Effect of endurance training with selenium on IL-17 and IL-18 in heart tissue in rats exposed to cadmium poisoning

Efecto del entrenamiento de resistencia con selenio en IL-17 e IL-18 en tejido cardíaco en ratas expuestas a envenenamiento por cadmio

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Abstract

Interleukin-17 (IL-17) and interleukin-18 (IL-18) are Proinflammatory cytokines. The main purpose of this study is analysis of the effect of endurance training, along with using selenium, on IL-17 and IL-18 in heart tissue of rats exposed to cadmium poisoning. in this empirical study, 30 Sprague Dawley male Rats were selected and placed randomly in 6 groups with 5 rats in each group: 1) control 2) sham 3) cadmium 4) selenium with cadmium 5) endurance training with cadmium and 6) endurance training with selenium and cadmium. During 8 weeks, the rats in groups 3, 4, 5 and 6 took 2mg/kg peritoneum cadmium daily. Groups 4 and 6 used 0.23mg/kg selenium daily and groups 5 and 6 done endurance practices 3 sessions per week. For analysis of the data, Kolmogorov-Smirnov test, independent t-test and two-way ANOVA were used (p≤0.05). 8 weeks of endurance training and 8 weeks of using selenium could leave significant effect on reduction of IL-17 and IL-18 expression of rats poisoned by cadmium (p=0.001). Moreover, the interactive effect of endurance training and using selenium on reduction of IL-17 and IL_18 expression in rats poisoned by cadmium was significant (p=0.001). 8 weeks of using selenium with endurance training could improve proinflammatory cytokines in rats poisoned with cadmium.

Keywords: cadmium, endurance training, selenium, IL-17, IL-18.

Resumen

La interleucina-17 (IL-17) y la interleucina-18 (IL-18) son citocinas proinflamatorias. El objetivo principal de este estudio es el análisis del efecto del entrenamiento de resistencia, junto con el uso de selenio, en IL-17 e IL-18 en tejido cardíaco de ratas expuestas a envenenamiento por cadmio. En este estudio empírico, se seleccionaron 30 ratas macho Sprague Dawley y se colocaron al azar en 6 grupos con 5 ratas en cada grupo: 1) control 2) simulacro 3) cadmio 4) selenio con cadmio 5) entrenamiento de resistencia con cadmio y 6) entrenamiento de resistencia con selenio y cadmio. Durante 8 semanas, las ratas en los grupos 3, 4, 5 y 6 tomaron 2 mg / kg de peritoneo cadmio diariamente. Los grupos 4 y 6 usaron 0.23mg / kg de selenio diariamente y los grupos 5 y 6 realizaron prácticas de resistencia 3 sesiones por semana. Para el análisis de los datos, se utilizaron la prueba de Kolmogorov-Smirnov, la prueba t independiente y el ANOVA de dos vías (p≤0.05). 8 semanas de entrenamiento de resistencia y 8 semanas de uso de selenio podrían dejar un efecto significativo en la reducción de la expresión de IL-17 e IL-18 de ratas envenenadas por cadmio (p = 0.001). Además, el efecto interactivo del entrenamiento de resistencia y el uso de selenio en la reducción de la expresión de IL-17 e IL_18 en ratas envenenadas por cadmio fue significativo (p=0,001). 8 semanas de uso de selenio con entrenamiento de resistencia podrían mejorar las citocinas proinflamatorias en ratas envenenadas con cadmio.

Palabras clave: cadmio, entrenamiento de resistencia, selenio, IL-17, IL-18.

Today, environmental pollution is one of the main problems of human health at industrial and developed countries. Wide spread studies show that exposition to air pollution and inhale of heavy metals in the air and using foods poisoned by these materials can cause worsening of inflammation in hear and vessels and ultimately, cardiovascular diseases and even death[1,2]. Moreover, toxic effects of the heavy metals may cause dysfunction in different tracts of body such as cardiovascular system through production of free radicals and as a result of increasing inflammation[1,3]. In fact, one of the factors increasing inflammation and causing spread of cardiovascular diseases can be the cadmium in the air and soil[4]. In fact, evidences show that exposition to cadmium is correlated to increased risk of cardiovascular diseases including high blood pressure and heart tissue damage[5]. The products containing cadmium including batteries, electronic devices, jewelry and toys and the fertilizers containing cadmium endanger people through the soil and food[6,7]. According to the investigations, in people with inflammatory cardiovascular diseases, the cadmium content is very high[8].cadmium can increases the amount of inflammatory cytokines like interleukins, which can develop the atherogenic plaques in coroner arteries[9]. With regard to harmful effects of cadmium on cardiovascular tract and increasing rise of possibility of exposition to air pollution on one hand and the effect of incorrect lifestyle including inactivity[10] and inadequate nutrition exposed to soil and fertilizers contaminated by cadmium[11,12] on the other hand; different strategies have been provided by scholars to neutralize damaging effects of cadmium on inflammation in cardiovascular system. In other words, many studies have revealed that nutrition and physical practice can have effective role in improvement of inflammation caused by cadmium[13-17,18-20]. In fact, some food supplements can neutralize the inflammatory effects of cadmium. One of the supplements with opposite effect of cadmium, which can decrease its harmful effects, can be selenium[13]. In some studies, it has been referred that selenium can neutralize negative effects of cadmium. Moreover, it has been emphasized in a study that people exposed to forcible intake of cadmium can reduce the level of this poison in different tissues by taking selenium in specific rate[13]. Furthermore, Chen et al found in a study that selenium can decrease negative effects of cadmium through empowering the antioxidant system[14]. On the other hand, Abdolhafez et al took wide range studies and mentioned that using selenium as a medicine can effectively improve oxidative pressure, inflammation and common disorders relevant to inhale of heavy metals in the air. In fact, they remind that selenium contains a strong therapeutic potential to be used to treat heart and respiratory inflammatory diseases[15]. Moreover, selenium can decrease inflammatory cytokines like interleukin-17 (IL-17) and interleukin-18 (IL-18) induced by heavy metals such as lead (pb) and cadmium (Cd)[16]. Sung et al conducted a study on rats and found that selenium can act as a strong inhibitory substance for inflammation through decreasing IL-18 gene expression[17].

Recent studies have shown that inflammation plays key role in Coronary artery disease (CAD). Moreover, inflammation can increase two inflammatory factors including IL-17 and IL-18 in heart tissue, which can be a factor for progress of inflammation and cardiovascular diseases in different people. Moreover, the amount of IL-18 in majority of cardiovascular patients is in high level, which can show its direct relation with cardiovascular diseases[21]. Another inflammatory cytokine playing key role in cardiovascular diseases is IL-17. The IL-17 is a proinflammatory cytokine derived from CD4; although it could be mentioned that can play key role in progress of inflammatory diseases in tissue[22].

In addition to food supplements, physical activity can be considered as a known and applied method to decrease inflammation and to decrease risk of cardiovascular diseases[23]. Blair et al have reported that regular physical activity and sport can be in reverse correlation with blood levels of inflammatory markers and can remove chronic inflammation[18]. Additionally, Kohut et al suggested that type of activity can affect inflammatory mediators and can decrease the serum IL-18 as a result of regular aerobic practices compared to flexibility[19]. At the same time, Lingard et al observed reduction of serum IL-18 after 8 weeks of endurance practices[20]. In a study, Duzova H et al studied the effect of two types of training plan of running on treadmill (Extreme Exercise at 85% Max. Oxygen Consumption with Slope and Exercise Style: 50 to 60% Maximum Oxygen Consumption without Tilt) and found that the level of the cytokine after 8 weeks was increased in those using extreme exercise and no change was observed in the other group[24]. Tasha et al found in a study (2017) that taking physical practices, along with intake of an antioxidant supplement, can cause protection of heart tissue against cadmium harmful effects[25]. At last, it should be mentioned that majority of studies have separately studied the effects of selenium[16,17] and sport activities[18-20] on levels of IL-17 and IL-18 in situations of exposing to cadmium. However, according to the previous studies, no study was found on analysis of interactive effects of the two factors. According to harmful effects of cadmium, the present study is aimed that analysis of interactive effects of endurance training and using selenium on decreasing inflammation in heart tissue of rats poisoned by cadmium.

Methods

This study is an empirical research. In order to implement this study, 30 Sprague Dawley male Rats with approximate age of 8 weeks were bought from Shiraz Institute pasture and were then transferred to the sport physiology lab of Islamic Azad University, Marvdasht Branch. After 1 week of adjustment with laboratory environment, rats were placed in 6 groups with 5 rats in each group: 1) control 2) sham 3) cadmium 4) selenium with cadmium 5) endurance training with cadmium and 6) endurance training with selenium and cadmium. The study duration was 8 weeks. During the 8 weeks, groups 3, 4, 5 and 6 took 2mg/kg peritoneum cadmium daily[26]. Groups 4 and 6 used 0.23mg/kg selenium daily[27] and groups 5 and 6 done endurance practices 3 sessions per week[28]. It should be mentioned that rats in group 2 took the peritoneum cadmium in whole study period.

The protocol of endurance training included 60 minutes running on treadmill with speed of 65-75% and maximum oxygen intake for 8 weeks and 3 sessions per week. The protocol of endurance training was as follows: the rats used to take warm up on treadmill in each session for 5 minutes with speed of 50-60% and maximum oxygen intake. Then, they took endurance practices with intensity of 65% and maximum speed in week 1; 70% maximum speed in week 2; 75% and maximum speed from week 3. At the end, rats cooled 5 minutes with intensity of 50-60% and maximum oxygen intake. At the first, to determine maximum oxygen intake, Bedford (1979) standard test was used[29]. This test contains 10 steps with 3 minutes in each step. The speed in step 1 was equal to 0.3km/h and 0.3km/h speed was added to the treadmill in next steps; although slope was equal to 0 in all steps. In each step of test that rats were unable to continue, speed in that step was considered equal to speed of animal in maximum oxygen intake. At the end of study period, 48hrs after last practice session, rats were anesthetized by ketamine and xylacin and their heart tissue was taken to measure research variables.

For molecular analysis in gene expression level, the RNA was firstly extracted from the heart tissue based on the protocol of the company (Sinagen, Iran). Then using light adsorption property along wavelength of 260nm and using the following equation, the density and the purity of RNA sample was obtained quantitatively.

$C\ (\mu g/\mu l) = A260\times \varepsilon\times d/1000$

After RNA extraction with high purity and density, cDNA synthesis was done for all samples based on manufacturing company and then, the synthesized cDNA was used to take reverse transcription reaction. At the first, the designed primers relevant to genes were studied. Then, analysis of gene expression was done using PCR q-RT quantitative method. The sequence of primers used in the study includes:

IL-17 (f)	CCGTTCCACTTCACCCTG
IL-17 (r)	GTCCAACTTCCCCTCAGC
IL-18 (f)	ATGTCTACCCTCTCCTGT
IL-18 (r)	TTCCATTTTGTTGTGTCCTG

For purpose of analysis of research data, SPSS software and Kolmogorov-Smirnov test and independent t-test and also two-way ANOVA were used ($p\leq0.05$).

Results

In table 1, the amount of IL-17 and IL-18 gene expression is presented in 6 study groups. In table 2, results of independent t-test show significant difference in amount of Il-17 gene expression (t=-0.24 and p=0.81) and IL-18 (t=1.58 and p=0.15) between control and sham groups. Moreover, the results show that expression of IL-17 (t=11.43, p=0.001) and IL-18 (t=4.50, p=0.002) in cadmium group is significantly higher than control group. The results of two-way ANOVA in table 3 show that 8 weeks of endurance training can have significant effect on decreased expression of IL-17 (F=83.17 and p=0.001) with impact level of 0.83 and IL-18 (F=19.82 and p=0.001) with impact level of 0.55 in rats poisoned by cadmium. 8 weeks of using selenium could have significant effect on reduction of IL-17 gene expression (F=110.28, p=0.001 with impact level of 0.87) and IL-18 (F=21.21, p=0.001 with impact level of 0.57) in rats poisoned with cadmium. Moreover, the interactive effect of endurance training and using selenium on decreased expression of IL-17 (F=90.88, p=0.001 with impact level of 0.85) and IL-18 (F=18.61, p=0.001 with impact level of 0.53) was significant on rats poisoned by cadmium.

Table 1. IL-17 and IL-18 gene expression level in 6 groups

Variable Group	IL-17 (M±SD)	IL-18 (M±SD)
Control	0.0144±0.0041	0.0053±0.0003
Sham	0.0152±0.0068	0.0047±0.0007
Cadmium	0.8128±0.1561	0.9134±0.4506
Selenium and cadmium	0.0259±0.0073	0.0144±0.0045
Endurance training and cadmium	0.0802±0.0797	0.0298±0.0076
Endurance training and selenium and cadmium	0.0421±0.0079	0.0005±0.0001

Table 2. Results of independent t-test to compare IL-17 and IL-17 expression in control, sham and cadmium groups

Group		Variable value	T	Df	Sig
Control	Cadmium	IL-17	11.43	8	0.001
		Il-18	4.50	8	0.002
	Sham	IL-17	-0.24	8	0.81
		IL-18	1.58	8	0.15

Table 3. Results of two-way ANOVA to analyze the effects of endurance training and using selenium on expression of IL-17 and IL-18 in rats poisoned with cadmium

Variable	Value factor	F	Sig	Impact level
IL-17	Training	63.17	0.001	0.83
	Selenium	110.28	0.001	0.87
	Endurance training and selenium	90.88	0.001	0.85
IL-18	Endurance training	19.82	0.001	0.55
	Selenium	21.21	0.001	0.57
	Endurance training and selenium	18.61	0.001	0.53

Discussion

The results obtained from this study show that both endurance training and using selenium can cause significant decrease in Il-17 and IL-18 in heart tissue of rats poisoned with cadmium. In fact, this study showed that endurance training can cause significant decrease in IL-17 and IL-18, which is not in consistence with results of some studies. Leick et al (1007) reported increased level of Il-18 in obese women and men after 8 weeks of endurance practices with intensity of 70% with maximum oxygen consumption[30]. At the same time, the effect of intensity of practice on IL-17 and IL-18 in some studies can be considered as an important factor. For example, in a study conducted by Duzova H et al, the effect of two types of running practice on treadmill (practice with speed of 85% and maximum oxygen use with slope and light practice: 50-60% maximum oxygen use) was studied. They found that after 8 weeks training, level of the cytokines in groups with endurance training was increased; although no significant change was observed in another group[24].

Golzari et al found that using 8 weeks of combined endurance and strengthening training can't increase Il-17 level and was even decreased in some people, which was as a result of low intensity of practices[31]. On the contrary, Tofighi et al mentioned after a semi-empirical study that intense practices could have no significant effect on IL-17 levels compared to the time before practice and the reason was short time of practices[32]. Therefore, another important factor in secretion of these cytokines can be also the training time. In fact, majority of studies have reported increased of the cytokine and the mechanism is probably relevant to intensity of sport practices, which can cause release of proinflammatory cytokines through leucocytes and skeleton muscles. On the other hand, the Kohut et al found in their study that taking aerobic practices can decrease IL-18 levels[20]. Moreover, Lindegaard et al found after implementation of a protocol of aerobic practices with average intensity that these practices can significantly decrease level of inflammatory cytokines such as IL-17[21]. Also, it has been mentioned in some studies that endurance practices under maximum can adjust the negative effects of cadmium in the body and can protect heart tissue[25]. Additionally, Mirdar et al conducted a study on fertile rats poisoned by cadmium and found that taking endurance training of swimming can cause significant reduction of cadmium in the body of these animals, which can decrease liver and cardiovascular risk[33]. This means that type of intensity and the time of aerobic practices, which was almost long-time and with average intensity in this study, can be significant factors in reducing inflammatory cytokines caused by environmental pollution such as exposition to cadmium. Tofighi et al conducted a semi-empirical study and claimed that severe practices can have no significant effect on IL-17 levels compared to the time before practice, which was because of short time of practices[32].

Therefore, another important factor in secretion of these cytokines can be the practicing time. In fact, majority of studies have reported increase in the said cytokine and the mechanism is probably because of intensity of sport practices, which can release proinflammatory cytokines and anti-inflammatory cytokines through leucocytes and skeleton muscles[34]. Moreover, the gene expression of Il-17 and IL-18 was significantly decreased in this study in the groups using selenium, which can be a positive sign of effectiveness of selenium in improvement of cardiovascular inflammation caused by forcible use of cadmium metal. In reality, some studies have emphasized that people exposed to forcible intake of cadmium can decrease the cadmium content in different tissues through getting specific amount of selenium[14]. Selenium has antioxidant and anti-inflammatory impacts and can improve immune system[35]. Moreover, selenium can decrease inflammatory cytokines induced by heavy metals such as Pb and Cd[36]. Furthermore, selenium can somehow cause reduction of toxicity of immune system induced by cadmium through expression of immune cytokines[37]. Selenium can decrease toxicity induced by medicines and heavy metals such as cadmium[38]. Also, some studies have referred that selenium can decrease infalammatory cytokines induced by cadmium such as Il-17 and IL-18 through reducing the cadmium content in heart tissue[39]. Moreover, Alizadeh et

al found that using antioxidant supplements, along with continuous endurance training, can regulate the inflammatory responses through suppression of CK, CRP and IL-17; which can be usually increased as a result of severe practices[40]. Therefore, endurance training and using selenium in people who have to inhale cadmium can decrease activity of inflammatory cytokines[41].

Moreover, this study has analyzed the interactive effect of endurance training with using selenium on levels of IL-17 and IL-18 and results showed significant reduction of levels of the two said cytokines in heart tissue of rats poisoned by cadmium it seems that aerobic activity can decrease activity of inflammatory cytokines through its antioxidant mechanisms with increasing antioxidant enzymes on one hand[41,43] and selenium has been introduced as a part of activation system of antioxidant system on the other hand. In fact, selenium is a part of glutathione peroxidase enzyme[44], which can protect heart against oxdative pressure and ultimately, heart tissue inflammation[45]. In reality, selenium plays regulative role in inflammatory anti-oxidative system[46]. Moreover, selenium can decrease inflammation in different tissues such as heart through affecting P38MAPK path[47]. As a result, with activation of anti-inflammatory enzymes such as glutathione peroxidase, the inflammatory cytokines can be decreased in heart tissue of rats[47-49]. At last, despite to all controls on gender, race and weight of animals; environmental factors (e.g. light, temperature and noise, …), training plan and food of animals; lack of measurement of cadmium absorption rate and selenium in heart tissue and lack of controlling night activity can be limitations in this study. Despite to mentioned, according to forcible intake of cadmium in the air and foods and destructive effects of that on health of heart tissue; scholars should pay attention to controlled analysis of cost-effective and safe non-pharmaceutical strategies like HIIT practices and herbal antioxidant supplements, especially in presence of other pollutants in animal treatments for long time as fundamental research to take further human studies[50-53].

Conclusions

The results obtained from this study showed that taking regular aerobic practices, along with using selenium antioxidant supplement, can cause significant decrease in IL-17 and IL-18 levels, which can increase inflammation as a result of intake of cadmium. Therefore, such practices, along with using selenium, can protect heart tissue against the inflammation caused by intake of cadmium.

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References

1. Gurer H, Ercal N. Can antioxidants be beneficial in treatment of lead poisoning? Free Radic Biol Med 2000; 29(10): 927–945.
2. Simkhovich BZ, Kleinman MT, Kloner RA. Air Pollution and Cardiovascular Injury. Epidemiology, Toxicology, and Mechanisms. Jam Coll Cardiol 2008; 52(9): 719-726.
3. Ademuyiwa O, Agarwal R, Chandra R, Behari JR. Lead-induced phospholipidosis and cholesterolgenesis in rat tissues. Chem Biol Interact 2009; 179: 314–320.
4. Christopher JK, Hame tt, Prapavessis H, Chris Bald J, Varo N, Schoenbeck V, et al. Effects of exercise training on 5 inflammatory markers associated with cardiovascular risk. American heart J 2006; 151(2): 367-387.
5. Puri VN. Cadmium induced hypertension. Clin Exp Hypertens 1999; 21: 79-84.
6. Ding YH, Young CN, Luan X, Li J, Rafols JA, Clark JC, et al. Exercise preconditioning ameliorates inflammatory injury in ischemic rats during reperfusion. Acta neuropathol (Berl) 2005; 109(3):237-46.
7. Laura E, Dick S, Paul L, Erik S. Exercise, cognition and Alzheimer's disease: More is not necessarily better. Neurosci Biobehav Rev 2006; 30: 562–575.
8. Aggarwal BB, Harikumar KB. Potential therapeutic effects of curcumin, the antiinflammatory agent, against neurodegenerative, cardiovascular, pulmonary, metabolic, utoimmune and neoplastic diseases. Int J Biochem Cell Biol 2009; 41(1):40-59.
9. Anthony Z, Eza L, Bagus PPW, Xin J, Komang S, Grace DS. High Dietary Taurine Reduces Apoptosis and Atherosclerosis in the Left Main Coronary Artery; Association With Reduced CCAAT/Enhancer Binding Protein Homologous Protein and Total Plasma Homocysteine but not Lipidemia. Hypertension 2009; 53: 1017-1022.
10. Jarup L, Akesson A. Current status of cadmium as an environmental health problem. Toxicol Appl Pharmacol 2009; 238: 201-208.
11. Subramanyam G, Bhaskar M, Govindappa S. The role of cadmium in induction of atherosclerosis in rabbits. Indian Heart J 1992; 44: 177–180.
12. Mlynek V, Skoczyńska A. The proinflammatory activity of cadmium. Postepy Hig Med Dosw 2005; 59: 1-8.
13. Kippler M, Lonnerdal B, Goessler W. Cadmium interacts with the transport of essential micronutrients in the mammary gland—a study in rural Bangladeshi women. Toxicology 2009; 257(1–2):64–9.
14. Chen M, Li X, Fan R, Cao C, Yao H, Xu S. Selenium antagonizes cadmium-induced apoptosis in chicken spleen but not involving Nrf2-regulated antioxidant response. Ecotoxicol Environ Saf 2017; 4(145):503-510
15. Abedelhaffez A, El-Aziz E, Abdel Aziz M, Ahmed A. Lung injury induced by Bisphenol A: A food contaminant, is ameliorated by selenium supplementation. Pathophysiology 2017; 24:81–89
16. Sun GX, Chen Y, Liu CP, Li S, Fu J. Effect of Selenium Against Lead-Induced Damage on the Gene Expression of Heat Shock Proteins and Inflammatory Cytokines in Peripheral Blood Lymphocytes of Chickens. Biol Trace Elem Res 2016; 172: 474–480.
17. Song H, Kim J, Lee HK, Park HJ, Nam J, Park GB, Kim YS, et al. Selenium inhibits migration of murine melanoma cells via down-modulation of IL-18 expression. Int Immunopharmacol 2011; 11(12): 2208-13.
18. Blair SN, Cheng Y, Holder JS. Is physical activity or physical fitness more

important in defining health benefits? Med Sci Sports Exerc 2001; 33(6): 379-399

19. Kohut ML, McCann DA, Russell DW, Konopka DN, Cunnick JE, Franke WD. Aerobic exercise, but not flexibility/resistance exercise, reduces serum IL-18, CRP, and IL-6 independent of beta-blockers, BMI, and psychosocial factors in older adults. Brain Behav Immun 2006; 20(3): 201-209
20. Lindegaard B, Hansen T, Hvid G, van Hall G, Plomgaard P, Ditlevsen S. The effect of strength and endurance training on insulin sensitivity and fat distribution in human immunodeficiency virus-infected patients with lipodystrophy. J Clin Endocrinol Metab 2008; 93(10): 3860-3869.
21. Barbara JMH, Jefferis A, Olia Papacosta A, Christopher G, Owen BS, Goya Wannamethee A, et al. Interleukin 18 and coronary heart disease: Prospective study and systematic review. Atherosclerosis 2011; 219(2):970
22. Moseley TA, Haudenschild DR, Rose L, Reddi AH. Interleukin-17 family and IL-17 receptors". Cytokine Growth Factor Rev 2003; 14(2):155–74.
23. Tuomisto K, Jousilahti P, Sundvall J, Pajunen P, Salomaa V. C-reactive protein, interleukin-6 and tumor necrosis factor alpha as predictors of incident coronary and cardiovascular events and total mortality. A population-based, prospective study. Thromb Haemost 2006; 95(3): 511-518
24. Duzova H, Karakoc Y, Hanifi MT, Yilmaz ZD, Kilinc E. Effects of acute moderate and strenuous exercise bouts on IL-17 production and inflammatory response in trained rats. Journal of Sports Science and Medicine 2009; 8: 219 – 224.
25. Tasha D, Samson N, Vincent W, Felix O. Effects of Phytic Acid and Exercise on Some Serum Analytes in Rats Orally Exposed to Diets Supplemented with Cadmium. Biol Trace Elem Res 2012; 151: 400.
26. Gregory S, William F, Tom S. Correlation of hepatic metallothionein concentrations with acute cadmium toxicity in the mouse. Toxicology and Applied Pharmacology 1977; 39(1): 61-69.
27. Thijssen S, Maringwa J, Faes C, Lambrichts I, Van Kerkhove E. Chronic exposure of mice to environmentally relevant, low doses of cadmium leads to early renal damage, not predicted by blood or urine cadmium levels. Toxicology 2007; 229(1-2): 145-156.
28. Agha-Alinejad H, Haftchenari SH, MatinHomaei H. Effect of a Period of Endurance Training on Serum Il-8 Concentration and Tumor Volume in Breast Cancer Bearing Mice. Iranian Journal of Endocrinology and Metabolism 2014; 16(1): 28-32.
29. Bedford T, Tipton C, Wilson N, Oppliger R, Gisolfi C. Maximum oxygen consumption of rats and its changes with various experimental procedures. Applied Physiology 1979; 47(6): 1278-1283.
30. Leick L, Lindegaard B, Stensvold D, Plomgaard P, Saltin B, Pilegaard H. Adipose tissue interleukin-18 mRNA and plasma interleukin-18: effect of obesity and exercise. Obesity 2007; 15(2): 356-63.
31. Golzari Z, Shabkhiz F, Soudi S, Kordi MR, Hashemi SM. Combined exercise training reduces IFN-β and IL-17 levels in the plasma and the supernatant of peripheral blood mononuclear cells in women with multiple sclerosis. Int Immunopharmacol 2010; 10(11): 1415-9.
32. Tofighee A, Khazaei H, Jalili a. Comparison of Effect of One Course of Intense Exercise (Wingate test) on Serum Levels of Interleukin-17 in Different Groups of Athletes. Asian J Sports Med 2014; 5(4): e22769.
33. Mirdar S, Arab A, Hedayati M, Hajizadeh A. The effect of a course of swimming training program on the levels of lung hypoxia induced invasion of newborns in pregnant rats. Qom Univ Med Sci J 2013; 7(3): 11-20.
34. Rosendal L, Sogaard K, Kjaer M, Sjogaard G, Langberg H, Kristiansen J. Increase in interstitial interleukin-6 of human skeletal muscle with repetitive low-force exercise. Journal of Applied Physiology 2005; 98(2): 477-481.
35. El-Boshy ME, Risha EF, Abdelhamid FM, Mubarak MS, Hadda TB. Protective effects of selenium against cadmium induced hematological disturbances, immunosuppressive, oxidative stress and hepatorenal damage in rats. J Trace Elem Med Biol 2015; 29: 104–10.
36. Sun L, Zhang N, Zhu M, Zhao L, Zhou J, Qi T. Prevention of Aflatoxin B1 Hepatoxicity by Dietary Selenium Is Associated with Inhibition of Cytochrome P450 Isozymes and Up-Regulation of 6 Selenoprotein Genes in Chick Liver. J Nutr 2016; 147(8): 789-797.
37. Xu F, Liu S, Li S. Effects of selenium and cadmium on changes in the gene expression of immune cytokines in chicken splenic lymphocytes. Biol Trace Elem Res 2015; 165:214–221.
38. Hu Y, Spengler ML, Kuropatwinski KK, Comas M, Jackson M, Chernov MV, Gleiberman AS, Fedtsova N, Rustum YM, Gudkov AV, Antoch M. Selenium is a modulator of circadian clock that protects mice from the toxicity of a chemotherapeutic drug via upregulation of the core clock protein, BMAL1. Oncotarget 2011;410-411.
39. Rusolo F, Pucci B, Colonna G, Capone F, Guerriero E, et al. Evaluation of Selenite Effects on Selenoproteins and Cytokinome in Human Hepatoma Cell Lines. Molecules 2013; 18:2549-2562.
40. Alizadeh H, Bazgir B, Daryanoosh F, Koushki M, Sobhani V. Effect of aerobic exercise and fish oil supplements on plasma levels of inflammatory indexes in mice. Medical Journal of the Islamic Republic of Iran 2014; 28(6).
41. Rodríguez T, Pinilla E, Mariño M, Moncó C. Evaluation of the influence of physical activity on the plasma concentrations of several trace metals. Eur J Appl Physiol Occup Physiol 1996; 73(3-4):299-303.
42. Lambertucci RH, Levada-Pires AC, Rossoni LV, Curi R, Pithon-Curi TC. Effects of aerobic exercise training on antioxidant enzyme activities and mRNA levels in soleus muscle from young and aged rats. Mech ageing Dev 2006; 128:267-75.
43. Terblanche SE. The effects of exhaustive exercise on the activity levels of catalase in various tissues of male and female rats. Cell Biol Int 1998; 23: 749-53.
44. Trumbo PR. The level of evidence for permitting a qualified health claim: FDA's review of the evidence for selenium and cancer and vitamin E and heart disease. The Journal of nutrition 2005; 135(2): 354-6.
45. Nawrot TS, Staessen JA, Roels HA, Den Hond E, Thijs L, Fagard RH, et al. Blood pressure and blood selenium: a cross-sectional and longitudinal population study. European heart journal 2007; 28(5): 628-33.
46. Brigelius-Flohe R, Banning A, Kny M, Bol GF. Redox events in interleukin-1 signaling. Archives of biochemistry and biophysics 2004; 423(1): 66-73.
47. Karimi P, Bayat Makou R, Dehgan P, Salimi Movahed MR. Selenium relieves inflammation in oxidized-LDL activated platelets via p38MAPK pathway. AMUJ 2014; 17(82): 63-75.
48. Heidari S, Imani M, Mostafavi SM. A Validated and Rapid HPLC Method for Quantification of Human Serum Albumin in Interferon beta-1a Biopharmaceutical Formulation. MedBioTech Journal. 2017;1(01):29.
49. Obidoa P, Ugueche U. In-vitro Investigation of Ocular E-Coli Infection via Norfloxacin. Medbiotech Journal. 2017;01(02):96-103.
50. Riahi A. Oil-in-Water Emulsion-Solvent Evaporation Fabrication of Polycaprolactone Containing Piroxicam for Drug Release. Medbiotech Journal. 2018;02(01):14-20.
51. Kalenik, E. N., Salakhova, V. B., Mikhaylovsky, M. N., Zhelezniakova, M. E., Bulgakov, A. V., & Oshchepkov, A. A. (2018). Psychophysiologic features and personal-adaptive potential of students with limited abilities. Electronic Journal of General Medicine, 15(6).
52. Kulkarni, V. S., Gupta, A. K., & Bhawsar, S. (2019). Formulation and evaluation of activated charcoal peel off mask. International Journal of Pharmacy Research & Technology, 9 (2), 44-48.
53. Özer G, Ergün U, İnan LE. Headache in Multiple Sclerosis from a Different Perspective: A Prospective Study. J Clin Exp Invest. 2018;9(1):9-13. https://doi.org/10.5799/jcei.413052