

The Protective Effects of Virgin Coconut Oil on High-Fat Diet Induced Rat Liver

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ABSTRACT

BACKGROUND AND OBJECTIVE: A high-fat diet can disrupt the antioxidant system and damage the liver. One of the most important ways to control non-alcoholic fatty liver is to use natural compounds with antioxidant properties. Therefore, this study was performed to evaluate the effect of coconut oil on cholesterol, triglyceride and antioxidant status in high-fat diet- induced rat liver.

METHODS: In this experimental study, 30 male rats were randomly divided into 6 groups of 5 including: 1) control group, 2 and 3) control+10% and 8% virgin coconut oil, 4) only receiving high fat diet, and 5 and 6) receiving high fat diet+10% and 8% virgin coconut oil. Coconut oil was prepared daily and mixed with animal food. At the end of the study, the rats were anesthetized and liver tissue was isolated and used for antioxidant tests.

FINDINGS: In this study, the levels of triglyceride (159 ± 11.5) in the high-fat diet group increased significantly compared to the control (64 ± 4.2) ($p < 0.001$). Treatment of high-fat diet group with coconut oil at doses of 8% (104.5 ± 9.1) and 10% (97.5 ± 8.2) was able to reduce triglyceride levels ($p < 0.05$) significantly. Cholesterol (118 ± 6.7) in the high-fat diet group increased significantly compared to the control (60 ± 6.6) ($p < 0.001$). Treatment of high-fat diet group with coconut oil at a dose of 10% (94 ± 5.3) was able to reduce cholesterol ($p < 0.01$) significantly.

CONCLUSION: According to the results of this study, virgin coconut oil can be useful in the treatment of fatty liver by reducing lipids and increasing antioxidants.

KEY WORDS: Coconut Oil, Fatty Liver, Rat.

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Introduction

Non-Alcoholic Fatty Liver Disease (NAFLD) is caused by a variety of factors, including insulin resistance, obesity, blood lipid disorders, diabetes, sedentary lifestyle, and a high-fat diet (1-4). The most important mechanisms involved in non-alcoholic fatty liver include changes in lipid metabolism, changes in insulin signaling, mitochondrial dysfunction, inflammation, and oxidative stress (5-8).

One of the most important ways to control non-alcoholic fatty liver is to use natural compounds with antioxidant properties (9-14). In this regard, vegetable oils such as coconut oil can be useful. Coconut oil is prepared in two ways: Copra Oil and Virgin Coconut Oil (VCO). Copra oil has been reported to have no positive effect on blood lipids and may even increase blood lipids. But the effective and therapeutic form of coconut oil is Virgin coconut oil. Virgin coconut oil is able to significantly reduce the concentration of cholesterol and levels of phospholipids, triglycerides and LDL (Low-Density Lipoprotein) and also increase the serum level of HDL (High-Density Lipoprotein) (15).

It has been reported that virgin coconut oil has beneficial effects on lipid parameters by reducing lipogenesis and increasing fatty acid catabolism (16). Other beneficial effects of virgin coconut oil include antioxidant, anti-inflammatory, analgesic, anti-aging, anti-bacterial and chemical protective activities. Coconut oil is known as a very useful nutrient that is rich in polyphenol compounds (17). These data suggest that virgin oil can be beneficial in improving fatty liver through its antioxidant and hypolipidemic properties. Therefore, the aim of this study was to investigate the antioxidant effects of virgin coconut oil on an animal model of non-alcoholic fatty liver.

Methods

In this experimental study, after approval by the ethics committee of Hamadan University of Medical Sciences with ethics code IR.UMSHA.REC.1397.550, male Wistar rats aged 8 weeks after two weeks of adaptation to the new environment (temperature of 22 ± 2 °C with standard food and exposed to natural light/dark cycles and proper ventilation), were randomly divided into 6 groups of 5:

1-Healthy control group

2-Healthy control group+8% virgin coconut oil (VCO)

3-Healthy control group+10% virgin coconut oil (VCO)

4-High fat diet group (HFD)

5-High fat diet group (HFD)+8% virgin coconut oil (VCO)

6-High fat diet (HFD)+10% virgin coconut oil (VCO).

At the end of the eighth week of treatment and after overnight fasting, the animals were anesthetized through ketamine injection (Sigma-Aldrich, USA) and then blood samples were collected. In addition, the isolated liver was washed with PBS (Phosphate Buffer Saline) buffer and immediately frozen in liquid nitrogen and stored at -80 °C and finally used for antioxidant tests. Doses of 8% and 10% of virgin coconut oil were more effective than other doses, according to previous reports in rats. Therefore, in order to evaluate the antioxidant effects in this study, treatment with the mentioned doses was performed (18). Virgin coconut oil was prepared according to previous studies (19).

All of the tools were prepared from Sigma-Aldrich (USA). Blood chemistry factors were measured using biochemical kits of Pars Azmun Company according to the existing instructions (20, 21). This method is based on the ability of homogenized tissue to reduce ferric (Fe^{3+}) ions to ferrous (Fe^{2+}) ions. The regeneration process is performed in the presence of a substance called TPTZ (Tripyridyl-S-triazine, Sigma-Aldrich). The Fe^{2+} -TPTZ complex forms a color complex with a maximum absorption of 593 nm. TAC levels were reported in terms of nmol/mg protein (22-24). Lipid oxidation was measured according to previous studies. MDA was reported in terms of U/mg protein (25). The total oxidant content of homogenized liver samples was measured by oxidation of ferrous to ferric iron under moderate acidity using Xylenol orange dye.

TAC levels were reported based on nmol/mg protein (26). Descriptive statistics of mean, median, standard deviation and interquartile range as well as graphs of data were used to describe the collected data. To evaluate the effect of coconut oil and to compare the groups, one-way analysis of variance test based on Bootstrap method and Bayesian approach were used with respect to the appropriate previous distribution of response variables in Stan statistical software in R3.6.1 development environment, as well as the statistical packages of Ggplot2, BRMS and Quantreg. Furthermore, for abnormal data with abnormal distribution values, a non-parametric test was used and $p < 0.05$ was considered significant.

Results

In this study, the levels of triglyceride (159 ± 11.5) in the high-fat diet group increased significantly compared to the control (64 ± 4.2) ($p<0.001$). Treatment of high-fat diet group with coconut oil at doses of 8% (104.5 ± 9.1) and 10% (97.5 ± 8.2) was able to reduce triglyceride levels ($p<0.05$) significantly. Cholesterol (118 ± 6.7) in the high-fat diet group increased significantly compared to the control (60 ± 6.6) ($p<0.001$). Treatment of high-fat diet group with coconut oil at a dose of 10% (94 ± 5.3) was able to reduce cholesterol ($p<0.01$) significantly (Table 1). Lipid peroxidation activity was significantly increased in the high-fat diet group compared to the control group ($p<0.001$). This marker showed a significant decrease in the group receiving high-fat diet+10% virgin coconut oil and also in the group receiving high-fat diet+8% virgin coconut oil compared to the group receiving high-fat diet ($p<0.05$) (Figure 1). There was a significant increase in TOS in the group

receiving high-fat diet compared to the control group ($p<0.001$). The amount of TOS in the control group receiving coconut oil at a dose of 10% compared to the control group showed a significant decrease (Figure 2) ($p<0.05$). The amount of TOS in the group receiving high-fat diet+10% virgin coconut oil ($p<0.001$) and also the group receiving high-fat diet+8% virgin coconut oil ($p<0.01$) showed a significant decrease compared to the group receiving high-fat diet. In the group receiving high-fat diet compared to the control group, the amount of TAC was significantly reduced ($p<0.001$). The level of TAC in the control group receiving coconut oil at doses of 8 and 10% did not show a significant increase compared to the control group. The amount of TAC in the group receiving high-fat diet+10% virgin coconut oil ($p<0.05$) and also the group receiving high-fat diet+8% virgin coconut oil ($p<0.01$) showed a significant decrease compared to the group receiving high-fat diet (Figure 3).

Table 1. The effect of virgin coconut oil on cholesterol and triglyceride levels in different treatment groups

Study groups	Cholesterol (mg/dl)	triglyceride (mg/dl)
Healthy control group	60 ± 6.6^a	64 ± 4.2^A
Healthy control group+8% virgin coconut oil (VCO)	62 ± 4.7^a	62.5 ± 7.2^A
Healthy control group+10% virgin coconut oil (VCO)	56 ± 3.3^a	60 ± 3.7^A
High Fat Diet (HFD) Group	118 ± 6.7^b	159 ± 11.5^B
HFD+8% virgin coconut oil (VCO)	$104.5\pm9.1^{b*}$	$104.5\pm7.6^{B*}$
HFD+10% virgin coconut oil (VCO)	$94\pm5.3^{b*}$	$97.5\pm8.2^{B*}$

Non-similar Latin letters indicate significant differences and similar Latin letters indicate no significant differences between groups ($p<0.001$). (*) indicates a significant difference with the group receiving high-fat diet (HFD).

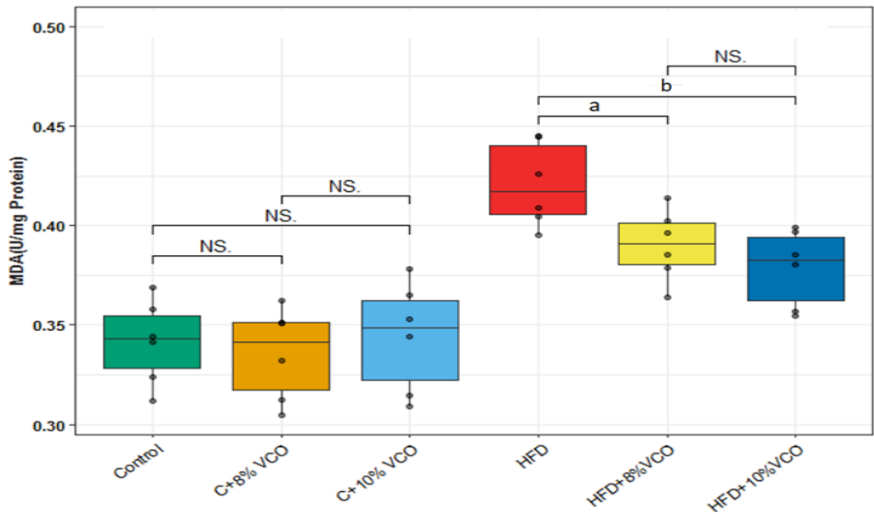


Figure 1. Effect of virgin coconut oil on malondialdehyde (MDA) in liver tissue. There was a statistically significant difference between the high-fat diet group and the groups of HFD+8% VCO and also the HFD+10% VCO, so that the mean MDA in the groups with VCO intervention was higher than the group of high-fat diet without intervention. C: Control, HFD: high-fat diet, VCO: virgin coconut oil, NS: no significance. Significance was shown as $p<0.05^a$ and $p<0.01^b$ in comparison with untreated HFD group.

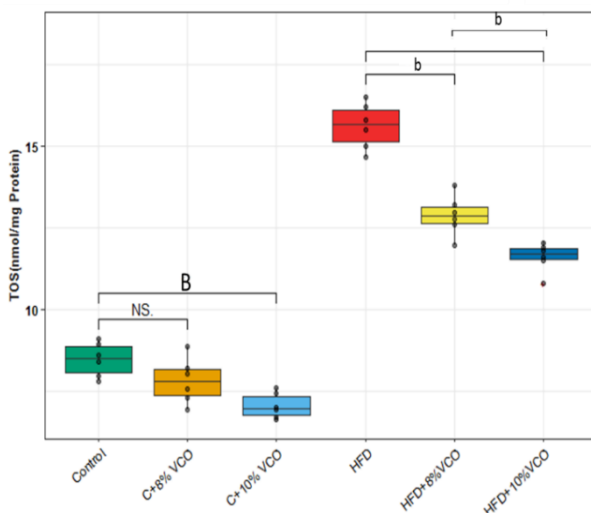


Figure 2. Effect of virgin coconut oil on total oxidative state (TOS) of liver tissue. There was a significant difference between the control group and the control group treated with 10% VCO. Moreover, a significant difference was observed between the high-fat diet group and the groups of HFD+8% VCO and also the HFD+10% VCO, so that the mean total oxidation was reduced in the groups with VCO intervention compared to the high-fat diet group without intervention. NS: No significance. Significance was shown as $p < 0.01^b$ and $p < 0.001^c$ compared to untreated HFD group and $p < 0.01^B$ compared to control.

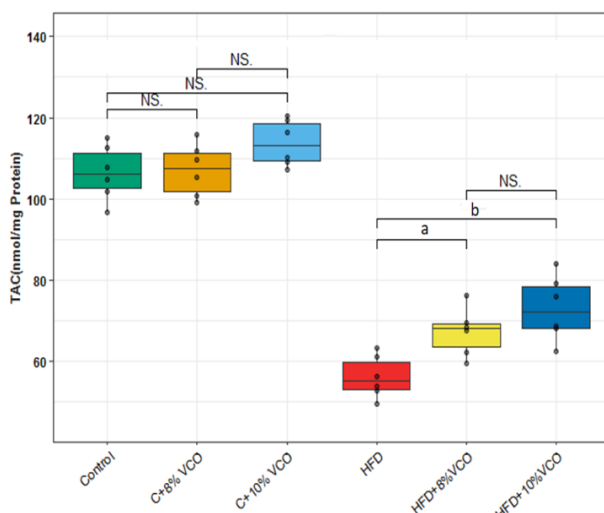


Figure 3. Effect of virgin coconut oil on total antioxidant capacity (TAC) in liver tissue. There was a significant difference between the high-fat diet group and the groups of HFD+8% VCO and also the HFD+10% VCO, so that the mean total antioxidant capacity was increased in the groups with VCO intervention compared to the high-fat diet group without intervention. There was no statistically significant difference between the two groups of HFD+8% VCO and HFD+10% VCO. NS: No significance. Significance was shown as $p < 0.05^a$ and $p < 0.01^b$ in comparison with untreated HFD group.

Discussion

The present study showed that HFD in rats increased oxidative factors including TOS and decreased TAC. Treatment of hyperlipidemic rats with virgin oil showed that it has a beneficial effect on the oxidant-antioxidant system and increased antioxidant factors such as TAC and decreased TOS. 10% virgin coconut oil was more effective.

In this study, cholesterol and triglyceride levels increased in the high-fat group, while it showed a significant decrease in rats receiving virgin coconut oil. This process can be effective in reducing the accumulation of fat in the liver. The biological effect of virgin coconut oil is probably due to its high polyphenols such as ferric acid, vanillic acid, p-coumaric acid, syringic acid, and caffeic acid (27). Feranil et al. in a cohort study administering coconut oil showed that this compound increased HDL levels (28). The hydroxyl group of phenolic compounds is able to trap free radicals produced in the process of non-alcoholic fatty liver and control oxidative stress (29-31).

Increased fat deposition in the liver increases oxidative stress by increasing the level of MDA, a marker of lipid peroxides (32). In this study, the amount of MDA was reduced by coconut oil. It has been shown that accumulation of fat and increased MDA in the liver due to consumption of high-fat diet, disrupts the expression of inflammatory factors and genes involved in fatty acid synthesis, which eventually progresses to non-alcoholic fatty liver, fibrosis, and cirrhosis (33). Newell-Fugate et al. showed that the administration of virgin oil reduced inflammation (34).

The present study showed that high-fat diet in rats increased oxidative factors such as TOS and decreased TAC. Treatment of rats with high-fat diet using virgin coconut oil showed that it has a beneficial effect on the oxidant-antioxidant system and increased TAC and decreased TOS. Consistent with the present study, Famurewa et al. showed that treatment of rats with virgin coconut oil improves antioxidant status, reduces TOS levels and increases TAC (35).

Ferulic acid is a phenolic compound with effective antioxidant activity and anti-inflammatory activity that is abundant in virgin oils. The strong anti-inflammatory and antioxidant properties of ferulic acid have been proven. This compound reduces lipid accumulation and is able to inhibit oxidative stress by binding to free radicals (36). Ferulic acid has been shown to be effective in improving fatty liver by inhibiting inflammatory pathways (37).

P-coumaric acid is another compound in coconut oil that has high antioxidant power (38). Nevin et al. showed that administration of coconut oil increased antioxidant enzymes and decreased lipid peroxidation (17). Babu et al. also showed that virgin coconut oil due to its phenolic compounds increases antioxidant activity and decreases lipid index and blood pressure (39). The researchers reported that phenolic compounds significantly reduced inflammatory cytokines, increased antioxidant potency, and decreased interleukin-6 production (40, 41). Famurewa et al. showed that administration of virgin oil in normal rats reduces liver enzymes and increases antioxidant activity (35). Administration of coconut oil to male rats has been

reported to increase antioxidant enzymes and decrease lipid peroxidation (17). The results of this study showed that this oil can be useful in the treatment and prevention of non-alcoholic fatty liver due to its anti-inflammatory, antioxidant and cholesterol lowering activity. Therefore, in this study, virgin coconut oil reduced lipid indexes and improved antioxidant status in non-alcoholic fatty liver.

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References

1. Ratzliff V, Bellentani S, Cortez-Pinto H, Day C, Marchesini G. A position statement on NAFLD/NASH based on the EASL 2009 special conference. *J Hepatol*. 2010;53(2):372-84.
2. Rafrat M, Nabavi S, Somi MH, Homayouni-Rad A, Asghari-Jafarabadi Rad M. The effect of probiotic and conventional yogurt consumptions on anthropometric parameters in individuals with non alcoholic fatty liver disease. *J Babol Univ Med Sci*. 2014;16(9):55-62. [In Persian]
3. Efati M, Khorrami M, Zarei Mahmmodabadi A, Raouf Sarshoori J. Induction of an Animal Model of Non-Alcoholic Fatty Liver Disease Using a Formulated High-Fat Diet. *J Babol Univ Med Sci*. 2016;18(11):57-62. [In Persian]
4. Fattahi A, Darabi M, Farzadi L, Salmassi A, Latifi Z, Mehdizadeh A, et al. Effects of dietary omega-3 and -6 supplementations on phospholipid fatty acid composition in mice uterus during window of pre-implantation. *Theriogenology*. 2018;108:97-102.
5. Serviddio G, Bellanti F, Villani R, Tamborra R, Zerbini C, Blonda M, et al. Effects of dietary fatty acids and cholesterol excess on liver injury: a lipidomic approach. *Redox biol*. 2016;9:296-305.
6. Youshari N, Ebrahimi-Mameghani M, Asghari-Jafarabadi M, Youshari N. Association between dietary fructose and lipid profile in non-alcoholic fatty liver disease. *J Babol Univ Med Sci*. 2014;16(10):23-30. [In Persian]
7. Shahebrahimi K, Zulnoorian Sh, Almasi A, Sharifi A, Keshavarz AA, Farshchian N. A comparison of the therapeutic effects of metformin, pioglitazone and vitamin E in patients with non-alcoholic fatty liver. *J Babol Univ Med Sci*. 2017;19(9):32-8. [In Persian]
8. Heidarian E, Rafieian-Kopaei M, Ashrafi K. The effect of hydroalcoholic extract of *Allium latifolium* on the liver phosphatidate phosphatase and serum lipid profile in hyperlipidemic rats. *J Babol Univ Med Sci*. 2013;15(4):37-46. [In Persian]
9. Nasri H, Rafieian-Kopaei M. Preventive and Curative effect of garlic on nephrotoxic effect of gentamicin in rat. *J Babol Univ Med Sci*. 2014;16(2):42-8. [In Persian]
10. Abbasi-Oshaghi E, Khodadadi I, Tavilani H, Mirzaei F, Goodarzi MT. Dill-normalized liver lipid accumulation, oxidative stress, and low-density lipoprotein receptor levels in high cholesterol fed hamsters. *ARYA Atheroscler*. 2018;14(5):218-24.
11. Abbasi-Oshaghi E, Noori Sorkhani A, Rezaei A. Effects of walnut on lipid profile as well as the expression of sterol-regulatory element binding protein-1c (SREBP-1c) and peroxisome proliferator activated receptors α (PPAR α) in diabetic rat. *Food Nutr Sci*. 2012;3(2):255-9.
12. Abbasi-Oshaghi E, Mirzaei F, Mirzaei A. Effects of ZnO nanoparticles on intestinal function and structure in normal/high fat diet-fed rats and Caco-2 cells. *Nanomedicine (Lond)*. 2018;13(21):2791-816.
13. Pouyandeh Ravan A, Bahmani M, Ghasemi Basir HR, Salehi I, Abbasi Oshaghi E. Hepatoprotective effects of *Vaccinium arctostaphylos* against CCl₄-induced acute liver injury in rats. *J Basic Clin Physiol Pharmacol*. 2017;28(5):463-71.
14. Ghorbani M, Amiri I, Khodadadi I, Fattahi A, Atabakhsh M, Tavilani H. Influence of BHT inclusion on post-thaw attributes of human semen. *Syst Biol Reprod Med*. 2015;61(1):57-61.
15. Nevin KG, Rajamohan T. Beneficial effects of virgin coconut oil on lipid parameters and in vitro LDL oxidation. *Clin Biochem*. 2004;37(9):830-5.
16. Sheela DL, Nazeem PA, Narayanankutty A, Manalil JJ, Raghavamenon AC. In silico and wet lab studies reveal the cholesterol lowering efficacy of lauric acid, a medium chain fat of coconut oil. *Plant Foods Hum Nutr*. 2016;71(4):410-5.
17. Nevin KG, Rajamohan T. Virgin coconut oil supplemented diet increases the antioxidant status in rats. *Food chem*. 2006;99(2):260-6.
18. Mirzaei F, Khazaei M, Komaki A, Amiri I, Jalili C. The Effects of Virgin Coconut Oil on Prevention of Alzheimer's Disease. *Jundishapur J Nat Pharm Prod*. 2019;14(4):e67747.

- 19.Mirzaei F, Khazaei M, Komaki A, Amiri I, Jalili C. Virgin coconut oil (VCO) by normalizing NLRP3 inflammasome showed potential neuroprotective effects in Amyloid- β induced toxicity and high-fat diet fed rat. *Food Chem Toxicol*. 2018;118:68-83.
- 20.Amirasouli H, Asefy Z, kazerouni F, Taghikhani M. Study of serum cystatin C as a reliable marker for metabolic syndrome. *J Diabetes Metab Disord*. 2011;10:1-4.
- 21.Shahryari J, Poormorteza M, Noori-Sorkhani A, Divsalar K, Abbasi-Oshaghi E. The Effect of Concomitant Ethanol and Opium Consumption on Lipid Profiles and Atherosclerosis in Golden Syrian Hamster's Aorta. *Addict Health*. 2013;5(3-4):83-9.
- 22.Mirzaei F, Khazaei M, Komaki A, Amiri I, Jalili C. Multitarget Effects of Coconut Oil (Virgin Type) on A β -Induced Alzheimer's Disease Animal Model. *Arch Neurosci*. 2019;6(2):e85715.
- 23.Abbasi Oshaghi E, Khodadadi I, Mirzaei F, Khazaei M, Tavalani H, Goodarzi MT. Methanolic extract of dill leaves inhibits AGEs formation and shows potential hepatoprotective effects in CCl₄ Induced liver toxicity in rat. *J Pharm (Cairo)*. 2017;2017:6081374.
- 24.Abbasi-Oshaghi E, Mirzaei F, Pourjafar M. NLRP3 inflammasome, oxidative stress, and apoptosis induced in the intestine and liver of rats treated with titanium dioxide nanoparticles: in vivo and in vitro study. *Int J Nanomedicine*. 2019;14:1919-36.
- 25.Koyuncuoğlu T, Vızdıklar C, Üren D, Yılmaz H, Yıldırım Ç, Atal SS, et al. Obestatin improves oxidative brain damage and memory dysfunction in rats induced with an epileptic seizure. *Peptides*. 2017;90:37-47.
- 26.Tavalani H, Setarehbadi R, Fattahi A, Nasrollahi SH, Karimi J, Shafiee G, et al. The Relationship between Plasma Antioxidant Enzymes Activity and Sex Hormones during the Menstrual Cycle. *Med Lab J*. 2014;7(4):34-40.
- 27.Marina AM, Che Man YB, Nazimah SAH, Amin I. Antioxidant capacity and phenolic acids of virgin coconut oil. *Int J Food Sci Nutr*. 2009;60(Suppl 2):114-23.
- 28.Feranil AB, Duazo PL, Kuzawa CW, Adair LS. Coconut oil is associated with a beneficial lipid profile in premenopausal women in the Philippines. *Asia Pac J Clin Nutr*. 2011;20(2):190-5.
- 29.Hirohata M, Hasegawa K, Tsutsumi-Yasuhara S, Ohhashi Y, Ookoshi T, Ono K, et al. The anti-amyloidogenic effect is exerted against Alzheimer's β -amyloid fibrils in vitro by preferential and reversible binding of flavonoids to the amyloid fibril structure. *Biochemistry*. 2007;46(7):1888-99.
- 30.Kheiripour N, Karimi J, Khodadadi I, Tavalani H, Goodarzi MT, Hashemnia M. Hepatoprotective Effects of Silymarin on Liver Injury via Irisin Upregulation and Oxidative Stress Reduction in Rats with Type 2 Diabetes. *Iran J Med Sci*. 2019;44(2):108-17.
- 31.Piri H, Seyyed-Attaran F, Gheibi N, Najafipour R, Sirati-Sabet M, Asl-Fallah S, et al. Structural Characterization of the Recombinant Human Fibroblast Growth Factor Receptor 2b Kinase Domain Upon Interaction with Flavonoids. *Jundishapur J Nat Pharm Prod*. 2019;14(2):e12499.
- 32.Karimi J, Mohammadalipour A, Sheikh N, Khodadadi I, Hashemnia M, Goudarzi F, et al. Protective effects of combined Losartan and Nilotinib on carbon tetrachloride (CCl₄)-induced liver fibrosis in rats. *Drug Chem Toxicol*. 2020;43(5):468-78.
- 33.Matsuzawa-Nagata N, Takamura T, Ando H, Nakamura S, Kurita S, Misu H, et al. Increased oxidative stress precedes the onset of high-fat diet-induced insulin resistance and obesity. *Metabolism*. 2008;57(8):1071-7.
- 34.Newell-Fugate AE, Lenz K, Skenandore C, Nowak RA, White BA, Braundmeier-Fleming A. Effects of coconut oil on glycemia, inflammation, and urogenital microbial parameters in female Ossabaw mini-pigs. *PLoS One*. 2017;12(7):e0179542.
- 35.Famurewa AC, Ekeleme-Egedigwe CA, Nwali SC, Agbo NN, Obi JN, Ezechukwu GC. Dietary Supplementation with Virgin Coconut Oil Improves Lipid Profile and Hepatic Antioxidant Status and Has Potential Benefits on Cardiovascular Risk Indices in Normal Rats. *J Diet Suppl*. 2018;15(3):330-42.
- 36.Fernando WM, Martins IJ, Goozee KG, Brennan CS, Jayasena V, Martins RN. The role of dietary coconut for the prevention and treatment of Alzheimer's disease: potential mechanisms of action. *Br J Nutr*. 2015;114(1):1-14.

- 37.He G-Y, Xie M, Gao Y, Huang J-G. Sodium Ferulate Attenuates Oxidative Stress Induced Inflammation via Suppressing NALP3 and NF- κ B Signal Pathway. *Sichuan Da Xue Xue Bao Yi Xue Ban*. 2015;46(3):367-71.
- 38.Konishi Y, Hitomi Y, Yoshioka E. Intestinal absorption of p-coumaric and gallic acids in rats after oral administration. *J Agric Food Chem*. 2004;52(9):2527-32.
- 39.Babu AS, Veluswamy SK, Arena R, Guazzi M, Lavie CJ. Virgin coconut oil and its potential cardioprotective effects. *Postgrad Med*. 2014;126(7):76-83.
- 40.Gauliard B, Grieve D, Wilson R, Crozier A, Jenkins C, Mullen WD, et al. The effects of dietary phenolic compounds on cytokine and antioxidant production by A549 cells. *J Med Food*. 2008;11(2):382-4.
- 41.Haghdoost-Yazdi H, Piri H, Faraji A, Fraidouni N, Dargahi T, Mahmudi M, et al. Pretreatment with potassium channel blockers of 4-aminopyridine and tetraethylammonium attenuates behavioural symptoms of Parkinsonism induced by intrastriatal injection of 6-hydroxydopamine; the role of lipid peroxidation. *Neurol Res*. 2016;38(4):294-300.