

Effect of Water and Lipid Soluble Antioxidant on Oxidative Stress Biomarker and Lipid Profile in High Fat-Fed Rats

Ali Abdulhussein Alkhafaji¹, Falahshari², Usama Ramadhan³

¹Researcher, ²Assistant Professor, ³Professor,

^{1,2,3}Department of Clinical Laboratory Sciences,

College of Pharmacy, University of Basrah, Basrah, Iraq

Article Information

Received: Aug 28, 2023

Accepted: Sep 20, 2023

Published: Oct 23, 2023

Keywords: Antioxidant; NAFLD; high-fat diet; CO enzyme 10; Thiocctic acid; L-carnitine; Vitamin C.

ABSTRACT

Hyperlipidemia refers to elevated levels of lipids (such as cholesterol and triglycerides) in the blood. It is a common condition that can increase the risk of cardiovascular diseases, such as heart attacks and strokes. Managing hyperlipidemia typically involves lifestyle modifications and, in some cases, medication. The prevalence of obesity and type 2 diabetes mellitus (T2DM), contributing to the burden of Hyperlipidemia, is not projected to decline in the foreseeable future. A high-fat diet is associated with increased oxidative stress and free-radical activity. Oxidative stress plays a role in Hyperlipidemia development, and many antioxidants reverse the free radical action and delay liver damage, like vitamin C and alpha-lipoic acid, ubiquinone 10, and L-carnitine, 32 male and female rats weighing 150-200 grams were divided into four groups. The various antioxidants used in different combinations in treated group 3 were water-soluble vitamin C, L-carnitine, lipid-soluble antioxidants ubiquinone and alpha lipoic acid given to group 4 orally. The result of this study was a significant increase in Malondialdehyde MDA level in the high fat-fed group and a decrease in Superoxide dismutase SOD and Glutathione peroxidase GPx an elevation in a lipid profile, LDL, vLDL Triglyceride, and reduction in HDL, a significant reduction in Malondialdehyde level and increase in Superoxide dismutase and Glutathione peroxidase level and decrease Lipid profile level in antioxidant group 3 and 4. The role of antioxidants as protective agents against oxidative stress decreases free radicals' activity by increasing the scavenging properties of antioxidants.

Introduction

Your largest internal organ is the liver, The liver is the central organ in all metabolic processes. Fats are metabolised in the liver cells to be used as fuel.(1) The daily bile production ranges from 800 to 1,000 cc. Bile, which can be yellow, brownish, or olive green, is collected in tiny ducts and sent on its way to the primary bile duct, which carries it to the duodenum. Bile is essential for the digestion and absorption of lipids.(2)

Hyperlipidemia is characterized by elevated lipids (cholesterol and triglycerides) levels in the blood. It is a common health concern that increases the risk of cardiovascular diseases. Lifestyle factors, such as poor diet, lack of exercise, and genetic predisposition, contribute to its development. Managing hyperlipidemia involves adopting a heart-healthy diet, engaging in regular physical activity, maintaining a healthy weight, and sometimes taking prescribed medications. Regular monitoring of lipid levels through blood tests is essential to assess the effectiveness of the management plan. By addressing hyperlipidemia, individuals can reduce

their risk of heart attacks, strokes, and other cardiovascular complications(3). Oxidative Stress is an imbalance between the production of reactive species (RS) and AO defences. Hans Selye developed the "stress concept" in 1936 to explain how animals react to acute nonspecific noxious agents, including colds, surgical trauma, and medications. He described stress as the body's generalised response to any demand. Paniker et al. demonstrated in the latter part of the 1970s that red blood cell exposure to hydrogen peroxide (H₂O₂) generates "oxidative stress," which is connected to glutathione reductase activity.(1)(4)

Antioxidants Due to their capacity to lower oxidative stress, antioxidants are crucial for preserving human health and preventing and treating illnesses.(5)(6)

L-carnitine is an antioxidant that lessens cellular metabolic stress. It has many benefits in some physio-pathological systems. End-stage renal disease (ESRD), coronary artery disease, and liver damage are just a few of the illnesses for which L-carnitine has been advocated recently.(7)(8)(9)

Alpha-lipoic acid is also known as thioctic acid. The liver and other tissue mitochondria produce alpha-lipoic acid, a naturally occurring antioxidant essential to metabolism(10)(11)

Vitamin C is abundant in citrus fruits, which continue to be the principal source of this vitamin in humans. However, supplements with a synthetic form are also offered. Vitamin C enhances various physiological processes in people and lowers oxidative cell damage.(12)(13)

All human cell membranes naturally contain the extremely lipophilic chemical coenzyme Q10 (CoQ10), which is essential to the oxidative phosphorylation process. It supports energy transfer from carbs and fatty acids into the energy-dense adenosine triphosphate by acting as an electron transporter from complexes I and II to complex III.(14)(15)(16)

Materials and Methods

Animal care

Thirty-two (32) male and female Wistar rats weighing 150-200 gram were obtained from The University of Basrah, Faculty of Veterinary Medicine's animal house. Were housed and separated into four groups (8 animals in each group) at the animal house of the College of Pharmacy/university of Basrah. The rats were housed in a light-controlled, air-conditioned atmosphere at a constant temperature and supplied with food and water. Noisiness and harsh handling were avoided to reduce stress. The animals used in this study were treated in conformity with the National Institute of Health (NIH) guidelines for handling laboratory animals.

Preparation of antioxidant supplementation

The antioxidant supplementation was bought from private pharmacies in Basrah as tablets. The tablets were crushed by using a mortar to convert them to powder, then dissolved in distilled water to obtain a suitable form of solution or suspension for administration orally to the rats. The various antioxidants were used in different combinations, treating group three (Vitamin 15 mg/kg and L-carnitine 20 mg/kg) and treating group four (Thioctic acid 20mg/kg, and Coenzyme 10 20mg/kg) orally.

Animal treatment

The rats were divided into four groups.

control group 1: Rats in this group have a normal diet. Rats in this group were given D.W(2ml/kg) orally by feeding gavage for 30 days to expose the rats to the same level of stress.

Group 2 high-fat diet group: Rats in this group are fed a high-fat diet. Rats in this group were given D.W(2ml/kg) orally by feeding gavage for 30 days to expose the rats to the same level of stress.

Group 3 (water-soluble antioxidant group): Rats in this group are fed with a high-fat diet and given water-soluble antioxidants (L-carnitine and vitamin C) for 30 days by feeding gavage.

Group 4 (lipid-soluble antioxidant group): Rats in this group are fed with a high-fat diet and given lipid-soluble antioxidants (Thioctic acid and co-enzyme 10) for 30 days by feeding gavage.

Blood sampling

The blood samples were collected directly from the hearts of rats via the rat dissection process. Blood sample volumes of 3-5 ml were collected into a gel tube and left for 15 minutes to clot. The serum was separated by centrifugation at 6000 rpm for 15 minutes. The supernatants are collected carefully by using a micropipette, and the sample is stored in an aliquot at (-20c) in the freezer for analysis time.

Statistical Analysis

Data are expressed as Means $\pm$ standard deviation (SD) of samples. Analysis was made by using SPSS (statistical package for social sciences) for Windows (version 27) and Microsoft Office (2022). Differences among different groups were compared by one-way analysis of variance (ANOVA). Statistically significant was accepted at a level of $P \leq 0.05$

Results

The study was designed to investigate the effect of antioxidants in high-fat diet-fed rats, investigate the lipid profile and oxidative stress measurement, Antioxidants were given orally in solution form for 30 days, blood serum was taken for laboratory measurement of MDA, SOD, GPx, LDL, vLDL, TG, HDL, TC)

Serum MDA

Table 1 shows a significant increase ($p < 0.05$) in MDA levels in high-fat diet-fed group 2 compared to MDA level in the control group 1 and lipid-soluble treated antioxidants group 4 and a slight increase in MDA level in water-soluble treated antioxidants group 3 but its non-significant difference compared to control group 1 and lipid-soluble treated antioxidants group 4 and its significant difference compared to high-fat fed group 2

Table 1: Effect of Different Antioxidants on Serum MDA level.

Groups	MDA (micromole/L)	F Statistic LSD	P value
G1: Control	21.862 $\pm$ 0.676 c	3.762	0.0271 ^S
G2: High fat fed group	35.064 $\pm$ 8.492 a		
G3: Water soluble antioxidants	25.39 $\pm$ 1.611 b		
G4: Lipid soluble antioxidants	20.19 $\pm$ 1.417 c		

-Data presented as (mean standard error), with a sample size (N) of 5.

The Least Squared Difference (LSD) test reveals statistically significant differences across groups that experienced differing litter sizes.

NS means there was no discernible distinction between the groups ($p > 0.05$).

S: $p < 0.05$ indicates a statistically significant difference between groups

HS = Very large and statistically significant difference ($p < 0.01$)

Serum SOD

Table 2 shows a significant decrease in SOD levels in the high-fat diet group ($p < 0.05$) compared to Control group 1 and shows an increase in SOD levels in lipid-soluble treated antioxidants group 4 and water-soluble treated antioxidant group 3, and its significant ($p < 0.05$) compared to another high-fat diet group 2 and control group 1

Table 2: Effect of Different Antioxidants on Serum SOD level.

Groups	SOD (micromole/min/ml)	F Statistic LSD	P value
G1: Control	3.358 ± 0.440 b	3.318	0.0351 ^S
G2: High fat fed group	2.396 ± 1.116 a		
G3: Water soluble antioxidants	3.992 ± 0.945 c		
G4: Lipid soluble antioxidants	4.208 ± 0.417 c		

-Data presented as (mean standard error), with a sample size (N) of 5.

The Least Squared Difference (LSD) test reveals statistically significant differences across groups that experienced differing litter sizes.

NS means there was no discernible distinction between the groups ($p > 0.05$).

S: $p < 0.05$ indicates a statistically significant difference between groups

HS = Very large and statistically significant difference ($p < 0.01$)

Serum GPx

Table 3 shows a high significant decrease in GPx level in high-fat diet group 2 ($P < 0.01$) compared to control group 1 and shows significant increase in GPx level in water-soluble antioxidant treated group 3 ($p < 0.01$) and lipid soluble antioxidant group 4 compared to control group 1 and high-fat diet group 2.

Table 3: Effect of Different Antioxidants on Serum GPx level.

Groups	GPx (U/L)	F Statistic LSD	P value
G1: Control	825.104 ± 15.793 b	4.461	0.0016 ^{HS}
G2: High fat fed group	735.33 ± 27.542 c		
G3: Water soluble antioxidants	926.038 ± 119.371 a		
G4: Lipid soluble antioxidants	895.33 ± 173.406 a		

-Data presented as (mean standard error), with a sample size (N) of 5.

The Least Squared Difference (LSD) test reveals statistically significant differences across groups that experienced differing litter sizes.

NS means there was no discernible distinction between the groups ($p > 0.05$).

S: $p < 0.05$ indicates a statistically significant difference between groups

HS = Very large and statistically significant difference ($p < 0.01$)

Serum Total Cholesterol (TC)

Table 4 show a highly significant ($p \leq 0.01$) increase in serum TC in high-fat diet group 2 compared to the other three groups and show a non-significant difference in Group 3 and Group 4 antioxidant-treated group but there a significant difference between the control group 1 and group 3 and group 4.

Table 4: Effect of Different Antioxidants on Serum TC level.

Groups	TC (mg/dl)	F Statistic LSD	P value
G1: Control	73.500 ± 0.691 b	3.932	0.0074 ^{HS}
G2: High fat fed group	88.532 ± 1.153 a		
G3: Water soluble antioxidants	68.808 ± 2.162 c		
G4: Lipid soluble antioxidants	70.114 ± 3.573 c		

-Data presented as (mean standard error), with a sample size (N) of 5.

The Least Squared Difference (LSD) test reveals statistically significant differences across groups that experienced differing litter sizes.

NS means there was no discernible distinction between the groups ($p > 0.05$).

S: $p < 0.05$ indicates a statistically significant difference between groups

HS = Very large and statistically significant difference ($p < 0.01$)

Serum Triglycerides (TG)

Table 5 show a significant ($p \leq 0.05$) increase in TG level in the high-fat diet group compared to the other three groups and show a significant decrease ($p \leq 0.05$) in group 4, lipid-soluble antioxidant-treated compared to other groups.

Table 5: Effect of Different Antioxidants on Serum TG level.

Groups	TG (mg/dl)	F Statistic LSD	P value
G1: Control	92.134 ± 5.839 b	3.625	0.0286 ^S
G2: High fat fed group	101.730 ± 12.094 a		
G3: Water soluble antioxidants	83.828 ± 8.655 b c		
G4: Lipid soluble antioxidants	67.812 ± 5.501 d		

-Data presented as (mean standard error), with a sample size (N) of 5.

The Least Squared Difference (LSD) test reveals statistically significant differences across groups that experienced differing litter sizes.

NS means there was no discernible distinction between the groups ($p > 0.05$).

S: $p < 0.05$ indicates a statistically significant difference between groups

HS = Very large and statistically significant difference ($p < 0.01$)

Serum HDL

Table 6 show a high significant ($p \leq 0.01$) decrease in HDL levels in high-fat diet group 2 compared to the other three groups and show significant increase ($p \leq 0.01$) in HDL levels in antioxidants treated groups 3 & 4 compared to control group 1.

Table 6: Effect of Different Antioxidants on Serum HDL level.

Groups	HDL (mg/dl)	F Statistic LSD	P value
G1: Control	60.476 ± 3.718 a	4.292	0.0045 ^{HS}
G2: High fat fed group	40.530 ± 2.244 d		
G3: Water soluble antioxidants	56.836 ± 2.058 b		
G4: Lipid soluble antioxidants	52.404 ± 5.956 c		

-Data presented as (mean standard error), with a sample size (N) of 5.

The Least Squared Difference (LSD) test reveals statistically significant differences across

groups that experienced differing litter sizes.

NS means there was no discernible distinction between the groups ($p > 0.05$).

S: $p < 0.05$ indicates a statistically significant difference between groups

HS = Very large and statistically significant difference ($p < 0.01$)

Serum vLDL

Table 7 show a significant increase in vLDL ($p \leq 0.05$) in high-fat diet group 2 compared to the other three groups and show a significant ($p \leq 0.05$) decrease in antioxidants treated groups 3 & 4 compared to control and high-fat diet groups.

Table 7: Effect of Different Antioxidants on Serum vLDL level.

Groups	VLDL (mg/dl)	F Statistic LSD	P value
G1: Control	18.426 $\pm$ 1.168 b	3.112	0.0426 ^S
G2: High fat fed group	24.942 $\pm$ 2.406 a		
G3: Water soluble antioxidants	16.760 $\pm$ 1.731 c		
G4: Lipid soluble antioxidants	13.558 $\pm$ 1.099 d		

-Data presented as (mean standard error), with a sample size (N) of 5.

The Least Squared Difference (LSD) test reveals statistically significant differences across groups that experienced differing litter sizes.

NS means there was no discernible distinction between the groups ($p > 0.05$).

S: $p < 0.05$ indicates a statistically significant difference between groups

HS = Very large and statistically significant difference ($p < 0.01$)

Serum LDL

Table 8 show a significant ($p \leq 0.05$) increase in LDL levels in the high-fat diet group compared to the other three groups and show a decrease in LDL levels in the antioxidants groups 3 & 4 compared to high-fat diet group ($p \leq 0.05$) but not to control group 1 which is the lowest value.

Table 8: Effect of Different Antioxidants on Serum LDL level.

Groups	LDL (mg/dl)	F Statistic LSD	P value
G1: Control	31.446 $\pm$ 4.015 d	3.315	0.0329 ^S
G2: High fat fed group	45.944 $\pm$ 1.024 a		
G3: Water soluble antioxidants	35.732 $\pm$ 1.592 b		
G4: Lipid soluble antioxidants	33.124 $\pm$ 4.624 c		

-Data presented as (mean standard error), with a sample size (N) of 5.

The Least Squared Difference (LSD) test reveals statistically significant differences across groups that experienced differing litter sizes.

NS means there was no discernible distinction between the groups ($p > 0.05$).

S: $p < 0.05$ indicates a statistically significant difference between groups

HS = Very large and statistically significant difference ($p < 0.01$)

Discussion

There is mounting evidence linking the pathophysiology of nonalcoholic fatty liver disease (NAFLD) to elevated oxidative stress caused by an increase in free radical generation due to a high-fat diet combined with a reduction in antioxidant defences. (17) Excessive consumption of a high-fat diet has been shown to increase mitochondrial respiration, leading to elevated superoxides, free radicals, and oxidative stress. The studies show that antioxidants decrease the level of oxidative biomarkers. Table 1 shows a significant increase in MDA levels in high-fat diet-fed group 2 that the high-fat diet increased oxidative biomarkers and caused various (18)inflammatory processes leading to liver disease and cardiovascular disease compared to MDA levels in the control group 1, while antioxidant groups 3 &4 show decrease in MDA level that indicates of antioxidant effect on reverse oxidative stress (19)and lead to decrease the harmful effect of high-fat diet many studies showing the effectiveness of lipid and water soluble antioxidants on decrease the MDA level.(20)

Table 2 show a significant decrease in SOD levels in the high-fat diet group ($p < 0.05$) compared to Control group 1 that indicates high-fat diet decreases SOD level and increase free radicals activity, leading to oxidative stress activity (21)and Table 2 shows an increase in SOD levels in lipid-soluble treated antioxidants group 4 and water-soluble treated antioxidant group 3 and its significant ($p < 0.05$) compare to another high-fat diet group 2 and control group 1 that indicate antioxidant intake lead to increase SOD activity and decrease free radicals and reduce oxidative stress as many studies show that benefit of antioxidant.(22)(18)

Table 3 shows a highly significant decrease in GPx level in high-fat diet group 2 ($P < 0.01$) compared to control group 1. Many studies show high fat-rich diet induces oxidative stress and a decline in GPx level (23), with a significant increase in GPx level in water-soluble antioxidant-treated group 3 ($p < 0.01$) and lipid soluble antioxidant group 4 compared to the control group 1 and high-fat diet group 2 Many studies show that antioxidant increase glutathione peroxidase activity. (24)(25)

Table 4 shows a highly significant ($p \leq 0.01$) increase in serum TC in high-fat diet group 2 compared to the other three groups, that mean high-fat diet increases total cholesterol and increases lipid peroxidation and oxidative stress and liver injury and atherosclerosis risk and Diabetics risk factor, in contrast to high-fat group Antioxidant group 3 & 4 show a significant decrease in total cholesterol and decrease the risk of liver injury by reducing lipid peroxidation and oxidative stress and Cardiovascular risk factor by decreasing lipid profile.(26) (27)

Table 5 shows a significant ($p \leq 0.05$) increase in TG level in the high-fat diet group compared to the other three groups. This means a High-fat diet increases TG and increases the risk of NAFLD and cardiovascular and stroke risk (28)in otherwise, Table 5 showed a significant decrease ($p \leq 0.05$) in group 4, lipid-soluble antioxidant-treated compared to other groups. Many studies show that co-Q10 can decrease TG levels and contrast the high-fat diet effect.(29)

Table 6 shows high significant ($p \leq 0.01$) decrease in HDL levels in high-fat diet group 2 compared to the other three groups, which means that a high-fat diet decreases the good type of lipoprotein and increases bad ones and increases liver injury and cardiovascular disease and show a significant increase ($p \leq 0.01$) in HDL levels in antioxidant-treated groups 3 & 4 compared to control group 1many studies show antioxidants increase HDL and improve lipid profile. When patients with Hyperlipidemia take L-carnitine supplements, their HDL cholesterol and triglyceride levels improve significantly compared to when they took a placebo.(30)

Table 7 shows a significant increase in vLDL ($p \leq 0.05$) in high-fat diet group 2 compared to the other three groups and show a significant ($p \leq 0.05$) decrease in antioxidants treated groups 3 & 4 compared to control and high-fat diet groups many studies show high-fat diet increase vLDL and all Noxious lipoprotein (31) and many studies show antioxidant decrease level of vLDL and

protect action on liver and another vital system(32)

Table 8 show a significant ($p \leq 0.05$) increase in LDL levels in the high-fat diet group compared to the other three groups, which indicate that a high-fat diet increases LDL level and increase fatty liver risk and oxidative stress damage action and increase cardiovascular diseases (33) and Antioxidants groups 3 & 4 show decrease in LDL levels compared to high-fat diet group ($p \leq 0.05$) but not to control group 1 which is the least value Many studies show that antioxidant are decrease the level of LDL and have protective action on liver and cardiovascular system against atherosclerosis(34)

Conclusion

Oral administration of water or lipid soluble antioxidants like L-carnitine and vitamin C or Coenzyme 10 and alpha lipoic acid as a combination in treated Hyperlipidemia shows improvement in lipid profile biomarkers. Avoid a high-fat diet because it's associated with harmful effects through increased oxidative stress biomarker and lipid profile, leading to obesity, liver disease, atherosclerosis risk and diabetic disease. A significant decrease in MDA levels in antioxidant-treated groups was associated with a decreased oxidative stress effect and an increase in GPx and SOD levels as the scavenger action of antioxidants against free radicals.

Conflict of Interest: The authors declare no conflict of interest.

Ethical Consideration: Ethical permission was taken from the ethics review committee of the College of Pharmacy/ University of Basrah.

Source of Funding: Self.

References

1. Mooli RGR, Mukhi D, Ramakrishnan SK. Oxidative Stress and Redox Signaling in the Pathophysiology of Liver Diseases. *Compr Physiol*. 2022 Apr 1;12(2):3167–92.
2. Abdel-Misih SRZ, Bloomston M. Liver Anatomy. Vol. 90, *Surgical Clinics of North America*. W.B. Saunders; 2010. p. 643–53.
3. Stewart J, McCallin T, Martinez J, Chacko S, Yusuf S. Hyperlipidemia Practice Gaps [Internet]. Available from: <http://pedsinreview.aappublications.org/>
4. Pizzino G, Irrera N, Cucinotta M, Pallio G, Mannino F, Arcoraci V, et al. Oxidative Stress: Harms and Benefits for Human Health. Vol. 2017, *Oxidative Medicine and Cellular Longevity*. Hindawi Limited; 2017.
5. Hoorsan H, Simbar M, Tehrani FR, Fathi F, Mosaffa N, Riazi H, et al. The effectiveness of antioxidant therapy (vitamin C) in an experimentally induced mouse model of ovarian endometriosis. *Women's Health*. 2022;18.
6. Shari F. Study the antioxidant of Matricaria chamomilla (Chamomile) powder: In vitro and vivo. 2023 Mar 15;8.
7. Oh H, Park CH, Jun DW. Impact of L-Carnitine Supplementation on Liver Enzyme Normalization in Patients with Chronic Liver Disease: A Meta-Analysis of Randomized TrialsS1. Vol. 12, *Journal of Personalized Medicine*. MDPI; 2022.
8. Kepka A, Ochocinska A, Borzym-kluczyk M, Skorupa E, Stasiewicz-jarocka B, Chojnowska S, et al. Preventive role of l-carnitine and balanced diet in Alzheimer's disease. *Nutrients*. 2020 Jul 1;12(7):1–21.
9. Tuama R, Shari F, Ramadhan U. The Effect of Antioxidants on Electrolytes in Vancomycin-Streptozotocin Induced Diabetes Kidney Disease in Rabbits. *Indian Journal of Forensic Medicine & Toxicology*. 2021 Jun 2;15:3971–8.

10. Kravchenko L V., Aksenov I V., Nikitin NS, Guseva G V., Avrenyeva LI, Trusov N V., et al. Lipoic acid exacerbates oxidative stress and lipid accumulation in the liver of wistar rats fed a hypercaloric choline-deficient diet. *Nutrients*. 2021 Jun 1;13(6).
11. Hameed BJ, Ramadhan UH. Xanthine oxidase inhibitory, antihyperuricemic, anti-inflammatory, antinociceptive activity of α -lipoic acid in gouty arthritis model. *Asian Journal of Pharmaceutical and Clinical Research*. 2018 Dec 1;11(12):483–7.
12. Gęgotek A, Skrzydlewska E. Antioxidative and Anti-Inflammatory Activity of Ascorbic Acid. Vol. 11, *Antioxidants*. MDPI; 2022.
13. Matroad S, Ramadhan U, Al-Mahmood R. EFFECT OF SOWING DATE AND TREATMENT WITH ASCORBIC ACID ON GROWTH AND YIELD OF FLAX (*Linum usitatissimum* L.). 2018 Apr 9;7:493–507.
14. Mantle D, Lopez-Lluch G, Hargreaves IP. Coenzyme Q10 Metabolism: A Review of Unresolved Issues. Vol. 24, *International Journal of Molecular Sciences*. MDPI; 2023.
15. Arenas-Jal M, Suñé-Negre JM, García-Montoya E. Coenzyme Q10 supplementation: Efficacy, safety, and formulation challenges. Vol. 19, *Comprehensive Reviews in Food Science and Food Safety*. Blackwell Publishing Inc.; 2020. p. 574–94.
16. Saber B, Ramadhan U, Abdulkareem Q. The Combined Effect of Coenzyme Q10 and Magnesium Ion on Advanced Glycation End Products Formed by Methylglyoxal in Rabbits. 2022 Oct 1;6.
17. Lasker S, Rahman MM, Parvez F, Zamila M, Miah P, Nahar K, et al. High-fat diet-induced metabolic syndrome and oxidative stress in obese rats are ameliorated by yogurt supplementation. *Sci Rep*. 2019 Dec 1;9(1).
18. Fallah M, Askari G, Soleimani A, Feizi A, Asemi Z. Clinical trial of the effects of coenzyme q10 supplementation on biomarkers of inflammation and oxidative stress in diabetic hemodialysis patients. *Int J Prev Med*. 2019;10(1):12.
19. Tripathi AK, Ray AK, Mishra SK, Bishen SM, Mishra H, Khurana A. Molecular and Therapeutic Insights of Alpha-Lipoic Acid as a Potential Molecule for Disease Prevention. Vol. 33, *Revista Brasileira de Farmacognosia*. Springer Science and Business Media Deutschland GmbH; 2023. p. 272–87.
20. Shahsavar A, Rajabi H, Gharakhanlou R, Dehkhoda MR. Effect of Aerobic Training and L-carnitine on MDA, GPX and Hippocampal Neurogenesis in Diabetic Rats. Vol. 12, *IRANIAN JOURNAL OF DIABETES AND OBESITY*.
21. Yodoshi T, Orkin S, Arce-Clachar AC, Bramlage K, Su W, Fei L, et al. Identifying Predictors of Response to Vitamin E for the Treatment of Pediatric Nonalcoholic Steatohepatitis. *Journal of Parenteral and Enteral Nutrition*. 2020 Sep 1;44(7):1301–7.
22. Miazek K, Beton K, Śliwińska A, Brożek-Pluska B. The Effect of β -Carotene, Tocopherols and Ascorbic Acid as Anti-Oxidant Molecules on Human and Animal In Vitro/In Vivo Studies: A Review of Research Design and Analytical Techniques Used. Vol. 12, *Biomolecules*. MDPI; 2022.
23. Shi Y, Zhong L, Zhong H, Zhang J, Che C, Fu G, et al. Taurine supplements in high-fat diets improve survival of juvenile *Monopterus albus* by reducing lipid deposition and intestinal damage. *Aquaculture*. 2022 Jan 30;547:737431.
24. Divković A, Karasalihović Z, Rumora Samarin I, Sabitović D, Radić K, Golub N, et al. Effect of Alpha Lipoic Acid Supplementation on Oxidative Stress and Lipid Parameters in Women Diagnosed with Low-Grade Squamous Intraepithelial Lesions (LSILs): A Double-

- Blind, Randomized, Placebo-Controlled Trial. *Antioxidants* [Internet]. 2023 Aug 25;12(9):1670. Available from: <https://www.mdpi.com/2076-3921/12/9/1670>
25. Stote KS, Burns G, Mears K, Sweeney M, Blanton C. The Effect of Berry Consumption on Oxidative Stress Biomarkers: A Systematic Review of Randomized Controlled Trials in Humans. Vol. 12, *Antioxidants*. Multidisciplinary Digital Publishing Institute (MDPI); 2023.
 26. Gao Y sheng, Chen Y ke, Wang Q ju, Wang G qin, Lin L li, Chen X mei, et al. L-carnitine can improve the population growth and anti-stress ability of rotifer (*Brachionus rotundiformis*) under ammonia stress. *Aquac Rep*. 2021 Jul 1;20.
 27. Albrahim T, Robert AA. Lycopene Effects on Metabolic Syndrome and Kidney Injury in Rats Fed a High-Fat Diet: An Experimental Study. *ACS Omega*. 2022 Sep 6;7(35):30930–8.
 28. Lasker S, Rahman MM, Parvez F, Zamila M, Miah P, Nahar K, et al. High-fat diet-induced metabolic syndrome and oxidative stress in obese rats are ameliorated by yogurt supplementation. *Sci Rep*. 2019 Dec 1;9(1).
 29. Sousa GM de, Cazarin CBB, Maróstica Junior MR, Lamas C de A, Quitete VHAC, Pastore GM, et al. The effect of α -terpineol enantiomers on biomarkers of rats fed a high-fat diet. *Heliyon*. 2020 Apr 1;6(4).
 30. Chen L, Xue S, Dai B, Zhao H. Effects of Coix Seed Oil on High Fat Diet-Induced Obesity and Dyslipidemia. *Foods*. 2022 Oct 1;11(20).
 31. Nasr LR, Saber ME, Hussam B, Salma AR, Muzaffar I. The effect of vanadium on rat hypercholesterolemia in the presence and absence of statins. *Afr J Pharm Pharmacol*. 2017 Oct 22;11(39):509–16.
 32. Casagrande D, Waib PH, Jordão Júnior AA. Mechanisms of action and effects of the administration of Coenzyme Q10 on metabolic syndrome. Vol. 13, *Journal of Nutrition and Intermediary Metabolism*. Elsevier Inc; 2018. p. 26–32.
 33. Mollace R, Macrì R, Nicita M, Musolino V, Gliozzi M, Carresi C, et al. Bergamot Polyphenolic Extract Combined with Albedo and Pulp Fibres Counteracts Changes in Gut Microbiota Associated with High-Fat Diet: Implications for Lipoprotein Size Re-Arrangement. *Int J Mol Sci*. 2023 Aug 1;24(16).
 34. Garkuwa UA, Saleh MIA, Alhassan A, Kawu MU. Alpha lipoic acid improved blood glucose level and lipid profile in type-2 diabetic Wistar rats. *Gadau Journal of Pure and Allied Sciences* [Internet]. 2023 Aug 13;2(2):106–12. Available from: <https://gadaufos.com/gjpas/index.php/journal/article/view/107>