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Original Research Article

Anti-inflammatory effects of basil seeds consumption in high-intensity resistance training individuals

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Abstract

A high nutritious diet along with regular exercise is essential to maintain physical and psychological health. Physical inactivity leads to chronic low grade inflammation and is the leading risk factor for obesity and many other diseases. Few studies revealed that strenuous exercise may also promote systemic low grade inflammation and increase the pro - inflammatory cytokines. The inflammatory cytokines increase the risk of morbidity. Recently much research has been going on natural and synthetic formulations that bring exercise benefits. One such herb with health promoting bio active compounds is *Ocimum basilicum*.

Aim: We aimed to find out the anti-inflammatory and anti-obesity effect of basil seeds supplementation in both non exercisers and high intensity resistance training healthy male individuals.

Materials and Methods: The study included 150 healthy male individuals in the age group of21-35 years. The participants were divided into three groups: Non-exercise individuals who consumed basil seeds (Basil seeds group BS, n=50), High intensity resistance training group (HIRT, n=50) and HIRT group along with basil seeds supplementation (BS+HIRT, n=50). These 3 groups underwent 8 weeks of intervention. BS and BS+HIRT participants consumed 10 gm of basil seeds soaked in one litre of water, 6 days/week. High intensity training included 8 weeks with 5 sessions per week. We measured lnterleukin-6 (IL-6), Tumor necrosis factor– α (TNF-α) and leptin levels at the baseline and after 8 weeks of intervention. Blood samples were obtained after overnight fasting.

Results: At the baseline mean value of IL-6 is 30.05 pg/ml, TNF –α is 34.07pg/ml and leptin is 8.34ng/ml in all the three groups. There was significant reduction in IL-6 and TNF –α and leptin in BS group after consumption of basil seeds for 8 weeks (23.6±2.19pg/ml, 18.01±1.73pg/ml, 3.77±1.12ng/ml respectively with $p<0.001$). The HIRT group showed significant elevation in IL-6 (46.85±4.16pg/ml, $p<0.001$) and TNF–α (81.24±4.14pg/ml, $p<0.001$) after 8 weeks of resistance training. IL-6 and TNF–α levels were less in BS +HIRT (40.01±4.11 pg/ml, 54.77±5.34 pg/ml respectively; $p<0.001$) compared to HIRT group. Leptin levels were reduced from 8.35±1.44 ng/ml to 3.77±o.79 ng/ml with $p<0.001$ in all the three groups after 8 weeks of intervention.

Conclusions: Basil seeds supplementation reduced the pro-inflammatory status. The reduction in leptin levels concluded that basil seeds have anti-obesity properties in both non-exercisers and resistance training individuals.

Key words: Basil seeds, anti-inflammation, HIRT, IL-6, TNF–α, Leptin

Introduction

Physical inactivity leads to chronic low grade systemic inflammation which is the fundamental cause for many life style disorders. The best way to prevent and treat the chronic diseases is lifestyle modification. Change in diet and physical training protects against development of chronic diseases. There are controversies regarding the intensity and type of exercise beneficialto health. Studies suggest that mild to moderate intensity exercise is beneficial over strenuous/high intensity exercise. Strenuous exercise acts as a stressor and raise the inflammatory markers to produce pro-inflammatory condition. [1]. During resistance training this inflammation is essential to repair the injury incurred during exercise[2]. Over a period of time continuous training turns the pro- inflammatory status to anti-inflammatory condition to repair tissue injury, initially caused by exercise[3,4].

Few studies state that adaptation to exercise is poor in some individuals. Continuous exercise, particularly in which eccentric contractions are used; may lead to chronic inflammatory status[5]. This chronic inflammation may become the prime cause for osteoarthritis [6], rheumatoid arthritis [7], cardiac arrhythmias [8] few musculoskeletal disorders and morbidity [9]. It is essential to reduce the inflammatory reaction due to strength training to derive complete benefits of exercise. In addition, for most of the people exercise has become impractical because of various reasons. This lead to search for dietary supplements that produce benefits similar to exercise and enhance the exercise performance [10]. To maintain immune function, exercisers should consume well balanced diet with anti-oxidant and anti-inflammatory actions. Substances like AICAR (5-aminoimidazole-4- carboxamide-1-b-D-ribofuranoside), selective PPAR-δ (Peroxisome proliferator –activated receptor delta) agonist: GW1516 [11], resveratrol [12], ursolic acid[13]have been identified to have exercise mimicking effects.

Another herb with anti inflammatory, anti-oxidant and anti obesity properties is *Ocimum basilicum*. *O. Basilicum* belongs to Laminaceae family. The leaves and seeds are edible and havemany medicinal properties. It has wide range of pharmacological actions including anti-viral, anti-bacterial, anti-microbial, anti-oxidant and anti-inflammatory properties[14]. Basil seeds contain 42%-63% of carbohydrates [15], 9.7%-33% of fats [16], 14.8gm/100gm dry weight of proteins and high amount of cellulose and hemicelluloses [15]. The seeds are rich source of alpha- linolenic acid (ALA) (49.3-52.4%), linoleic acid (23.6-26%),oleic acid (10.3-12.3%), palmitic acid (8-9.2%), stearic acid (3.6-3.8%), otherpoly unsaturated fatty acids phenolic compounds, flavanoids, alkaloids, saponins andterpenoids (0.134mg/g). They also possess anti-oxidant activity [17].The phytochemical compounds present in the seeds with anti-inflammatory actions are ricinoleic acid, gamabufotalin, colchicine, beclomethasone and prednisone. The anti-obesity and anti-oxidant properties are due to the presence of beta carotene, levodopa, retinol, retinyl acetate triaziquone and vincamine[18]. ALA, the omega 3 fatty acid component of basil seeds is an anti-inflammatory agent and suppress the release of anti-inflammatory cytokines from immune cells. The ω-3 fatty acid series have the capacity to minimise the inflammation. ALA can alter the membrane lipid composition of cell membranes, energy expenditure, decreases formation of reactive oxygen species and activates peroxisome proliferator-activated receptor (PPAR). The PPAR decreases the activation of pathways whichcause inflammation. In addition ALA accumulated in the adipose tissue can modify the leptin synthesis and release from adipose tissue and indirectly regulates obesity [19]. There are only few human studies on the anti-inflammatory and anti-obesity effect of basil seeds. To assess the anti-inflammatory and anti-obesity properties we selected IL-6, TNF-α, and leptin. We aimed to study the effect of basil seeds consumption on the levels of IL-6, TNF-α, and leptin in both non-exercisers and high intensity resistance training individuals.

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Materials and Methods

The study group included healthy male individuals between the age of 20-35 years. Institutionalethical committee approval was obtained. All the subjects signed on the informed consent. Anthropometric data was collected by using a portable In Body 270 compact body compositionanalyser. The subjects were recruited as three groups. The first group (basil seeds - BS) included50 physically inactive individuals. BS group consumed 10gm of soaked basil seeds for 8 weeks. The second group (HIRT, n=50) of healthy male subjects underwent high resistance training for 8 weeks. During the training programme a total of 26 exercise types were included. RT consisted of 10 upper body(bench press, cable cross over, shoulder press, lateral raise, biceps curl, concentration curl, barbell elbow extension and kick back) and 10 lower body training exercises (squat, leg press, leg extension, seated/standing calf raise, sit–up, leg curl, back extension, sit up, stiff leg,dead lift and abdominal crunch). Participants performed 5 sets of 10- 15 repetitions with a 30 seconds rest between the repetitions, 5times/week for 8 weeks. Intensity of exercise is determined by calculating target heart rate according to American heartassociation. The target heart is 70-85% of maximum heart rate. The third group (BS+HIRT) with 50 male healthy subjects underwent high resistance training as well as consumed 10gm ofsoaked basil seeds for 8 weeks.

Basil seeds were purchased from local market. 10gm packets were prepared and provided to BS and BS+HIRTgroup. Subjects were instructed to soak them in 1 litre of water during night time and consume the basil (sabja) seeds water early in the morning on empty stomach. They were continuously monitored throughout the study. Subjects performed exercises using weights and machines under the supervision of a trained instructor. All the subjects signed on the informed consent.Anthropometric data was collected by using a portable InBody 270 compact body composition analyser. Blood samples were collected before and after 8 weeks of intervention. Serum was separated by centrifuge machine (3000rpm for 3min) and it was stored at -80^{o}C until assayed. SerumIL-6, TNF-α, and leptin were estimated by using ELISA kits.

Statistical analysis

Statistical analysis carried out by SPSS 21.0 version. Data were expressed as mean and standard deviation (SD). Paired T test, Pearson correlation were used. One way ANOVA was analysed by post hoc test. The study power was calculated at 0.95. The significance level was considered to be at $p<0.05$.

Results

The demographic features of the three groups were tabulated in Table – 1. Data were expressed in mean and standard deviation. The effect of basil seeds consumption on TNF- α, IL-6 and leptin were analysed. There was a significant difference in the levels of TNF- α, IL-6, Leptin after 8 weeks of intervention. In the BS group significant decrease in TNF-α (23.6±2.19pg/ml) and IL-6 levels (18.01±1.73pg/ml) was observed after consumption of basil seeds.In HIRT group there was significant increase in TNF- α (81.24±4.14 pg/ml) and IL-6 (46.85±4.16 pg/ml). The increase in levels can be attributed to their release from actively contracting muscles.

Table 1: Characteristics of the three different intervention groups.

Group	Age (Yrs)	BMI	Waist /Hip ratio
BS (n=50)	27.11 ±3.91	25.88 ±4.67	0.92±0.067
HIRT(n=50)	26. 80 ±4.51	24.89 ±4.68	0.85±0.067
BS+HIRT(n=50)	27.12 ±3.75	26.34 ±4.60	0.85±0.064

In HIRT+BS group though there was increase in TNF- α (54.77±5.34pg/ml)and IL-6 (40.01±4.11 pg/ml); but their levels were less than the HIRT group levels, indicating that basil seeds have anti-inflammatory action. In all the three groups the leptin levels were reduced significantly from 8.35±1.44ng/ml to 3.77±0.79 ($P<0.001$). Pearson correlation between TNF-α, IL-6 and leptin were analysed. There was significant correlation between TNF-α and IL-6 (r=0.93, n=150) in all the three groups. But there was insignificant correlation of TNF- α and

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IL-6with leptin.

Table 2: Paired 't' test results of TNF- α

TNF- α (pg/ml)	BS	HIRT	HIRT+BS
	Mean±SD	Mean±SD	Mean±SD
At the baseline	34.47±3.01	33.89±3.46	33.86±3.49
After 8weeks	23.6±2.19	81.24±4.14	54.77±5.34
P Value	<0.001	<0.001	<0.001

Fig 1: Paired't' test results TNF-α

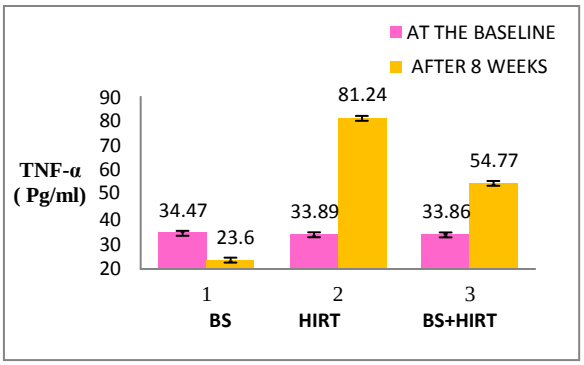

Table 3: Paired 't' test results for IL-6

IL-6 (pg/ml)	BS	HIRT	HIRt+BS
	Mean±SD	Mean±SD	Mean±SD
At the baseline	28.26±2.03	31.07±2.47	30.82±3.19
After 8 weeks	18.01±1.73	46.85±4.16	40.01±4.11
P Value	<0.001	<0.001	<0.001

Fig 2: Paired 't' test results for IL-6

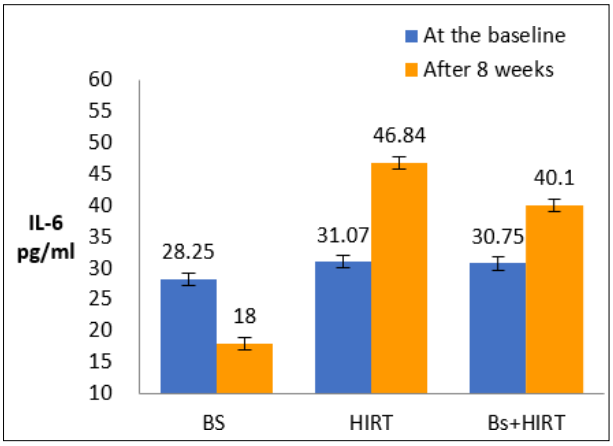

Table 4: Paired 't' test results for Leptin

LEPTIN (ng/ml)	BS	HIRT	HIRT+BS	TOTAL
	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD
At the baseline	8.24±1.86	8.45±1.28	8.35±1.12	8.35±1.44
After 8 weeks	3.77±1.12	3.79±0.58	3.79±0.58	3.77±0.79
P Value	<0.001	<0.001	<0.001	<0.001

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Fig 3 - Leptin paired 't' test

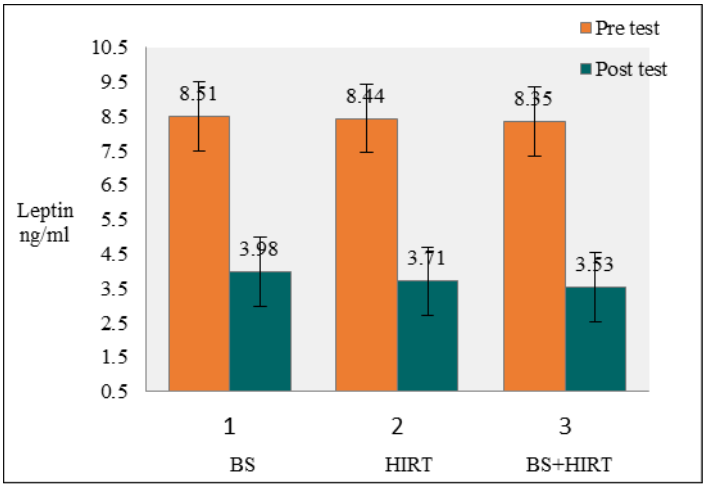

Table 5: Pearson Correlation test between TNF- α, IL – 6, Leptin

Variables		correlation coefficient (r)	P value
TNF- α	IL6	0.93	<0.001
	LEPTIN	-0.002	0.98
IL- 6	LEPTIN	-0.03	0.78

Discussion

It is well known that exercise induces certain hormonal and immunological changes akin to stress. During exercise skeletal muscle, adipose tissue and immune cells release an array of cytokines which modulate the metabolism and immune response of the individual (20). The cytokines are removed from the circulation within short period to inhibit the inflammation in the injured or exercising tissues. The degree of cytokine release depends on the intensity, duration of exercise and the individual response to exercise (21). Few studies reveal that strenuous exercise for prolonged period may not clear the cytokines from circulation. This may lead to chronic low grade inflammatory state and potentiate significant pathological immune response in skeletal muscle and articular cartilage (22). If sufficient recovery is not allowed; the cytokines hinder muscle function. The cytokines stimulate the formation of free radicals and cause damage to contractile proteins (23, 24). The inflammatory reaction is due to rise in pro inflammatory cytokines such as interleukins – 6, 8, 15, 1beta and TNF-α (17). During exercise training the major source of IL-6 is skeletal muscle and a small amount of IL-6 is secreted fromadipocytes of adipose tissue and macrophages. Exercise induces transcription of IL-6 genein skeletal muscles and also stimulates release of TNF-α from adipose tissue and macrophages. Our results showed that 8 weeks of HIRT induced significant increase in both IL-6 and TNF-α.The rise in IL-6 levels in HIRT are consistent with many studies; but the rise in TNF-αlevels in HIRT group are in contradiction with the previous studies. Data suggests that IL-6 causes anti-inflammation by decreasing the production and release ofTNF-α from adipose tissue and monocyte series (21). In contrast to it we observed rise in TNF-α levels. The possible mechanism of the post exercise rise in IL-6 and TNF-α may be the high volume training during the 8 weeks programme. During HIRT training the muscles undergo both eccentric and concentric type of contractions. More over muscle injury is also more in HIRT, releasing high amount ofcytokines. The structural damage is severe in HIRT and inflammatory reactions might last for several days. More over the rise also can be due tocollection of the samples immediately afterexercise.

In our study basil seeds supplementation decreased IL-6 and TNF-α in both non-exercisers and resistance training individuals. The decrease in cytokines can be due to the anti-inflammatory activity of basil seeds (25). Basil seeds might have decreased the release of these cytokines

from macrophages, Natural killer cells and adipose tissue, without affecting the release from skeletal muscle. Basil seeds reduce the PPAR (peroxisome proliferator-activated receptors), systemic inflammation related genes such as Nuclear factor kappa B (NF κB). Basil seeds consumption down regulates the expression of pro inflammatory cytokines genes in macrophages. It also blocks macrophage infiltration in the adipocytes by inhibiting the Ccl2 gene and reduces the percentage of foam cells. Our results were in line with *in vitro* performedon co cultured adipocytes and macrophages. (26, 27).ALA, the ω-3 PUFA content of basil seeds decrease the pro-inflammatory cytokines release from neutrophils(28, 29). In addition basil seeds supply specific micro nutrients that attenuate immune dysfunction(25).

We also tested the effect of basil seeds supplementation on leptin levels. The pre test leptin levels were more than normal in all the three groups (Normal range: 2-5.6 ng/ml in lean males). The serum leptin levels reduced significantly in all the three groups. The combined effect of HIRT, BS supplementation caused more reduction when compared to the other two groups. Many studies revealed that diet can modulate leptin levels and especially fatty acid compositionof diet have more impact on leptin production. *In vitro* and *In vivo* studies showed that ω-3fatty acids consumption decreases leptin gene expression (30, 31). In basil seeds the amount of alpha linolenic acid is more and we assumed that ALA might have decreased leptin levels. Basil seedshave high dietary fibre content in the form of cellulose, hemicelluloses and lignin. The high fibre hinders carbohydrate absorption from the gut and reduces insulin levels also. Leptin levels are lowered as a consequence of lowered blood glucose and insulin (25). ALA exerts its action on fat metabolism. Itreduces fat deposition in the adipose tissue and reduces serum levels of cholesterol, LDL and VLDL. Altered fat metabolism decreases leptin production in the adipose tissue (31). In addition, exercise decreases fat mass and increases skeletal muscle mass. Studiesindicate that leptin levels correlate with the amount of body fat mass. So the reduction in fat mass feedback to inhibit leptin secretion. Leptin secretion is also regulated by cytokines released from immune cells. IL-6 and TNF-α promote leptin mRNA secretion from adipose tissue. In HIRT+BS group, the reduced cytokine levels might have decreased leptin secretion.Conclusion:

Basil seeds have strong anti-inflammatory properties. They can modulate inflammatory response of the immune system cells both in physically inactive people and high volume training individuals. Anti obesity effect is of basil seeds slightly less than the exercise training effect. Much research is needed to know the dose and duration of consumption of basil seeds for effective body weight reduction. Basil seeds consumption promotes the exercise performance by reducing the inflammatory cytokines.

Limitations: we could not assess the intensity of the training by calculating Vo2 max. Instead of Vo2 max, target heart rate was calculated for assessing the intensity of exercise.

Conflict of interest: No

Financial aid: Self aided

research**References**

1. Silveira LS, AntunesBde M, Minari AL, Dos Santos RV, Neto JC, Lira FS. Macrophage Polarization: Implications on Metabolic Diseases and the Role of Exercise. Crit Rev Eukaryot Gene Expr. 2016;26(2):115-32.

2. Oishi Y, Manabe I. Macrophages in inflammation, repair and regeneration. Int. Immunol. 2018 Oct 29;30(11):511-528.
3. Pedersen BK. Anti-inflammatory effects of exercise: role in diabetes and cardiovascular disease. Eur J Clin Invest. 2017 Aug;47(8):600-611.
4. Roca-Rodríguez Mdel M, Garrido-Sánchez L, García-Almeida JM, Ruiz-Nava J, Alcaide-Torres J, Gómez-González A,*et al*. Effects of exercise on inflammation in cardiac rehabilitation. Nutr Hosp. 2015 Jun 1;31(6):2633-40.
5. Howatson G, van Someren KA. The prevention and treatment of exercise-induced muscle damage. Sports Med. 2008;38(6):483-503.
6. Akeson G, Malemud CJ. A Role for Soluble IL-6 Receptor in Osteoarthritis. J FunctMorpholKinesiol. 2017;2(3):27.
7. Yoshida Y, Tanaka T. Interleukin 6 and rheumatoid arthritis. Biomed Res Int. 2014;2014:698313.
8. Benito B, Gay-Jordi G, Serrano-Mollar A, Guasch E, Shi Y, Tardif JC,*et al*. Cardiac arrhythmogenicremodeling in a rat model of long-term intensive exercise training. Circulation. 2011 Jan 4;123(1):13-22.
9. Docherty S, Harley R, McAuley JJ, Crowe LAN, Pedret C, Kirwan PD,*et al*. The effect of exercise on cytokines: implications for musculoskeletal health: a narrative review. BMC Sports Sci Med Rehabil. 2022 Jan 6;14(1):5.
10. Goodyear LJ. The exercise pill--too good to be true? N Engl J Med. 2008 Oct 23;359(17):1842-4.
11. Narkar VA, Downes M, Yu RT, Embler E, Wang YX, Banayo E,*et al*. AMPK and PPAR delta agonists are exercise mimetics. Cell. 2008 Aug 8;134 (3):405-15.
12. Lagouge M, Argmann C, Gerhart-Hines Z, Meziane H, Lerin C, Daussin F,*et al*. Resveratrol improves mitochondrial function and protects against metabolic disease by activating SIRT1 and PGC-1alpha. Cell. 2006 Dec 15;127(6):1109-22.
13. Kunkel SD, Elmore CJ, Bongers KS, Ebert SM, Fox DK, Dyle MC,*et al*. Ursolic acid increases skeletal muscle and brown fat and decreases diet-induced obesity, glucose intolerance and fatty liver disease. PLoS One. 2012;7(6):e39332.
14. Bilal A, Jahan N, Ahmed A, Bilal SN, Habib S, Hajra, S. Phytochemical and pharmacological studies on Ocimum basilicum Linn-A review. Int. J Curr. Res. Rev.2012;4:73-83.
15. Mathews S, Singhal RS, Kulkarni PR. Ocimum basilicum: A new non-conventional source of fiber. Food Chem. 1993; 47:399-401.
16. Kakaraparthi PS, Srinivas KVNS, Kumar JK, Kumar AN, Kumar A. Composition of herb and seed oil and antimicrobial activity of the essential oil of two varieties of Ocimum basilicum harvested at short time. J Plant Dev. 2015;22:59-76.
17. Mezeyová I, Hegedűsová A, Hegedűs O, Vargová A, Timoracká M, Šlosár M,*et al*. Basil seeds as a source of antioxidants affected by fortification with selenium. Folia Horticulture. 2020;32(1):11-20
18. Subash-Babu P, Mohammed Alowaidh H, Al-Harbi LN, Shamlan G, Aloud AA, AlSedairy SA,et al. Ocimum basilicum L. Methanol Extract Enhances Mitochondrial Efficiency and Decreases Adipokine Levels in Maturing Adipocytes Which Regulate Macrophage Systemic Inflammation. Molecules. 2022 Feb 18;27(4):1388.
19. Zebrowska A, Hall B, Stolecka-Warzecha A, Stanula A, Sadowska-Krępa E. The Effect of Omega-3 Fatty Acid Supplementation on Serum Adipocytokines, Lipid Profile and Biochemical Markers of Inflammation in Recreational Runners. Nutrients. 2021 Jan 29;13(2):456.
20. Pedersen BK, Hofman-Goetz L. Exercise and the immune system: regulation, integration, and adaptation. Physiol Rev. 2000;80:1055-81.
21. Cerqueira É, Marinho DA, Neiva HP, Lourenço O. Inflammatory Effects of High and Moderate Intensity Exercise-A Systematic Review. Front Physiol. 2020 Jan 9;10:1550.
22. Morais GP, Chemerka C, Masson A, Seerattan RA, da Rocha AL, Krawetz R,*et al*. Excessive downhill training leads to early onset of knee osteoarthritis. OsteoarthrCartil.

2021;29(6):870-81.
23. Cheng AJ, Jude B, Lanner JT. Intramuscular mechanisms of overtraining. Redox Biol. 2020 Aug;35:101480.
24. VanderVeen BN, Fix DK, Montalvo RN, Counts BR, Smuder AJ, Murphy EA,*et al*. The regulation of skeletal muscle fatigability and mitochondrial function by chronically elevated interleukin-6. Exp Physiol. 2019;104 (3):385-97.
25. Nieman DC, Konrad M, Henson DA, Kennerly K, Shanely RA, Wallner-Liebmann SJ. Variance in the acute inflammatory response to prolonged cycling is linked to exercise intensity. J Interferon Cytokine Res. 2012 Jan;32(1):12-7.
26. Takeuchi H, Takahashi-Muto C, Nagase M, Kassai M, Tanaka-Yachi R, Kiyose C. Anti-inflammatory Effects of Extracts of Sweet Basil (*Ocimum basilicum* L.) on a Co-culture of 3T3-L1 Adipocytes and RAW264.7 Macrophages. J Oleo Sci. 2020 May2; 69(5):487-493.
27. Żebrowska A, Hall B, Stolecka-Warzecha A, Stanula A, Sadowska-Krępa E. The Effect of Omega-3 Fatty Acid Supplementation on Serum Adipocytokines, Lipid Profile and Biochemical Markers of Inflammation in Recreational Runners. Nutrients. 2021 Jan 29;13(2):456.
28. Singh S, Nair V, Jain S, Gupta YK. Evaluation of anti-inflammatory activity of plant lipids containing alpha-linolenic acid. Indian J Exp. Biol. 2008;46:453-456.
29. AhmadniayMotlagh H, Aalipanah E, Mazidi M, Faghih S. Effect of flaxseed consumption on central obesity, serum lipids, and adiponectin level in overweight or obese women: A randomised controlled clinical trial. Int J ClinPract. 2021 Oct;75(10):e14592.
30. Mostowik M, Gajos G, Zalewski J, Nessler J, Undas A. Omega-3 polyunsaturated fatty acids increase plasma adiponectin to leptin ratio in stable coronary artery disease. Cardiovasc Drugs Ther. 2013 Aug;27(4):289-95.
31. Reseland JE, Haugen F, Hollung K, Solvoll K, Halvorsen B, Brude IR,*et al*. Reduction of leptin gene expression by dietary polyunsaturated fatty acids. J Lipid Res. 2001 May;42(5):743-50.