.39±1.63, and 24.14±1.93 *mg/dl*), respectively Figure (3)

In the same time data presented in figure (4) showed significant increase in the very low density lipoprotein cholesterol (VLDL-C) levels in hyper-lipidemic diet group (HLD) during 1st, 2nd, 3rd, and 4th weeks of the experimental period (33.56± 0.62, 34.12±0.46, 34.76±0.45, and 34.96±0.51*mg/dl)*, when compared with the control (ND) group (30.44±0.45, 30.96±0.65, 31.44±0.47 and 31.92±0.33 *mg/dl*), respectively.

On the contrary the results recorded for HDL-C levels showed significant ($P \leq 0.05$) decrease in hyperlipidemic diet (HLD); (20.20±3.13, 18.40± 2.88, 16.00± 2.00, and 14.20± 1.64*mg/dl)* during 1st, 2nd, 3rd and 4th week of the experimental periods, as compared with normal diet (ND) group (24.00±1.81, 27.60±3.04, 29.00±1.58, and 29.80±1.92*mg/dl*), respectively Figure (5).

Moreover, groups subjected to hyperlipidemic diet and supplemented with low dose of virgin olive oil (HLD + LVOO) or high dose of virgin olive oil (HLD + HVOO), revealed a significant ($P \leq 0.05$) decrease in TG, TC, LDL-C, VLDL-C, levels, as compared with both hyperlipidemic diet group and normal diet (HLD+ND) group. Meanwhile; there was a significant increase in HDL-C of rats subjected with hyperlipidemic diet (HLD) group, as compared with all other groups. Furthermore, group subjected to hyperlipidemic diet and supplemented with normal diet (HLD+ND), indicated non, difference in their serum lipid profile, as compared with that of both control (ND) and hyperlipidemic (HLD) groups.

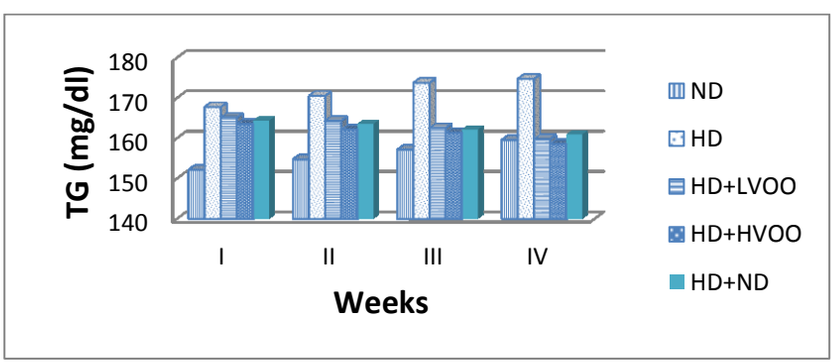

Figure (1): Effect of olive oil administration on TG in serum of hyperlipidemic rats.

ND= Control, HLD= Hyperlipidemic diet, HLD+LVOO = Hyperlipidemic diet + low dose of virgin olive oil, HLD+HVOO= Hyperlipidemic diet + high dose of virgin olive oil, HLD+ND= Hyperlipidemic diet followed by normal diet.

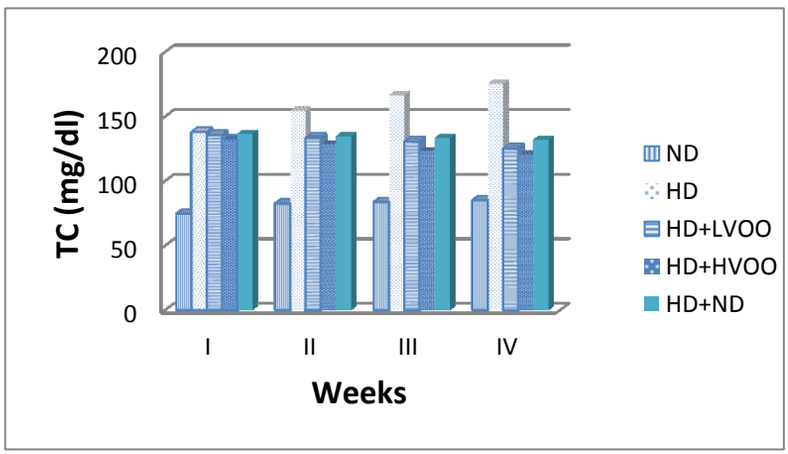

Figure (2): Effect of olive oil administration on TC in serum of hyperlipidemic rats.

ND= Control, HLD= Hyperlipidemic diet, HLD+LVOO = Hyperlipidemic diet + low dose of virgin olive oil, HLD+HVOO= Hyperlipidemic diet + high dose of virgin olive oil, HLD+ND= Hyperlipidemic diet followed by normal diet.

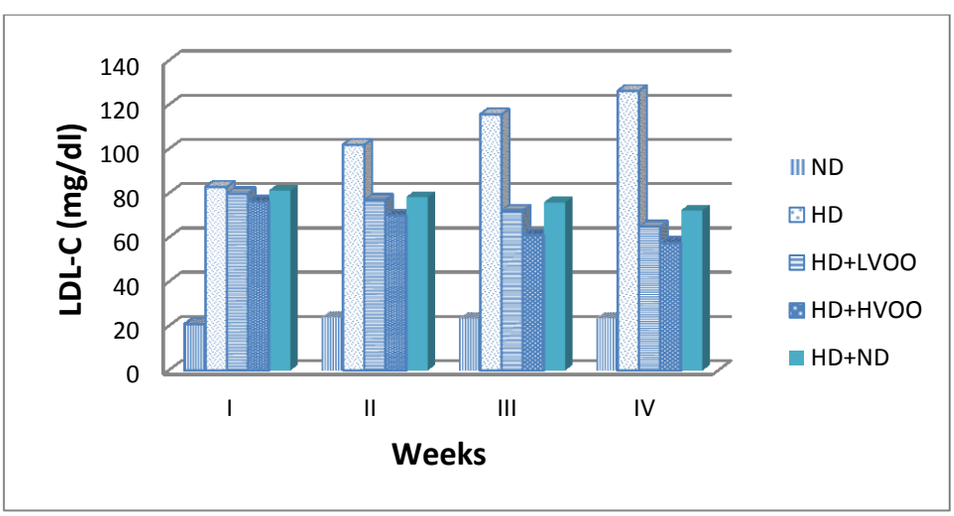

Figure (3): Effect of olive oil administration on LDL-C content in serum of hyperlipidemic rats.

ND= Control, HLD= Hyperlipidemic diet, HLD+LVOO = Hyperlipidemic diet + low dose of virgin olive oil, HLD+HVOO= Hyperlipidemic diet + high dose of virgin olive oil, HLD+ND= Hyperlipidemic diet followed by normal diet.

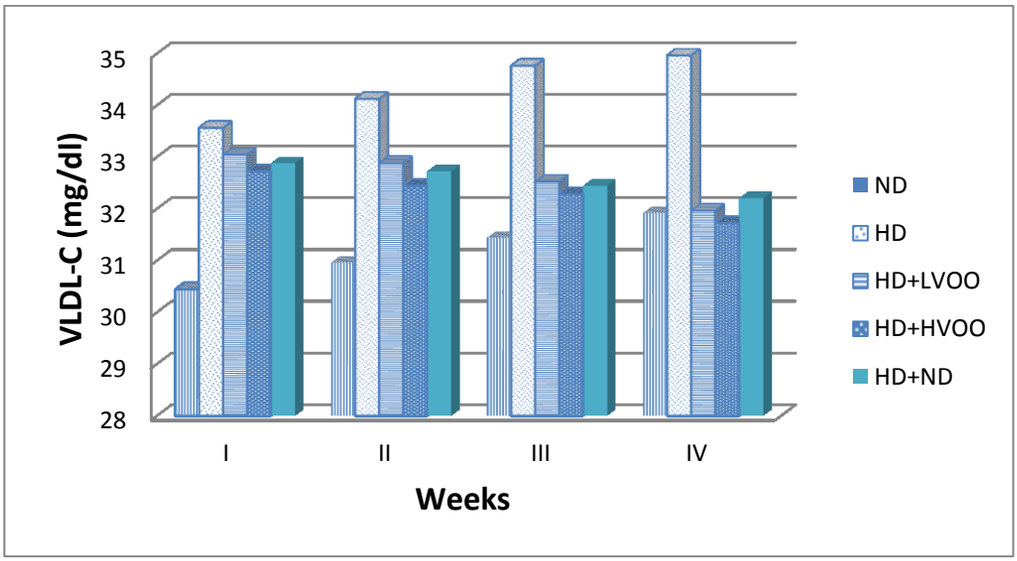

Figure (4): Effect of olive oil administration on VLDL-C content in serum of hyperlipidemic rats.

ND= Control, HLD= Hyperlipidemic diet, HLD+LVOO = Hyperlipidemic diet + low dose of virgin olive oil, HLD+HVOO= Hyperlipidemic diet + high dose of virgin olive oil, HLD+ND= Hyperlipidemic diet followed by normal diet.

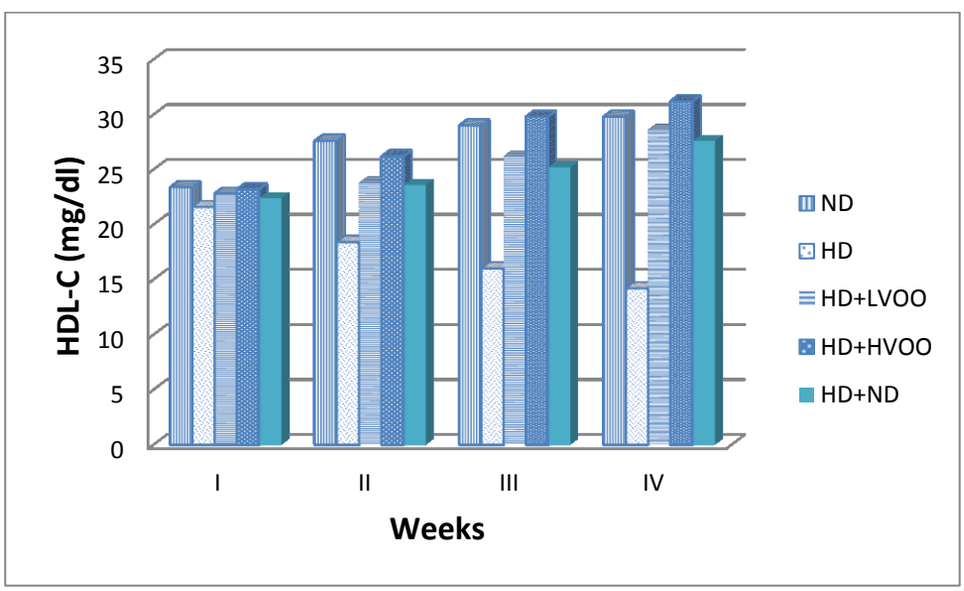

Figure 5): Effect of olive oil administration on HDL-C content in serum of hyperlipidemic rats.

ND= Control, HLD= Hyperlipidemic diet, HLD+LVOO = Hyperlipidemic diet + low dose of virgin olive oil, HLD+HVOO= Hyperlipidemic diet + high dose of virgin olive oil, HLD+ND= Hyperlipidemic diet followed by normal diet.

Discussion

Prolonged consumption of high fat diet (HFD) is causing hyperlipidemia, that represents one of the major causes promoting atherosclerosis in human and cardiovascular disorder in experimental animals (Kratz, 2015), additionally hypercholesterolemia appears critical to the atherogenic process and tends to lead serious cardiovascular disease (Kratz, 2015).

In the present study, feeding rats on high fat diet, induced a significant increase in serum levels TG, TC, LDL-C, and VLDL-C, . While serum levels of HDL-C) was decreased significantly. These results agree with those of other studies, demonstrating similar hyperlipidemic pattern further suggesting initiation of atherosclerotic process (Elias *et al*., 2017).

Several mechanisms related to initiation and development of atherosclerosis caused by lipids. In this context, increased TG promote production of the atherogrenic triglyceride rich lipoproteins (TGRLs) comprising TG and VLDL-C (Elias *et al*., 2017). This leads to enhanced thrombogenic tendency by increasing circulating factor VII levels (Saigo *et al*., 2004).A report by (Wang *et al*., 2009) suggested TGRLs can promote direct endothelia damage through its ability to cross the endothelial barrier and enter the arterial wall, (Wang *et al*., 2009), in addition in playing a role as marker of endothelium dysfunction (Schwartz and Reaven, 2012). Moreover, disorder in TG metabolism may promote atherogenesis by increasing the expression of adhesion molecules. The concentrations of adhesion molecules, including intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), therefore, increased levels of TG and VLDL-C, as detected in this study can be considered as a marker for the incidence of atherosclerosis (Perona *et al*., 2006). Other researchers have indicated that elevated levels of TC and LDL-C are unique in being sufficient to drive development of atherosclerosis even in the absence of other known risk factors (Glass and Witztum, 2001). LDL-C has essential physiological role as a carrier for transporting cholesterol to peripheral tissues, raise in LDL-C levels are related to increased risk of cardiovascular disease (CVD) (Glass and Witztum, 2001).Oxidation of LDL-C by peroxidation of lipid components of this lipoprotein, results in production of Ox-LDL-C (Covas, 2007, thus, intracellular cholesterol accumulates, converting macrophages into lipid laden foam cells, characteristic of early atherosclerotic lesions (Hansson, 2009). However, Ox-LDL-C was suggested also to produce other actions that promote atherosclerosis. In this respect, reported that Ox-LDL-C may directly damage the endothelium and contribute to atheroma, plaque formation. While, HDL-C was found to have an effect that reversing cholesterol transport (Moore et al., 2013), and inhibit the oxidation of LDL-C thus neutralize the effect of Hyperlipidemia due to

oxidized-LDL-C (Ox-LDL-C) (Mannarino and Pirro, 2008). However, a reciprocal relation between the concentration of LDL-C and HDL-C has been reported Moreno and Mitjavila, 2003).

Results of the current study indicated that low dose of virgin olive oil (LVOO) or high dose of virgin olive oil (HVOO) administration to rats fed normal or hyperlipidemic diet (HLD) caused a significant decrease in the serum levels of TG, TC, LDL-C, VLDL-C, while a significant elevation was seen in HDL-C. Similarly, (Rosa *et al.,* 2017; Elias *et al*., 2017; Khan *et al*., 2017 and Farahat *et al*., 2019), found that virgin olive oil reduced serum TG, TC, LDL-C and VLDL-C, and increased HDL-cholesterol level. It has been suggested by these authors that, the health effects of OO on cardiovascular risk factors are due to its high content of MUFAs, such as oleic acid, that suggested to improve serum lipid profile, through a decrease in TC, LDL-C and TGs and increase in HDL-C (Moreno and Mitjavila, 2003).

References

- Allain, C. C.; Poon, L. S.; Chan, C. S. G.; Richmond, W. and Fu, P.C.(1966): Enzymatic determination of total serum cholesterol. Clin. Chem., 20: 470-475.
- AOAC (2012): Association official Analytical Chemists International. Official Methods of Analysis, 16th revision, 41.1.36. AOAC international, Gaithersburg
- Covas MI . (2007): Olive oil and the cardiovascular system. Pharmacol. Res.; 55: 175-86Elias, S.; Wisam, S.; Luai, A.; Massad, B.; Nimer, A. (2017): Lipotoxicity in Obesity: Benefit of Olive Oil. *Obesity and Lipotoxicity*; Advances in Experimental Medicine and Biology, 960: 5-26.
- Elias, S.; Wisam, S.; Luai, A.; Massad, B.; Nimer, A. (2017): Lipotoxicity in Obesity: Benefit of Olive Oil. Obesity and Lipotoxicity; Advances in Experimental Medicine and Biology, 960: 5-26.
- Farahat, A. A.; Sawiress F. A. and Aghwider A. A. (2019): Effect of Olive Oil Supplementation on Lipid Profile and Oxidative Status in rats. *J.VET.MED. RESEARCH 2019, 25.*
- Festi, D.; Colecchia, A.; Sacco, T.; Bondi, M.; Roda, E. and Marchesini, G. (2004): Hepatic steatosis in obese patients: clinical aspects and prognostic significance. Obesity Reviews, 5: 27- 42.
- Fossati, P. and Prencipe, L. (1982): Serum triglycerides determined colorimetrically with an enzyme that produces hydrogen peroxide. Clin. Chem. 28(10): 2077-2080.

- Friedewald, W.T., Levy R.I. and Fredrickson D. S. (1972): Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin. Chem.,*18 (6): 499-502.
- Glass, C.K. and Witztum, J. L. (2001): Atherosclerosis: The road ahead. Cell, 104:503-516.
- Hansson, G.K.; and Robertson, A. K. (2006): Inflammation and atherosclerosis. Annu. Rev. Pathol., 1:297-329.
- Keaney, J. F. Jr. (2000): Atherosclerosis from lesion formation to plaque activation and endothelial dysfunction. Mol. Aspects. Med., 21: 99–166.
- Khan, T.M.; Iqbal, S. and Rashid, M.A. (2017): Comparison of lipid lowering effect of extra virgin olive oil and atorvastatin in dyslipidaemia in type 2 diabetes mellitus. J. Ayub. Med. Coll. Abbottabad., 29(1): 83-6.
- Kratz, M.(2015): Dietary cholesterol, atherosclerosis and coronary heart disease. Hand book Exp. Pharmacol., (170): 195-213.
- Lioyd–Jones (2010): Cardiovascular Risk Prediction Basic Concepts, Current Status, and Future Directions, Volume 121, Issue 15, 20 April 2010; Pages 1768-1777.
- Lopez-Virella, M.FP.; Stone, S. and Ellis, J.A.(1977): Colwell Cholesterol determination in high-density lipoproteins separated by three different methods. Clin. Chem., 23(5):882-884.
- Mannarino, E., and Pirro, M. (2008). Molecular Biology of Atherosclerosis. Clin. Cases Miner Bone Metab. 5, 57–62.
- Moore, K. J., Sheedy, F. J., and Fisher, E. A. (2013). Macrophages in Atherosclerosis: a Dynamic Balance. *Nat. Rev. Immunol.* 13, 709–721.
- Moreno, J.J. and Mitjavila, M.T. (2003): The degree of unsaturation of dietary fatty acids and the development of atherosclerosis. J. Nutr. Biochem.,14(4): 182-195.
- Moreno, L. R.; Munoz, H.R.; Miranda, M.L.; Costa, A.F.; Jimenez, L. and Vallejo, L. (2012): Olive oil polyphenols decrease blood pressure and improve endothelial function in young women with mild hypertension. American J. of hypertension, 25 (12): 1299- 1304.
- NRC, (1977): National Research Council. Nutrients Requirements of Rats (2^{ed}). National Academy of Science. Washington, DC., USA. 1977.
- Otunola, G.A.; Oloyede, O.B; Oladiji, A.T. and Afolayan, A.A. (2010): Effects of diet-induced hypercholesterolemia on the lipid profile and some enzyme activities in female Wistar rats. African J. of Biochemistry Res.,4 (6) 149-154.
- Perona, J.S.; Cabello-Moruno, R. and Ruız-Gutıerrez, V. (2006): The role of virgin olive oil components in the modulation of endothelial function. J. Nutr. Biochem., 17: 429–45.

- Rosa, C.R.; Urpı, S.M.; Sacanella, E.; Arranz, S.; Corella, D.; Castaner, O.; Lamuela, R.R.; Salas, S.J.; Lapetra, J.; Portillo, M.P. and Estruch, R. (2017): Anti-Inflammatory Effects of the Mediterranean Diet in the Early and Late Stages of Atheroma Plaque Development. J. Nutr. 146:1684–93.
- Russo, M.V.; De Leonardis, A. and Macciola, V. (2005): Solid phase extraction gas-chromatographic method to determine free cholesterol in animal fats. J. Food Compos. Anal., 18: 617- 624.
- Saigo, M.; Priscilla, Y. H. and Waters, D. D. (2004). Role of thrombotic and fibrinolytic factors in acute coronary syndromes. Issue May–June 2004, Pages 524-538.
- Satheesh, M. and Pari, L., (2008): Effect of pterostilbene on lipids and lipid profiles in streptozotocin-nicotinamide induced type 2 diabetes mellitus. J. Appl. Biomed., 6:31-37.
- Schwartz E .A and Reaven P. D. (2012) Lipolysis of triglyceride-rich lipoproteins, vascular inflammation, and atherosclerosis *:* BBA Molecular and Cell Biology of Lipids : Issue May 2012, Pages 858-866
- Snedecor, G.W. and Cochran, W.G. (1980): Statistical methods. 7th edition. Iowa state university press. Ames.
- Wang, L. Gill, R. S. Pedersen, T. L, Higgins, L, J. Newman J W. and Rutledge, J., C. (2009). Triglyceride-rich lipoprotein lipolysis releases neutral and oxidized FFAs that induce endothelial cell inflammation: Journal of Lipid Research. Issue .February 01,2009 , 204 -213
- Wood, S.C.; Seeley, R.J.; Rushing, P.A.; D'Alessio, D. and Tso, P. (2003): Controlled high-fat diet induces an obese syndrome in rats. J. Nutr. Metabol., 133: (1) 1081- 1087.
- Yang, R. and Barouch, L. A. (2007): Leptin signaling and obesity: cardiovascular consequences. Circ. Res., 101:545– 59.