



## Effect of High Intensity Interval Training and Honey Consumption on Some Inflammatory Indices in Sedentary Subjects

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### Abstract

**Background:** The sedentary lifestyle has been introduced as one of the main causes of disease and a predictor of morbidity and mortality. Inflammation is an essential contributor to the pathogenesis of diseases. The aim of the present study was to investigate the effect of high-intensity interval training and honey consumption on IL-6, IL-12 and TNF- $\alpha$  levels in sedentary individuals.

**Methods:** Thirty-eight young, healthy and inactive men were assigned to one of the following interventions: Exercise+placebo (EP), Exercise+Supplement (ES), Supplement (S) and Placebo (P). Subjects in the exercise groups underwent a supervised HIIT program over 8 weeks. Exercise at each session comprised 2 min high intensity training with the intensity of 80-90% of heart rate max interspersed by low-intensity intervals of walking for 1 minute. Throughout the study, the subjects in supplement groups received 5 cc/kg body mass of 13% honey dissolved in plain water within 30-60 min before each exercise session. The subjects in placebo groups were administered with an equal volume of water solution with 5 gr sucrose. Before and 72h after the experimental period blood samples were collected to assess plasma levels of IL-6, IL-12, and TNF- $\alpha$ .

**Results:** We observed that IL-6 levels significantly decreased in ES and E groups from pretest to posttest and there was a significant difference between the ES and control groups ( $P$ value=0.023). However, no significant changes were observed for IL-12 and TNF- $\alpha$  ( $P$ value>0.05).

**Conclusions:** HIIT program along with honey consumption over 8 weeks could have favorable effects on inflammatory indices such as IL-6 in subjects with sedentary life-style.

**Keywords:** HIIT, Honey, Inflammation, IL-6, TNF- $\alpha$ , IL-12.

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and chronic inflammation elevating its biomarkers in circulation.<sup>7</sup> It has been indicated that people with sedentary behavior have greater BMI, higher systolic blood pressure and insulin resistance as well as elevated levels of inflammatory cytokines. People who spend more time sitting present a worse inflammatory profile.<sup>7</sup>

Lifestyle modifications, on the other hand, such as physical activity and a healthy diet may favorably modulate inflammatory responses and immune system function.<sup>8-11</sup> The effect of exercise training on inflammation has been explored in numerous studies and various results have been achieved.<sup>12-16</sup> Few studies have indicated an inverse relationship between biomarkers of inflammation and cardiorespiratory fitness.<sup>17,18</sup> For instance, Fischer et al., (2004) reported that 10 weeks of endurance training decreased IL-6 levels.<sup>16</sup> According to ACSM guidelines, 150 min moderate-intensity exercise is recommended for inactive subjects to achieved health benefits of exercise.<sup>19</sup> Nonetheless, recommendations of physical activity for inactive individuals include moderate to vigorous continuous exercise throughout the week. Recently, high-intensity interval training (HIIT) programs have attracted attention because of being time-efficient. Since lack of time is one of the common barriers if exercise participation, HIIT programs with low volume can be a proper strategy that can be considered by fitness professionals.<sup>20</sup> Fisher et al., (2015) reported that 6 weeks of HIIT protocol improved lipid profile, Body fat %, and cardiovascular fitness in overweight and obese male individuals.<sup>21</sup> Gerosa-Neto et al., (2016) also reported that BMI, weight, and IL-6 significantly reduced but TNF- $\alpha$  levels increased following 16 weeks of HIIT program in overweight and obese adults.<sup>22</sup> Although some researchers have investigated the effects of HIIT programs in different aspects, they have not been investigated as much as other modalities of exercise training and the health benefits of HIIT training programs needs to be further elucidated.

Besides, diet and consuming healthy nutrients is another component of life style. Health benefits of honey on humans have been claimed by nutritionists.<sup>23,24</sup> It is a healthy nutrient comprised of carbohydrate as well as vitamins and minerals and is a strong antioxidant. It has a potential therapeutic role in the treatment of diseases due to its anti-inflammatory, antioxidant and antimicrobial properties.<sup>24</sup> Fukuda et al., (2011) indicated that honey induces neutrophils that possess antitumor activity.<sup>25</sup> Jalili et al., (2010) reported that pre-exercise honey consumption could attenuate the immune system response to a single bout of aerobic exercise.<sup>26</sup> Carbohydrate ingestion during exercise sessions has been recommended by exercise nutritionists. Due to its nutritional value and health benefits,

## Introduction

The sedentary lifestyle has been introduced as one of the causes of disease and a predictor of morbidity and mortality. It is a risk factor for cardiovascular disease (CVD) the prevalence of which is increasing in societies.<sup>1,2</sup> Inflammation is contributed to the pathogenesis of several chronic diseases such as CVD.<sup>3,4</sup> During the state of inflammation some biomarkers including CRP, TNF- $\alpha$ , IL-1, IL-6 and, IL-12 is elevated.<sup>4,5</sup> Accordingly, Ito et al., (2003) reported that blood levels of IL-6 and its hepatic byproduct C-reactive protein (CRP) can reflect the magnitude of plaque inflammation. They suggested that therapeutic modulations of inflammatory biomarkers can feasibly prevent atherosclerosis and upcoming cardiovascular diseases.<sup>6</sup> Physical inactivity can independently result in acute

honey may be a suitable alternative to other common sources of carbohydrate such as sucrose. However, little is known about the benefits of honey as a sport supplement.

Overall, based on the aforementioned statements we assumed that honey consumption prior to exercise along with HIIT program over 8 weeks could have favorable effect on biomarkers of inflammation in subjects with sedentary lifestyle.

**Materials and Methods**

Thirty-eight healthy, inactive volunteers participated in this study. First, the participants were informed about the experimental procedure and the study protocol and then they gave the written consent. The study procedures were in accordance with the ethical standards of the Helsinki Declaration of 1975, as revised in 2000 (available at [http://www.wma.net/e/policy/17-c\\_e.html](http://www.wma.net/e/policy/17-c_e.html)) and the trial was registered with the trial ID: UMIN000039156. Inclusion criteria were healthy state, inactive life-style, age range between 20-30 yrs, and exclusion criteria included tobacco use, medicine and supplement intake. None of the participants had a history of smoking, heart diseases, and regular physical activity. They were all inactive based on the evaluations by the physical activity questionnaire (PAQ). The subjects were randomly assigned to the following groups: 1- Exercise+placebo (EP, N=10), 2- Exercise+Supplement (ES, N=10), 3- Supplement (S, N=10) and 4- Placebo (P, N=8) (figure 1). Simple randomization was applied in the present study and 2 subjects in the control group did not attend the lab for post-test evaluations due to personal reasons.

Subjects in the exercise groups underwent a supervised high-intensity interval training program over 8 weeks. Exercise at each session comprised 2 min high-intensity training with the intensity of 80-90% of heart rate max interspersed by low-intensity intervals of walking for 1 minute. Each exercise session lasted 40-50 min and the frequency of exercise training was 4 sessions a week. Each exercise session preceded by 10-15 min warm-up and followed by 5-10 min cool down. The intensity of exercise was determined based on each participants' maximal heart rate. The heart rate throughout the exercise was monitored by the polar heart rate monitor (PE3000, Polar

Electro, Kemple, Finland). The participants were required to follow their usual diet and abstain from taking any supplements throughout the experimental period. Moreover, a 24-hour diet recall questionnaire was completed before the first assessment session and the participants were asked to replicate it preceding the second assessment session. Throughout the study, the subjects in supplement groups received 5 cc/kg body mass of 13% honey dissolved in plain water within 30-60 min before each exercise session. The subjects in placebo groups were administered with an equal volume of water solution with 5 gr sucrose. The supplement and placebo were provided in a covered bottle to mask the supplementation.

At the first attendance to the lab, the basic measurements of weight, height, body mass index, height, and body fat percentage were done. Body mass index (BMI) was calculated as body weight (kg) divided by height (m<sup>2</sup>). The skinfolds were measured using skin fold caliper (slim guide, USA) on the right side of the body at chest, abdominal, and suprailiac sites. Skin fold measurements were performed in triplicate and average values were used to estimate fat percent using the Jackson-Pollack equation. The assessments were replicated at the end of the experimental period.

Before and 72h after the experimental period, the participants were asked to attend the lab following an overnight (8-10 h) fasting and blood samples were taken from antecubital vein. The samples were then centrifuged at 3000 r.p.m for 15 min to separate plasma samples. The plasma samples were then frozen and stored at -80 °C for subsequent assessments of IL-6, IL-12 and TNF-a. IL-6, TNF-a, and IL-12 were assessed through ELIZA methods using commercial kits (IL-6: Sanquin, Netherlands, IL-12: Invitrogen, USA, and TNF-a: Invitrogen, USA).

Data are presented as Mean±SD. Normal distribution of data was confirmed using the Kolmogorov–Smirnov test and parametric statistical tests were applied. Since there were no significant inter-group differences at the pre-test. To determine the difference between groups, the post-test data was subtracted from the pre-test and then the results (Δ) were analyzed using the one-way ANOVA test. Tukey's post hoc test was used to determine the differences when ANOVA reached significance level. Statistical significance was set at Pvalue<0.05.

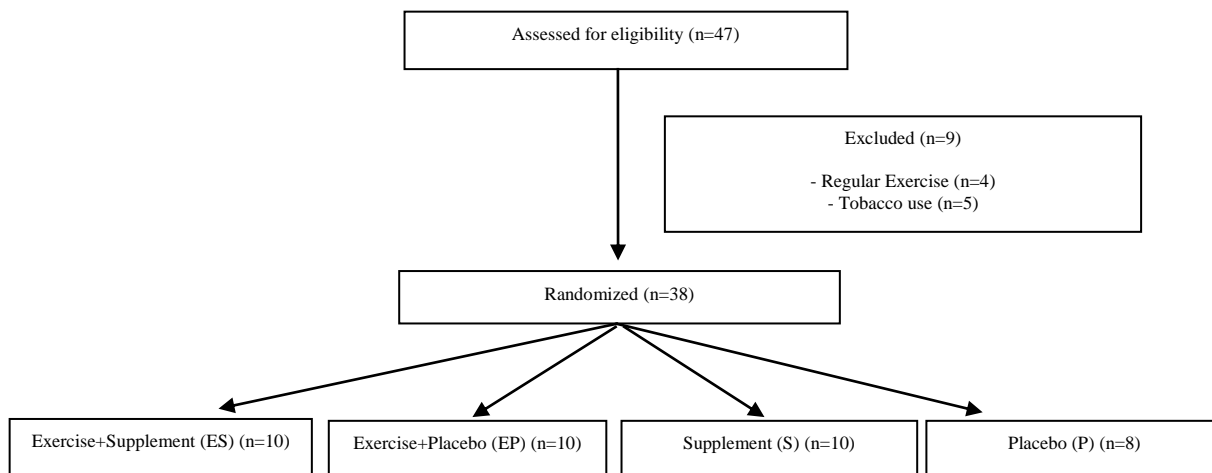


Figure 1. Participant recruitment flow chart

**Results**

Data indicate that there was no significant difference among groups regarding baseline characteristics. The mean and SD for variables are also presented in table 1.

There were no significant inter-group differences at baseline regarding all variables (Pvalue>0.05). We observed that IL-6 levels significantly decreased in ES and EP groups

from pre-test to posttest and there was a significant difference between the ES and control groups (Pvalue=0.023) (table 1, figure 2). However, no significant changes were observed for TNF-a levels from pre-test to posttest with no significant inter-group differences (Pvalue=0.400). Moreover, mean values of IL-12 decreased in exercise groups from pre-test to posttest but it was not statistically significant and the difference between exercise groups and the control did not reach significance level (Pvalue=0.283) (table 1).

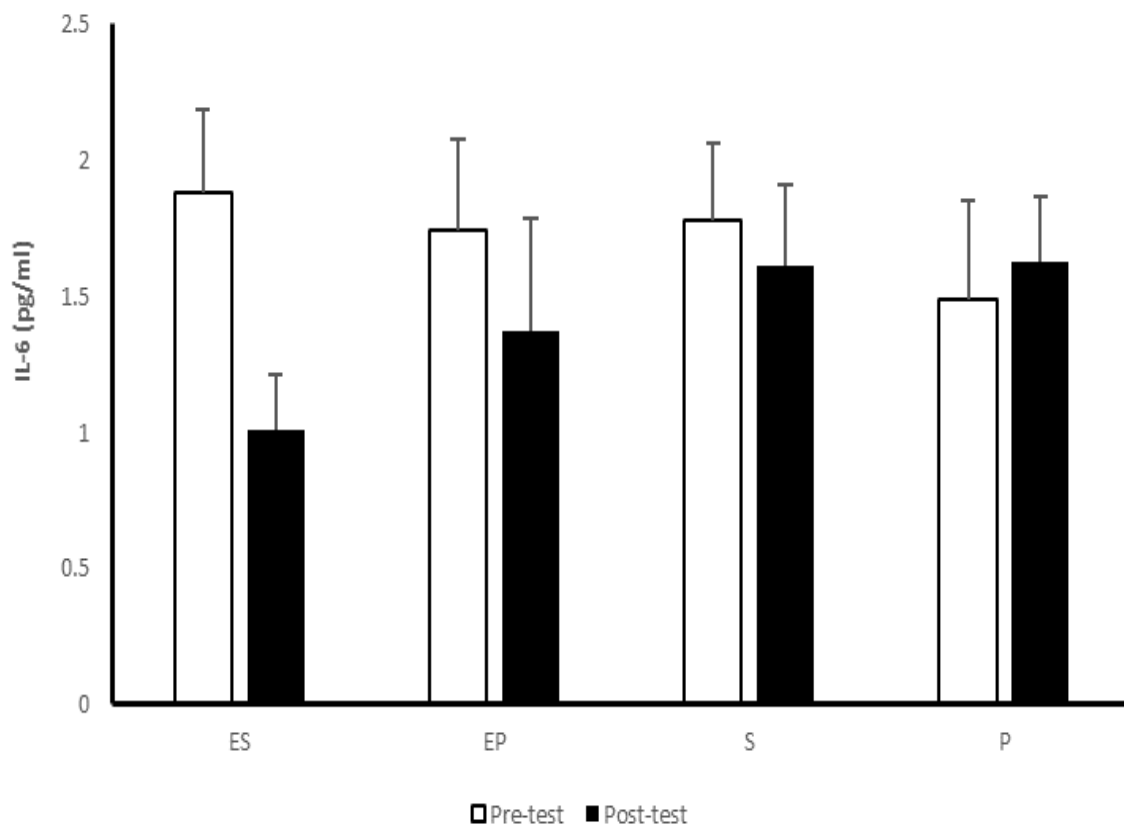
**Table 1. Mean±SD values of variables**

Variables	Groups	IL-6 (pg/ml)		IL-12 (pg/ml)		TNF-a (pg/ml)	
		Pre-test	Post-test	Pre-test	Post-test	Pre-test	Post-test
Exercise+Supplement (ES)		1.88 ± 0.31	1.01 ± 0.2*#	1.79 ± 0.22	1.6 ± 0.2	3.52 ± 0.45	3.43 ± 0.42
Exercise+Placebo (EP)		1.74 ± 0.34	1.37 ± 0.42	1.71 ± 0.29	1.49 ± 0.25	2.98 ± 0.53	2.91 ± 0.49
Supplement (S)		1.78 ± 0.28	1.61 ± 0.30	1.72 ± 0.31	1.59 ± 0.31	3.62 ± 0.6	3.69 ± 0.58
Placebo (P)		1.49 ± 0.36	1.63 ± 0.24	1.56 ± 0.30	1.60 ± 0.28	3.41 ± 0.43	3.46 ± 0.4

\* Significantly (Pvalue<0.05) different with pre-exercise

# Significantly (Pvalue<0.05) different with the placebo

Abbreviations: ES, exercise plus supplement; E, exercise; S, supplement; C, control; IL-6, interleukin 6; IL-12, interleukin 12; TNF-a, tumor necrosis factor a



**Figure 2. IL-6 levels at pre-test and post-test in the experimental and control groups**

\* Significantly (Pvalue<0.05) different with the placebo

# Significantly (Pvalue<0.05) different with pre-test

## Discussion

In this study, we investigated the effect of high-intensity interval training along with honey consumption on some inflammatory markers in sedentary male subjects. The results indicated that honey consumption along with HIIT could decrease IL-6 levels but had no remarkable effect on IL-12 and TNF- $\alpha$  in inactive subjects.

Regarding effects of HIIT on IL-6 our finding is consistent with Hadiono et al., (2019), Gerosa-Neto et al., (2016).<sup>22,27</sup> Hadiono et al., (2019) indicated that the HIIT program for 6 weeks decreased IL-6 levels in obese participants to a larger extent than medium intensity training (MIT).<sup>27</sup> They suggested that, HIIT exercise is more effective than MIT to alter IL-6 levels. Gerosta-Neto et al., (2016) also investigated the effect of HIIT on inflammatory indices in overweight and obese subjects.<sup>22</sup> They found that 16 weeks of HIIT significantly increased IL-6 levels. These findings support the hypothesis that HIIT program has the potential to reduce the concentration of pro-inflammatory markers. Regular exercise training is known to exert an anti-inflammatory effect, especially in overweight and sedentary subjects.<sup>14</sup> Another possible reason would be the changes in body fat percentage, especially visceral body fat, following regular exercise participation. IL-6 is mainly secreted by adipose tissue, particularly visceral adipose tissue. Jae et al., (2006) indicated that there is an association between body fat percent and levels of inflammatory indices and lower levels of inflammatory factors is accompanied by lower fat percent.<sup>28</sup> HIIT has been suggested to increase energy expenditure to a larger extent than continuous forms of exercise which can be maintained for hours postexercise.<sup>29</sup> Thus, it can be effective in reducing visceral adipose tissue. Moreover, IL-6 release from adipose tissue is enhanced by sympathetic stimulation. On the other hand, regular physical activity causes a decrease in sympathetic stimulation which can result in lower IL-6 release. Unlike our results, it has been indicated that a single bout of HIIT can increase circulatory levels of IL-6. This is comparable with our study as unlike our study, they have conducted single-session exercise investigating acute effect of HIIT on inflammatory markers. It has been suggested that IL-6 release during exercise can inhibit pro-inflammatory cytokine production and up-regulate the transcription of anti-inflammatory cytokines such as IL-10.<sup>30,31</sup> Exercise intensity is a key modulator of IL-6 release as during high-intensity efforts IL-6 release can be elevated and during active rest intervals it can be removed by kidney and liver.<sup>32</sup> Therefore, an adaptation to IL-6 production and release may occur at long-term training to decrease resting levels of IL-6. On the other side, previous studies have indicated that the ingestion of carbohydrates during exercise may have an ergogenic effect and can ameliorate the response of inflammatory biomarkers. However, Miles et al., (2007) reported that a single bout of exercise with and without carbohydrate ingestion increased IL-6 levels.<sup>33</sup> Sim et al., (2011) also reported similar results indicating that carbohydrate ingestion during exercise has no remarkable effect on post-exercise IL-6 response.<sup>34</sup> Honey consumption has been suggested to alter the immune response to exercise. Jalili et al., (2010) reported that exercise-induced white blood cell count in

sedentary subjects can be attenuated by honey ingestion.<sup>26</sup> Wan Ghazali et al., indicated that honey can exert anti-inflammatory effects in chronic smokers.<sup>35</sup> We assumed that honey consumption before exercise over 8 weeks of training may have a favorable effect on resting levels of IL-6 which was approved in the present study.

However, neither the HIIT program nor honey administration had a remarkable effect on resting levels of TNF- $\alpha$  and IL-12 in sedentary subjects. It is in line with Hadiono et al., (2016) who reported that HIIT had no significant effect on TNF- $\alpha$  levels in obese subjects.<sup>27</sup> In contrast, Gerosta-Neto et al., (2016) reported that HIIT increases blood levels of TNF- $\alpha$ .<sup>22</sup> There is a discrepancy in the literature with this regard which can be attributable to differences in exercise modality, characteristics of the subjects, baseline levels of markers and the assessment time-point. Elevated levels of inflammatory biomarkers reported by Gerosta-Neto et al may be due to posttest assessments.<sup>22</sup> Assessment of inflammatory indices very close to the latest exercise session may result in false elevation of the markers. Yet, we assessed blood levels of the markers 72 postexercise. Furthermore, in the present study, we observed that honey consumption during HIIT program had no additive effect to cause any alteration in resting levels of IL-12 and TNF- $\alpha$  in sedentary subjects. The reason behind this finding is not clear but we assume that IL-12 and TNF- $\alpha$  levels would have been affected if they were above physiological levels, as it has been suggested that honey can exert anti-inflammatory effects in subjects with elevated levels of inflammatory indices such as chronic smokers.<sup>35</sup>

Overall, high-intensity interval training accompanied by honey consumption over 8 weeks could have favorable effects on inflammatory indices such as IL-6 in subjects with the sedentary life-style.

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## Conflict of Interest

The authors declare that they have no conflict of interest.

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