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Simultaneous Effect of Atorvastatin and Combined Training on lipid and hepatic enzymes in Rats induced Non-Alcoholic Fatty Liver Disease

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ABSTRACT

Introduction: Non-alcoholic fatty liver disease (NAFLD) is one of the most common liver diseases, the prevalence of which is increasing. This study aimed to evaluate the effect of atorvastatin and combined training in NAFLD-induced rats.

Methods: This study was conducted on 21 male Wistar rats, divided into two groups: 1) HFFD + combined training + atorvastatin and 2) HFFD + atorvastatin. The groups received HFFD for 15 weeks to induce NAFLD. Atorvastatin was administrated at the dose of 2mg/kg/day. The interventions (atorvastatin and combined training) were performed for eight weeks.

Results: Alanine transaminase (ALT) was significantly reduced, and high-density lipoprotein (HDL) was increased in the HFFD + atorvastatin group. Low-density lipoprotein (LDL) decreased significantly in the HFFD + combined training + atorvastatin. There was no significant difference in the aspartate transaminase (AST), triglyceride (TG), alkaline phosphatase (ALP), and weight between the groups.

Conclusion: Based on the findings, Atorvastatin, along with combined training, improved NAFLD. Therefore, they can be used to reduce the complications of NAFLD. However, more studies are needed to confirm the results.

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Introduction

Non-alcoholic fatty liver disease (NAFLD) is an exceedingly prevalent chronic liver condition that encompasses a broad range of hepatic steatosis leading to cirrhosis (1). The incidence of this ailment is on the rise, with approximately 2.9 to 7.1% of the general population in Iran grappling with NAFLD (2). Multiple investigations have demonstrated a significant relationship between NAFLD and obesity, type 2 diabetes, cardiovascular disease, as well as sedentary behavior (3). Aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), and other markers of hepatic diseases may be helpful to surrogate measures of NAFLD (4). Accordingly, measurement of aminotransferases, blood lipids (Triglyceride (TG), Total Cholesterol (TC), low-density lipoproteins (LDL), and high-density lipoproteins (HDL), and insulin resistance (IR) are often used in clinical settings to detect NAFLD (5). Currently, there are no FDA-approved pharmacological interventions for treating NAFLD (6). Consequently, the primary action in addressing this affliction involves altering one's lifestyle by reducing the consumption of a diet high in fat and carbohydrates while increasing physical activity (7). Mainly, physical activity exerts its beneficial effects through the enhancement of lipolysis and secretion of pro-inflammatory cytokines, thereby playing a pivotal role in the regulation and control of inflammatory conditions such as NAFLD (8). Lack of physical activity, which encompasses a dearth of bodily movement and exercise, stands as a fundamental component within the realm of cardiovascular risk factors, manifesting as an influential determinant for the

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emergence of various debilitating conditions such as cardiovascular diseases, diabetes, and other causes of death. The absence of regular physical exertion can serve as a remarkable indicator in predicting the occurrence of these health issues. Regardless of whether an individual possesses exceptional stamina or formidable muscular power, athletes, owing to their consistent engagement in rigorous athletic endeavors, exhibit significantly diminished levels of TG, TC, and LDL while concurrently indicating elevated levels of HDL, which confers an enhanced ability to ward off the aforementioned cardiovascular ailments (9).

Resistance training (RT), which emphasizes muscle mass and fortitude, has been recognized as an effective modality for eliciting beneficial effects on the human body. Especially, RT has yielded analogous metabolic advantages compared to aerobic activities while imposing a lesser burden on the cardiorespiratory system (10). Simultaneously, a novel form of training, denoted as intense interval training (HIIT), has garnered considerable attention due to its time-saving nature and heightened efficacy. This revolutionary training approach was instrumental in improving body composition and effectively inducing weight reduction through intermittent and high-intensity exertions, unveiling its potential as a promising intervention in physical fitness and well-being (11). HIIT is characterized by the repetition of brief and intense training sessions, followed by periods of rest or low-intensity exercise. HIIT (12) increases the transfer of free fatty acids (FFAs) from adipose tissue, ultimately resulting in β-oxidation. This biochemical pathway involves the breakdown of FFAs, resulting in the generation of energy for bodily functions (13). On the other hand, combined training in middle-aged women does not have a positive effect on inflammatory factors and adipokines (14).

Among the widely utilized medications are cholesterol-lowering drugs, particularly statins, which operate by exerting control over the production of cholesterol by inhibiting a critical regulatory enzyme within the cholesterol synthesis pathway (15). Furthermore, atorvastatin, a type of statin, has been shown to possess other beneficial therapeutic effects, even when administered at low doses (16). These additional effects encompass anti-inflammatory and antioxidant properties identified in various studies (17). For instance, atorvastatin has been shown to protect cellular structure from damage caused by ischemia and insufficient blood supply to tissues and prevent the loss of antioxidant enzyme activity (18, 19). Considering the information above, the objective of the present study revolves around evaluating the concurrent impact of atorvastatin administration and combined training in male rats with NAFLD. The purpose of this investigation is to examine the effects of atorvastatin, both alone and in combination with exercise training, on the pathology and potential amelioration of NAFLD in male rats. Incorporating exercise training into the study design is particularly important as it permits the study to examine the synergistic effects that may result from both atorvastatin therapy and combined exercise (endurance and resistance). This study can provide a deeper understanding of the interplay between pharmacological interventions and lifestyle modifications in managing NAFLD, thereby contributing to developing more effective treatment strategies for this prevalent liver disorder.

Material and Method

Animal and Design

In this experimental study, 21 male Wistar rats (270-370g) were obtained from Shahid Mirghani Research Institute (Golestan, Iran) and subjected to a 12:12h dark/light cycle at 20-24°C with unrestricted access to food and water. NAFLD was induced in the animals following the protocol of Eslami et al. after a week of acclimation to the environment (20). Blood and liver samples were collected after 15 weeks from five randomly selected rats to assess alanine aminotransferase (ALT) levels and liver tissue changes, which revealed the presence of NAFLD. Subsequently, the rats were divided into two groups: high-fat-fructose diet (HFFD) + atorvastatin (n=8) and HFFD + combined training (CT) + atorvastatin 2mg/kg (dissolved in 6% DMSO, gavage) (Raha Pharmaceutical co, Iran) (n=8), with the interventions being administered for eight weeks. HFFD consists of 45% fructose and 35% olive oil consumed by gavage.

Measurement of Biochemical Indices

The rats were anesthetized through intraperitoneal injection of ketamine (50mg/kg) and xylazine (5mg/kg, Merck, Germany) (21),

with the levels of aminotransferases and alkaline phosphatase (ALP) determined through standard enzymatic techniques, and TG, LDL, and HDL levels evaluated using an auto-analyzer (BT-3500, Biotecnica Instruments, Italy) (22).

Combined Training Protocol

Tables 1 and 2 contain the protocol for resistance training and HIIT, respectively (23).

Table 1. Protocol of resistance training

	Session	1st	2nd	3rd	4th	5th	6th	7th	8th	9th
1st week	Repetition	1	1	1	1	1	1	1	-	-
	%	0%	20%	30%	40%	30%	20%	0%	-	-
2nd week	Repetition	0	1	2	2	2	1	0	-	-
	%	0%	20%	30%	40%	30%	20%	20%	-	-
3rd week	Repetition	0	1	1	1	1	1	1	1	-
	%	20%	30%	40%	50%	40%	30%	20%	0%	-
4th week	Repetition	0	1	1	1	1	1	1	1	1
	%	0%	20%	30%	40%	50%	40%	30%	20%0	0
5th week	Repetition	0	1	1	1	2	1	1	1	1
	%	0%	20%	30%	40%	50%	40%	30%	20%	0%
6th week	Repetition	0	1	1	1	1	2	1	1	1
	%	0%	30%	40%	50%	60%	50%	40%	30%	0%
7th week	Repetition	1	1	1	2	2	1	1	-	-
	%	0%	40%	50%	60%	50%	40%	0%	-	-
8th week	Repetition	1	1	2	3	1	1	1	-	-
	%	0%	40%	50%	60%	50%	40%	0%	-	-

Table 2. Protocol of HIIT

Week	1st	2nd	3rd	4th	5th	6th	7th	8th
Repetition	2	2	3	4	4	5	6	6
Min	2	2	2	2	2	2	2	2
%	90%	90%	90%	90%	90%	90%	90%	90%

Statistical Analysis

The distribution of data was determined using the Shapiro-Wilk test. At the same time, the homogeneity of variances was checked using Levene's test, and the mean of the desired variables was compared using One-way analysis of variance (ANOVA), all analyzed using SPSS software version 16 at a significance level of P≤0.05.

Ethical Statement

The research followed the guidelines outlined in the publication "Guide for the Care and Use of Laboratory Animals" by the US National Institutes of Health (NIH publication No. 85–23, revised 1996). The study protocol was approved by the ethics committee in the local jurisdiction (IR.SSRC.REC.1402.119). Every endeavor was undertaken to mitigate animal distress and limit the number of animals employed.

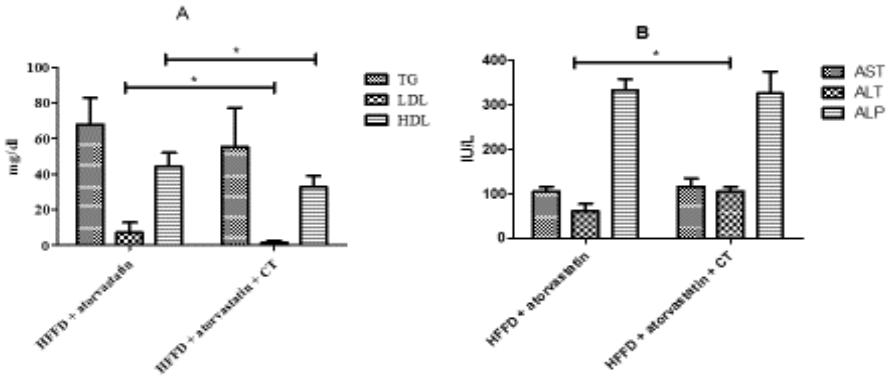

Figure 1. Mean and SD of biochemical parameters in eight weeks of interventions. A: lipid profile, B: liver enzymes

Results

There is no notable disparity in the magnitude of serum TG (P= 0.293), AST (P= 0.251), and ALP (0.749) between the two groups. Consequently, the administration of atorvastatin in isolation yielded for eight weeks a marginal decline in ALT

(P=0.000) and elevation in HDL (P= 0.019) levels. Conversely, co-administration of atorvastatin and CT caused a significant reduction in LDL (P=0.024) level in HFFD + CT + atorvastatin compared to HFFD + atorvastatin (Table 3). The average weight over eight consecutive weeks did not exhibit any noteworthy variance between the two groups. The outcomes of the ANOVA were employed to compare weight in eight consecutive weeks, presented in Table 4 and Figure 2.

Table 3. Average of biochemical parameters in eight weeks of interventions

Group	TG	LDL	HDL	LDL/HDL	ALT	AST	ALP
HFFD + Atorvastatin	62.75 ± 10.81	8.62 ± 5.15	47.02 ± 4.91	0.11 ± 0.10	66.85 ± 9.99	101.78 ± 7.38	342.50 ± 14.10
HFFD + CT + Atorvastatin	66.60 ± 13.14	1.01 ± 0.26	31.46 ± 5.79	0.03 ± 0.007	103.27 ± 7.96	112.53 ± 17.34	314.67 ± 44.44
P	0.293	0.024*	0.019*	0.053	0.000*	0.251	0.749
F	1.230	7.016	7.816	4.798	34.575	1.485	0.108

*Significant: P≤0.05

Table 4. Average of weight in eight weeks of interventions

Group	W1	W2	W3	W4	W5	W6	W7	W8
HFFD + Atorvastatin	332.74 ± 33.92	329.85 ± 34.19	326.93 ± 38.82	336.45 ± 43.10	369.02 ± 42.10	359.12 ± 43.08	360.48 ± 40.37	370.23 ± 38.93
HFFD + CT + Atorvastatin	375.15 ± 46.57	360.65 ± 33.22	368.66 ± 37.94	375.92 ± 40.56	365.06 ± 21.20	372.08 ± 19.73	382.26 ± 19.92	383.85 ± 19.78
P	0.115	0.149	0.092	0.136	0.833	0.495	0.233	0.441
F	2.977	2.448	3.464	2.625	0.047	0.502	1.613	0.643

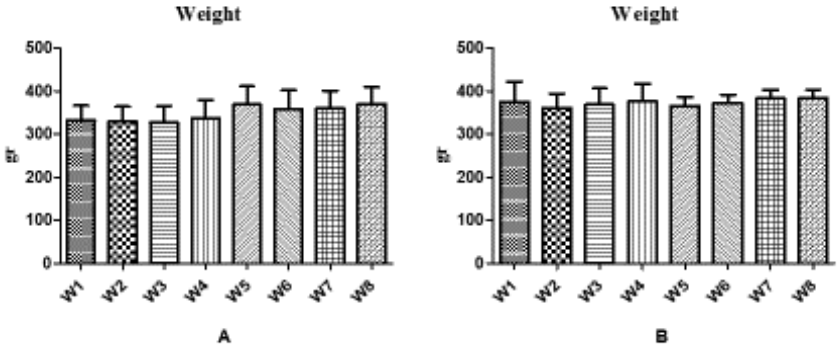

Figure 2. Mean and SD of weight in study groups during intervention. A: HFFD + atorvastatin, B: HFFD + atorvastatin + CT

Discussion

The findings indicate that the administration of atorvastatin for eight weeks significantly reduced ALT levels and elevation of HDL levels. Conversely, engaging in CT concurrently with atorvastatin administration decreases serum LDL levels. Other biochemical parameters did not show significant changes. Various studies exploring the impact of training, including different types, intensities, and durations, on liver enzymes in individuals with NAFLD have yielded conflicting results. For instance, a study demonstrated that 12 weeks of HIIT decreased liver fat and liver enzymes such as ALT and AST in NAFLD patients (24). Another investigation revealed that both HIIT and resistance training led to a reduction in liver fat content in individuals with NAFLD. Furthermore, the plasma concentration of AST did not experience a significant alteration following either type of training, whereas the concentration of ALT exhibited a significant decrease in both groups (25). There have been a limited number of trials that have examined the effects of combined training in patients with NAFLD. Houghton et al. demonstrated that a 12-week intervention involving combined training resulted in a significant reduction in liver fat content,

regardless of any accompanying weight loss. However, this intervention did not impact the liver enzymes AST and ALT (26). Another study showed that 12 weeks of HIIT training improved obesity indices more effectively than moderate-intensity training (MIT) (27). Pekkala et al. showed that HIIT and MIT are equally effective in combating obesity (28). The results of the present study indicated that combined training is associated with a decrease in HDL levels, which was in line with the results of Mirghani et al. (29). Piano et al. examined the effects of endurance training alone or in conjunction with resistance training on patients with NAFLD to ascertain the impact of exercise training on individuals with NAFLD. The findings indicated that combined training, encompassing both endurance and resistance exercises, yielded greater efficacy in reducing the prevalence of NAFLD than endurance training alone. Additionally, Hallsworth et al. discovered no significant decrease in ALT levels after an eight-week training period. However, Baba et al. demonstrated that a three-month regimen of aerobic training coupled with a dietary intervention led to a decrease in aminotransferase levels, although no significant alterations were observed in the lipid profile. The inconsistency in the findings about the lipid profile may be ascribed to the variances in the type and duration of the training sessions.

Hepatic enzyme activity is affected by various factors, including the duration, intensity, type, and mode of exercise. Training background, subject characteristics, physical fitness level, and exercise type should also be considered, as each can contribute to these discrepancies. Ebrahimi et al. conducted a study demonstrating that an eight-week period of moderate and vigorous aerobic exercise did not yield any discernible impact on the liver enzymes of rats fed a diet high in fat. Conversely, Mirdar et al. observed that levels of aminotransferases increased post-exercise, which contradicts the investigation findings mentioned above. The elevation of circulating aminotransferase levels can potentially be attributed to muscular damage resulting from exercise. Haghigi et al. affirmed that pharmacotherapy, physical activity, and dietary interventions exhibit similar efficacy in mitigating the severity of liver disease as determined by ultrasound.

Atorvastatin reduces cholesterol by inhibiting the enzyme HMG-CoA reductase in the liver and is rapidly absorbed through the gastrointestinal tract. Most therapeutic drugs for treating various ailments undergo metabolism within the liver. Consequently, these metabolic transformations have the potential to generate harmful metabolites, resulting in the possibility of acute and chronic liver damage in the event of enzyme system disruption. The current investigation demonstrated that atorvastatin alone reduced ALT levels and increased HDL levels. Conversely, Eslami et al. revealed that the administration of atorvastatin at a dosage of 10mg/kg over eight weeks was associated with a decrease in aminotransferase and triglyceride levels, as well as an increase in LDL levels (22). In this particular context, applying atorvastatin at 10 mg/kg/day in rats with NAFLD for eight weeks yielded positive enhancement in the quantities of TG, cholesterol, and liver enzymes (30). Mirghani et al. showed that concurrent training is the most suitable type of training to improve cardiovascular factors by preventing the reduction of HDL levels by comparing eight weeks of strength training and concurrent training on men (31). In a study, the effect of aerobic exercise was investigated on the expression of genes related to lipid metabolism (MAPK P38 and UCP-1). The results indicated that 12 weeks of aerobic training (five sessions per week) is associated with decreased MAPK P38 gene expression in subcutaneous adipose tissue (32). The results of this study indicated that CT does not make a significant difference in the weight of rats fed HFD. In contrast, another study shows that endurance exercise improves anthropometric indices (33).

Conclusion

Based on the results, administration of atorvastatin in conjunction with combined training leads to a reduction in ALT and LDL levels and an increase in HDL levels. Consequently, a regimen combining training and atorvastatin administration seems feasible for treating patients with NAFLD by taking advantage of both approaches.

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Conflict of Interest

The authors declare no conflict of interest regarding the publication of this article.

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References

1. Maurice J, Manousou P. Non-alcoholic fatty liver disease. Clin Med (Lond). 2018;18(3):245-50.
2. Khoonsari M, Mohammad Hosseini Azar M, Ghavam R, Hatami K, Asobar M, Gholami A, et al. Clinical Manifestations and Diagnosis of Non-Alcoholic Fatty Liver Disease. Iranian Journal of Pathology. 2017;12(2):99-105.
3. Hassen G, Singh A, Belete G, Jain N, De la Hoz I, Camacho-Leon GP, et al. Nonalcoholic Fatty Liver Disease: An Emerging Modern-Day Risk Factor for Cardiovascular Disease. Cureus. 2022;14(5):e25495.
4. LaBrecque DR, Abbas Z, Anania F, Ferenci P, Khan AG, Goh K-L, et al. World Gastroenterology Organisation global guidelines: Nonalcoholic fatty liver disease and nonalcoholic steatohepatitis. Journal of clinical gastroenterology. 2014;48(6):467-73.
5. Anderson EL, Howe LD, Jones HE, Higgins JP, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PloS one. 2015;10(10):e0140908.
6. Chen JYS, Chua D, Lim CO, Ho WX, Tan NS. Lessons on Drug Development: A Literature Review of Challenges Faced in Nonalcoholic Fatty Liver Disease (NAFLD) Clinical Trials. International Journal of Molecular Sciences. 2023;24(1):158.
7. Tsamos G, Vasdeki D, Koufakis T, Michou V, Makedou K, Tzimagiorgis G. Therapeutic Potentials of Reducing Liver Fat in Non-Alcoholic Fatty Liver Disease: Close Association with Type 2 Diabetes. Metabolites. 2023;13(4).
8. Callegari IOM, Rocha GZ, Oliveira AG. Physical exercise, health, and disease treatment: The role of macrophages. Front Physiol. 2023;14:1061353.
9. Ambroży T, Rydzik Ł, Obmiński Z, Spieszny M, Szczepanik A, Ambroży D, et al. Effect of High-Intensity Strength and Endurance Training in the Form of Small Circuits on Changes in Lipid Levels in Men Aged 35–40 Years. Journal of Clinical Medicine. 2022;11(17):5146.
10. Hallsworth K, Fattakhova G, Hollingsworth KG, Thoma C, Moore S, Taylor R, et al. Resistance exercise reduces liver fat and its mediators in non-alcoholic fatty liver disease independent of weight loss. Gut. 2011;60(9):1278-83.
11. Guo Z, Li M, Cai J, Gong W, Liu Y, Liu Z. Effect of High-Intensity Interval Training vs. Moderate-Intensity Continuous Training on Fat Loss and Cardiorespiratory Fitness in the Young and Middle-Aged a Systematic Review and Meta-Analysis. Int J Environ Res Public Health. 2023;20(6).
12. Atakan MM, Li Y, Koşar Ş N, Turnagöl HH, Yan X. Evidence-Based Effects of High-Intensity Interval Training on Exercise Capacity and Health: A Review with Historical Perspective. Int J Environ Res Public Health. 2021;18(13).
13. Savikj M, Stocks B, Sato S, Caidahl K, Krook A, Deshmukh AS, et al. Exercise timing influences multi-tissue metabolome and skeletal muscle proteome profiles in type 2 diabetic patients – A randomized crossover trial. Metabolism. 2022;135:155268.
14. Banitalebi E, Mardanpour Shahrekordi Z, Kazemi AR, Bagheri L, Amani Shalamzari S, Faramarzi M. Comparing the Effects of Eight Weeks of Combined Training (Endurance and Resistance) in Different Orders on Inflammatory Factors and Adipokines Among Elderly Females. Women's Health Bulletin. 2016;3(2):1-10.
15. Schonewille M, de Boer JF, Mele L, Wolters H, Bloks VW, Wolters JC, et al. Statins increase hepatic cholesterol synthesis and stimulate fecal cholesterol elimination in mice. J Lipid Res. 2016;57(8):1455-64.
16. Zhou Q, Liao JK. Pleiotropic effects of statins. - Basic research and clinical perspectives. Circ J. 2010;74(5):818-26.
17. J D. Beneficial cardiovascular pleiotropic effects of statins. Circulation. 2004;109(23):39-43.
18. Parlakgumus HA, Aka Bolat F, Bulgan Kilicdag E, Simsek E, Parlakgumus A. Atorvastatin for ovarian torsion: effects on follicle counts, AMH, and VEGF expression. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2014;175:186-90.
19. Gottmann U, Brinkkoetter PT, Hoeger S, Gutermann K, Coutinho ZM, Tobias Ruf SH, et al. Atorvastatin donor pretreatment prevents ischemia/reperfusion injury in renal transplantation in rats: possible role for aldose-reductase inhibition. Transplantation. 2007;84(6):755-62.
20. Eslami Z, Mirghani SJ, Eghbal Moghanlou A, Norouzi A, Naseh H, Joshaghani H, et al. An Efficient Model of Non-alcoholic Fatty Liver Disease (NAFLD) Versus Current Experimental Models: Effects of Fructose, Fat, and Carbon Tetrachloride on NAFLD. Hepat Mon. 2021;21(8):e117696.
21. Eslami Z, Rezaei Ghomi M, Saidi A, Mousavi SV, Farhadi M, Sheikh Robati N, et al. Endurance Training and Exogenous Adenosine Infusion Mitigate Hippocampal Inflammation and Cell Death in a Rat Model of Cerebral Ischemia/Reperfusion Injury: A Randomized Controlled Trial. Arch Neurosci. 2022;9(1):e119236.
22. Eslami Z, Mohammadnajad Panah kandi Y, Norouzi A, Eghbal Moghanlou A, Sheikh arabi M, Kazeminejad V, et al. Changes in Blood Lipids and Enzymatic Reactions in Response to Atorvastatin Administration Following a High-Fat Diet in a NAFLD Rat Model. Medical Laboratory Journal. 2022;16(3):7-13.
23. Leandro CG, Levada AC, Hirabara SM, Manhães-de-Castro R, De-Castro CB, Curi R, et al. A program of

moderate physical training for Wistar rats based on maximal oxygen consumption. J Strength Cond Res. 2007;21(3):751-6.
24. Hallsworth K, Thoma C, Hollingsworth KG, Cassidy S, Anstee QM, Day CP, et al. Modified high-intensity interval training reduces liver fat and improves cardiac function in non-alcoholic fatty liver disease: a randomized controlled trial. Clin Sci (Lond). 2015;129(12):1097-105.
25. Galedari M, Kaki A. The Effect of 12 Weeks High Intensity Interval Training and Resistance Training on Liver Fat, Liver Enzymes and Insulin Resistance in Men with Nonalcoholic Fatty Liver. Jundishapur Scientific Medical Journal. 2017;16(5):493-503.
26. Houghton D, Thoma C, Hallsworth K, Cassidy S, Hardy T, Burt AD, et al. Exercise Reduces Liver Lipids and Visceral Adiposity in Patients With Nonalcoholic Steatohepatitis in a Randomized Controlled Trial. Clin Gastroenterol Hepatol. 2017;15(1):96-102.e3.
27. Mirghani SJ, Azarbayjani MA, Peeri M. Effects of Endurance Training and Isocaloric High Intensity Interval Training on Anthropometric Indices and Insulin Resistance in High Fat Diet-Fed Wistar Rats. Medical Laboratory Journal. 2018;12(6):12-8.
28. Pekkala S, Rafiei M, Eslami Z, Ghaderi M, Moghanlou A, Sharifian S, et al. High-intensity interval training and moderate intensity training with exogenous adenosine counteract development of obesity in rats. Science & Sports. 2022;37(5-6):477-85.
29. Mirghani SJ, Alinejad HA, Azarbayjan MA, Mazidi A, Mirghani SA. Influence of strength, endurance and concurrent training on the lipid profile and blood testosterone and cortisol response in young male wrestlers. Baltic Journal Of Health And Physical Activity. 2014;6(1).
30. Eslami Z, Moghanlou AE, Kandi Y, Arabi MS, Norouzi A, Joshaghani H. Atorvastatin and Flaxseed Effects on Biochemical Indices and Hepatic Fat of NAFLD Model in Rats. Adv Biomed Res. 2023;12:98.
31. Mirghani SJ, Agha-Alinejad H, Azarbayjani MA, Arshadi S, Mazidi A, Mirghani SA. Effect of 8 Weeks Concurrent Training on Blood Lipid Profile and Body Mass Index in Young Men. International Medical Journal. 2012;19:260-3.
32. Zahra Eslami YMP, Shohreh Sharifian , Abdorreza Eghbal Moghanlou , Seyed Reza Sheikh , Seyed Javad Mirghani. Evaluation of the effect of aerobic exercise on UCP1 and MAPK p38 heat factor gene expression in subcutaneous adipose tissue in male Wistar rats fed a high-fat diet. Feyz. 2021;25(4):1020-30.
33. Mirghani SJ, Azarbayjani MA, Peeri M, keshtkar A. Investigating Effects of Vitamin D Injection during a Course of Endurance Training On Anthropometrical Parameters of Wistar Rats with High-Fat Diet-Induced Obesity. Medical Laboratory Journal. 2019;13(6):36-43.