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Original article

Function of Alpha-Lipoic Acid in Rabbits as An Antioxidant and to Lower Lipid Levels

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ABSTRACT

As a thiol-replenishing and redox-modulating agent in cells, Alpha lipoic acid 'ALA—also known as 'thioctic acid, 1,2-dithiolane-3-pentanoic acid, 1,2dithiolane-3-valeric acid, or 6,8-thioctic acid—has attracted a lot of medicinal interest. Naturally, alpha lipoic acid is needed as a cofactor for the oxidative decarboxylation responses of the glucose digesting system to lose life. Thus, the goal of this investigation was to draw attention to how thioctic acid affects lipid profile. Critical papers were found by a deliberate search of PubMed/Medline, Scopus, Web of Science, Cochrane Library, and Embase through October 2023. The rabbits were given an oral dose of 60 mg/kg BW of thioctic acid. Rabbits were given the tried measurements daily for a period of 12 weeks. The results demonstrated that thioctic acid caused a critical (PB/0.05) decrease in the levels of glucose, "TBARS", "cholesterol", triglycerides "TG", low density lipoprotein "LDL", and very low-density lipoprotein "VLDL", while the level of high-density lipoprotein "HDL" increased in comparison to the control group.

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INTRODUCTION

One particular type of antioxidant is thioctic acid, which has the ability to quickly neutralize free radicals, is amphiphilic, and does not have any detrimental side effects [1]. Because of its unique qualities, which enable it to travel to all regions of the body and enter areas of the cell that most other antioxidants cannot, thioctic acid demonstrates anti-inflammatory properties as well. It dissolves in fat and water equally. thioctic acid is a chemical that functions through multiple mechanisms and is employed as a potent antioxidant in various disorders involving age-dependent oxidative damage. It may reduce aging and lengthen longevity in cardiovascular disorders such as ischemic heart disease, hypertension, heart failure, and atherosclerosis.

Numerous studies have demonstrated that thioctic acid improves vascular function and reduces the amount of atherosclerotic plaque [2]. The primary vasoconstrictor, endothelin I, is inhibited by thioctic acid in the vascular overproduction [3]. Moreover, thioctic acid dramatically boosts the production production NO^-, the main vasodilator; it may also improve endothelium-dependent NO^-mediated vasodilation and the redox status of the plasma. In addition, thioctic acid reduces ENOS phosphorylation loss, improving endothelial function. By defending against the risk factors for cardiovascular disease, thioctic acid may also reduce the risk of CVD by positively affecting blood lipid profiles, plaque formation, 'LDL' oxidation, and hypertension [2]. Alpha lipoic acid can replenish glutathione, vitamins E and C,

metal chelate, and scavenge reactive oxygen species [4]. Additionally, Alpha lipoic acid possesses anti-inflammatory qualities that help restore vascular health and lower the load of atherosclerotic plaque. It has been demonstrated that thioctic acid metabolites have antioxidant effects. Therefore, Alpha lipoic acid in its reduced form can enhance antioxidant qualities. Because it can raise glutathione levels within cells, thioctic acid has been shown to be an excellent direct chelator of hazardous metals [5]. It also provides substantial indirect support for metal chelation.

METHODS

Tested compound

The impact of Alpha lipoic acid on the "glucose and lipid profile" of male rabbits was examined in this work. The thioctic acid was bought for therapeutic purposes from the Al-Bayda city public market.

Animals and treatments

An adult male from New Zealand Six-month-old white rabbits were employed. Over the course of the 12-week experiment, each animal was kept in its own cage and had its weight checked every week. Water and food were given out on a daily basis. Randomly, ten mature male rabbits were divided into two groups, each having five rabbits in it: Group I: Rabbits were used as the control group every day for a period of 12 weeks. Group II: For 12 weeks in a row, the rabbits received daily gavage treatments of Alpha lipoic acid at a dose of 60 mg/kg BW [6]. Blood enzymatic activity and biochemical parameters Samples of blood were promptly put on ice. Samples were centrifuged at 860 xg for 20 minutes to extract plasma, which was then kept at -20°C until needed for analysis. Plasma glucose concentrations in stored plasma samples were determined using the procedure described in [7]. Triglycerides 'TG' and cholesterol plasma concentrations were measured using the techniques described in [8], respectively. The levels of "high-density lipoprotein" 'HDL' were measured using the procedures outlined in [9].

Data analysis

The formula for calculating low-density lipoprotein 'LDL' was cholesterol-'TG/5+HDL'. To compute very low-density lipoprotein 'VLDL', 'TG' values were divided by a factor of 5. Data were examined using statistical methods in accordance with [10]. At a significance level of 5%, the F test was utilized to ascertain the statistical significance of the variation in the values of the treated and control animals. The statistical analysis of the study's data was conducted using Duncan's Multiple Range Test [11].

RESULTS

The table below compares various parameters and lipid profiles between the groups that received thioctic acid treatment and the control group. The data is presented as mean ± standard error. Significant differences between the groups are denoted by different superscripts (a, b). The glucose levels in the control group were significantly higher (113.40 ± 0.415 mg/dl) compared to the Alpha lipoic acid -treated group (96.92 ± 2.773 mg/dl). This indicates that Alpha lipoic acid has a substantial effect in lowering blood glucose levels. The levels of Thiobarbituric Acid Reactive Substances "TBARS", a marker of oxidative stress, were significantly reduced in the Alpha lipoic acid -treated group (1.015 ± 0.025 nmol/ml) compared to the control group (1.568 ± 0.027 nmol/ml). This demonstrates the antioxidant properties of Alpha lipoic acid in reducing lipid peroxidation. Total cholesterol levels were slightly lower in the thioctic acid group (116.04 ± 0.705 mg/dl) compared to the control group (119.66 ± 0.544 mg/dl), showing a modest but significant reduction in cholesterol due to thioctic acid treatment.

Triglycerides levels in the thioctic acid -treated group (50.68 ± 1.098 mg/dl) were significantly lower than those in the control group (57.15 ± 0.955 mg/dl), indicating that Alpha lipoic acid effectively reduces triglyceride levels. The "HDL" levels, considered the "good" cholesterol, were significantly higher in the Alpha lipoic acid group (61.30 ± 0.694 mg/dl) compared to the control group (56.47 ± 0.485 mg/dl). This suggests that thioctic acid improves the lipid profile by increasing HDL levels. "LDL" levels, known as "bad" cholesterol, were significantly reduced in the Alpha lipoic acid -treated group (55.33 ± 0.746 mg/dl) compared to the control group (60.18 ± 0.648 mg/dl). This further supports the lipid-lowering effect of thioctic acid.

The results indicate that Alpha lipoic acid has a significant effect on lowering blood "glucose", reducing oxidative stress, and improving lipid profiles in rabbits. Alpha lipoic acid treatment leads to lower levels of "glucose", "TBARS", cholesterol, triglycerides, and "LDL", while increasing "HDL" levels. These findings highlight the potential therapeutic benefits of Alpha lipoic acid as an antioxidant and lipid-lowering agent.

Table 1. Plasma biochemistry of male rabbits treated with Alpha lipoic acid

Items	Control	Alpha lipoic acid
Glucose (mg/dl)	113.40 ± 0.415[a]	96.92±2.773[b]
TBARS (nmol/ml)	1.568±0.027[a]	1.015±0.025[b]
Cholesterol (mg/dl)	119.66± 0.544 [a]	116.04±0.705[b]
TG (mg/dl)	57.15± 0.955 [a]	50.68±1.098[b]
HDL (mg/dl)	56.47± 0.485 [a]	61.30±0.694[b]
LDL (mg/dl)	60.18± 0.648 [a]	55.3 3 ± 0.746[b]

Each treatment group has five values, which are expressed as means ± SEM. The means of the rows that did not have the same superscript letter (a, b) differed considerably, $p<0.05$.

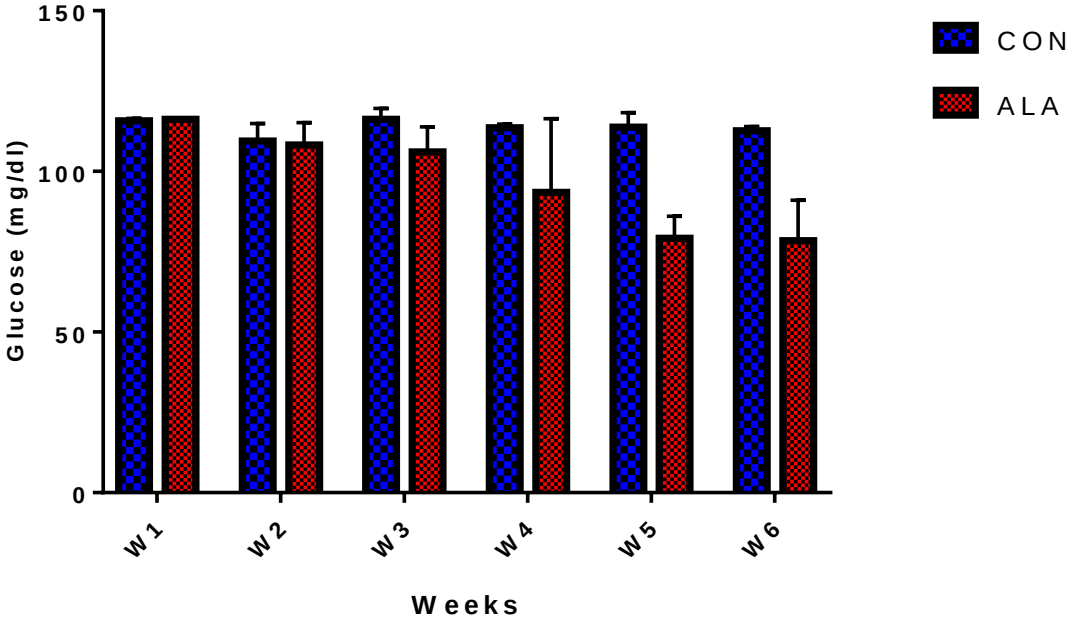

Figure 1. Changes in blood plasma of glucose during treatment of male rabbits with, Alpha lipoic acid

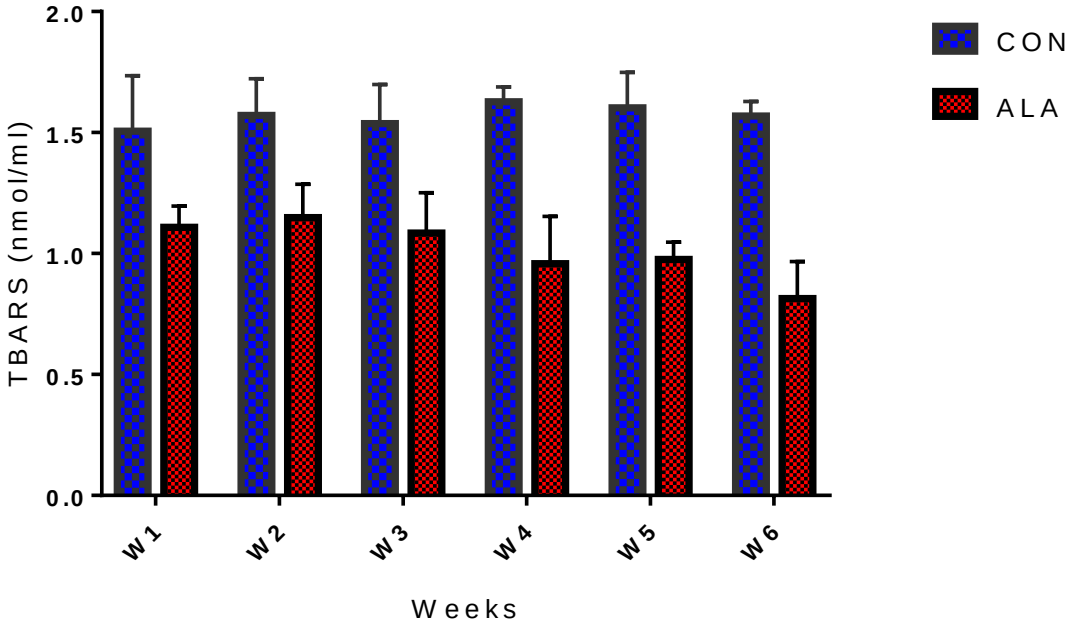

Figure 2. Changes in blood plasma of "TBARS" during treatment of male rabbits with, Alpha lipoic acid

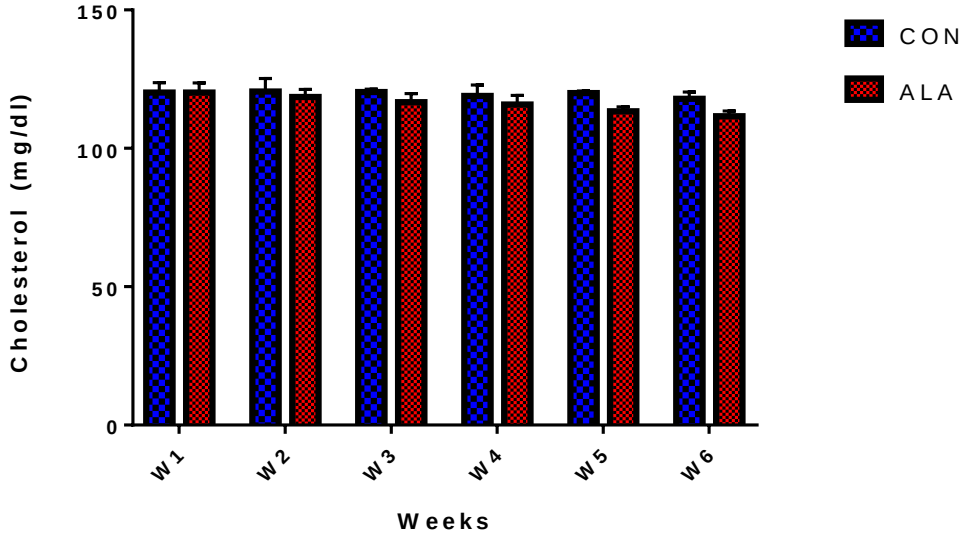

Figure 3. Change in blood plasma of cholesterol "TC" during treatment of male rabbits with , Alpha lipoic acid

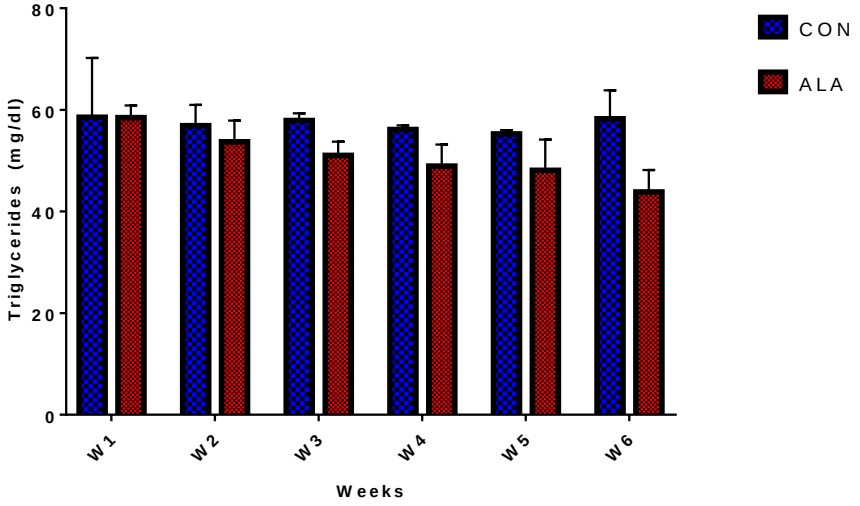

Figure 4. Change in blood plasma of triglyceride "TG" during treatment of male rabbits with, Alpha lipoic acid

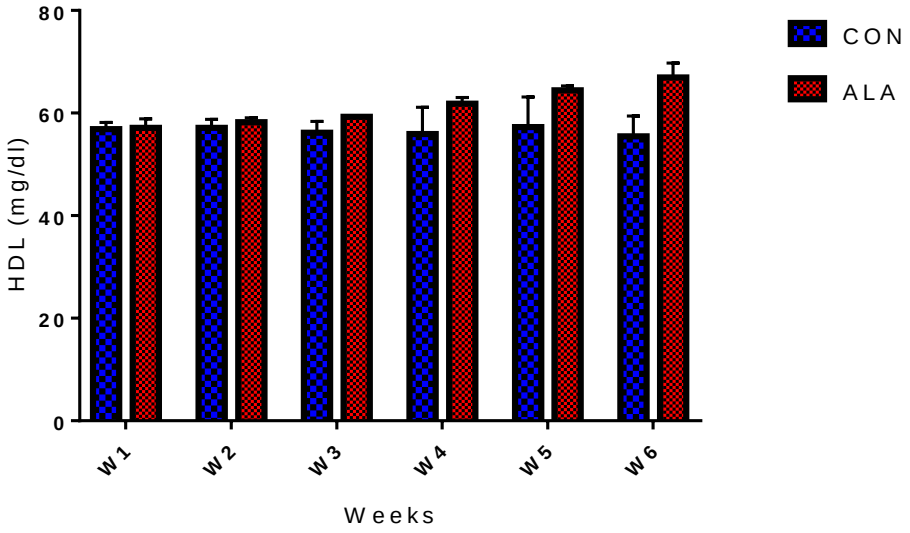

Figure 5. Changes in the activity of plasma high density lipoprotein during treatment of male rabbits with, Alpha lipoic acid

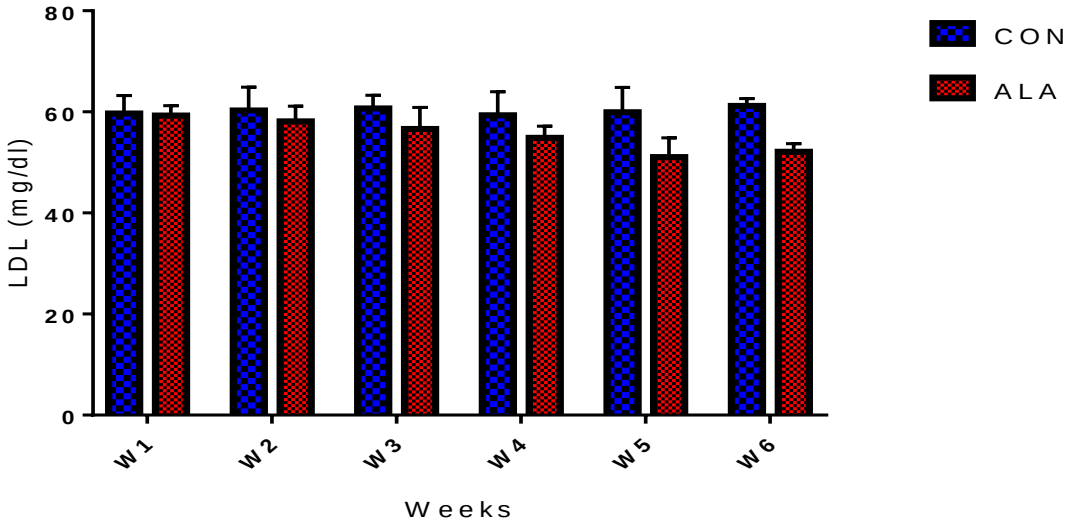

Figure 6. Changes in the activity of plasma "LDL" during treatment of male rabbits with, Alpha lipoic acid

DISCUSSION

The Alpha lipoic acid supplementation on serum lipid profile, despite prior research on the positive benefits of alpha lipoic acid on a number of disorders and plasma levels of lipid profile [12]. Both humans and animals manufacture alpha lipoic acid, a potent natural antioxidant. This antioxidant is essential for the blood, kidneys, and liver's lipid metabolism. It is also crucial cofactor for enzymes involved in the metabolism of energy [13].

It has recently been demonstrated that alpha lipoic acid may influence lipid metabolism, which in turn may alter the plasma lipid profile. The plasma levels of TG and TC decreased significantly between the groups, according to our findings. Our findings are consistent with those of [14], who found that giving obese individuals with impaired glucose tolerance (IGT) 600 mg/day of thioctic acid for two weeks significantly reduced the levels of 'TG' and TC in their serum. Additionally, additional studies have demonstrated that supplementing with alpha lipoic acid has favorable effects on 'TG' and 'TC' [15]. Conversely, de Oliveira et al. observed no rise in 'TC' and 'TG' levels in the serum [16]. We still don't know the precise processes by which alpha lipoic acid might influence 'TG'.

Adenosine monophosphate-activated protein kinase (AMPK) activation may boost mitochondrial fatty acid beta-oxidation, which could be the mechanism by which 'ALA' lowers cholesterol. The aforementioned protein kinase inhibits fatty acid synthase and acetyl-CoA carboxylase activity, which decreases lipogenesis [17]. The second likely mechanism involves thioctic acid [18] lowering plasma glucose levels, which facilitates an increase in cyclic adenosine monophosphate (cAMP) [19], lowering blood insulin levels [20].

Our research showed that there were no appreciable variations in the groups' plasma levels of 'HDL-C' and 'LDL-C'. Our findings are consistent with those of [21], who after 12 weeks observed no difference in the groups' plasma levels of 'HDL-C' and 'LDL-C'. Similar results have also been found in a number of other investigations [22], however our results were not supported by some of the earlier research. [12]. Certain investigations have proposed that alpha lipoic acid may improve 'TC' or 'LDL' via the following mechanisms: (i) reduced 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase activity and increased lipoprotein lipase activity; (ii) liver expression of the LDL receptor, which facilitates the transfer of cholesterol to the liver, and increased expression of apolipoprotein A [23], and (iii) elevated adiponectin levels in the serum, which enhance fatty acid b-oxidation [24]. Furthermore, some research has demonstrated that alpha lipoic acid can suppress the hepatic production of lipogenic genes, including sterol regulatory element binding protein-1c (SREBP1-c) and carbohydrate responsive element binding protein (ChREBP) [25].

Even though its exact mechanism is yet unknown, thioctic acid, in its reduced form, DHLA, demonstrates a protective measure against free radical activity. In our investigation, the 'TBARS 'level, as determined by 'MDA' concentration, was considerably lower in the group treated with alpha lipoic acid than in the untreated group (AT), suggesting that alpha lipoic acid may have antioxidant properties in addition to its hypocholesterolemic effects. These results were consistent with earlier research that suggested alpha lipoic acid could be a powerful source of metabolic antioxidants to scavenge free radicals both in vivo and in vitro [26].

CONCLUSION

The body can produce alpha lipoic acid or consume it through supplements. Alpha lipoic acid has been the buzz of the town lately, particularly among young people who work out. This is because it aids in weight loss. Our research attempts to show that alpha lipoic acid has additional significant impacts, as suggested by the studies in the literature. Many studies have shown that alpha lipoic acid can be helpful in the treatment of diabetes because of its antioxidant and antidiabetic qualities. However, because alpha lipoic acid can cause hypoglycemia, it is important to use caution when combining alpha lipoic acid supplementation with hypoglycemic medications. In rabbits, Alpha lipoic acid exhibits strong antioxidant and cholesterol-lowering characteristics, pointing to a possible therapeutic use for the treatment of oxidative stress and lipid diseases. It is necessary to conduct more research to examine its clinical applicability in humans.

Conflict of interest. Not declared

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وظيفة حمض ألفا ليبويك في الأرانب كمضاد للأكسدة وخافض لمستويات الدهون

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المستخلص

يهدف هذا البحث إلى دراسة دور حمض ألفا ليبويك كمضاد للأكسدة وخافض للدهون في الأرانب. حمض ألفا ليبويك هو مركب كيميائي يتميز بخصائصه الفريدة كمضاد للأكسدة وقدرته على تعديل مستويات الدهون في الجسم. تم إجراء البحث على مجموعة من الأرانب التي تلقت جرعات يومية من حمض ألفا ليبويك بجرعة 60 ملغ/كغ من وزن الجسم لمدة 12 أسبوعًا. أظهرت النتائج أن حمض ألفا ليبويك أدى إلى انخفاض كبير في مستويات الجلوكوز، والـ TBARS (مؤشر للإجهاد التأكسدي)، والكوليسترول، والدهون الثلاثية، والبروتين الدهني منخفض الكثافة، والبروتين الدهني منخفض الكثافة جدًا في الأرانب مقارنة بالمجموعة الضابطة. في المقابل، شهدت مستويات البروتين الدهني عالي الكثافة ارتفاعًا ملحوظًا. تشير هذه النتائج إلى أن حمض ألفا ليبويك يمتلك خصائص مضادة للأكسدة وقدرات فعالة في تحسين ملف الدهون في الجسم، مما يجعله مرشحًا محتملاً للاستخدام في الوقاية والعلاج من اضطرابات الدهون والأمراض المرتبطة بالإجهاد التأكسدي.

الكلمات المفتاحية. الفا ليبوليك اسيد ؛ كولستيرول,TBARS ؛ ارانب.