The Effect of Eight Weeks of Combined Exercise With and Without Supplementation of Cinnamon on Hematological and Liver Enzymes AST, ALT, and ALP in Female Amphetamine Addicts

Moradi, M. , Ali-Akbari Bidokhti, M. , Ghofrani, M.

Abstract

Objective: The present study aimed at investigating the effect of eight weeks of combined exercise with and without the supplementation of cinnamon on hematological factors of liver enzymes in female amphetamine addicts. **Method:** In this quasi-experimental study, 48 women addicted to amphetamine were divided into four groups. The exercise program was performed for eight weeks (three days a week). Cinnamon supplement was taken as a 500-mg capsule twice a day after breakfast and lunch. Blood samples were taken to measure hematological factors and liver enzymes. To compare the groups, MANOVA test was used and paired t-tests were run for measuring intra-group changes. **Results:** The results of this study showed no significant difference in hematological variables and liver enzymes between the groups ($P \geq 0.05$). However, t-test showed a significant reduction of white blood cells in all groups, while the reduction of hematocrit and red blood cells was observed only in the supplement group ($P < 0.05$). **Conclusion:** The combined exercise along with the supplementation of cinnamon can be effective in the hematologic factors of addicts.

Keywords: combined exercise, cinnamon supplement, hematologic, liver enzymes, female amphetamine addicts

Moradi, M. ,
Master's Holder of Sports Physiology, Sistan and Baluchestan University, Zahedan, Iran
Ali-Akbari Bidokhti, M. ,
Ph.D. Student, Department of Sports Physiology, Birjand University, Birjand, Iran, Email: aliakbaribidokhti@yahoo.com
Ghofrani, M.
Assistant Professor, Department of Physical Education, Sistan and Baluchestan University, Zahedan, Iran

Research on Addiction Quarterly Journal of Drug Abuse
Presidency of the I. R. of Iran
Drug Control Headquarters
Department for Research and Education
Vol. 12, No. 47, Autumn 2018
http://www.etiadpajohi.ir

Introduction

Drug use is a major dilemma in many human societies, which, in addition to social and behavioral disorders, affect different aspects of one's physical health and imposes huge financial damage on the individual, the community, and the family (Karam et al, 2004). Currently, the pattern of drug use is changing throughout the world in that the use of traditional substances, such as opium is being replaced by the use of new industrial substances, including amphetamines. Amphetamine-type stimulants takes the second rank after cannabis in the world with about 38 million consumers in the world (Bamdad, Fallahi Khoshkanab, Dalvandi, & Khoda'ei Ardakani, 2013). The main position of the effect of amphetamines is the central nervous system, especially the serotonin neurons. For this reason, this substance belongs to the group of neurotoxin compounds. Amphetamines produce side effects on various body tissues, including heart, kidneys, and liver, and lead to the stimulation of the body's endocrine system, the pituitary-hypothalamic-thyroid axis, and the adrenal gland. Its consumption also increases body temperature and ACTH and cortisol secretion (Bagheri Haghighi, Fattahi, Forouzanfar, & Hemayatkhahi Jahromi, 2012). Drug dependence and abuse in women are growing more than those in men. The factors effective in the prevalence of substance use in women include stress, negative mood in relationships, disturbed and conflicting family environment, violence against them, addicted spouses, mental illnesses, and sexual violence (Vafamand, 2012). Addiction is a chronic disease that requires long-term treatment, and the use of medication has not been a successful method to prevent addiction relapse and reduce the desire to consume substance (Hosseini, Ala'ea, Naderi, Sharifi, & Zahed, 2009).

Blood is a heterogeneous connective tissue that has numerous elements and compounds being influenced by the internal factors of the body and the outside environment (Mousavizadeh, Ebrahimi, & Nikbakht, 2009). Physical activity generally increases the power to do physical work and causes changes in the body, including the peripheral blood erythrocyte system. On the other hand, inactivity reduces plasma volume and the total volume of red blood cells, which ultimately results in lowering blood volume and decreasing the body's efficiency (Dubnov & Constantine, 2004). Research on various hematological indices reveals contradictory findings. The effect of physical activity on the level of hemoglobin and red blood cells, the percentage of transferrin concentration, serum iron, and hematocrit indicates the decrease, increase, or constancy of these factors (Mousavizadeh et al., 2009). The enzymes of Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), and Alkaline Phosphatase (ALP) are considered as the most important indicators of liver health function (Vozarova et al., 2002; Larson et al., 2008). Studies have shown that drug use, alcohol drinking, obesity, overweight, and exercise may increase liver enzymes activity (Giannini, Testa & Savarino, 2005; Suzuki et al., 2005;

Lawlar et al., 2005). Lawlar et al. (2005) conducted a study on the effect of exercise on liver enzymes. The results of this study indicated that regular exercises from light to moderate levels lead to the reduced activity of liver enzymes and reduced disease symptoms in people. Long-term exercises have been proved able to increase liver enzymes (Skenderi, Kavouras, Anastasiou, Yiannakouris, & Matalas, 2006). Suzuki et al. (2005) have shown that weight loss and regular exercise significantly reduce serum alanine aminotransferase, while drug use increases this enzyme.

Cinnamon is a plant with the scientific name of zeylanicum. Cinnamon is also considered one of the medicinal plants in traditional medicine. The study of books on Iranian ancient medicine, such as The Canon of Medicine by Avicenna and "Kitab al-saydala fi al-tibb" (Book on the Pharmacopoeia of Medicine by Abū Rayḥān Muḥammad ibn Aḥmad Al-Bīrūnī shows that this plant is used to treat many disorders, including digestion and diarrhea, removal of halitosis, dyspnea, accelerated blood flow, menstrual and postpartum births, sleeplessness, and poor eyesight (Vahidi, Dashti, Mojdeh, & Soltani, 2012). The medicinal effects of this plant are indebted to the compounds available in the essential oil (ester oil) or the extract of cinnamon. These substances include cinnamaldehyde, eugenol, candenyl, coumarin and other compounds (Paranagama et al., 2001).

Askari, Rashidkhani, & Hekmatdoost (2014) reported a decrease in plasma levels of liver enzymes after taking 1500 milligrams of cinnamon daily in patients with fatty liver. Cinnamon facilitates blood circulation; accordingly, the proper bloodstream provides oxygenation to the body cells and also eliminates blood contamination (Wainstein, Stern, Heller & Boaz, 2011). Moreover, cinnamon consumption is very useful for the treatment of anemia. The combination of cinnamic aldehyde available in cinnamon stimulates the immune system and helps this system in attacking infectious agents (Rose, 1999). Additionally, cinnamon prevents the non-enzymatic sugar metabolism of hemoglobin and low-density lipoprotein (LDL) oxidation due to its anti-oxidant activity (Baker, 2008).

Sport activities will lead to a serious reduction of drug use tendency by eliminating temptation and craving, interest in diversity, and curiosity. Meanwhile, considering easy access to drugs, one of the most important ways of preventing people from drug use is their inclination towards exercise (Fontes-Ribeiro, 2011). Drug use among women has serious consequences, such as rejection, addicted generations, the decrease of communication with ordinary people, and the increase of communication with drug addicts. In addition, women have the motherhood responsibility and bringing up of the future generation and, thereby, the presence of the addicted mother in the family can seriously harm the spouse and children and, consequently, society. Therefore, we need to accept women's addiction as a major problem and seek methods of addiction prevention and treatment in women.

The aim of this study was to investigate the effect of eight weeks of combined exercise with and without the supplementation of cinnamon on hematological factors of liver enzymes in female amphetamine addicts.

Method

Population, sample, and sampling method

The present study is a quasi-experimental one with four groups of random substitution, which has obtained ethics approval in research (IR.SSRI. REC.1395.111 code) from the Institute of Physical Education and Sports Sciences. The statistical population of this study consisted of female patients who had enrolled in Zahedan addiction treatment clinics in 2016. A sample of 48 people was selected from among those willing to participate in the study via convenience sampling method. The entry criteria of this study were lack of regular exercise, no history of blood diseases or diseases affecting hematological factors, and a seven-year period of addiction. The sample was randomly divided into four 12-person groups, namely practice-placebo, practice-supplement, supplement, and placebo. Participants signed a consent form after they were aware of their training goals and practices, and they were assured about the confidentiality of information.

Procedure

After grouping, participants received oral 500-gram placebo capsules (starch) and cinnamon twice a day after breakfast and lunch. The prepared cinnamon and starch were sent to the Herbarium section of the Faculty of Pharmacy, University of Tehran, and its purity was determined and each of them was prepared in the form of powders. Then, they were sent to a herbal pharmacy in Karaj and 500-mg capsules of cinnamon and starch were prepared over there. The capsules were similar to each other in color, shape, material, and size (Mirfeizi et al., 2014). The supplement and practice-supplement groups took 500-mg cinnamon capsules, and the practice-placebo and placebo groups took 500-mg starch capsules for eight weeks.

In terms of physical training, participants were first familiarized with the work environment and, then, referred to the training site to do the desired movements. An anaerobic circle training of six stations with the following features was conducted: each station took 15 seconds (sit-up, Swedish swim, butterfly, pair jump, scissors, walking on the paw) where 45 seconds of rest between each station was considered in three turns, and at the end of the circle training, the four-meter route was walked via kickback for three minutes, and the knee-high back was opted for with an intensity of 60-80% of the maximum heart rate with an increasing rate of 5% per week, 15 minutes of aerobic training (jugging) at five minutes of rest between the two exercises. A 10-minute warm-up at the start and a 5-minute cool-down at the end of the training for eight weeks (three days at 10 am each week) (Farzad et al., 2011). To determine

cardiovascular fitness, the participants performed the average Rockport Walk Test at the beginning and end of the course (Arazi, Jourbonian, & Asghari, 2012). Oxygen consumption was considered as VO2max. Then, 24 hours before and after the training program, 10 cc blood from the venous vein was taken in the sitting position. The participants were also asked to come there while fasting for at least 12 hours. From seven to eight, blood sampling was carried out. Blood samples were poured into test tubes containing Ethylenediaminetetraacetic acid (EDTA). Three cc of blood was transferred to the laboratory for CBC and the remainder was separated in terms of centrifugation and plasma for 10 minutes at a rate of 3000 rpm and was stored at -70 ° C in the freezer (Mir, Attarzadeh Hosseini, Mirsa'eadi, & Hejazi, 2016).

For the analysis of hematological factors and liver enzymes of blood cells, they were counted via cell counter XL22 device (made in Switzerland). In addition, the blood plasma volume was calculated using the Dill-Costill equation (Dill & Costill, 1974).

$$PVb = (1\text{-}HCTb/100) \times 100$$
$$BVb = 100 \text{ ml}$$
$$BVa = BVb \times (HGBb/HGBa)$$
$$RCVa = BVa \times HCTa$$
$$PVa = BVa \times RCVa$$

In this formula, BV represents blood volume, RCV indicates red blood cell volume, a denotes after exercise, and b shows before exercise.

The measurement of liver enzymes of aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase was performed using kits of the Iranian Biosystem Company and the 3000-BTT auto analyst device (jointly made in Japan-Germany).

Results

The descriptive statistics of the study pertaining to participants' physiological characteristics are presented in Table 1.

Table 1: Descriptive Statistics Pertaining to Physiological Characteristics of Participants

Variable	*Test type*	*Practice-Placebo*	*Practice-Supplement*	*Supplement*	*Placebo*
Age (years)	-	23.25±5.13	26.41±3.77	26.72±2.74	33.18±3.09
Height (cm)	-	153±0.08	156±0.07	159±0.04	155±0.08
Weight (kg)	Pretest	45.06±6.27	47.83±6.05	47.45±9.35	5.58±11.58
	Posttest	45.23±7.41	48.93±5.52	47.7±9.8	51.32±10.98
Body mass index (kg / m 2)	Pretest	19.17±2.28	19.43±2.51	19.45±3.18	20.99±4.96
	Posttest	19.32±2.91	2.10±5.52	18.86±20.68	21.36±5.02
Waist to hip (m)	Pretest	0.89±0.05	0.86±0.05	0.85±0.08	0.91±0.13
	Posttest	0.85±0.17	0.88±0.06	0.82±0.16	0.85±0.09
Maximum oxygen consumption (ml/kg/min)	Pretest	51.13±5.80	56.01±7.92	46.6±7.34	58.82±9.52
	Posttest	56.44±10.39	57.60±8.67	50.36±9.11	53.93±10.74

After assuring about the normal distribution of the data via Kolmogorov-Smirnov test; paired sample t-test, MANOVA test, and Tukey's post hoc test were run to investigate the variation in the post-test. The significance level was considered as P <0.05. Data were analyzed by SPSS20. The magnitudes of changes in hematological factors and liver enzymes of the study groups in the pre-test and post-test phases have been presented in Tables 2 and 3.

Table 2: Hematological Factors and Plasma Volume for Each Group

Variable	*Test type*	*Practice-Placebo*	*Practice-Supplement*	*Supplement*	*Placebo*	*Sig.*
White blood cell (10^3 per micro liters)	Pretest	9.34±2.03	8.78±2.26	7.1±1.12	7.5±2.47	0.08
	Posttest	7.04±1.75	7.11±1.58	6.07±1.03	5.82±1.54	
	Within-group Sig.	0.001	0.003	0.007	0.033	
Red blood cell (10^6 per micro liters)	Pretest	4.59±0.422	4.92±0.552	5.05±0.506	4.96±0.657	0.13
	Posttest	4.46±0.591	4.82±0.366	4.63±0.515	5.1±1.04	
	Within-group Sig.	0.196	0.884	0.001	0.705	
Hemoglobin (g / dl)	Pretest	13.6±0.899	13.63±0.891	13.15±1.2	13.71±1.77	0.52
	Posttest	13.77±0.898	13.84±1.27	13.26±0.937	13.82±1.2	
	Within-group Sig.	0.554	0.4446	0.587	0.766	
Hematocrit (percent)	Pretest	41.9±2.06	41.83±2.04	41.2±2.84	43.58±4.06	0.21
	Posttest	41.37±2.38	41.76±2.75	39.85±2.78	41.55±1.42	
	Within-group Sig.	0.505	0.933	0.022	0.104	
Platelet (10^3 per µl)	Pretest	106.41±3.34	74.23±3.35	64.25±3.27	95.67±3.4	0.66
	Posttest	104.23±3.28	80.92±3.34	62.36±3.25	77.58±3.63	
	Within-group Sig.	0.753	0.958	0.877	0.148	
Plasma volume (percent)	Pretest	58.10±2.06	58.16±2.04	58.79±2.84	56.41±4.06	0.75
	Posttest	58.13±5.75	57.57±5.55	59.78±5.06	57.95±5.20	
	Within-group Sig.	0.987	0.747	0.503	0.499	

As it has been shown in Table 2, paired sample t-test showed a significant reduction after training compared to pre-training in white blood cell values in the practice-supplement group (P <0.01), placebo group (P <0.001)), supplement group (P <0.01), and placebo group (P <0.05). Also, there was a significant decrease between the pretest and posttest in the values of red blood

cells (P <0.001) and in hematocrit values in the supplement group (P <0.05). In other groups, there was no significant difference before and after training in red blood cells and hematocrit values (P≥0.05). There was no significant difference in the pre- and post-training phases in hemoglobin, platelet, and plasma volume of the groups (P≥0.05).

The values of liver enzymes are presented in Table 3.

Table 3: Hepatic Enzyme Values for Each Group

Variable	*Test type*	*Practice-Placebo*	*Practice-Supplement*	*Supplement*	*Placebo*	*Sig.*
Aspartate Aminotransferase (International Unit)	Pretest	19.83±6.72	23.91±12.08	22.16±7.25	25.75±10.34	
	Posttest	20.66±8.79	17.83±4.04	15.83±2.94	14.83±2.75	
	Between-group Sig.	0.801	0.091	0.005	0.003	0.46
Alanine Aminotransferase (International Unit)	Pretest	22.91±12.37	23.83±22.24	23.66±6.3	23.33±7.67	
	Posttest	25.66±9.86	27.91±18.09	19.5±10.6	13.83±3.66	0.99
	Between-group Sig.	0.586	0.493	0.207	0.005	
Alkaline phosphatase (International Unit)	Pretest	337.91±101	369.41±211.18	298.41±81.64	373.25±183.12	
	Posttest	282.25±97.15	238.66±127.91	203.41±84.77	259.5±270.2	0.67
	Between-group Sig.	0.046	0.001	0.002	0.007	

As it can be observed, paired sample t-test showed a significant reduction after training compared to pre-training in aspartate aminotransferase values in the supplement group (P <0.01) and placebo group (P <0.01); however, no significant difference was observed in the practice-supplement and practice-placebo groups (P≥0.05). A significant decrease in the levels of alanine aminotransferase was observed after training in the placebo group (P <0.01); however, there was no significant difference in the levels of alanine aminotransferase in other groups (P≥0.05). On the other hand, paired sample t-test showed a significant decrease after training compared to pre-training in alkaline phosphatase values in all groups, i.e. practice-supplement (P <0.001), practice-placebo (P <0.05), supplement (P <0.01), and placebo groups (P <0.01).

Discussion and Conclusion

This study was conducted on 48 amphetamine addicts who were on the verge of abstinence in order to examine hematological factors and hepatic enzymes after eight weeks of combined exercise with and without cinnamon supplementation. The results of the study showed no significant difference in the hematologic factors among the groups. However, the white blood cells showed a significant

decrease after the training and exercise in the placebo, supplement, practice-supplement, and practice-placebo groups. Also, red blood cells and hematocrit showed a significant decrease in the supplement group. The research findings indicate that the proposed training did not create any change in the hematologic factors except in white blood cells.

Patlar & Keskin stated that exercise and training under the maximum level did not significantly change the average corpuscular volume, the concentration of hemoglobin, and red blood cells, which is consistent with the findings of the present study (Patallar & Kaskin, 2007). Mousavizadeh et al. (2009) observed a significant decrease in hemoglobin, red blood cells, and hematocrit in studying the effect of aerobic training on hematological indices of students. Ghanbari Niaki & Mohammadi (2010) reported that the anaerobic RAST activity increases the hemoglobin and red blood cells, which is not consistent with the findings of the present study. Ahmadizad, & Besami (2010) also observed a significant increase in the number of platelets and plasma volume and a significant reduction in hematocrit after three types of resistance activities, which is not consistent with the results of the present study.

Decreased hemoglobin and hematocrit concentrations due to exercise is associated with increased plasma volume. This condition causes the blood to be diluted and improves blood flow properties (Szygula, 1990). The destruction of red blood cells and hemoglobin is known as hemoglobin trauma where the following factors speed up its degradation: 1. RBC life, 2. Physical and body pressure, 3. Red blood cell deformation, 4. Red blood cell concentration, 5. Increased temperature, 6. Decreased blood glucose (Requena, 2017).

Based on the findings of this study, the plasma volume in the exercise group increased by 1.65%. The factors contributing to the increase of plasma volume include exercise intensity, exercise duration, repetition of exercises, and level of individuals' readiness (Bejder, Andersen, Goetze, Aachmann-Andersen, & Nordsborg, 2017; Afolabi et al., 2016). Exercise intensity is likely to be the main driver of increased plasma volume arising from exercise. The increase in plasma volume occurs mainly due to two mechanisms. First, exercise and practice increase the secretion of antidiuretic hormone (ADH) and aldosterone, which causes water retention by the kidneys and results in increased blood plasma levels. Second, exercise increases the amount of plasma protein, especially albumin, and whenever plasma protein concentrations increase, osmotic pressure increases and, thereby, the binding of water molecules to them occurs late in the recovery period. As a result, more liquid remains in the blood and these two mechanisms together increase blood plasma levels. Due to increased plasma volume and reduced hemoglobin and hematocrit, blood viscosity level decreases. The reduction of blood viscosity is beneficial because the blood performs the responsibility of its own transfusion well due to the ease of flow in the vessel (Bejder et al., 2017; Afolabi et al., 2016). On the other hand, the intake of some foods and medicine, such as cinnamon can facilitate blood circulation

(Vahidi et al., 2012). According to the findings of this study, this influence can be due to increased plasma volume and hematocrit, which requires doing more research to achieve definite results on the mechanism of the effect of cinnamon on blood circulation facilitation.

The results of the present study showed no significant difference between the groups in terms of liver enzymes, i.e. aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase. However, the alkaline phosphatase enzyme significantly decreased in all groups. Liver tissue is one of the organs that is constantly in contact with toxic compounds because of its ability to neutralize toxic substances or to change their biological form. It should be kept in mind that the liver's ability in metabolic changes is limited; thus, if the encounter of liver tissues with different toxins is more than a certain amount that cannot excrete it in some way, it will inevitably cause abnormalities in the structure and function of the liver (Valente et al., 2016). Amphetamines appear to lower cells, including hepatocytes. This combination damages DNA and leads to a decrease in energy production due to a defect in the function of mitochondrial enzymes, the increased activity of lysozyme enzymes, and the oxidation of cytoplasmic proteins. Therefore, it can lead hepatocyte cells to death (Valente et al., 2016; Montiel-Duarte et al., 2002).

Aminotransferases are normally present in liver cells; therefore, they are released with the membrane damage and cell death, which can be a sign of liver tissue damage (Fatahi, Forouzanfar, & Bagheri Haghighi, 2012). In this regard, Bagheri Haghighi, Fattahi, Forouzanfar, & Reza'ea Jahromi (2012) examined the effect of different doses of amphetamines on liver cells of Wistar rats for two weeks and showed that hepatocyte cells in the experimental group underwent damage and reduction. Accordingly, in the present study, participants have probably experienced damage hepatic cells and a decrease in the hepatic enzymes during the study period since they were on the verge of withdrawal from drug use.

In the present study, in the practice-placebo group, the levels of aspartate aminotransferase and alanine aminotransferase increased significantly. In this regard, Asad et al. investigated the effect of eight weeks of endurance training on liver enzymes in female addicts under methadone maintenance treatment and showed that endurance training had no significant effect on the levels of aspartate aminotransferase and alanine aminotransferase (Asad, Haddadi, Nejad, & Soukhteh Zari, 2013). However, Davoudi, Mousavi, & Nikbakht (2012) concluded that eight weeks of aerobic and endurance exercise training could reduce liver enzymes and liver parenchymal density and could prevent the malignancy while these findings are not consistent with those of the present research.

Also, in the present study, liver enzymes of aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase in the supplement group were reduced by 28%, 17%, and 31%, respectively; in addition, aspartate

aminotransferase and alkaline phosphatase decreased significantly in this group. The results of this study are consistent with those of the study carried out by Askari et al. (2014) where the reduction of plasma levels of liver enzymes after the daily intake of 1500 milligrams of cinnamon in patients with fatty liver. Cinnamon supplement has phenolic and non-phenolic compounds, such as cinnamic acid derivatives and coumarins, and it also has antioxidant properties. These compounds act as regenerative agents, or as potent inhibitors of peroxide radicals, and prevent oxidative reactions. Cinnamon has an inhibitory effect on the hepatocyte oxidation system and prevents the destruction of liver cells and reduces the release of liver enzymes into the circulation (Kemali Rousta, Ghavami, Elhami Rad, & Azizinejad, 2014).

This research suffered from some limitations, such as no control of participants' stress, mental conditions, and the rate of smoking. It is suggested that future research employ groups with different doses of cinnamon supplementation and various sports exercises (endurance and resistance). Regarding the findings of this study, it can generally be concluded that combined exercise with cinnamon supplementation can reduce the white blood cells and liver enzymes of aspartate aminotransferase and alkaline phosphatase in amphetamine addicted women.

Reference

Afolabi, B. B., Oladipo, O. O., Akanmu, A. S., Abudu, O. O., Sofola, O. A., & Broughton Pipkin, F. (2016). Volume regulatory hormones and plasma volume in pregnant women with sickle cell disorder. *Journal of the Renin-Angiotensin-Aldosterone System*, *17*(3), 1470320316670444.

Ahmadizad, S., & Bassami, M. (2010). Interaction effects of time of day and sub-maximal treadmill exercise on the main determinants of blood fluidity. *Clinical hemorheology and microcirculation*, *45*(2-4), 177-184.

Arazi, H., Jourbonian, A., & Asghari, E. (2012). Comparison of Concurrent (Resistance-Aerobic) and Aerobic Training on VO2max Lipid Profile, Blood Glucose and Blood Pressure in Middle Aged Men at Risk for Cardiovascular Disease, *Journal of Shahid Sadoughi University of Medical Sciences*, 20 (5), 627-638.

Asad, M. R., Haddadi, F., Nejad, M. R., & Sokhtehzari, S. (2013). Effect of eight weeks endurance exercise on liver enzymes in stopping drug women with methadone. *Journal of Paramedical Sciences*, 4(2), 68-71.

Askari, F., Rashidkhani, B., & Hekmatdoost, A. (2014). Cinnamon may have therapeutic benefits on lipid profile, liver enzymes, insulin resistance, and high-sensitivity C-reactive protein in nonalcoholic fatty liver disease patients. *Nutrition research*, *34*(2), 143-148.

Bagheri Haghighi, A., Fattahi, E., Foruzanfar, M., & Hemayatkhah Jahromi, V. (2012). Evaluation of the Effect of 3.4-Methylindiax-Amphetamine (Ecstasy) on the Hepatic Textural Structure in Rats, *Journal of Semnan Medical Sciences University*, 13 (3), 368-375.

Baker, W. L., Gutierrez-Williams, G., White, C. M., Kluger, J., & Coleman, C. I. (2008). Effect of cinnamon on glucose control and lipid parameters. *Diabetes care*, *31*(1), 41-43.

Bamdad, M., Fallahi Khoshkanab, M., Dalvandi A., & Khodayi Ardakani, M. (2013). Impact of Spiritual Care on Spiritual Health of hospitalized Amphetamine Dependents, *Journal of Psychiatric Nursing, 1* (3), 10-18.

Bejder, J., Andersen, A. B., Goetze, J. P., Aachmann-Andersen, N. J., & Nordsborg, N. B. (2017). Plasma volume reduction and hematological fluctuations in high-level athletes after an increased training load. *Scandinavian journal of medicine & science in sports*, *27*(12), 1605-1615.

Davoudi, M., Mousavi, H., & Nikbakht, M. (2012). The effect of eight weeks of endurance training on liver parenchyma and hepatic enzymes, *Journal of Shahrekord University of Medical Sciences*, 14 (10), 84-90.

Dill, D. B., & Costill, D. L. (1974). Calculation of percentage changes in volumes of blood, plasma, and red cells in dehydration. *Journal of applied physiology*, *37*(2), 247-248.

Dubnov, G., & Constantini, N. W. (2004). Prevalence of iron depletion and anemia in top-level basketball players. *International journal of sport nutrition and exercise metabolism*, *14*(1), 30-37.

Farzad, B., Gharakhanlou, R., Bayati, M., Agha Ali Nejad, H., Bahraminejad, M., Mehrabian, F., & Plouyi, E. (2011). Effect of Severe Periodic Exercise Period on Aerobic, Anaerobic, and Hematological Indicators of Athletic Performance, *Journal of Research in Sports Sciences*, 10, 69-88.

Fattahi, E., Foruzanfar, M., & Bagheri Haghighi, A. (2012). Effect of Methylene Dioxymetamutamin on Hepatocytes and Alanine Aminotransferase Enzyme, Aspartate Aminotransferase, and Alkaline Phosphatase in Rats, *Journal of Gorgan University of Medical Sciences*, 14 (4), 24-30.

Fontes-Ribeiro, C., Marques, E., C Pereira, F., P Silva, A., & RA Macedo, T. (2011). May exercise prevent addiction?. *Current neuropharmacology*, *9*(1), 45-48.

Ghanbari Niaki, A., & Mohammadi, S. (2010). Effect of 4 weeks of RAST Anaerobic Exercise on Hematological Changes in Male Cake Boxers, *Journal of Research in Sports Sciences*, 5 (10), 75-87.

Giannini, E. G., Testa, R., & Savarino, V. (2005). Liver enzyme alteration: a guide for clinicians. *Canadian medical association journal*, *172*(3), 367-379.

Hosseini, M., Alaei, H. A., Naderi, A., Sharifi, M. R., & Zahed, R. (2009). Treadmill exercise reduces self-administration of morphine in male rats. *Pathophysiology*, *16*(1), 3-7.

Kamali Roosta, L., Ghavami, M., Elhami Rad, A., & Azizi-Nejad, R. (2014). Antioxidant and Chelating Extract of Cinnamon Extract, *Journal of Food Technology & Nutrition*, 11 (2), 37-46.

Karam, G. A., Reisi, M., Kaseb, A. A., Khaksari, M., Mohammadi, A., & Mahmoodi, M. (2004). Effects of opium addiction on some serum factors in addicts with non-insulin-dependent diabetes mellitus. *Addiction biology*, *9*(1), 53-58.

Larson-Meyer, D. E., Newcomer, B. R., Heilbronn, L. K., Volaufova, J., Smith, S. R., Alfonso, A. J., & Ravussin, E. (2008). Effect of 6-month calorie restriction and exercise on serum and liver lipids and markers of liver function. *Obesity*, *16*(6), 1355-1362.

Lawlor, D. A., Sattar, N., Smith, G. D., & Ebrahim, S. (2005). The associations of physical activity and adiposity with alanine aminotransferase and gamma-glutamyltransferase. *American journal of epidemiology*, *161*(11), 1081-1088.

Mir, E., Attarzadeh Hosseini, R., Mirsa'eadi, M., & Hejazi, K. (2016). Effects of Eight Weeks Selected Combined Exercises on Humoral Immune and Hematological Index in Inactive Older Men, *Iranian Journal of Aging*, 11 (1), 20-29.

Mirfeizi, M., Mehdizadeh Tourzani, Z., Mirfeizi, Z., Asghari Jafar-Abadi, M., Rezvani, H., & Shoghi, M. (2014). The Effect of Cinnamon on Blood Glucose and Blood Flow Control in Patients with Type 2 Diabetes: a Double-Blind Clinical Trial, *Journal of Mashhad University of Medical Sciences*, 57 (3), 533-541.

Montiel-Duarte, C., Varela-Rey, M., Osés-Prieto, J. A., López-Zabalza, M. J., Beitia, G., Cenarruzabeitia, E., & Iraburu, M. J. (2002). 3, 4-Methylenedioxymethamphetamine ("Ecstasy") induces apoptosis of cultured rat liver cells. *Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease*, *1588*(1), 26-32.

Mousavizadeh, M., Ebrahimi, K., & Nikbakht, H. (2009). Effect of an Aerobic Exercise Course on Hematological Indices of Female Students, *Scientific Journal of Iranian Blood Transfusion Organization*, 6 (3), 227-231.

Paranagama, P. A., Wimalasena, S., Jayatilake, G. S., Jayawardena, A. L., Senanayake, U. M., & Mubarak, A. M. (2001). A comparison of essential oil constituents of bark, leaf, root and fruit of cinnamon (Cinnamomum zeylanicum Blum) grown in Sri Lanka. *Journal of the National Science Foundation of Sri Lanka*, *29*(3-4).

Patlar, S., & Keskin, E. (2007). The effects of glycerol supplement on various hematologic parameters in sedentariness and the athletes who exercise regularly. *Exercise*, *1*, 23-35.

Requena, B., García, I., Suárez-Arrones, L., de Villarreal, E. S., Orellana, J. N., & Santalla, A. (2017). Off-season effects on functional performance, body composition, and blood parameters in top-level professional soccer players. *The Journal of Strength & Conditioning Research*, *31*(4), 939-946.

Rose, J. O. H. A. N. N. E. (1999). Herbal and nutritional support for the immune system. *Clinical Nutrition Insight*, *6*(2), 1-4.

Skenderi, K. P., Kavouras, S. A., Anastasiou, C. A., Yiannakouris, N., & Matalas, A. L. (2006). Exertional rhabdomyolysis during a 246-km continuous running race. *Medicine & Science in Sports & Exercise*, *38*(6), 1054-1057.

Suzuki, A., Lindor, K., St Saver, J., Lymp, J., Mendes, F., Muto, A., & Angulo, P. (2005). Effect of changes on body weight and lifestyle in nonalcoholic fatty liver disease. *Journal of hematology*, *43*(6), 1060-1066.

Szygula, Z. (1990). Erythrocytic system under the influence of physical exercise and training. *Sports Medicine*, *10*(3), 181-197.

Vafamand, E., Kargarfard, M., & Marandi, M. (2012). Effect of eight-week aerobic training on serotonin and dopamine levels in addicted women in Isfahan Central Prison, *Journal of Isfahan Medical School*, 30 (204), 1336-1347.

Vahidi, A., Dashti, M. H., Mojdeh, M., & Soltani, H. R. (2012). Effects of cinnamon on learning and short memory in mice. *Medical Science Journal of Islamic Azad University-Tehran Medical Branch*, *22*(2), 105-109.

Valente, M. J., Araújo, A. M., Silva, R., de Lourdes Bastos, M., Carvalho, F., De Pinho, P. G., & Carvalho, M. (2016). 3, 4-Methylenedioxypyrovalerone (MDPV): in vitro mechanisms of hepatotoxicity under normothermic and hyperthermic conditions. *Archives of toxicology*, *90*(8), 1959-1973.

Vozarova, B., Stefan, N., Lindsay, R. S., Saremi, A., Pratley, R. E., Bogardus, C., & Tataranni, P. A. (2002). High alanine aminotransferase is associated with decreased hepatic insulin sensitivity and predicts the development of type 2 diabetes. *Diabetes*, *51*(6), 1889-1895.

Wainstein, J., Stern, N., Heller, S., & Boaz, M. (2011). Dietary cinnamon supplementation and changes in systolic blood pressure in subjects with type 2 diabetes. *Journal of medicinal food*, *14*(12), 1505-1510.