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Effect of six weeks of high intensity interval training and zinc supplement on serum creatine kinase and uric acid levels in futsal players

Malihe Saeedy[1], Nahid Bijeh[2]*, Ziba Shoorideh[3]

*1 M.A graduate in Sports Physiology, Faculty of Physical Education and Sport Sciences, Ferdowsi University of Mashhad, Mashhad, Iran, 2 *(Corresponding Author) Associate Professor in Sports Physiology Department, Faculty of Physical Education and Sport Sciences, Ferdowsi University of Mashhad, Mashhad, Iran, 3 Graduate in Sports Physiology, Faculty of Physical Education and Sport Sciences, Ferdowsi University of Mashhad, Mashhad*

ABSTRACT:

Background: strenuous training-induced reactive oxygen species is associated with several chronic diseases by damaging cell proteins and membrane lipids; it seems uric acid as a major intracellular antioxidant could lower membranous lipid peroxidation and muscle damage. The aim of this study was to examine the effect of six weeks of high-intensity interval training with and without zinc on serum Creatine Kinase and uric acid in female futsal players.

Methods: Thirty-two female futsal players were randomly divided into four groups: placebo, Zinc, HIT and Zinc+HIT. All subjects had to attend futsal-specific training three sessions per week. Zinc and Placebo groups took 30 mg day−1 of zinc gluconate or dextrose, respectively; HIT groups accomplished high-intensity interval training contained 6 to 10 repetitions of a 30-second running at 100% of VO_{2peak} with a 4-minutes rest between efforts, during six weeks.

Results: After six weeks, Creatine Kinase levels augmented insignificantly from 83.98 to 120.19 (P=0.101) in placebo, from 99.58 to 150.1(P=0.167) in HIT and from 81.07 to 107.90 (P=0.152) in HIT+Zinc group; while Creatine Kinase levels increased significantly from 66.86 to 124.81(P=0.004) only in Zinc group. Uric acid levels increased in all groups (Placebo (P=1), Zinc (P=0.317), HIT (P=0.157), Zinc+HIT (P=1)) insignificantly.

Conclusions: The findings indicated that after six weeks, serum Creatine Kinase and uric acid levels increased insignificantly in all groups; Creatine Kinase levels augmented significantly, only in Zinc group. Zinc as an antioxidant supplement could not decrease the muscle damage,

Correspondence Information
Faculty of Physical Education and Sport Sciences, Ferdowsi University of Mashhad, Mashhad, Iran.
E-mail: bijeh@ferdowsi.um.ac.ir, Tel: 98513880540.

and even increased the serum Creatine Kinase as a marker of muscle damage, significantly.

KEY WORDS: High intensity interval training, Zinc supplementation, Creatine Kinase, Uric acid, Futsal players.

INTRODUCTION

Oxidative stress is a condition, in which the cellular productions of pro-oxidants go beyond the body's physiological capacity to remove (1). Damaging cell proteins, DNA and cellular membrane lipids (2); oxidative stress is associated with several chronic diseases such as atherosclerosis, related cardiovascular disorders, mutagenesis, cancer, neurodegenerative disorders and type 2 diabetes mellitus (3).

Reactive oxygen and nitrogen species (RONS) production, during or after High-intensity interval training (HIT) may be because of both the high oxygen consumption, as well as the high anaerobic metabolism (2). Free radicals-induced cell membrane damage leads to an increase in levels of plasma Creatine Kinase (CK) that is a marker of cell damage and inflammatory conditions (4-6). In addition, the mechanical stress during physical activity causes some slight tears in the muscle fibers; thus concentrations of CK and LDH enzymes increase in bloodstream (5-7). Oxidative stress may enhance the primary muscle damage and make the recovery period longer (6). In this regard, acute and long-term impact of three types of training including endurance, sprint and combined training (endurance-sprint) were examined on the rats in a study. CK levels in the long-term training were observed higher compared to acute one; more, CK levels augmented in the combination group rather than the other groups (8). Furthermore, Deminice et al (2011) indicated an increase in serum CK (67%) and uric acid (25%) levels after a bout of hypertrophy resistance traditional interval training; while after a bout of resistance circuit training, it was observed an increase in CK (33%) without any change in the oxidative stress biomarker (1). In contrast, Gharahdaghi et al (2013) reported that four weeks of high intensity aerobic interval training, reduced the markers of muscle damage in soccer players at rest and exhaustion time (9).

It is thought that membranous lipid peroxidation due to free radicals, can be reduced by increasing the body's antioxidant capacity; in this way, the release of intracellular enzymes such as CK to the extracellular space, may be reduced and ultimately the muscle damage decreases (4, 7).

It is worth noting that the antioxidant system containing antioxidant enzymes such as superoxide dismutase, catalase, glutathione peroxidase and a set of small molecules like uric acid and bilirubin, protects the body against the RONS (10,11). Low-molecular-weight compounds as uric acid can either prevent ROS formation or scavenge the radical species and convert them into a less active molecule. Plus, they avoid the transformation of less active ROS like $O_2^{\bullet-}$ into more potent forms as $HO^{\bullet}$ and enhance the resistance of sensitive biological targets to ROS attack and contribute to the repair of radical-induced damage. The location of uric acid is in Ubiquitary and its particular function is scavenge of HO radicals; uric acid traps peroxyl radicals in aqueous phases and therefore contribute to the plasma antioxidant defence (12).

It is expressed that elevation of serum uric acid concentration, occurs as a physiologic response to increased oxidative stress for example, during acute exercise; providing a counter-regulatory increase in antioxidant defenses (13). Plus, Uric acid (UA) as a major intracellular antioxidant (14) can lower the rate of lipid peroxidation but cannot prevent its initiation (2). In this regard, researchers

observed that after 20 minutes of intense aerobic exercise, an increase in uric acid levels, improved serum antioxidant capacity and suppressed increased oxidative stress factor (8-iso-PGF 2) (15).On the contrary, Bergholm et al (1999) reported that high-intensity training (running at 70% to 80% VO_{2max}) during 3 months caused a reduction in soluble antioxidants like uric acid (16).

Molshatzki et al (2015) expressed that it is thought high serum uric acid levels are associated with numerous vascular risk factors, but UA is also a major natural antioxidant and higher levels of it, have been linked to slower progression of several neurodegenerative disease through mechanisms involving chelating Fenton reaction transitional metals and increasing antioxidant enzyme activity like Superoxide dismutase; the researchers indicated that low UA levels in patients with preexisting cardiovascular disease, are associated with poorer cognitive function (17,18). More, Amaro et al (2016) reported a beneficial effect of UA therapy on ischemic stroke progression in patients treated with alteplase, by receiving 1000 mg of UA before the end of alteplase infusion (19).

Also, studies showed that use of antioxidant supplement alleviates cell damage (20,21). In this respect, zinc (required for the activity of more than 300 enzymes) as an antioxidant, plays an essential role in preventing free radicals-induced damage during inflammatory processes by stabilizing the cell membrane (3, 22). The lucrative effects of zinc supplementation on various diseases like acute diarrhea in infants, cold, and so on have been reported in different investigations (22,23); however, our data on the effect of zinc supplementation on muscle damage are quite limited.

Cavas et al (2004) stated that vitamin-mineral supplementation along with swim training, attenuated the oxidative stress as well as CK, LDH, AST levels while antioxidant levels increased (20). By contrast, Padervand et al (2014) noticed that 6 weeks of ginger supplementation had no significant effect on CK levels and the antioxidant supplement failed to prevent or decrease the lipid peroxidation, inflammation and muscle damage (24).

We encountered some inconsistent and insufficient findings on the effects of exercise and use of antioxidant supplements on cell damage markers and uric acid levels. More, neither the impact of HIT nor the effect of HIT with zinc supplementation on cell damage and UA levels, have yet been studied؛so in this study, we examined the effect of six weeks of HIT with and without zinc supplementation on serum uric acid and CK levels in female futsal players to find out the relationship between the exercise-induced muscle damage and blood uric acid levels.

METHODS

This semi-experimental study is one of applied researches, containing pre-test and post-test phases with four groups. First, the study subject was declared throughout female futsal clubs in Mashhad city; then, out of 50 volunteers, 32 female futsal players (mean age 23.31 ± 3.89 years, height 162.25 ± 5.85 cm, weight 55.21 ± 6.29 kg, BMI 20.93 ± 1.74 kg/m^2) with at least four years of sports background attended this study. During two months before intervention, all athletes had regularly taken part in futsal team trainings only two sessions per week. Present study was approved by the ethics committee of Ferdowsi University of Mashhad by code 61681.

The nature of the study was orally announced in all female futsal clubs around Mashhad city by the researcher; next, personal and contact information of futsal players who were interested in the cooperation was recorded, and then 32 individuals were purposefully selected from 50 volunteers. The objectives, the research process and researcher's expectations from the athletes were described in detail in a meeting; afterwards, a consent form, a demographic questionnaire, medical questionnaire and Kaiser Physical Activity questionnaire were filled out by all participants. The height and weight were measured by Seca

220 Stadiometer (Germany) with a sensitivity of 5 mm and 100 g, respectively as well as their BMI was evaluated by body composition analyzer, Inbody 720 (South Korea).

In pre-test phase and Twenty-four hours before intervention, blood samples were collected. The subjects were randomly divided into four groups: placebo (n=8), Zinc (n=8), HIT (n=8) and Zinc+HIT (n=8); then, they were influenced by the interventions for six weeks. Lastly, in post-test phase and 24 hours after the last training session, blood samples were collected again.

Plus, the exact time of both blood sampling was announced to the players, and blood samples were taken at least three hours after their last meal, so that their bladder, stomach and intestines were not full. The subjects were also asked to register their diet over three days before the primary blood sampling in a recall questionnaire and follow the same diet in the secondary blood sampling. It should be noted that none of the participants were in their menstrual period at the moment of primary and secondary blood sampling.

Blood samples (7 cc) were collected in a sport salon of Ferdowsi University of Mashhad before futsal training at 17:00 to 18:00. The blood samples were centrifuged for five minutes at 3000 rpm to detach the serum. Next, they were frozen at -20°C. Finally, concentration of serum uric acid and CK were measured by Autoanalyzer Biochemistry device (Mindray BS800) made in China as well as Pars Azmoon kit made in Iran, respectively.

It should be noticed that the subjects were supposed to attend futsal league competitions two months later; in other words, the beginning of our project and their preparation phase, were at the same time. More, the participants were eliminated from our survey, if they were absent from training more than two sessions.

Training Protocol

All subjects had to attend futsal-specific training three sessions a week with the start of the study. In addition to futsal training in every session, HIT and HIT+Zinc groups had to perform HIT protocol as below (Fig 1), after their warm-up and before futsal-specific training. HIT contained 6 to 10 repetitions of 30-second running at 100% of VO_{2peak} with a 4-minutes rest between efforts (25). The training intensity was estimated by formula “Heart Rate Maximum (HRM) = 220 - age” and it was controlled by Heart Rate Monitors (Polar).

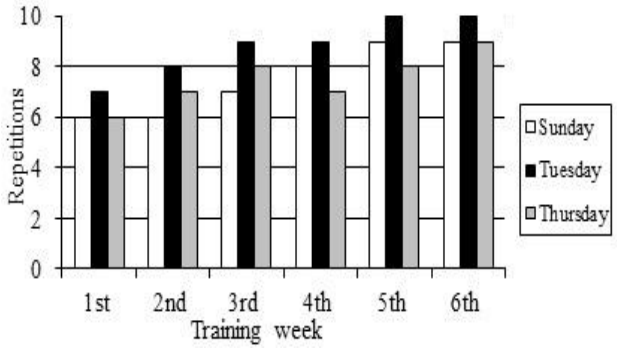

Fig 1. HIT Protocol

Supplementation Protocol

Our subjects in Zinc and Zinc+HIT groups took Zinc (30 mg of zinc gluconate (26) distributed by Nature Made Nutritional Products made in U.S.A), and the subjects in placebo group consumed dextrose (27), two hours after dinner, every day. The subjects had no history of using supplements at least two months prior to our project; more, they were asked to avoid using any other supplement during the study period.

STATISTICAL RESULTS

Using SPSS version 16, the mean and SD of data were calculated by Descriptive Statistics. Data distribution normality and homogeneity of variance were respectively analyzed by Shapiro-Wilk and Levene’s test. The paired-sample t-test and Tukey ’s post hoc analysis were also utilized to compare the differences within groups and between ones, respectively. Then, Wilcoxon and Mann-Whitney U tests were respectively used for comparing the differences within groups and between groups in variable with the distribution other than normal. More, statistical significance was considered at P values ≤ 0.05.

RESULTS

After six weeks, CK levels augmented insignificantly from 83.98 to 120.19 (P=0.101) in placebo group, from 99.58 to 150.1(P=0.167) in HIT group and from 81.07 to 107.90 (P=0.152) in HIT+ Zinc group; while CK levels increased significantly from 66.86 to 124.81(P=0.004) only in Zinc group (Table. 1 & Fig. 2(a)). In addition, we observed an increase in uric acid levels in all groups which were not significant (Table. 2 & Fig. 2(b)).

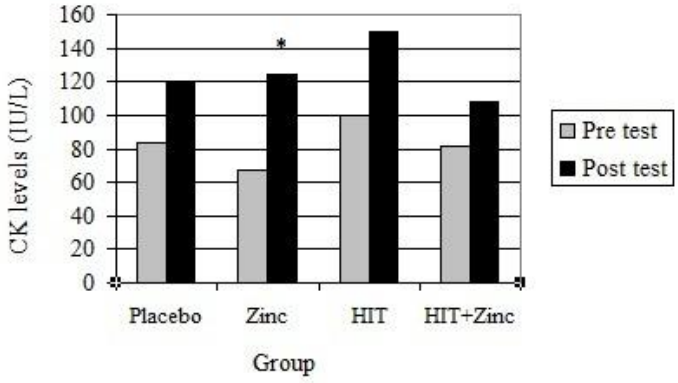

Fig 2(a). CK levels before and after the interventions.

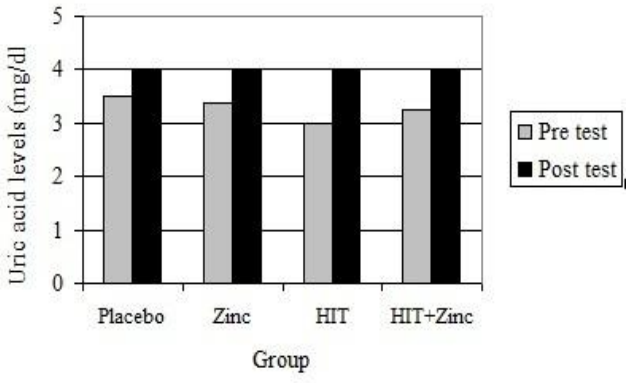

Fig 2(b). Uric acid levels before and after the interventions.

Table 1
Differences within groups of CK levels before and after the interventions. *P≤ 0.05 vs before

Variable	Groups	Phases		Differences			
		Pre-test	Post-test	Within Groups		Between Groups	
		Mean ± SD	Mean ± SD	t	Significance Level	F	Significance Level
CK (IU/L)	Placebo	83.98±22.86	120.19±44.32	-1/888	0.101	0.987	0.413
	Zinc	66.86±16.28	124.81±38.84	-4.140	0.004*		
	HIT	99.58±25.33	150.1±59.23	-1.542	0.167		
	HIT+Zinc	81.07±0.29	107.90±57.58	-1.606	0.152		

Table 2
Differences within groups of uric acid before and after the interventions. *P≤ 0.05 vs before

Variable	Groups	Mean Rank	Sum of Ranks	Difference Within Groups		Difference Between Groups	
				Z	Significance Level	K^2	Significance Level
Uric acid (mg/dl)	Placebo	2.50	5	0	1	0/518	0.915
		2.50	5				
	Zinc	0	0	-1	0.317		
		1	1				
	HIT	0	0	-1.414	0.157		
		1.50	3				
	HIT+Zinc	3.75	7.50	0	1		
		2.50	7.50				

DISCUSSION

This study revealed that CK and uric acid levels increased in female futsal players after six weeks of intervention (Placebo, Zinc, HIT, HIT+Zinc); but there was a significant increase in CK levels only in Zinc group.

We confronted a lack of investigations on the effect of HIT and zinc supplement on uric acid and CK levels. Our findings were not confirmed in some studies: Bogdanis et al (2013) notified that three weeks of HIT could attenuate CK levels and improved antioxidant status in healthy humans(2). Azizi et al (2012) expressed that use of vitamin-mineral supplement along with vigorous swimming training during 4 weeks could lower CK levels and improve inflammatory indices in elite female swimmers (21). Cumming et al (2014) revealed that use of antioxidant supplementation (E+C vitamin) during 11 weeks, declined the uric acid levels (28). These contradictions possibly rooted in the different training programs (various intensity, duration, volume and rest periods of the training), various supplementation way (type of supplement, consumption dose, time of consumption) and also diverse individual characteristics like fitness level, gender and genetic variation or heredity (4, 24).

In contrast, Sahebozamani et al (2015) observed that the repeated bouts of eccentric exercise did not show any effects on Creatine kinase values in male college students (29). Mirzaei et al (2013) reported that a single bout of resistance exercise had no effect on levels of uric acid and total antioxidant capacity in male athletes and non-athletes (10). Green et al (1998) examined the effect of different exercise intensity on serum uric acid concentration. They declared that uric acid concentration progressively increased in cycling at 120% VO_{2max} while prolonged sub-maximal exercise was not capable of an increase in uric acid concentration (30).

Reactive oxygen species cause the oxidative stress and lipid peroxidation of the cell membrane; they play an important role in the initiation and expansion of muscle fiber damage after primary mechanical damage through exercise (6). Muscle damage is accompanied with the destruction of myofibrillar structures and especially the Z lines (31). Instability of cell membrane and secretion of intracellular proteins to extracellular space, increases blood CK levels (7).

The antioxidant system protects the body against these free radicals. Blood uric acid concentration is significantly associated with total antioxidant capacity (2, 4). Uric acid is considered as a major intracellular antioxidant

(one third of total antioxidant capacity concentration) (2, 14); thus, an increase in uric acid levels probably lessens free radicals-induced damage and especially muscle damage. Although, this hypothesis was not confirmed in our study but we witnessed insignificant increase in uric acid levels. It seems that the formation of uric acid is due to the fast-twitch fibers activities during conditions of high energy utilization or high intensity exercise such as HIT; thus, HIT is lonely able to increase antioxidant capacity through increasing the concentration of uric acid (30). More, produce of the free radicals probably occurs in the anaerobic activities due to ischemic and reperfusion. In ischemic situation, xanthine is formed through anaerobic metabolism; then xanthine dehydrogenase is converted to xanthine oxidase and in reperfusion, hypoxanthine is oxidized to uric acid by xanthine oxidase (catalytic enzyme) (10)

It was suggested that increased cortisol levels during exercise contributing to muscle damage, released endogenous purines from the muscle tissue (protein degradation); also, the exercise caused an increase in serum uric acid due to renal clearance decrease which were declared as possible mechanisms of increased uric acid levels in this study (31).

Itahana et al (2014) reported that although high uric acid causes gout, it has been linked with human longevity because of its hypothetical antioxidant function. Recent studies reveal that p53 which has significant roles in cellular metabolism, contributes to tumor suppression by its antioxidant function, while there is a beneficial link between p53 and uric acid; UA transporter SLC2A9 (also known asGLUT9) is a direct p53 target gene and a key downstream effector in the reduction of reactive oxygen species (ROS) through transporting UA as a source of antioxidant (32).

Teixeira et al (2009) investigated the effect of four weeks of antioxidant supplement use (alpha-tocopherol, vitamin C, zinc, and magnesium) on muscle damage, inflammation and lipid peroxidation in kayakers being affected by exercise. After exercise, IL-6 and CK levels augmented in both groups (placebo and supplement group) (33). This result is consistent with our finding as zinc consumption failed to decline exercise-induced muscle damage. Its mechanism is unknown yet.

In response to exercise, the antioxidants release into the bloodstream from its reserves in muscle tissue; it is thought that taking the antioxidants as a supplementation may increase the antioxidant reserves in the muscle tissues and thus increases the antioxidants release into the bloodstream (4, 6). In the cell membrane, zinc has a crucial role in maintaining the membrane integrity; it binds to thiol groups of biomolecules and protects them from oxidation. It also enhances the activities of antioxidant proteins, enzymes and molecules and reduces the activities of oxidant-promoting enzymes as inducible nitric oxide synthase (iNOS) and NADPH oxidase; this way, zinc prohibits from the generation of lipid peroxidation products. More, zinc stimulates the expression of heavy metal-binding protein metallothionein as an excellent scavenger of HO (34-36), however, beneficial effect of zinc on the cell membrane integrity was not proved in our study and serum CK levels augmented, significantly. Its mechanism has not been understood yet. Lastly, we encountered the conflicting results and the lack of studies on the impact of antioxidant supplements, especially zinc on the muscle damage and also uric acid levels; we need more investigations to evaluate and compare the results, in order to understand possible correlation between uric acid and muscle damage.

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REFERENCES

1. Deminice R, Sicchieri T, Mialich MS, Milani F, Ovidio PP, Jordao AA, *Oxidative stress biomarker responses to an acute session of hypertrophy-resistance traditional interval training and circuit training*. J Strength Cond Res, 2011. **25**(3): p.798-804.

2. Bogdanis G, Stavrinou P, Fatouros I, Philippou A, Chatzinikolaou A, Draganidis D, et al, *Short-term high-intensity interval exercise training attenuates oxidative stress responses and improves antioxidant status in healthy humans*. Food chem toxicol, 2013. **61**: p. 171-7.

3. Prasad AS, *Discovery of human zinc deficiency: its impact on human health and disease*. Adv in Nutr: An Int Rev J, 2013. **4**(2): p.176-190.

4. Malekyian finin E, Shavandi N, Saremi A, Tabibi Rad S, *Effect of short term Rezvin supplementation on total antioxidant capacity, super oxide dismutase and cratine kinase in elite wemen vollyball players.* Iran J Nutr Sci Food Technol, 2013. **8**(3): p.86-79.

5. White JP, Wilson JM, Austin KG, Greer BK, John NS, Panton LB, *Effect of carbohydrate-protein supplement timing on acute exercise-induced muscle damage*. Int Soc Sports Nutr, 2008. **31**: p.315-26.

6. Rabienejad A, Joshagani HR, Farzaneh Hesari A, Aghaalinejad H, Khoshdel M, *Effect of vitamin C and E supplementation on lipid peroxidation and delayed onset muscle soreness in professional basketball players*. J Gorgan Univ Med Sci, 2014. **16**(2): p.12-20.

7. Zarghami Khameneh A, Jafari A, *The effect of different doses of caffeine and a single bout of resistent exhaustive on muscle damage indices in male vollyball players*. J Kashan Univ Med Sci, 2014. **18**(33): p.220-8.

8. Gaeini A.A, Sheikholeslam Vatani D, Ashrafi Helen J, Mogharnesi M, *Effects of acute and long term of three types of sprint, endurance and combination trainings on plasma LDH, CK and MDA levels in rats*. J Sport Biosci, 2010. **8**: p.5-20.

9. Gharahdaghi N, Kordi MR, Safaei M, Arabloueisani M, *Adaptive responses of myofibrillar disruption symptoms to high intensity interval aerobic training in soccer players*. J Am Sci, 2013. **9**(4): p.241-45.

10. Mirzaei B, Rahmani-nia F, Rashidlamir A, Gharemani Moghaddam M, *Comparison of resistance exercise on blood total antioxidant capacity, bilirubin and uric acid between athlete and non-athlete elderly men*. JME, 2013. **3**(2): .p129-39.

11. Ibrahim M., Mabrouk M., Tanko Y, *Association between Physical Activity and Serum Bilirubin Levels and Its Potential Modulating Effect in Trained and Untrained Adult Males*. IJAEP, 2016. **5**(1): p.36-42. 11.

12. Lamprecht, M, *Antioxidants in Sport Nutrition* .First ed: CRC Press, 2014.

13. Waring S. W., Webb D. J., Maxwell S. R., *Systemic uric acid administration increases serum antioxidant capacity in healthy volunteers.* Journal of cardiovascular pharmacology, 2001. **38**(3): p.365-371.

14. Mortazavi Moghaddam S.Gh, Zarban A, *Comparison of uric acid concentration and plasma antioxidant capacity in young smokers and non-smokers.* J Birjand Univ Med Sci, 2009. **16**(2): p.24-30.

15. Waring W, Convery A, Mishra V, Shenkin A, Webb D, Maxwell S, *Uric acid reduces exercise-induced oxidative stress in healthy adults*. Clin Sci, 2003. **105**(4): p.425-30.

16. Bergholm R, Mäkimattila S, Valkonen M, Liu M-l, Lahdenperä S, Taskinen M-R, et al, *Intense physical training decreases circulating antioxidants and endothelium-dependent vasodilatation in vivo.* Atherosclerosis, 1999. **145**(2): p.341-9.

17. Molshatzki N., Weinstein G., Streifler J. Y., Goldbourt U., Tanne D, *Serum uric Acid and subsequent cognitive performance in patients with pre-existing cardiovascular disease*. PloS one, 2015. **10**(3): e0120862.

18. Cutler G.R., Camandola S., Malott F.K., Edelhauser A.M., Mattson P.M., *The role of uric acid and methyl derivatives in the prevention of age-related neurodegenerative disorders*. Current topics in medicinal chemistry, 2015. **15**(21): p. 2233-2238.

19. Amaro S., Laredo C., Renú A., Llull L., Rudilosso S., Obach V., Chamorro Á, *Uric Acid Therapy Prevents Early Ischemic Stroke Progression*. Stroke, 2016. **47**(11): p. 2874-2876.

20. Cavas L, Tarhan L, *Effects of vitamin-mineral supplementation on cardiac marker and radical scavenging enzymes, and MDA levels in young swimmers*. Int J Sport Nutr Exercise Metab, 2004. **14**(2): p.133-46.

21. Azizi M, Razmjou S, Rajabi H, *Investigation of corrolation between inflammation, oxidative stress and muscle damage indices after intense swimming training and vitamin-mineral supplement consumption*. Sport Physiol, 2012. **13**: p.47-62.

22. Prasad AS, *Zinc in human health: effect of zinc on immune cells*. Mol Med Cam Ma New York, 2008. **14**(5/6): p.353.

23. Maiguma M, Suzuki Y, Suzuki H, Okazaki K, Aizawa M, Muto M, et al, *Dietary zinc is a key environmental modifier in the progression of IgA nephropathy*. PloS one, 2014; **9**(2): p.90558.

24. Padervand S, Hassani A, Kalalian Moghaddam H, Donyaei A, *The effect of taking ginger supplement and progressive endurance training on cellular damage in non-athlete men*. J Knowledge Health, 2014. **9**(2): p.9-13.

25. Siahkohian M. Khodadadi D, *The effect of high intensity interval training and moderate continuous training on aerobic and anaerobic indices in athlete men* .Sports physiol, 2013. **18**: p.39-52.

26. Asghari S, Hossein Zadeh M.J, Mohajeri Tehrani M.R, Sehat M, *The effect of Zinc supplementation on serum lipids level and hs-CRP in diabetic individuals with over weight*. IJDLD, 2011. **10**(6): p.614-20.

27. Gaeini A.A, Choobineh S, Shafiei Neek L, Satarifard S, Mahmod Zadeh M, Allahyar beigi KH, *The effect of zinc supplementation on serum testosterone and plasma lactate in male cyclists after one bout of exhaustive exercise*. J Sharekord univ med sci, 2012. **14**(3): p.51-61.

28. Cumming K.T, Raastad T, Holden G, Bastani N.E, Schneeberger D, Paronetto M.P, et al, *Effects of vitamin C and E supplementation on endogenous antioxidant systems and heat shock proteins in response to endurance training*. Physiol Reports, 2014. **2**(12142): p.1-14.

29. Sahebozamani M., and Mohammadi H, *The effect of repeated bouts of eccentric exercise on some of Biochemical markers of delayed onset muscle soreness.* IJAEP, 2015. **4**(1): p. 34-39.

30. Green HJ, Fraser I, *Differential effects of exercise intensity on serum uric acid concentration*. Med sci sports exercise, 1988. **20**(1): p.55-9.

31. Hazar S, Hazar M, Korkmaz Ş, Bayil S, *The effect of graded maximal aerobic exercise on some metabolic hormones, muscle damage and some metabolic end products in sportsmen*. Sci. Res. Essays, 2011. **6**(6): p.1337-43.

32. Itahana Y., Han R., Barbier S., Lei Z., Rozen S., Itahana K, *The uric acid transporter SLC2A9 is a direct target gene of the tumor suppressor p53 contributing to antioxidant defense*. Oncogene, 2015. **34**(14): p. 1799-1810.

33. Teixeira VH, Valente HF, Casal SI, Marques AF, Moreira PA, *Antioxidants do not prevent postexercise peroxidation and may delay muscle recovery. Med Sci Sports Exercise,* 2009. **41**(9): p.1752-60.

34. Prasad AS, *Zinc: role in immunity, oxidative stress and chronic inflammation*. Curr Opin Clin Nutr Metab Care, 2009. **12**(6): p.646-52.

35. Prasad AS, *Clinical, immunological, anti-inflammatory and antioxidant roles of zinc*. Exp gerontol, 2008. **43**(5): p. 370-7.

36. Rahman I, Bagchi D, *Inflammation, Advancing Age and Nutrition: Research and Clinical Interventions*.First ed. USA: Academic Press, Technology & Engineering, 2013.