# Effect of Chlorella vulgaris supplementation with eccentric exercise on serum interleukin 6 and insulin resistance in overweight men

**Article** *in* Sport Sciences for Health · September 2020

DOI: 10.1007/s11332-020-00656-0

CITATIONS
0

READS
76

**3 authors:**

Mohammad Samadi
Baqiyatallah University of Medical Sciences,Tehran,Iran.
**18** PUBLICATIONS **112** CITATIONS
SEE PROFILE

Hossein Shirvani
**56** PUBLICATIONS **154** CITATIONS
SEE PROFILE

Ali Akbar Shafeie
**2** PUBLICATIONS **0** CITATIONS
SEE PROFILE

Sport Sciences for Health
https://doi.org/10.1007/s11332-020-00656-0

ORIGINAL ARTICLE

# Effect of *Chlorella vulgaris* supplementation with eccentric exercise on serum interleukin 6 and insulin resistance in overweight men

**Mohammad Samadi**[1] · **Hossein Shirvani**[1] · **Ali Akbar Shafeie**[1]

Received: 11 February 2020 / Accepted: 14 May 2020


## Abstract

**Purpose** Overweight can lead to the down-regulation of insulin sensitivity and cytokine profile. In this regard, non-pharmacological interventions such as exercise and supplementation are recommended. Therefore, the aim of this study was to investigate the synergistic effect of Chlorella vulgaris supplementation with acute eccentric exercise on serum levels of interleukin-6 and insulin resistance in overweight men.

**Methods** Thirty subjects (aged 22.8 ± 2.1 years, BMI 27.1 ± 9.6 kg/m$^2$) were randomly divided into three equal groups: exercise [just perform acute eccentric exercise test (AEE)], Chlorella vulgaris (for 7 days and then AEE), placebo (for 7 days and then AEE). Blood sampling was performed in 4 stages: day 1 (before supplementation) and day 7 (after supplementation), after AEE and 24 h after AEE. Subjects of the supplement group received *Chlorella vulgaris* supplement (300 mg) four times daily for 1 week, and the placebo group consumed similar dextrose tablets. Exercise groups just perform AEE. AEE test included a 20-min treadmill run at a speed of 9 km/h with a negative 10% slope. Serum levels of IL-6, insulin, and glucose were measured by Elisa kit. Also, the hip circumference and knee range of motion (ROM) was measured at four stages.

**Results** At the end of the study, there was a significant decrease in IL-6 levels in the *Chlorella vulgaris* group compared to the other two groups at 24 h after AEE test ($P < 0.01$). There was also a significant decrease in insulin resistance levels in the supplement group compared to the other two groups at 24 h after AEE test ($P < 0.02$). Also, the knee ROM decreased significantly in all three groups ($P < 0.05$).

**Conclusion** *Chlorella vulgaris* with acute eccentric exercise can have a more modulating effect on serum IL-6, insulin resistance and other characteristics in overweight men compared to acute eccentric exercise without chlorella.

**Keywords** Insulin resistance · *Chlorella vulgaris* · Cytokine · Eccentric exercise · Overweight

## Introduction

In inactive people, gaining weight and obesity is strongly associated decrease the range of motion (ROM) and increase in waist-hip ratio or waist-to-hip ratio (WHR) with distribution of chronic diseases including hypertension, disorder in blood lipids' and insulin resistance, which are all risk factors for cardiovascular diseases (CVD). Also, inactive lifestyle increases the risk of developing CVD [1]. The WHR is the dimensionless ratio of the circumference of the waist to that of the hips. WHR is used as a measurement of obesity, which in turn is a possible indicator of other more serious health conditions. Also, obesity is associated with poorer range of motion and Tegner scores following hamstring auto graft anterior cruciate ligament reconstruction in Asians. Exercise training improve ROM in obese people. It has been show that physical activity significantly reduces risk factor of CVD [2]. It is suggesting that, in the treatment of overweight, physical activity should be accompanied by weight-loss diet.

Doing heavy and unusual physical activities and/or activities associated with extrovert contractions such as running downhill, plyometric exercises and extrovert contractions caused by exercise are followed by increasing overly inflammatory factors in the muscle [3]. Christiansen et al. show that acute exercise increases circulating inflammatory markers in overweight and obese compared with lean subjects [4]. Muscular function disorder that occurs as a result of muscular incandescence and injury leads to a decrease in daily

✉ Hossein Shirvani
shirvani@bmsu.ac.ir

[1] Exercise Physiology Research Center, Life Style Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran

Published online: 02 June 2020

exercise and performance in normal people and athletes [5]. The morphological changes caused by extrovert contractions lead to inflammatory responses [6]. Chemokines (signaling proteins) are brought out from injured muscles and make inflammatory cells such as neutrophils and macrophages more active [7]. Due to the accumulation of inflammatory cells at the spot of injury, the level of Bradykinin, Leukotrienes, and prostaglandins also increase at the same time, which are the same reasons of creation in muscle tissue and increased overly inflammatory factors [8]. Therefore, reducing post-workout muscle injury through decreasing inflammatory responses seems critical. Recent findings indicate that physical activity increases the systemic level of a number of cytokines with anti-inflammatory properties, and the skeletal muscle has recently been recognized as an endocrine member that induces the production and release of cytokines [9, 10]. An anti-inflammatory and antioxidant dietary supplement seems to be one of the ways to combat this injury [8]. Among the materials, polyphenols have recently received lots of attention due to their nutritional effects, polyphenols are phytochemical components amply found in plants [11]. The most important biological function of polyphenols is related to their antioxidant and anti-inflammatory properties [12]. In addition, researches in human and animal specimens have occasionally shown positive anti-inflammatory effects of polyphenols on muscular injuries caused by activities [13, 14].

In recent years, the tendency to use micro-seaweeds and underwater creatures as a diet or an alternative medicine has increased due to their high content of bioactive compounds. These small algae have a variety range of different nutrients such as minerals, Proteins, vitamins, fiber, omega-3s, chlorophylls, carotenoids and other bioactive compounds [15]. Using Chlorella supplement has shown that multiple effects on biochemical function, such as antioxidant effects have led to physical system increase in diabetic mice and also blood sugar reduction in diabetic animals. Some reportage about anti-inflammatory being of this supplement has also been reported. Farther more, some reportage about cytokine production and body immune system improvement has been reported. Chlorella has also reduced oxidative stress [16]. On the other hand, Interleukin 6 (IL-6) is a multiple-function protein which has an important role in defensing the host, rapid reaction phase and immune responses. IL-6 is one of the cytokines that has both anti-inflammatory and inflammatory properties and increases more to response to activities in the muscles compared to other cytokines [17], the primary cytokines found in bloodstream associated with severe infection include IL-6, interleukin 1 beta (IL-1β) and tumor necrosis factor alpha (TNF-α). In general, IL-6 is the first cytokine present in the bloodstream during exercise, and the appearance of IL-6 in the circulation is very obvious and occurs before other cytokines. Developing IL-6 level significantly increases (up to 100 times) in the response to exercise and decrease in the post-exercise period [18, 19].

Using herbal and chemical supplement with exercise training can improve physical performance and cellular hemostasis in different tissue [20, 21]. In a study, Lee et al. [22] examined the effects of Chlorella vulgaris on antioxidant status in smokers. After intervention, the results showed an increase in the activity of catalase and superoxide dismutase enzymes and a significant decrease in damages of lymphocytes' DNA were shown [22]. In a study, Ali Ashrafi et al. [23] divided the patient with non-alcoholic fatty liver disease (NAFLD) into the intervention and placebo groups, each groups consisted of 35 specimens. The results showed a decrease in alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) enzymes. Only the difference in ALP for the two groups was significant. At the end of the study, there was a significant decrease in TNF-α levels compared to the placebo group [23]. In another study, Lin et al. stated that chlorella supplement improves anaerobic exercise capacity and also reduces post-dehydration muscle inflammation after exercise training [24]. Farther more, Ebrahimi et al. observed weight-loss in groups that took this supplement [25]. Consistency of FSG and Hs-CRP Liver enzymes' serums were also significantly reduced. Consistency of insulin and HOMA serum were also significantly increased in *Chlorella vulgaris* supplementation group [26]. In a study, Horii et al. stated that high-intensity interval training (HIIT) exercise with use of chlorella supplement had a greater effect on exercise performance and muscular glycolytic and oxidative lactate metabolism compared to chlorella supplement taking or HIIT exercising [27]. Sibi et al. found that the use of *Chlorella vulgaris* supplement causes reduction in pro-inflammatory factors such as IL-6, interleukin 6 and TNF-α. This researcher also found that supplementation of Chlorella vulgaris prevent the production of anti-inflammatory cytokine and is also a good alternative to steroidal and non-steroidal anti-inflammatory drugs [28].

## Materials and methods

### Subjects

Subjects of this study included 30 non-athlete overweight men (average ± standard deviation; aged 22.8 ± 2.2 years; height 176.1 ± 4.9 cm; weight 86.7 ± 6.6 kg). The study was approved under the procedures of the local Ethics Committee of Baqiyatallah University of Medical Science. Subject were randomly divided into three equal groups: exercise [just perform acute eccentric exercise test (AEE)], *Chlorella vulgaris* (for 7 days and then AEE), placebo (for 7 days and then AEE). Blood sampling was performed in 4 stages: day 1

(before supplementation) and day 7 (after supplementation), after AEE and 24 h after AEE (Table 1). Waist circumference greater than 100 cm and BMI of 20–25 were the standards of participating in the study. At first, all subjects completed the health-related questionnaire. Before the study all the subjects were asked to complete the written testimonial. All the subjects were asked to avoid other physical and exercise activities, take no supplements and medicine, and do not smoke during the exercise period. From two weeks before the study until 3 days thereafter, specific dietary guidelines were provided to the subjects, which included guidelines on avoiding excessive eating foods containing polyphenols and antioxidants. Average knee's range of motion (ROM) was measured using a goniometer as well as the hip circumference (thigh circumference) was measured using a tape meter at all stages.

## Eccentric exercise

The subjects of the study took an acute eccentric exercise session (or AEE test) on the treadmill (German H/P casmus model) seven days after supplementation other group with *Chlorella vulgaris*. Before the main test, the subjects were warmed up on a treadmill with a 0-degree slope for 5 min at 50% of maximum heart rate. In order to do AEE test, subjects started running at the Razi University Physical Education Laboratory for 20 min at a speed of 9 km/h with a negative 10% slope [29].

## Supplement program

After randomly dividing the subjects during the study protocol, subjects of the groups (Chlorella vulgaris group) received Chlorella supplement tablet (300 mg) four times daily (one before breakfast, two before lunch, and one before dinner). Whereas the placebo group used 300 mg dextrose similar to the main supplement and the exercise group only did the acute eccentric exercise. Chlorella vulgarise (Alvomed, Bioprodukte, Prof. Steinberg Produktions- und Vertriebs GmbH & Co. KG, Germany) was produced by Iranian Green Tomorrow Company [25].

**Table 1** Baseline physiological characteristics of the experimental and control groups

| | *Chlorella vulgaris* | Placebo | Exercise |
|---|---|---|---|
| Height | 174.16 ± 4.83 | 175.81 ± 2.53 | 172.80 ± 4.42 |
| Weight | 82.45 ± 9.52 | 88.06 ± 6.37 | 81.20 ± 7.59 |
| BMI | 27.19 ± 1.85 | 28.51 ± 1.43 | 28.54 ± 1.23 |
| WHR | 0.96 ± 0.02 | 0.97 ± 0.01 | 0.94 ± 0.02 |
| BFP | 27.5 ± 2.2 | 28.9 ± 1.6 | 26.7 ± 1.5 |

*BMI* body mass index, *WHR* waist-to-hip ratio, *BFP* body fat percentage

## Measurement of hip circumference

In order to measure the thigh circumference, subjects were asked to stand upright, with both feet perpendicular to the ground and the soles of the feet completely on the ground. The legs were as open as the shoulder width and the foot measured was not weight-bearing. The distance between the pelvic hip joint and the outer epicondyle of the thigh was first measured and then the number was divided in two to determine the middle of the thigh. It was then marked with a marker to avoid re-measuring the next time [30]. Then it was marked with a marker to avoid re-measuring for the next times [30]. The same area was measured as the hip circumference at five measurement stages, namely pre-supplementation, post-supplementation, immediately after acute eccentric exercise and 24 h after exercise.

## Range of motion (ROM) measurement

In this study, to assess the range of motion of the knee, the person sleeps in a proneness and comfortable position on the exam bed and rests his foot flat (straight) on the bed. The goniometer axis is placed on the outer part of the knee on the tibia condyle and the fixed arm in the outer part of the thigh parallel to the long axis of the thigh and the movable arm is placed parallel to the longitudinal axis of the tibia. Now the person bends his/her knee and the knee flexion rate is measured [31, 32]

## Blood sampling and analysis

In each of the four stages of blood sampling, after 20 min resting in a sitting position and taking blood pressure, 8 ml of blood was taken from the antibiotic vein. After blood sampling, to separate the serum, the samples were centrifuged at 4 °C for 15 min and stored at − 80 °C. At the end of the study, a special kit was used for each of the IL-6, insulin and glucose factors. Glucose level was determined by enzymatic colorimetric method (Glucose oxidase, Pars Azmoon Company, Tehran, Iran) with a coefficient of variation (CV) of 3.3% sensitivity 5 (Mg/dl), glucose insulin level was determined by insulin kit and Sandwich ELISA method (Insulin, Mercedia, Uppsala, Sweden) with a coefficient of variation of 5.8% and sensitivity 1 (MU/l) and also by IL-6 kit using ELISA Sandwich method by using Human IL-6 kit (IL-6, Diaclon France) with a coefficient of variation of 3.5 and sensitivity percentage (Pm/ml). The IR index (IRHOMA-IR) was calculated [33]:

$$\text{HOMA-IR} = \text{fasting insulin } (\mu\text{U/ml}) \times \text{fasting glucose } (\text{mmol/l})/22.5$$

### Statistical analysis

The results were analyzed by SPSS software version 23. Physiological and anthropometric characteristics were presented descriptively. To determine the normality of the data, Shippo–Wilk test and within-group and inter-group differences were analyzed using repeated measurement method. Bonferroni post hoc test was used to determine any significant differences between groups. Significance level was considered in all calculations ($P < 0.05$).

## Results

The results obtained from analysis of individual characteristics and anthropometric characteristics of the research subjects are demonstrated in Table 1(mean ± SD). Table 2 shows the intra- and inter-group differences of stiffness parameters in Chlorella vulgaris, placebo, and exercise groups.

### Knee's range of motion

ROM levels decreased significantly in all groups (*Chlorella vulgaris*, placebo, and exercise) immediately and 24 h after AEE test compared to before acute eccentric exercise ($P < 0.05$) (Table 2).

### Thigh circumference

Thigh circumference increased in all groups (*Chlorella vulgaris*, placebo, and exercise) immediately after and 24 h after AEE test compared to before acute eccentric exercise ($P < 0.05$) (Table 2)

### Interleukin 6

The results of ANOVA test with repeated measurement showed significant difference between IL-6 levels in 3 groups (*Chlorella vulgaris*, placebo, exercise) at different steps of sampling (day 1, day 7, after AEE and 24 h after AEE). Thus, time course had a significant effect on IL-6 values ($P < 0.000$). Also, there was a significant decrease in IL-6 levels in Chlorella vulgaris group compared to other two groups (placebo group and exercise group) at 24 h after AEE test. Also we show the difference between IL-6 levels in the three groups (*Chlorella vulgaris*, placebo, exercise) at 24 h after AEE test was significant compared to before AEE test. The results of *T* test show that there is no significant difference between resting values of the three groups ($P > 0.05$). Serum IL-6 levels reached their lowest levels within 24 h AEE test (Fig. 1).

### Insulin resistance

The results of ANOVA test with repeated measurement showed significant difference between insulin resistance (IR) in 3 groups (*Chlorella vulgaris*, placebo, exercise) at different steps of sampling (day 1, day 7, after AEE and 24 h after AEE). Thus, in general, time had a significant effect on IL-6 values ($P < 0.000$). Also, there was a significant decrease in (IR) levels in supplement group compared to other 2 groups (placebo group and exercise group) at 24 h after AEE test. Also we show the difference between difference (IR) levels in the three groups (*Chlorella vulgaris*, placebo and

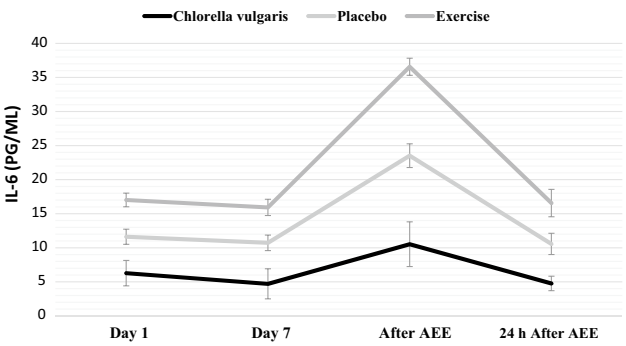


**Fig. 1** IL-6 levels in all groups (*Chlorella vulgaris*, placebo, exercise) day 1, day 7, immediately after AEE, 24 h after AEE). Data show as mean ± SD. *AEE* acute eccentric exercise test

**Table 2** Physiological characteristics of the experimental and control groups during protocol

| | Day 1 | Day 7 | After AEE | 24 h After AEE |
|---|---|---|---|---|
| ROM | | | | |
| *Chlorella vulgaris* | 140.36 ± 3.54 | 140.21 ± 3.51 | 139.01 ± 4.44 | 137.96 ± 4.13 |
| Placebo | 142.91 ± 4.57 | 142.71 ± 4.61 | 140.66 ± 5.74 | 137.96 ± 5.46 |
| Exercise | 141.62 ± 5.17 | 141.52 ± 5.47 | 137.86 ± 5.27 | 137.56 ± 5.37 |
| Thigh circumference (CM) | | | | |
| *Chlorella vulgaris* | 58.24 ± 0.83 | 58.60 ± 0.68 | 60.56 ± 0.47 | 64.43 ± 1.12 |
| Placebo | 58.72 ± 0.76 | 58.35 ± 0.72 | 60.13 ± 0.95 | 62.23 ± 1.18 |
| Exercise | 57.86 ± 1.17 | 58.24 ± 0.95 | 59.72 ± 1.00 | 62.20 ± 0.78 |

*AEE* Acute eccentric exercise test, *ROM* range of motion

exercise) at 24 h after AEE test was significant compared to before AEE test. By using t test it was recognized that there is no significant difference between resting values of IR in the three groups ($P^{>}0.024$). (IR) levels reached their lowest levels within 24 h after AEE test (Fig. 2).

## Discussion

In current study that aimed to evaluate simultaneous effect of *Chlorella vulgaris* supplementation on serum IL-6 level and insulin resistance after a session of intense acute eccentric exercise in overweight men. The results show that levels of serum IL-6 and insulin resistance in the supplement group significantly decreased. Therefore, according to significant effect of time and the effect of time and group interaction ($P<0.01$) on IL6 production and insulin resistance, it can be concluded that simultaneous use of *Chlorella vulgaris* supplementation and one session of intense acute eccentric exercise significantly decreases the serum IL-6 levels and insulin resistance after exercise and especially 24 h after exercise. Insulin resistance is defined as a defective glucose response to a specific amount of insulin, which is a metabolic state in which the tissue response to physiological insulin levels is lower than normal. In fact, insulin resistance is a condition in which the body's cells become resistant to the effects of insulin. Insulin resistance represents a major defect in maintaining normal blood sugar levels. For this reason, exercise training is associated with a decrease in insulin resistance [34], so that exercise increases glucose uptake from skeletal muscle by increasing protein carrier density on sarcolemma, and thereby insulin sensitivity increases and consequently insulin resistance decreases. Dungan et al. show that exercise acutely inhibits mTORC1 signaling, improvements in insulin-stimulated signaling [35]. After a single bout of exercise, the ability of insulin to stimulate glucose uptake is markedly improved locally in the previously active muscles. It is believed that at least part of the mechanism relates to an improved ability of insulin to stimulate translocation of glucose transporters (GLUT4) to the muscle membrane after exercise [36]. Also increasing postsynaptic messages, increasing glucose carrier protein, increasing glycogen and hexokinase synthesis, decreased diffusion and increased depletion of free fatty acid, increased muscle glucose transfer and changes in muscle structure are among possible mechanisms for decreasing insulin resistance after exercising [31]. Many researches have been done on effects of physical activity and insulin resistance decrease. Saltin et al. [37] showed that only intense physical activity (higher than or equal to 70% of maximal oxygen consumption) can lead to insulin resistance improvement [37, 38]. Whereas Sadrzadeh et al. [39] stated that light and moderate physical activity decreases insulin resistance parameter [39]. The reason could be gender and conditions of the test, the type of exercise protocol, or even a sudden change in the insulin resistance parameter. Also, Shundi et al. stated that combined aerobic training decreases blood glucose, weight, body fat percentage, and insulin resistance in women with type 2 diabetes [40]. On the other hand, Hansen et al. stated that intense interval program leads to more decreased fasting blood sugar, insulin and more increased insulin sensitivity [41]. By the way studies on chlorella vulgaris supplementation effects on insulin resistance and IL-6 are just getting started. Furthermore, no study has been done to investigate concurrent use of *Chlorella vulgaris* supplementation with exercise training so far except one or two studies. All studies have been conducted to investigate the effect of *Chlorella vulgaris* supplementation on the body. *Chlorella vulgaris* supplementation leads to decreased triglyceride by insulin resistance improvement, decreasing lipogenesis and subsequently by decreasing free fatty acids. Chlorella supplement are herbal supplement that can relieve the body from oxidative pressure caused by oxidative stress [30]. Mizoguchi et al. investigated the metabolic response to swimming exercise after 14 days of supplementation with chlorella in mice. Their results indicated a change in metabolism in mice that used chlorella [42]. Esmaieli et al. showed that there was no significant change in serum levels of ghrelin of supplementation group *Chlorella vulgaris* + aerobic training compared to aerobic training group [43], which can be considered as the result of amount and method of supplementation, the amount of supplement used, and uncontrolled diet of the subjects. Horii et al. investigated glycolytic and oxidative capacities in rats and showed that high-intensity exercise along with using chlorella vulgaris improves glycolytic and oxidative capacities [27]. Lin et al. stated that *Chlorella vulgaris* supplement anaerobic exercise capacity and also reduces muscle inflammation following exercise [24]. Lee et al. showed that *Chlorella vulgaris* supplement can lead to maintenance of body's

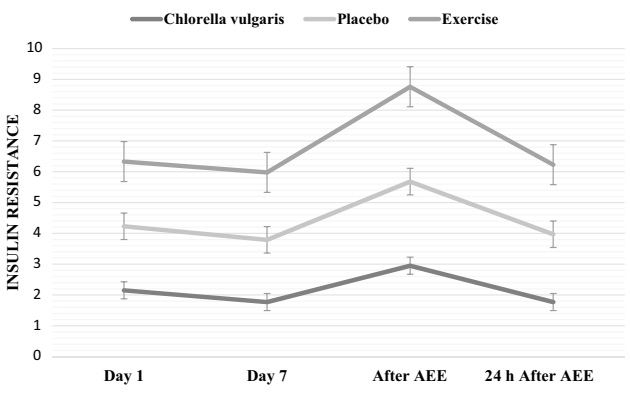


**Fig. 2** Insulin resistance (IR) levels in all groups (*Chlorella vulgaris*, placebo, exercise) day 1, day 7, immediately after AEE, 24 h after AEE). Data show as mean ± SD. *AEE* acute eccentric exercise test

plasma antioxidant status and improvement of activity status of antioxidant enzymes [22]. Whereas, Panahi et al. showed that 8 weeks of intense intermittent exercise with 4–10 repetitions for 30 s does not have significant changes in amount of plasma IL-6 levels, that the drawn result can be related to gender, time, and the type of training protocol and the duration of the exercise [44].

Reducing fat and improving insulin metabolism following exercise, along with supplementation with chlorella supplements, may be involved in lowering levels of inflammatory cytokines such as IL-6 [19]. Researchers believe that exercise, especially intense exercise causes autohypnosis or damage to muscle and plays an effective role in release of various substances such as intracellular proteins and cytokines [24], that IL-6 is one of the pro- and anti-inflammatory cytokines that has controlling effect on T-regulatory cells and affects the function of other inflammatory cells. Adipose tissue high levels of IL-6 so high production and secretion of IL-6 from adipose tissue causes negative regulation of metabolism and deficiency in muscle glycogen synthesis in overweight people, which ultimately plays an important role in increasing insulin resistance in body; thus, losing weight and fat following exercise will be associated with a decrease in IL-6 and consequently insulin resistance, overweight people generally have higher plasma concentrations of inflammatory markers (parameters) compared to normal people. From previous studies it is concluded that a session of eccentric and intense exercise is associated with a decrease in the level of pro-inflammatory interleukins [24], also using antioxidant and anti-inflammatory supplements can largely limit the increase of inflammatory cytokines and insulin resistance in obesity and overweight [17, 23]. However, few studies have been done on the use of *Chlorella vulgaris* supplementation with an intense eccentric training session, and most studies investigated the effect of Chlorella supplementation without exercise training or following other exercise protocols. What was found in this study was a significant decrease in insulin resistance and serum levels of interleukin-6. However, since this is the first study to examine the simultaneous effect of *Chlorella vulgaris* supplementation and an intense exercise session on insulin resistance and serum IL-6 levels, we should be precautious when we interpret data and to obtain more detailed and accurate results, more studies are required.

## Conclusion

An intense eccentric exercise session with 300 mg supplementation of *Chlorella vulgaris* for 7 days and 4 times daily results in decreased insulin resistance and serum levels of interleukin-6. In other words, an intense eccentric exercise session with increased metabolism and lipopenia (fat loss) results in decreased plasma levels and decreased inflammatory property of IL-6 and insulin resistance in overweight men. Finally, it can be concluded that an intense exercise session supplemented with *Chlorella vulgaris* can have more positive effects than doing this exercise without taking Chlorella vulgaris supplement on overweight men. However, since no research have been done on simultaneous effect of AEE and supplementation with *Chlorella vulgaris*, this study was done for the first time. Also for a better conclusion, future studies must be done with control of other effective variables and more subjects in longer time.

## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** The study was approved under the procedures of the local Ethics Committee of Baqiyatallah University of Medical Science. All procedures were carried out in line with the Declaration of Helsinki.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

## References


1. Gleeson M et al (2011) The anti-inflammatory effects of exercise: mechanisms and implications for the prevention and treatment of disease. Nat Rev Immunol 11(9):607
2. Wei M et al (1999) Relationship between low cardiorespiratory fitness and mortality in normal-weight, overweight, and obese men. JAMA 282(16):1547–1553
3. Kenney WL, Wilmore JH, Costill DL (2015) Physiology of sport and exercise. Human Kinetics
4. Christiansen T et al (2013) Acute exercise increases circulating inflammatory markers in overweight and obese compared with lean subjects. Eur J Appl Physiol 113(6):1635–1642
5. Tanabe Y et al (2015) Attenuation of indirect markers of eccentric exercise-induced muscle damage by curcumin. Eur J Appl Physiol 115(9):1949–1957
6. Clarkson PM, Hubal MJ (2002) Exercise-induced muscle damage in humans. Am J Phys Med Rehabil 81(11):S52–S69
7. Tidball JG (2011) Mechanisms of muscle injury, repair, and regeneration. Compr Physiol 1(4):2029–2062
8. Connolly DA, Sayers SP, McHugh MP (2003) Treatment and prevention of delayed onset muscle soreness. J Strength Cond Res 17(1):197–208
9. Petersen AMW, Pedersen BK (2005) The anti-inflammatory effect of exercise. J Appl Physiol 98(4):1154–1162
10. Pedersen B et al (2003) Searching for the exercise factor: is IL-6 a candidate? J Muscle Res Cell Motil 24(2–3):113
11. Malaguti M, Angeloni C, Hrelia S (2013) Polyphenols in exercise performance and prevention of exercise-induced muscle damage. Oxidative Med Cell Longev 2013(1):1–9
12. Kuehl KS et al (2010) Efficacy of tart cherry juice in reducing muscle pain during running: a randomized controlled trial. J Int Soc Sports Nutr 7(1):17

13. Davis JM et al (2007) Curcumin effects on inflammation and performance recovery following eccentric exercise-induced muscle damage. Am J Physiol Regul Integr Comp Physiol 292(6):R2168–R2173
14. Howatson G et al (2010) Influence of tart cherry juice on indices of recovery following marathon running. Scand J Med Sci Sports 20(6):843–852
15. Fallah AA et al (2018) Effect of Chlorella supplementation on cardiovascular risk factors: a meta-analysis of randomized controlled trials. Clin Nutr 37(6):1892–1901
16. Lee HS, Kim MK (2009) Effect of *Chlorella vulgaris* on glucose metabolism in Wistar rats fed high fat diet. J Med Food 12(5):1029–1037
17. Petersen A, Pedersen B (2006) The role of IL-6 in mediating the anti inflammatory. J Physiol Pharmacol 57(Suppl 10):43–51
18. Febbraio MA, Pedersen BK (2002) Muscle-derived interleukin-6: mechanisms for activation and possible biological roles. FASEB J 16(11):1335–1347
19. Suzuki K et al (2002) Systemic inflammatory response to exhaustive exercise cytokine kinetics. Exerc Immunol Rev 8:6–48
20. Arabzadeh E, Mirdar S, Moradiani H (2016) Nigella sativa supplementation attenuates exercise-induced bronchoconstriction in the maturing rat: a histometric and histologic study. Comp Clin Pathol 25(1):1–5
21. Arabzadeh E, Mirdar S, Fathi Z (2015) Measurement of levels of lung HIF-1α protein in response to tapering for 14-and 21-day with nigella sativa supplementation in maturing rat, with histological study. Sport Sci Health 11(2):195–202
22. Lee SH et al (2010) Six-week supplementation with Chlorella has favorable impact on antioxidant status in Korean male smokers. Nutrition 26(2):175–183
23. Aliashrafi S et al (2014) The effect of microalgae *Chlorella vulgaris* supplementation on inflammatory factors in non-alcoholic fatty liver disease (NAFLD): a double-blind randomized clinical trial. J Mazandaran Univ Med Sci 24(112):113–121
24. Lin C-P et al (2017) The effect of Chlorella supplementation on exercise performance and inflammation-related blood cells after dehydration: 3265 board# 170 June 2 200 PM-330 PM. Med Sci Sports Exerc 49(5S):930
25. Ebrahimi-Mameghani M et al (2017) Glucose homeostasis, insulin resistance and inflammatory biomarkers in patients with non-alcoholic fatty liver disease: beneficial effects of supplementation with microalgae *Chlorella vulgaris*: a double-blind placebo-controlled randomized clinical trial. Clin Nutr 36(4):1001–1006
26. Bagherniya M et al (2018) Medicinal plants and bioactive natural compounds in the treatment of non-alcoholic fatty liver disease: a clinical review. Pharmacol Res 130:213–240
27. Horii N et al (2017) High-intensity intermittent exercise training with chlorella intake accelerates exercise performance and muscle glycolytic and oxidative capacity in rats. Am J Physiol Regul Integr Comp Physiol 312(4):R520–R528
28. Sibi G, Rabina S (2016) Inhibition of pro-inflammatory mediators and cytokines by *Chlorella vulgaris* extracts. Pharmacogn Res 8(2):118
29. Oosthuyse T, Bosch A (2017) The effect of gender and menstrual phase on serum creatine kinase activity and muscle soreness following downhill running. Antioxidants 6(1):16
30. Segan DJ et al (1988) Weight lifting as a cause of bilateral upper extremity compartment syndrome. Physician Sportsmed 16(10):73–75
31. Van der Esch M et al (2007) Joint proprioception, muscle strength, and functional ability in patients with osteoarthritis of the knee. Arthritis Care Res 57(5):787–793
32. Dekker J (2013) Exercise and physical functioning in osteoarthritis: medical, neuromuscular and behavioral perspectives. Springer Science & Business Media, New York
33. Matthews D et al (1985) Homeostasis model assessment: insulin resistance and β-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 28(7):412–419
34. Arabzadeh E et al. (2020) Alteration of follistatin-like 1, neuron-derived neurotrophic factor, and vascular endothelial growth factor in diabetic cardiac muscle after moderate-intensity aerobic exercise with insulin. Sport Sci Health 1–9
35. Dungan CM, Gordon BS, Williamson DL (2019) Acute treadmill exercise discriminately improves the skeletal muscle insulin-stimulated growth signaling responses in mice lacking REDD1. Physiol Rep 7(4):e14011
36. Frøsig C, Richter EA (2009) Improved insulin sensitivity after exercise: focus on insulin signaling. Obesity 17(S3):S15–S20
37. Saltin B, Åstrand P (1993) Free fatty acids and exercise. Am J Clin Nutr 57(5):752S–758S
38. Salamat KM et al (2016) The response of pre-inflammatory cytokines factors to different exercises (endurance, resistance, concurrent) in overweight men. Alex J Med 52(4):367–370
39. Sadrzadeh N, Glembourtt MJ, Stevenson CL (2007) Peptide drug delivery strategies for the treatment of diabetes. J Pharm Sci 96(8):1925–1954
40. Shavandi N et al (2011) Relationship between adiponectin and insulin resistance in type II diabetic men after aerobic training. Arak Med Univ J 14(2):43–50
41. Hansen D et al (2009) Continuous low-to moderate-intensity exercise training is as effective as moderate-to high-intensity exercise training at lowering blood HbA 1c in obese type 2 diabetes patients. Diabetologia 52(9):1789–1797
42. Mizoguchi T et al (2011) Influence of Chlorella powder intake during swimming stress in mice. Biochem Biophys Res Commun 404(1):121–126
43. Esmaieli M, Abedi B, Fathollahi-Shoorabeh F (2018) Effect of aerobic training with Chlorella supplement on insulin resistance and serum ghrelin levels in obese women. Iran J Obstet Gynecol Infertil 21(10):48–56
44. Panahi Y et al (2012) Investigation of the effects of *Chlorella vulgaris* supplementation in patients with non-alcoholic fatty liver disease: a randomized clinical trial. Hepato-Gastroenterol 59:2099–2103