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Research Article



# The Effect of Eight Weeks of Hand-Selected Strength Exercises and the Cinnamon Supplementation on Inflammatory Biomarkers in Elderly Women with Osteoarthritis

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#### **Abstract**

**Background:** Osteoarthritis is the most common joint disease (arthropathy) and a cause of disability in aging ages. The prevalence rate of the osteoarthritis is different and is related to different indicators.

**Objectives:** The purpose of the present study was to investigate the effect of eight weeks of hand-selected exercises and cinnamon supplementation on inflammatory biomarkers in elderly women with osteoarthritis.

**Methods:** The participants of this study were 48 women with hand-osteoarthritis. They divided into four groups (strength exercises, cinnamon-honey supplementation, combinatory and control) randomly. The first group underwent the hand-selected strength exercises. The second group used the supplementations for 8 weeks. The third group also applied hand-selected exercises and supplements simultaneously. The fourth group also participated as a control group without any exercise or supplementation. Patients'  $TNf\alpha$  and IL6 levels were measured before and after applying the independent variables and were compared. The dependent t-test was used to compare between pre and posttest and the ANOVA test to compare  $TNf\alpha$  and IL6 levels between the four groups. The significance level  $P \le 0.05$  was considered.

**Results:** The results showed that by applying variables, the strength exercises and cinnamon-honey supplementary as well as the combination of exercises and supplementary have had a positive effect on inflammatory biomarkers and in fact, 8 weeks of resistance exercises and using cinnamon-honey supplements in women with hand osteoarthritis have led to a decrease in IL 6 and  ${\rm TNf}\alpha$  levels.

**Conclusions:** Therefore, it is recommended to use wrist resistance exercises with supplements (cinnamon and honey) to accelerate the recovery of the disease and improve the wrist inflammatory.

Keywords: Osteoarthritis, Cinnamon, Honey, Strength Exercises, Inflammatory Biomarkers

## 1. Background

Osteoarthritis is the most common joint disease (arthropathy) and a cause of disability in aging ages. The prevalence rate of the osteoarthritis is different and is related to different indicators. After the knee, with a prevalence of 33%, wrist osteoarthritis with a prevalence of 5.29% is the most common joint that affected. Research has shown that its prevalence in women is almost twice that of men. Also It often occurs in people over 55 years of age (1).

Based on the number of joints involved, there is a classification of osteoarthritis, which includes generalized osteoarthritis with involvement of more than 3 joints and localized osteoarthritis with involvement of less than 3

joints. In idiopathic osteoarthritis, localized involvement mainly involves involvement of the first carpometacarpal joints, the Heberden, the Bouchard and the knees and thighs (2).

A better cognition of the pathogenesis of the disease indicates that numerous local or general factors are involved in the development and progression of osteoarthritis (3, 4). Some of these factors include age, sex, race, genetics, bone density, sex hormones (estrogen, testosterone) endocrine or metabolic disorders, nutrition, obesity, major joint injuries, excessive pressure on joints caused by occupation or exercise, congenital and developmental disorders and defects in joint or ligamentous laxity and previous history of inflammatory or infectious arthritis (3, 4).

According to research, it can be concluded that both cy-

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tokine interleukin 6 (IL6) and tumor necrosis factor alpha (TNF $\alpha$ ) are responsible for altering cartilage homeostasis in degradation and catabolism of the joint, which causes to induce inflammatory process and to activate the parsers mediators of the joint and apoptosis (5).

Different ways have been suggested to reduce the effects of the disease:

Such as: Patients' awareness, proper nutrition, drug therapy and finally, exercise programs which each have its own significant benefits. Different studies on the medicinal plants and their constituents have demonstrated the anti-inflammatory effect of cinnamon. Various studies have also reported the anti-inflammatory properties of cinnamon and cinnamon oil. Also, the use of honey either in the form of feed or for topical use has reduced inflammation and pain in various joint diseases. It seems that the soothing effect of cinnamon on the arthritis progression is done without affecting the antibody response, which is due to its anti-inflammatory effect. Therefore, cinnamon and honey as a complementary therapy can be useful for the treatment of arthritis (6, 7).

Another important component of osteoarthritis healthcare in the elderly is exercise therapy. Exercise involves planned, regular and organized movements to improve or maintain one or more physical and motor fitness factors (8). Physical activity and exercise are key recommendations for the management of osteoarthritis of the hands and fingers. It is worth noting that studies have reported different results (9). Exercise has had from low to medium effects on reducing pain and inflammatory biomarkers, which have been reported by researchers. It seems that exercise is also likely to be effective in osteoarthritis, although limited evidence is available (10).

However, there is some debate as to which exercise and which type of exercise has the benefit or risk of progression of OA. This may be due to the evaluation of the effect of physical activity or new disease-modifying OA drugs which is currently based on radiographic criteria (e.g., Width space of articular) and non-correlation with clinical signs and symptoms (e.g. Pain and loss of strength and motor function). In addition, OA specifically manifests itself as a change in common space and bone (10).

Certainly, patients with this disease are looking for ways that, in addition to the best performance, has the least harm. The use of painkillers and corticosteroids reduces pain in patients, but the long-term adverse effects will occur with the onset of some diseases.

## 2. Objectives

In this regard, safe and low-cost methods include different exercises as well as changing eating habits. The benefits of using exercise and supplements have been studied in previous researches, but neither of these studies has jointly examined these two important factors and in addition, has not examined the variables involved in the disease in this way. Most of the studied researches have investigated a few factors separately and in some cases, the reported results have been contradictory. Therefore, in this study, the researcher is trying to investigate the effect of 8 weeks of hand-selected strength exercises and cinnamon and honey supplementation on some inflammatory biomarkers of patients with osteoarthritis.

#### 3. Methods

This is a quasi-experimental study with pre-test and post-test design with a control group. The statistical population of this study consisted of all women with hand osteoarthritis who have referred to Imam Reza Medical Center in Kermanshah. Among the people referred to this center, 48 were selected as a specimen and randomly divided into four groups of selected strength exercises (n = 12), cinnamon-honey supplement (n=12), combinatory (n=12) and control (n=12).

In this study, the first the levels of  ${\rm TNf}\alpha$  and IL6 biomarkers were measured and after applying the practical and complementary interventions, the mentioned variables were again measured and recorded in four groups after eight weeks. The subjects participated in the pre-test after completing the consent form and demographic questionnaire. Subjects had to answer the following questions:

Age, history of physical activity, history of skeletal problems, history of severe osteoporosis, history of Parkinson's disease, history of stroke or neuropathy, history of severe lumbar disc or orthopedic problems, ability to walk without the need for assistive devices, sufficient vision and hearing and work experience.

## 3.1. Method of Blood Sampling and Measuring Variables

To measure TNf  $\alpha$  and IL6 levels, 5 mL of blood was sampled from the brachial vein 24 hours before the start of the first session and supplementation use as well as 24 hours after the last exercises session in the fasting state. The samples were then centrifuged at 20,000 rpm for 20 min using a laboratory method and analyzed using ELISA kit.

#### 3.2. Procedure

The hand strength exercises intervention was performed for 8 weeks as suggested by Hennig et al. (Appendix 1 in Supplementary File). In this group, standard hand strengthening exercises was performed using simple tools (11). The second group used honey supplements and cinnamon powder twice a day for 8 weeks. The third group also received hand-selected exercises and cinnamon and honey supplements simultaneously. The fourth group also participated in this study without any exercise or supplementation and as a control group. Patients'  $TNf\alpha$  and IL6 levels were measured before and after applying the independent variables and compared with each other (11-13).

According to Hennig et al.'s suggestion (11), dosage of the honey and cinnamon is two tablespoons of honey daily (every morning) with one teaspoon of cinnamon dissolved in a cup of water.

Descriptive statistics were used to adjust and classify the data, calculate central tendency and dispersion indices such as mean and standard deviation as well as draw charts. For inferential analysis after examining the normality of the data by Shapiro wilk test, dependent t-test was used to compare between pretest and posttest groups and ANOVA test to compare  ${\rm TNf}\alpha$  and IL6 levels between the four groups. Data analysis was performed by SPSS software version 23 and the significance level P  $\leq$  0.05 was considered.

### 4. Results

Table 1 shows the mean and standard deviation of the individual characteristics of the subjects in the four groups of control, strength training, cinnamon and honey supplementation and combination group.

Also the frequency, mean and standard deviation of  $TNf\alpha$  (pg/mL) and IL6 (pg/mL) levels during the pre-test and post-test are shown in Table 2 in all four groups.

In this study, the Shapiro-Wilk test was used to determine the normality of the data distribution. The results showed that the distribution of data in the variables  ${\rm TNf}\alpha$  (pg/mL) and IL6 (pg/mL) was normal in both pre-test and post-test. Therefore, parametric statistics were used to investigate the research hypotheses. To investigate the effect of strength exercise, cinnamon-honey supplementation and combinatory, a pre-test and post-test intra-group design (t-dependent) was used for all four groups. The results showed that there is significant difference in the pre-test and post-test in all three variables in the control group, but there was significant difference in the pre-test and post-test in all variables  ${\rm TNf}\alpha$  and IL6 in the Cinnamon-Honey supplementation, strength training group and the

combinatory group. These results indicate that the application of the independent variable has a significant effect on the subjects in all three experimental groups and in all three variables.

In this study, ANOVA test was used to investigate the differences between groups. Comparison between groups in all variables in the pre-test showed that there was no significant difference between the groups (strength training, cinnamon-honey supplement, combinatory and control groups). But the comparison between the four groups at the post-test showed that there was a significant difference between the four groups at this stage.

Tukey test at 0.05 was used to investigate the differences between groups. Tukey post hoc test for variable  $TNf\alpha$  showed that there was a significant difference between the four groups at posttest (Table 3).

This means that both strength training and the use of cinnamon-honey and combination supplements have been able to reduce  ${\rm TNf}\alpha$  (pg /mL). Tukey post hoc test for IL6 showed that there was no significant difference between strength training group and cinnamon and Honey supplement in the post-test phase. There was also a significant difference between the strength training, combination and control groups as well as the other groups.

## 5. Discussion

The results showed that implementation of the strength exercise, cinnamon-honey supplementation and combination of exercises and supplementation could have a positive effect on inflammatory biomarkers. It is also worth noting that, eight weeks of resistance training and the use of cinnamon-honey supplementation and combinatory in women with wrist osteoarthritis has led to decrease levels of IL6 and  $\text{TNf}\alpha$ .

The results of the current study showed that IL6 level was significantly decreased. Numerous studies, such as those of Yamaoka-Tojo et al. (14) and Kohut et al. (15), have shown that regular physical activity has anti-inflammatory effects and is a treatment for a range of inflammatory diseases. In a study, Kohut et al. (15) examined the effect of physical activity on inflammatory factors in the elderly, and in their study, subjects performed aerobic exercise on a treadmill, hand-held ergometer, and bicyclist 3 times a week for 10 months. In their study, intensity of activity started from 45 to 60 percent of maximal heart rate and increased to 60 to 70 percent then percent of maximal heart rate was maintained between 65 to 80 percent for 10 months. The results showed that the IL6 inflammatory factors in the aerobic group had a significant decrease.

Table 1. Mean and Standard Deviation of Individual Characteristics of Subjects <sup>a</sup>						
Groups	Age, y	BMI, kg/m²	Weight, kg	Height, cm		
Control	$60\pm2.41$	$27.18 \pm 1.19$	$\textbf{74.5} \pm \textbf{4.71}$	$165.58 \pm 2.42$		
Strength training	$59.5 \pm 1.73$	$25.97 \pm 2.06$	$72.75 \pm 7.18$	$167.25 \pm 3.98$		
Cinnamon and honey supplements	$59.5 \pm 4.81$	$27.2\pm1.65$	$\textbf{75.58} \pm \textbf{4.64}$	$166.75 \pm 4.67$		
Combinatory	$59.08 \pm 2.57$	$26.54\pm2$	$74.08 \pm 5.56$	$167.08 \pm 4.18$		

<sup>&</sup>lt;sup>a</sup> Values are expressed as mean  $\pm$  SD.

 $\textbf{Table 2.} \ Mean \ and \ Standard \ Deviation \ of \ Research \ Variables \ in \ Four \ Groups \ (Control, Strength \ Training, Cinnamon \ and \ Honey \ Supplement \ and \ Combinatory)^{a}$ 

Groups	IL6 Leve	IL6 Level, pg/mL		TNf $lpha$ Level, pg/mL	
	Pre-Test	Post-Test	Pre-Test	Post-Test	
Control	$1.46\pm0.08$	$1.43\pm0.08$	$3.05\pm0.15$	$3.03 \pm 0.13$	
Strength training	$1.39\pm0.11$	$1.18\pm0.09$	$3.03\pm0.13$	$2.06\pm0.16$	
Cinnamon and honey supplements	$\textbf{1.45} \pm \textbf{0.1}$	$1.19\pm0.09$	$\textbf{3.05} \pm \textbf{0.16}$	$1.83 \pm 0.107$	
combinatory	$\textbf{1.45} \pm \textbf{0.1}$	$1.05\pm0.1$	$3.02\pm0.105$	$1.41\pm0.093$	

 $<sup>^{\</sup>mathrm{a}}$ Values are expressed as mean  $\pm$  SD.

**Table 3.** Tukey Post Hoc Test to to Examine the Differences Between Groups in TNflpha Variable and II 6 Levels

Variable	Mean Differences	P Value
TNf $\alpha$ , pg/mL		
Strength exercise		
Cinnamon-honey supplement	0.233 <sup>a</sup>	0.0001
Combinatory	0.65 <sup>a</sup>	0.0001
Control	0.966 <sup>a</sup>	0.0001
Cinnamon-honey supplement		
Combinatory	0.416 <sup>a</sup>	0.0001
Control	-2.1 <sup>a</sup>	0.0001
Combinatory		
Control	-1.616 <sup>a</sup>	0.0001
IL6, pg/mL		
Strength exercise		
Cinnamon-honey supplement	-0.008	0.997
Combinatory	0.125 <sup>a</sup>	0.013
Control	-0.25 <sup>a</sup>	0.0001
Cinnamon-honey supplement		
Combinatory	0.133 <sup>a</sup>	0.0001
Control	-0.241	0.0001
Combinatory		
Control	-0.375 <sup>a</sup>	0.0001

<sup>&</sup>lt;sup>a</sup> Significance level at the difference between the means is 0.05.

In explaining the cause it can be said that physical activity reduces the level of inflammatory cytokines and increases the production of anti-inflammatory cytokines such as IL6. The production of anti-inflammatory cytokines decreases the production of pro-inflammatory cytokines from adipose tissue (16).

Beta-adrenergic receptor activity is a mechanism that mediates the changes in inflammatory mediators induced by exercise and dietary supplementation. The activity of adipocytes Beta-adrenergic receptor increases the secretion of pro-inflammatory cytokines. Exercise reduces the beta-adrenergic receptor density (16, 17). Also, the results of this study showed that CRP levels were significant difference to pre-test. In a study by Colbert et al. (18), they found that after six months of physical activity, CRP levels did not change significantly, which was not consistent with the results of the present study. Another study reported that increasing men's physical activity to about 30 minutes of walking per day had no significant effect on CRP values. The reason for this may be due to the duration and type of exercise (19).

In another study which carried out on 424 elderly men and women, the effect of 12 months of walking for 150 minutes per week on serum IL6 levels was examined. The results showed that after 12 months of physical training, the level of IL6 decreased significantly (20). Due to the increased inflammatory index induced by age and its relationship to the fat mass in the body the most likely reason for the finding differences is due to differences in age and physical status of the participants in the present study

with their research (21).

Basically, IL6 and TNf $\alpha$  are indicators that most researchers expect to change during different exercise activities, but according to research, the rate of changes in IL6 and TNf $\alpha$  during exercise is different in healthy individuals (22). The results of the present study are consistent with the findings of Pischon et al. (23), Bolboli (22) and Pourvaghar (24).

Bolboli (22) showed that 8 weeks of aerobic exercise reduce IL6 and  $\text{TNf}\alpha$  levels in obese and elderly women and considered such exercises as an effective way to prevent and control risk factors for inflammatory diseases. Although the results of numerous studies have confirmed the decrease in IL6 and  $\text{TNf}\alpha$ , the results of Akhtari Shojaei (25) and Gaini et al. (26) differed. One possible reason for the inconsistency of the findings of the present study with the said research can be attributed to the age difference of the subjects (22).

It is also important to consider both of the intensity and duration of exercise as well as the time interval of blood sampling after end of the intervention for investigating the short-term and long-term effects of exercise on IL6 and TNf $\alpha$  (27). Other possible reasons of inconsistency in the results of the research can be mentioned in the characteristics of the subjects such as their fitness and gender. As physical fitness increases, the level of inflammation associated with physical activity decreases, as well as in men, the rate of inflammation responds to activity is at a low level (28). Regular exercise, by reducing sympathetic stimulation and increasing anti-inflammatory cytokines, inhibits the release of inflammatory mediators from adipose tissue and subsequently reduces the concentration of inflammatory markers (28, 29).

In a research, Pischon et al. (23) studied more than 800 healthy men and women and found that physical activity was inversely correlated with CRP and IL6 levels, as more repetition of physical activity decrease the systemic inflammation and improve insulin sensitivity. However, increased free radicals induced by vigorous exercise are thought to increase the possibility of IL6 and  $\text{TNf}\alpha$  inflammatory cytokines release (29); therefore, exercise intensity appears to be one of the factors influencing cytokine levels, that should be taken into consideration.

Due to the anti-inflammatory properties of cinnamon and honey and the effect of these substances on free radicals and increase insulin sensitivity, and improve endothelial function, levels of inflammatory markers are also reduced. interleukins are probably one potential pathway. In particular, there is evidence for the interference of IL6 and  $\text{TNf}\alpha$ . IL6 and  $\text{TNf}\alpha$  indices are significantly released from adipose tissue, especially visceral fat. Their release from

adipose tissue is enhanced by sympathetic stimulation, and since regular physical activity as well as cinnamon and honey modulates sympathetic stimulation, it is likely to decrease TNf $\alpha$ , and stimulate the production of IL6 (30). In this regard, the researchers showed that IL6 regulates the secretion of some inflammatory markers from the liver, whereas the main source of IL6 release is adipose tissue (about 30%). Therefore, lowering body fat levels following exercise and consuming honey and cinnamon is probably a factor in modulating IL6 production and ultimately reducing inflammation (31). Also, consuming cinnamon and honey and exercising regularly will increase endothelial nitric oxide and improve endothelial function and increase antioxidant agents. Thus, this process reduces systemic and topical inflammation and, consequently, reduces the production of inflammatory cytokines from the endothelial wall smooth muscle and shows its ultimate effect as a possible reduction of this inflammatory marker in the liver (30, 32).

## **Supplementary Material**

Supplementary material(s) is available here [To read supplementary materials, please refer to the journal website and open PDF/HTML].

# **Footnotes**

**Authors' Contribution:** Shayesteh Hassani designed the experimental set up the study, performed the experiments, and analyzed the data. Sedigheh Hosseinpour Delavare and Hassan Safikhani wrote the manuscript.

**Conflict of Interests:** The authors declare no conflict of interest regarding the compilation or publication of this article.

**Ethical Approval:** All experimental were reviewed and approved by Ethics Committee of Kermanshah university of Medical Sciences with code: IR.KUMS.REC.1398.548.

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## References

 DeChellis DM, Cortazzo MH. Regenerative medicine in the field of pain medicine: Prolotherapy, platelet-rich plasma therapy, and stem cell therapy—Theory and evidence. *Tech Reg Anesth Pain Manag*. 2011;15(2):74–80. doi: 10.1053/j.trap.2011.05.002.

- Wang Y, Wluka AE, Simpson JA, Giles GG, Graves SE, de Steiger RN, et al. Body weight at early and middle adulthood, weight gain and persistent overweight from early adulthood are predictors of the risk of total knee and hip replacement for osteoarthritis. *Rheumatology (Oxford)*. 2013;**52**(6):1033-41. doi: 10.1093/rheumatology/kes419. [PubMed: 23362222].
- Murphy SL, Schepens Niemiec S, Lyden AK, Kratz AL. Pain, fatigue, and physical activity in osteoarthritis: The moderating effects of pain-and fatigue-related activity interference. Arch Phys Med Rehabil. 2016;97(9 Suppl):S201-9. doi: 10.1016/j.apmr.2015.05.025. [PubMed: 27207435].
- 4. Luo X, Pietrobon R, Sun SX, Liu GG, Hey L. Estimates and patterns of direct health care expenditures among individuals with back pain in the United States. *Spine (Phila Pa 1976)*. 2004;**29**(1):79–86. doi: 10.1097/01.BRS.0000105527.13866.0F. [PubMed: 14699281].
- Akhtar N, Haqqi TM. Current nutraceuticals in the management of osteoarthritis: a review. *Ther Adv Musculoskelet Dis.* 2012;4(3):181–207. doi: 10.1177/1759720X11436238. [PubMed: 22850529]. [PubMed Central: PMC3400101]
- Rao PV, Gan SH. Cinnamon: a multifaceted medicinal plant. Evid Based Complement Alternat Med. 2014;2014:642942. doi: 10.1155/2014/642942.
  [PubMed: 24817901]. [PubMed Central: PMC4003790].
- 7. Lee J, Lew J, Kim T, Kang H. Effect of an herbal mixture of Cinnamon Cortex, Persicae Semen, and Natril Sulfas on collagen-induced arthritis and lipopolysaccharides-induced nuclear factor- $\kappa$  B signaling. *Chin | Integr Med.* 2016:1–6.
- 8. Shojaedin SS, Sayyah M, Mehrabian H, Sheikh Oveisi J, Barati AH, Razi M. Comparing the radiographic grading scales, knee pain, signs, movement dysfunctions and the quality of life related to osteoarthritis in ex-elite track and field athletes and non-athletes. *Feyz J Kashan Univ Med Sci.* 2012:16.
- 9. Altman RD, Hochberg MC, Moskowitz RW, Schnitzer TJ. Recommendations for the medical management of osteoarthritis of the hip and knee: 2000 update. American college of rheumatology subcommittee on osteoarthritis guidelines. *Arthrit Rheum*. 2000;43(9):1905-15. doi: 10.1002/1529-013I(200009)43:9<1905::Aid-anrI>3.0.Co;2-p.
- Fransen M, McConnell S, Fransen M. Exercise for osteoarthritis of the knee. Cochrane Database of Systematic Reviews. 2008. doi: 10.1002/14651858.CD004376.pub2.
- Hennig T, Haehre L, Hornburg VT, Mowinckel P, Norli ES, Kjeken I. Effect of home-based hand exercises in women with hand osteoarthritis: a randomised controlled trial. *Ann Rheum Dis.* 2015;74(8):1501–8. doi:10.1136/annrheumdis-2013-204808. [PubMed: 24667900].
- Majani G, Giardini A, Scotti A. Subjective impact of osteoarthritis flare-ups on patients' quality of life. Health Qual Life Outcomes. 2005;3:14. doi: 10.1186/1477-7525-3-14. [PubMed: 15771777]. [PubMed Central: PMC555754].
- Lerner D, Reed JI, Massarotti E, Wester LM, Burke TA. The work limitations questionnaire's validity and reliability among patients with osteoarthritis. *J Clin Epidemiol*. 2002;55(2):197–208. doi: 10.1016/s0895-4356(01)00424-3.
- Yamaoka-Tojo M, Tojo T, Wakaume K, Kameda R, Nemoto S, Takahira N, et al. Circulating interleukin-18: A specific biomarker for atherosclerosis-prone patients with metabolic syndrome. *Nutr Metab (Lond)*. 2011;8:3. doi: 10.1186/1743-7075-8-3. [PubMed: 21251304]. [PubMed Central: PMC3038890].
- Kohut ML, McCann DA, Russell DW, Konopka DN, Cunnick JE, Franke WD, et al. 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):201-9. doi: 10.1016/j.bbi.2005.12.002. [PubMed: 16504463].
- 16. Amani Shalamzari S, Agha Alinejad H, Gharakhanlou R, Molanouri Shamsi M, Talebi Badrabadi K. The effect of body composition and physical activity on basal levels of insulin, glucose, IL-18, IL-6 & CRP and their relationship with insulin resistance. Iran | Endocrinol Metab.

- 2009;11(6):699-706.
- Madsen EL, Bruun JM, Skogstrand K, Hougaard DM, Christiansen T, Richelsen B. Long-term weight loss decreases the nontraditional cardiovascular risk factors interleukin-18 and matrix metalloproteinase-9 in obese subjects. *Metabolism*. 2009;58(7):946– 53. doi: 10.1016/j.metabol.2009.02.031. [PubMed: 19409578].
- Colbert LH, Visser M, Simonsick EM, Tracy RP, Newman AB, Kritchevsky SB, et al. Physical activity, exercise, and inflammatory markers in older adults: findings from the Health, Aging and Body Composition Study. J Am Geriatr Soc. 2004;52(7):1098-104. doi: 10.1111/j.1532-5415.2004.52307.x. [PubMed: 15209647].
- Gray SR, Baker G, Wright A, Fitzsimons CF, Mutrie N, Nimmo MA, et al. The effect of a 12 week walking intervention on markers of insulin resistance and systemic inflammation. *Prev Med.* 2009;48(1):39-44. doi: 10.1016/j.ypmed.2008.10.013. [PubMed: 19010347].
- Nicklas BJ, Hsu FC, Brinkley TJ, Church T, Goodpaster BH, Kritchevsky SB, et al. Exercise training and plasma C-reactive protein and interleukin-6 in elderly people. J Am Geriatr Soc. 2008;56(11):2045–52. doi: 10.1111/j.1532-5415.2008.01994.x. [PubMed: 19016938]. [PubMed Central: PMC2683336].
- Sheikholeslami VD, Ahmadi S, Mojtahedi H, Marandi M, Ahmadi DK, Faraji H, et al. Influence of different intensities of resistance exercise on inflammatory markers in young healthy men. *Iran J Endocrinol Metab*. 2011.
- Bolboli L. [Effect of omega-3 consumption and participate in aerobic exercise on sICAM-1 and pro-inflammatory cytokines in obese elderly women]. Sport Physiol. 2014;6(21):79–94. Persian.
- Pischon T, Hankinson SE, Hotamisligil GS, Rifai N, Rimm EB. Leisure-time physical activity and reduced plasma levels of obesity-related inflammatory markers. *Obes Res.* 2003;11(9):1055–64. doi: 10.1038/oby.2003.145. [PubMed: 12972675].
- 24. Pourvaghar MJ. [Impact of a 2-month aerobic exercise on CRP of overweight female students]. KAUMS J. 2013;17(4):380-6. Persian.
- Akhtari Shojaei E, Farajov A, Jafari A. Effect of moderate aerobic cycling on some systemic inflammatory markers in healthy active collegiate men. *Int J Gen Med*. 2011;4:79–84. doi: 10.2147/IJGM.S15065. [PubMed: 21403796]. [PubMed Central: PMC3048343].
- Gaini A, Nazari A, Tabrizi A, Farahani A. [The effect of an eight-week aerobic training on high sensitivity C-reactive protein of high school students with different body mass indexes]. *Iran J Cardiovasc Nurs*. 2013;1(4):48-56. Persian.
- 27. Kasapis C, Thompson PD. The effects of physical activity on serum C-reactive protein and inflammatory markers: a systematic review. *J Am Coll Cardiol.* 2005;**45**(10):1563–9. doi: 10.1016/j.jacc.2004.12.077. [PubMed: 15893167].
- Mogharnasi M, Moosazadeh H. Effects of omega-3 fatty acid supplementation on the most sensitive of inflammatory marker the predictive of cardiovascular diseases (hs-CRP & IL-6) after aerobic exercise. Sport Physiology. 2014;6(21):137-52.
- Ziccardi P, Nappo F, Giugliano G, Esposito K, Marfella R, Cioffi M, et al. Reduction of inflammatory cytokine concentrations and improvement of endothelial functions in obese women after weight loss over one year. *Circulation*. 2002;105(7):804–9. doi: 10.1161/hc0702.104279. [PubMed: 11854119].
- Faramarzi M, Mousavi Ghahfarokhi SM, Khosravi N. [Effect of a course low intensity synchronize aerobic exercise on crp level changes in elderly women]. Res Sport Sci. 2011:103–14. Persian.
- Vakili J, Hosseinpour L. [The effects of 8 weeks aerobic exercise training along with green tea consumption on the cardiovascular risk factors in obese women]. J Pract Stud Bioscie Sport. 2015. Persian.
- 32. Choobineh S, Dabidy Roshan V, Gaieni AA. Effect of the continues and intermittence aerobic training on high-sensitive c-reactive protein in rats. J Mov Sci Sport. 2007;5(9):1-14.