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The Effect of High-Intensity Interval Training in the Presence of L-Carnitine on the Expression of MCT1, PGC-1, and CS in the Liver of Male Wistar Rats

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Abstract

Background: T Liver oxidative metabolism disorder is dependent on several factors that lead to liver diseases like non-alcoholic fatty liver disease. Our hypothesis was that the combination of high-intensity interval training (HIIT) and L-carnitine affects the expression of citrate synthase (CS), PGC-1α, and monocarboxylate transporter 1 (MCT1) in the liver of male Wistar rats.

Methods: Thirty-two male Wistar rats were divided into four groups ($n=8$): control, L-carnitine (200 mg/kg/d, four weeks, IP), HIIT, and HIIT + L-carnitine (200 mg/kg/d, four weeks, IP). HIIT training was performed for four weeks (five days a week); then, the animals were anesthetized, and their liver tissues were extracted for real-time PCR to measure MCT1, PGC-1α, and CS. SPSS 22 software was used to analyze the data obtained in different groups, with $P<0.05$ considered statistically significant.

Results: MCT1 expression significantly increased in the HIIT and HIIT + L-carnitine groups compared to the control group ($P<0.001$). PGC-1α expression significantly increased in the HIIT + L-carnitine group compared to the control and L-carnitine groups ($P<0.001$). Also, PGC-1α expression significantly increased in the HIIT group compared to the control group ($P<0.001$). Furthermore, CS expression significantly increased in all groups compared to the control group ($P<0.001$).

Conclusion: HIIT exercise combined with L-carnitine supplementation increases the expression of MCT1, PGC-1α, and CS in the liver. Therefore, it seems that performing HIIT exercises and taking L-carnitine supplements can prevent the consequences of fat accumulation in the liver.

Keywords: High-intensity interval training, MCT1, PGC-1α, CS gene

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Introduction

A metabolically flexible system can adapt its energy source (glucose and fatty acids) oxidation to the availability of fuel. Tissues can regulate their use of substrates based on the balance between fuel oxidation, the capacity of the tissue to store the substrate, and the metabolic demands resulting from this balance (1). There is competition between glucose, lipids, and their derivatives regarding their oxidation (2). For example, increasing glucose stores or other fuels, such as lactate, can reduce the oxidation of fatty acids in some tissues (3). Deficiencies in regulating metabolic interactions between fuel substrates are often associated with insulin resistance, accumulation of lipids, and mitochondrial defects (4). Among the cell energy metabolism regulators most effective in the biogenesis of liver mitochondria, one can point to peroxisome proliferator-activated receptor-γ coactivator-1α (PGC-1α) (5). Hepatocyte nuclear factor 4 alpha (HNF4α) and a glucocorticoid receptor called FOXO1 are two of the factors that PGC-1α can activate.

Moreover, PGC-1α can increase gluconeogenesis-related gene expression, including genes associated with oxidative phosphorylation, lipid transport, and fatty acid oxidation (6). Due to the role of PGC-1α in gluconeogenesis and lipid oxidation in the liver, increasing its levels in the liver could be a treatment strategy for fatty acid oxidation in patients with fatty liver. Studies have shown that complete loss of PGC-1α in the liver leads to starvation-induced steatosis,

which, along with decreased gluconeogenesis, increases insulin sensitivity and increases glucose tolerance (7).

A member of the SLC (solute carrier) transporter superfamily, monocarboxylate transporter 1 (MCT1), has an unclear role in liver function. MCT1 can transport L-lactate, a hepatic substrate used in gluconeogenesis, to the parenchymal cells of the liver (8). Another key regulatory enzyme in the metabolic pathway of energy production is citrate synthase (CS), which is commonly used as a marker to measure aerobic capacity and mitochondrial density in skeletal muscles (9). Furthermore, Liu et al. 2019 showed that exercise training restored renal function via activating CS and NADH: ubiquinone oxidoreductase (complex I) (10).

The physiological effect of the L-form of beta-hydroxy-gamma trimethylammonium butyrate, an amino acid-like molecule better known as carnitine, can be used to treat diabetes and liver and cardiovascular diseases. Some of its effects include a decrease in liver enzyme levels, an improvement in liver inflammation, and an increase in fat oxidation (11). L-carnitine facilitates lipid oxidation by transferring long-chain fatty acids to the mitochondrial matrix. L-carnitine is absorbed through active sodium-dependent transport and inactive transport through the intestines (12). It reduces triglyceride and cholesterol levels and improves heart and metabolic disorders (13). L-carnitine is a supplement that reduces weight gain and increases lipid catabolism (so-called lipid burning) (12).

Lipid profiles have been reported to improve in people who have received L-carnitine as a supplement and performed exercise training. It has been reported that L-carnitine improves training performance (12). The effects of exercise include increased mitochondrial content and improved muscle oxidative capacity (14) and insulin sensitivity (15). Glucose transporter, MDA, and PPAR-gamma in the liver and muscles also decrease (16). Liver tissue apoptosis rates are decreased by aerobic exercise in combination with L-carnitine in patients with type 2 diabetes (17). Acute sports exercises have been demonstrated to elevate the expression of PGC-1α, AMPK, and IRS-2 genes in the liver (18). HIIT can increase the fat transfer capacity of mitochondria by increasing the activity of carnitine palmitoyl transferase, an oxidative process-facilitating enzyme (19). It has also been reported that HIIT improves the oxidative direction in the muscles of animals with hypertension (20).

L-carnitine decreases fat mass and increases insulin sensitivity (13,21-23). Nevertheless, how the expression of genes involved in exercise and mitochondrial biogenesis is affected by L-carnitine is yet to be determined. Therefore, we conducted this study to investigate the effects of HIIT on the expression of MCT1, PGC-1α, and CS in the presence of L-carnitine in the liver of male Wistar rats.

Materials and Methods

Experimental protocols

Groups

Thirty-two male Wistar rats (185 ± 10 g) were kept at 24 ± 2 °C, 30–50% humidity, and a 12 h dark/light cycle with ad libitum access to water and food during the acclimatization and test period. The animals were randomly assigned to four groups ($n = 8$ in each group): 1) control, 2) L-carnitine, 3) HIIT, and 4) HIIT + L-carnitine. L-carnitine (Sigma, C0283) was used at 200 mg/kg/d IP for four weeks in all carnitine groups.

Training protocols

All groups were first acclimatized to the treadmill (speed of 15 m/min). The animals underwent an incremental running test to determine the training group's maximum speed (Vmax). In each run (speed of 6 m/min for two minutes), 2 m/min was added to their speed every 2 minutes, and this exercise continued until exhaustion. The last minute the rats could tolerate the applied speed was considered Vmax. The training protocol was repeated five times weekly for six weeks (24). Vmax was measured weekly, and the new Vmax was taken as the animals' relative speed for that week. Furthermore, in addition to the time spent on the main workout, 5 minutes for a warm-up and 5 minutes for cooling were also included in the protocol. Forty-eight hours after the end of the last training session, the animals were anesthetized with ketamine (100 mg/kg, IP) (Alfasan, Netherland) and xylazine (8 mg/kg) (Alfasan, Netherland), the liver tissues were extracted and stored at -80 °C until use.

Gene expression studies

RNA isolation, cDNA synthesis, and real-time PCR

For RNA extraction, according to the manufacturer's instructions (BioBasic, Total RNA EZ-10 Spin Column Kit, BS82312), the liver tissue (40 mg) was homogenized in a specific lysis buffer using a sonicator (Heilscher H200, Heilscher Inc., Germany). To synthesize the cDNA, 500 ng of total RNA was used according to the kit's instructions (Parstous, A101161). Real-time PCR was performed using an ABI StepOnePlus device. Each real-time PCR contained 10 µL SYBR green (Ampliqon, A325402), synthesized cDNA (100 ng), and forward and reverse primers (1µl from each primer), and the reaction volume was raised to 20 µL by adding distilled water. The annealing temperature was determined according to each primer's Tm and by gradient PCR performed in a Bio-Rad thermocycler (18s: 59 °C; CS: 60 °C; MCT1: 60 °C; PGC-1α: 62 °C). The thermal protocol in real-time PCR was as follows: 95 °C (5 min), 95 °C (15 sec), annealing temperature (45 seconds), 40 cycles, and after the thermal cycles were finished, the melt curve analysis was performed. We used 18S rRNA as a housekeeping gene. The relative expression of genes was determined

by the $2^{-\Delta\Delta Ct}$ method (20, 21). Specific primers (Sinacolon Inc.) were used to perform real-time PCR measurements (Table 1) (25).

Statistical analysis

The collected data were analyzed using SPSS 22 software. Tukey's post hoc and one-way ANOVA tests were used to assess inter-group relationships between the variables, and $P<0.05$ was the criterion for statistical significance in all tests.

Results

MCT1 expression significantly increased in the HIIT and HIIT + L-carnitine groups compared to the control group ($P<0.001$) (Figure 1). PGC-1α expression significantly increased in the HIIT + L-carnitine group compared to the control and L-carnitine groups ($P<0.001$). Also, PGC-1α expression significantly increased in the HIIT group compared to the control group ($P<0.001$) (Figure 2). Moreover, CS expression significantly increased in all three groups, HIIT + L-carnitine, HIIT, and L carnitine, compared to the control group ($P<0.001$) (Figure 3).

Discussion

The effect of HIIT exercise was assessed in the presence of L-carnitine on the expression of MCT1, PGC-1α, and CS genes in the liver of male Wistar rats. The study results showed that the expression of PGC-1α and CS genes increased in the HIIT + L-carnitine group compared to the control group.

The present study showed increased PGC-1α expression in liver tissue following HIIT training and HIIT combined with L-carnitine. PGC-1α is a key regulating factor of mitochondrial biogenesis (26) by affecting a signaling pathway that involves PPAR-α, mitochondrial transcription factor A (TFAM), nuclear respiratory factor-1, and 2 (NFR-1 and -2). PGC-1α needs SIRT1 to be regulated, which also requires AMPK activation by exercise or drugs (27); PGC-1α deacetylation (28) through SIRT1 is facilitated by the increase in intracellular NAD + (26,29) caused by phosphorylated AMPK. PGC-1α increases following the increase of AMPK with L-carnitine consumption, probably due to AMPK leading to the expression of PGC-1α (30).

Moreover, we demonstrated that the HIIT + L-carnitine group significantly increased MCT1 expression compared to other groups. Exercising above the lactate threshold causes lactate accumulation; the liver is necessary for drawing the lactate produced by exercise from the blood via the Cori cycle, and the MCT1 gene carries lactate to hepatocytes via the gluconeogenesis pathway (31). In our study, the expression of MCT1 as a lactate transporter increased in the HIIT group along with L-carnitine. HIIT exercise seems to allow lactate to be eliminated through gluconeogenesis. L-carnitine is an essential nutrient that protects cells in metabolic disorders through various physiological functions, such as antioxidant effects (32). We revealed that L-carnitine consumption in combination with HIIT increases the relative expression of MCT1, probably due to the antioxidant effect of L-carnitine, which has been reported in previous studies to prevent liver mitochondrial damage in favor of energy production (32). In the process of essential fatty acid beta-oxidization, fatty acids in the form of acyl-CoA cannot pass the mitochondrial membrane. However, their passage is made possible by the carnitine acyltransferase in the mitochondrial membrane after conjugating with carnitine to form CoA derivatives. L-carnitine accumulates to metabolize mitochondrial energy and its acyl derivatives, which increases mitochondrial function. L-carnitine also has antioxidant and free radical scavenging effects to prevent mitochondrial damage (33).

Our findings showed that the expression of the CS gene in all three groups, HIIT + L-carnitine, HIIT, and L carnitine, increased significantly compared to the control group. The increase in PGC-1α expression is probably responsible for increased CS expression following exercise and L-carnitine intake. In support of our results, Merrill et al demonstrated that increased expression of AMPK-PGC-1α is a possible reason for increased CS (34). CS is a valid biomarker for mitochondrial density and cellular metabolism, and the higher the CS activity, the higher the mitochondrial biogenesis. Moreover, CS activity as a biochemical marker is an oxidative adaptation in training intervention, and there is a relationship between changes in whole-body aerobic capacity and changes in CS activity (35). Also, acetylcholine can be transported to the cytosol as citrate and converted to fatty acids when the ATP and NADH ratio is disturbed in post-workout conditions. The increase in the CS gene is due to changes in mitochondrial enzymes that increase during exercise, which is associated with changes in oxygen delivery in favor of increased fat

Table 1. The primer sequences used to evaluate the effect of high-intensity interval training (HIIT) in the presence of L-carnitine on the expression of monocarboxylate transporter 1 (MCT1), peroxisome proliferator-activated receptor-γ coactivator-1α; (PGC-1α), and citrate synthase (CS) in the liver of male Wistar rats

Genes name	Forward primer	Reverse primer
CS	CGGTTCTTGATCCTGATGAGGG	ACTGTTGAGGGCTGTGATGGC
MCT1	GCTGTCATGTATGCCGGA	CAATCATAGTCAGAGCTGGG
PGC-1a	ACCCACAGGATCAGAACAAACC	GACAAATGCTCTTTGCTTTATTGC
18s	GCAATTATTCCCCATGAACG	GGCCTCACTAAACCATCCAA

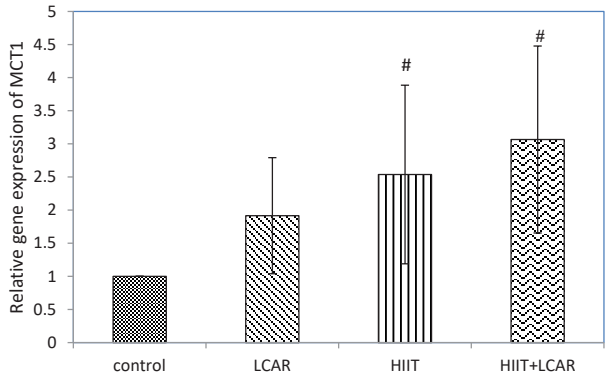

Figure 1. MCT1 gene expression relative to 18S rRNA. Gene expression was performed by real-time PCR in the studied groups ($n=8$). Data are expressed as mean ± SED. $P<0.05$ was considered as significant. # Statistically significant compared to the control group. MCT1: monocarboxylate transporter 1; HIIT: high-intensity interval training; LCAR: L-carnitine

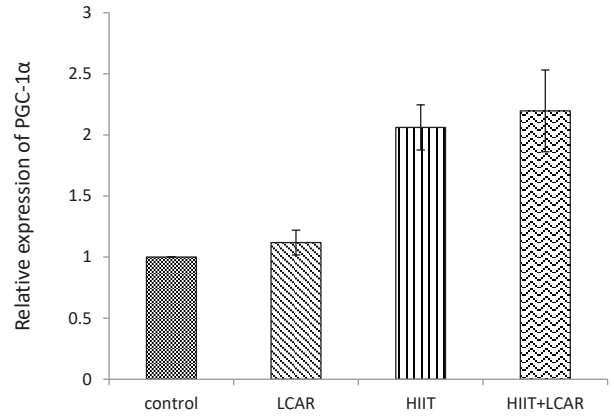

Figure 3. Citrate synthase gene expression relative to 18S rRNA. Gene expression was performed by real-time PCR in the studied groups ($n=8$). Data are expressed as mean ± SED. $P<0.05$ was considered significant. *Statistically significant compared to the control group. HIIT: high-intensity interval training; LCAR: L-carnitine

intake and a lower increase in lactate levels (36).

Conclusion

The overall results show that performing HIIT exercises combined with L-carnitine supplementation can improve the response of markers of oxidative metabolism in the liver. This improvement is associated with increased MCT1, CS, and PGC-1α expression. Moreover, although L-carnitine supplementation was associated with increased MCT1, CS, and PGC-1α, the changes were not significant. Increasing these factors in the liver can play a protective role against some liver diseases, including non-alcoholic fatty liver.

Authors' Contribution

Conceptualization: Mahdiyeh Haj Hosseini, Beydolah Shahouzehi.
Formal analysis: Mahdiyeh Haj Hosseini.
Investigation: Mahdiyeh Haj Hosseini, Beydolah Shahouzehi.
Methodology: Beydolah Shahouzehi.
Project administration: Mahdiyeh Haj Hosseini.
Visualization: Mahdiyeh Haj Hosseini.
Supervision: Mahdiyeh Haj Hosseini.

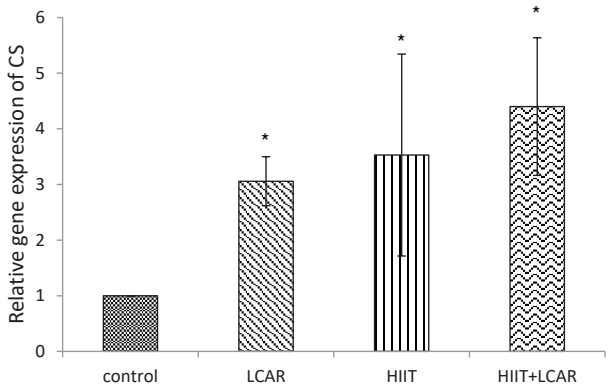

Figure 2. PGC-1a gene expression relative to 18S rRNA. Gene expression was performed by real-time PCR in the studied groups ($n=8$). Data are expressed as mean ± SD. $P<0.05$ was considered as significant. *Statistically significant compared to the control group. # statistically significant compared to the L-carnitine group. HIIT: high-intensity interval training; PGC1α: peroxisome proliferator-activated receptor-γ coactivator-1α; LCAR:L-carnitine

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Competing Interests

The authors declared no conflict of interest.

Ethical Approval

All procedures performed on animals were conducted following the ethical standards of the Kerman University of Medical Sciences (IR.KMU.REC.1398.356).

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References

1. Zhang S, Hulver MW, McMillan RP, Cline MA, Gilbert ER. The pivotal role of pyruvate dehydrogenase kinases in metabolic flexibility. Nutr Metab (Lond). 2014;11(1):10. doi: 10.1186/1743-7075-11-10.
2. Randle PJ. Regulatory interactions between lipids and carbohydrates: the glucose fatty acid cycle after 35 years. Diabetes Metab Rev. 1998;14(4):263-83. doi: 10.1002/(sici)1099-0895(199812)14:4<263::aid-dmr233>3.0.co;2-c.
3. Bielefeld DR, Vary TC, Neely JR. Inhibition of carnitine palmitoyl-CoA transferase activity and fatty acid oxidation by lactate and oxfenicine in cardiac muscle. J Mol Cell Cardiol. 1985;17(6):619-25. doi: 10.1016/s0022-2828(85)80030-4.
4. Mootha VK, Bunkenborg J, Olsen JV, Hjerrild M, Wisniewski JR, Stahl E, et al. Integrated analysis of protein composition, tissue diversity, and gene regulation in mouse mitochondria. Cell. 2003;115(5):629-40. doi: 10.1016/s0092-8674(03)00926-7.
5. Campos CV, Teixeira CJ, Payolla TB, Crisma AR, Murata GM, Amaral AG, et al. Changes in PGC-1α-dependent mitochondrial biogenesis are associated with inflexible hepatic energy metabolism in the offspring born to dexamethasone-treated mothers. Livers. 2021;1(4):201-20. doi: 10.3390/livers1040016.
6. Rius-Pérez S, Torres-Cuevas I, Millán I, Ortega Á L, Pérez S. PGC-1α, inflammation, and oxidative stress: an integrative view in metabolism. Oxid Med Cell Longev. 2020;2020:1452696. doi: 10.1155/2020/1452696.
7. Estall JL, Kahn M, Cooper MP, Fisher FM, Wu MK, Laznik

D, et al. Sensitivity of lipid metabolism and insulin signaling to genetic alterations in hepatic peroxisome proliferator-activated receptor-gamma coactivator-1alpha expression. Diabetes. 2009;58(7):1499-508. doi: 10.2337/db08-1571.
8. Droździk M, Szeląg-Pieniek S, Grzegółkowska J, Łapczuk-Romańska J, Post M, Domagała P, et al. Monocarboxylate transporter 1 (MCT1) in liver pathology. Int J Mol Sci. 2020;21(5):1606. doi: 10.3390/ijms21051606.
9. Latham CM, Fenger CK, White SH. Rapid communication: differential skeletal muscle mitochondrial characteristics of weanling racing-bred horses. J Anim Sci. 2019;97(8):3193-8. doi: 10.1093/jas/skz203.
10. Liu HW, Kao HH, Wu CH. Exercise training upregulates SIRT1 to attenuate inflammation and metabolic dysfunction in kidney and liver of diabetic db/db mice. Nutr Metab (Lond). 2019;16:22. doi: 10.1186/s12986-019-0349-4.
11. Savic D, Hodson L, Neubauer S, Pavlides M. The importance of the fatty acid transporter L-carnitine in non-alcoholic fatty liver disease (NAFLD). Nutrients. 2020;12(8):2178. doi: 10.3390/nu12082178.
12. Cha YS. Effects of L-carnitine on obesity, diabetes, and as an ergogenic aid. Asia Pac J Clin Nutr. 2008;17 Suppl 1:306-8.
13. Eskandari HG, Cimen MY, Tamer L, Kanik A, Atik U. Short term effects of L-carnitine on serum lipids in STZ-induced diabetic rats. Diabetes Res Clin Pract. 2004;66(2):129-32. doi: 10.1016/j.diabres.2004.03.005.
14. Karim S, Adams DH, Lalor PF. Hepatic expression and cellular distribution of the glucose transporter family. World J Gastroenterol. 2012;18(46):6771-81. doi: 10.3748/wjg.v18.i46.6771.
15. Holloszy JO, Coyle EF. Adaptations of skeletal muscle to endurance exercise and their metabolic consequences. J Appl Physiol Respir Environ Exerc Physiol. 1984;56(4):831-8. doi: 10.1152/jappl.1984.56.4.831.
16. Pala R, Genc E, Tuzcu M, Orhan C, Sahin N, Er B, et al. L-carnitine supplementation increases expression of PPAR-γ and glucose transporters in skeletal muscle of chronically and acutely exercised rats. Cell Mol Biol (Noisy-le-grand). 2018;64(1):1-6. doi: 10.14715/cmb/2018.64.1.1.
17. Jabbari E, Gholami M, Nikbakht H, Shakeri N, Ghazaliyan F. Effect of aerobic training and L-carnitine supplementation on some apoptotic factors in diabetic rat liver. Razi J Med Sci. 2019;26(7):131-40. [Persian].
18. Hoene M, Lehmann R, Hennige AM, Pohl AK, Häring HU, Schleicher ED, et al. Acute regulation of metabolic genes and insulin receptor substrates in the liver of mice by one single bout of treadmill exercise. J Physiol. 2009;587(1):241-52. doi: 10.1113/jphysiol.2008.160275.
19. Carnevali LC Jr, Eder R, Lira FS, Lima WP, Gonçalves DC, Zanchi NE, et al. Effects of high-intensity intermittent training on carnitine palmitoyl transferase activity in the gastrocnemius muscle of rats. Braz J Med Biol Res. 2012;45(8):777-83. doi: 10.1590/s0100-879x2012007500105.
20. Holloway TM, Bloemberg D, da Silva ML, Quadrilatero J, Spriet LL. High-intensity interval and endurance training are associated with divergent skeletal muscle adaptations in a rodent model of hypertension. Am J Physiol Regul Integr Comp Physiol. 2015;308(11):R927-34. doi: 10.1152/ajpregu.00048.2015.
21. Muniyappa R. Oral carnitine therapy and insulin resistance. Hypertension. 2010;55(2):e13. doi: 10.1161/hypertensionaha.109.147504.
22. Patel J, Goyal R, Bhatt P. Beneficial effects of levo-carnitine on lipid metabolism and cardiac function in neonatal streptozotocin rat model of diabetes. Int J Diabetes Metab. 2008;16(1):29-34. doi: 10.1159/000497650.
23. Rahbar AR, Shakerhosseini R, Saadat N, Taleban F, Pordal A, Gollestan B. Effect of L-carnitine on plasma glycemic and lipidemic profile in patients with type II diabetes mellitus. Eur J Clin Nutr. 2005;59(4):592-6. doi: 10.1038/sj.ejcn.1602109.
24. Leeuwenburgh C, Hollander J, Leichtweis S, Griffiths M, Gore M, Ji LL. Adaptations of glutathione antioxidant system to endurance training are tissue and muscle fiber specific. Am J Physiol. 1997;272(1 Pt 2):R363-9. doi: 10.1152/ajpregu.1997.272.1.R363.
25. Marefati H, Masoumi-Ardakani Y, Shakerian S, Habibi A, Aminizadeh S, Shahouzehi B. The effects of pyruvate dehydrogenase kinase 4 (PDK4) inhibition on metabolic flexibility during endurance training in skeletal muscles of streptozotocin-induced diabetic rats. J Kerman Univ Med Sci. 2020;27(4):304-17. doi: 10.22062/jkmu.2020.91017.
26. Yap KH, Yee GS, Candasamy M, Tan SC, Md S, Abdul Majeed AB, et al. Catalpol ameliorates insulin sensitivity and mitochondrial respiration in skeletal muscle of type-2 diabetic mice through insulin signaling pathway and AMPK/SIRT1/PGC-1α/PPAR-γ activation. Biomolecules. 2020;10(10):1360. doi: 10.3390/biom10101360.
27. Lim K, Jang J. L-carnitine supplement and running training improve skeletal muscle recovery after hindlimb suspension induced muscle atrophy. FASEB J. 2017;31(S1):799-6. doi: 10.1096/fasebj.31.1_supplement.799.6.
28. Cantó C, Auwerx J. PGC-1alpha, SIRT1 and AMPK, an energy sensing network that controls energy expenditure. Curr Opin Lipidol. 2009;20(2):98-105. doi: 10.1097/MOL.0b013e328328d0a4.
29. Bishop D, Edge J, Thomas C, Mercier J. High-intensity exercise acutely decreases the membrane content of MCT1 and MCT4 and buffer capacity in human skeletal muscle. J Appl Physiol (1985). 2007;102(2):616-21. doi: 10.1152/japplphysiol.00590.2006.
30. Shahouzehi B, Nasri H, Aminizadeh S, Masoumi-Ardakani Y. The effect of high-intensity interval training and L-carnitine on the expression of some pro-inflammatory genes in the liver and cardiac tissues of rats. J Kerman Univ Med Sci. 2021;28(1):56-68. doi: 10.22062/jkmu.2021.91564.
31. Lezi E, Lu J, Selfridge JE, Burns JM, Swerdlow RH. Lactate administration reproduces specific brain and liver exercise-related changes. J Neurochem. 2013;127(1):91-100. doi: 10.1111/jnc.12394.
32. Wang G, Zhao L, Jiang Q, Sun Y, Zhao D, Sun M, et al. Intestinal OCTN2- and MCT1-targeted drug delivery to improve oral bioavailability. Asian J Pharm Sci. 2020;15(2):158-73. doi: 10.1016/j.ajps.2020.02.002.
33. Gyawali A, Hyeon SJ, Ryu H, Kang YS. The alteration of L-carnitine transport and pretreatment effect under glutamate cytotoxicity on motor neuron-like NSC-34 lines. Pharmaceutics. 2021;13(4):551. doi: 10.3390/pharmaceutics13040551.
34. Merrill JF, Thomson DM, Hardman SE, Hepworth SD, Willie S, Hancock CR. Iron deficiency causes a shift in AMP-activated protein kinase (AMPK) subunit composition in rat skeletal muscle. Nutr Metab (Lond). 2012;9(1):104. doi: 10.1186/1743-7075-9-104.
35. Vigelsø A, Andersen NB, Dela F. The relationship between skeletal muscle mitochondrial citrate synthase activity and whole-body oxygen uptake adaptations in response to exercise training. Int J Physiol Pathophysiol Pharmacol. 2014;6(2):84-101.
36. Cochran AJ, Percival ME, Tricarico S, Little JP, Cermak N, Gillen JB, et al. Intermittent and continuous high-intensity exercise training induce similar acute but different chronic muscle adaptations. Exp Physiol. 2014;99(5):782-91. doi: 10.1113/expphysiol.2013.077453.