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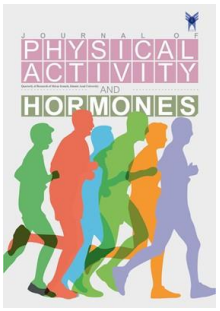

The effect of 4 weeks of bromelain supplementation on inflammatory indices after supermaximal weightlifting exercises

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Keywords
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Abstract

Introduction: Super Maximal has been considered as a method for enhancing the athletic performance of sportspeople; however, it can lead to injury, muscle fatigue, and increased serum enzyme concentrations, which come with side effects. The aim of the present study was to investigate the effect of 4 weeks of bromelain supplementation on inflammatory markers following maximal weightlifting exercises.

Material & Methods: The research was conducted using a pre-test and post-test design. The population and statistical participants of this research consisted of 11 female weightlifters with 3 to 5 years of training experience (age, weight and body mass index: 22 ± 7.5 years, 65 ± 8.5 kg and 24 ± 2.3) respectively. A sample was selected from the chosen weightlifting club in the city of Rasht, and consent forms were obtained from all participants. This study was conducted in four stages: (Stage One: 48 hour after normal training; Stage Two: 12 hours after supermaximal, followed by 30 days of bromelain supplementation+normal training; Stage Three: 12 hours after supermaximal, followed by 30 days of placebo plus normal training; Stage Four: 12 hours after supermaximal). In this study, blood samples were obtained for measurement of (white blood cell counts, serum IL-6 and LDH). For statistical analysis, ANOVA was used in SPSS version 26 with a $p<0.05$.

Results: The findings showed 4 weeks of bromelain supplementation had a significant reducing effect on serum IL-6 levels after supermaximal weightlifting exercises ($P < 0.05$), But it had no significant effect on other components.

Conclusion: Supermaximal exercises lead to significant inflammation; bromelain is likely one of the substances that influence this process. Based on the results of this study, bromelain could be used to manage inflammation levels in athletes.

1. Introduction

Weightlifting is a competitive sport that involves executing quick movements and strikes in competitions governed by the International Weightlifting Federation. It is an example of a strength and dynamic sport that leads to rapid muscular fatigue, high energy consumption, and power output in a short period of time (1). Muscle injuries resulting from weightlifting, which cause inflammatory responses, are very common among athletes during long-term training or competition, as inflammation occurs due to reactive proteins after exercise (2). Inflammation caused by reactive proteins often leads to muscle pain and decreased performance (3).

During intense exercise, the metabolic rate in working skeletal muscle increases more than 100 times compared to resting levels, leading to an increase in the production of reactive oxygen species (ROS), which creates an imbalance between antioxidants and ROS (4). A reduction in antioxidant defence may affect the elimination of ROS and lead to increased muscle pain; delayed onset muscle soreness depends on the type and intensity of exercise and typically peaks between 24 to 72 hours after exercise (5). This period is very important for athletes during training and competition when there is limited time for recovery (6).

It has been reported that reactive oxygen species (ROS) can affect metabolic processes such as transcription and gene expression, cell differentiation, and inflammatory responses. ROS is released not only from muscles but also from

endothelial and immune cells during periods of stimulation and significant changes during intense physical training (7). Consorti et al., (8) stated that inflammation and oxidative damage in muscle lead to fatigue and reduced performance due to excess ROS, which is mitigated by the consumption of fruit-derived polyphenols with antioxidant and anti-inflammatory properties. Bromelain is a proteolytic enzyme derived from pineapple that elicits an anti-inflammatory response by reducing the synthesis of prostaglandin E2 and cyclooxygenase-2 (9). This release includes the synthesis of cytokines such as interleukin-6 (IL-6) (10). IL-6 is expressed in human skeletal muscles in a fibre type-specific manner; thus, the level of absorption and, consequently, the intensity of muscle contraction affect the production of these cytokines. Additionally, about 30 percent of circulating IL-6 originates from adipose tissue (11). Regardless of the source of circulating cytokines, among the many markers of systemic inflammation, IL-6 has the highest concentration (12).

Skeletal muscle damage caused by exercise is a common consequence of intense physical activity (13). Many studies have shown that immediately after intense physical activity, biomarkers of skeletal muscle injury, such as lactate dehydrogenase (LDH), myoglobin levels, and creatine kinase, significantly increase, often reported to be more than 5 to 100 times higher than baseline (14). The study by Park et al. (14) observed athletes for a longer period after competition and found that these biomarkers of skeletal muscle injury return to normal within 7 to 10 days with proper recovery after the competition. However, these injuries may affect performance and limit potential during events, as athletes have only a limited time for recovery.

In the meantime, antioxidant and anti-inflammatory dietary supplements are common strategies typically used to reduce these damages (15). Theoretically, the consumption of antioxidants helps to inhibit the formation of ROS, as this mechanism occurs because antioxidants bind to metal ions, reduce the formation of hydrogen peroxide, quench superoxide and singlet oxygen, break the chain reaction, and improve recovery and muscle performance (16). Therefore, athletes should consume foods and beverages with sufficient nutrient content to meet their body's needs. Some athletes and coaches prepare supplements from natural and synthetic sources to meet their needs before and after training. Athletes aim to accelerate muscle recovery and increase energy during exercise (17). Natural supplements help to increase antioxidants and reduce fatigue in the body, enhancing athletes' performance (18). Nowadays, various supplements for muscle injury, recovery, and performance are available on the market; however, the U.S. Food and Drug Administration has warned that these supplements may contain additives and hazardous substances that can cause unwanted side effects. Previous studies have shown that about 38-90% of athletes or active populations consume supplements despite the lack of scientific evidence to support their effectiveness in enhancing performance and recovery (19). Bertuccioli et al., (9) reported that the anti-inflammatory effect of bromelain is associated with increased tissue permeability, facilitating edema absorption and accelerating the repair of damaged tissue, which may reduce muscle pain, facilitate muscular recovery, and enable faster recovery of contractile function.

Based on the conducted reviews, it can be stated that the research carried out has predominantly focused on male participants, with less attention paid to females. Furthermore, when studies have included women, they have mostly involved inactive individuals. Previous research indicates that the inclination and competition among women to partake in weightlifting exercises are relatively low. Nevertheless, given the limited studies in this area, further research appears necessary. It is important to investigate the effects and dosages of bromelain supplementation during a session of supermaximal exercise, and to conduct a more detailed analysis of the effects of this supplement on female athletes, in order to obtain more robust and comprehensive scientific results. It should also be noted that the training in the present study is to the point of exhaustion and is considered maximal, which could help address the research gap in this regard. Finally, it should be mentioned that this study will examine the effects of four weeks of bromelain supplementation on inflammatory markers following supermaximal weightlifting exercises.

2. Methodology

2.1. Materials and methods

The present research method was experimental..

2.2. Participants

The statistical sample consisted of 11 semi-professional female weightlifters in the city of Rasht, aged between 18 and 35 years. The participants were required not to use any supplements. If they sustained an injury during training, they were removed from the exercise. The stages of the training are specified in Figure 1. The research was registered with the Ethics Committee of the Islamic Azad University, Rasht Branch, under the number IR.IAU.RASHT.REC.1403.023.

The population and sample for this research consisted of 11 female weightlifters with 3 to 5 years of training experience in the city of Rasht, who voluntarily participated in the study. The inclusion criteria for the study were as follows: an age limit of 18 to 35 years; having a desirable physical condition to participate in the training sessions; approval by the medical committee of the Rasht Weightlifting Federation; continuous training for at least three years; possession of sports insurance; membership in the Guilan province weightlifting team; training at least three to a maximum of five times a week; and following a program that includes the main weightlifting movements, namely the snatch and the clean and jerk. The exclusion criteria included: lack of consent to participate in the current study; injury; treatment with anticoagulant, anti-inflammatory, or analgesic medications; undergoing specific physiotherapy treatments; engaging in risky behaviours and substance abuse (smoking, alcohol consumption); and physical activity other than weightlifting.

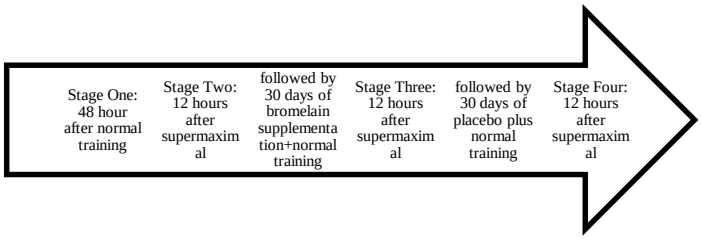

Fig 1. *Stages in Measurement of Sampling*

2.3. Measurements

Evaluation of Anthropometric Indices: Weight (in kilograms) was measured using a digital scale (Xiaomi, model XMTZC05HM, China), and height (in centimetres) was measured with a tape measure. The Body Mass Index (BMI) was then calculated based on weight divided by the square of height (kilograms per square metre).

2.4. Intervention

Supplementation Method with Bromelain: In this study, bromelain was administered in the form of capsules containing 200 mg from Anahil Salamat Permon Amin Company to the athletes (9).

Training Protocol: The maximum training programme involved participants performing a standard warm-up before the data collection session, which included lifting light weights to heavy weights: 3 repetitions at 70% of their one-repetition maximum (1RM), followed by 2 repetitions adjusted to 85% of 1RM, and finally 1 repetition at 90% to 95% of 1RM. After the warm-up, the participants performed 2 attempts with 100% of their 1RM, repeating this process until the athlete ultimately failed to lift the weight (20).

Table 1. *Weightlifting Exercise*

Movements	Time
Competitive lifts (Snatch & clean and jerk)	45-60 min
Rest	30 second
Strength training	15-30 min
Rest	1 min
Assistive exercises (if needed)	0-30 min
Cool down	0-15 min

* The rest between each exercise set in weightlifting is usually 30 seconds, and the rest between single and double lifts is 5 minutes.

Blood Sampling and Assessment of Inflammatory Indices: Inflammatory indices (CBC-dif, IL-6, and LDH) were evaluated from blood samples taken from the athletes after fasting. All the mentioned blood variables were assessed at four different intervals.

2.5. Statistical Methods

Descriptive statistics were employed to summarise the findings in terms of mean and standard deviation. In the inferential statistics section, a repeated measures analysis of variance (ANOVA) was conducted at a significance level of $\alpha < 0.05$ using SPSS version 26.

3. Results

The characteristics of the participants are shown in Table 2.

Table 2. *Participants' personal information in the pre-test (M ± SD)*

Measurement index	Standard deviation ± mean
Age (years)	22±7.5
Height (cm)	163.5±7.3
Weight (kg)	65.1±8.5
Body Mass Index (BMI) (kg.m^2)	24.2±2.3
WHR (waist-to-hip ratio in cm)	0.7±0.05

The Shapiro-Wilk test indicated that the data were normally distributed. The mean and standard deviation of the research variables are shown in Table 3. According to Machli's rule, equality of variance was observed, and the results of the repeated measures ANOVA test are reported in Table 3.

Table 3. *Mean and standard deviation of varibles*

Variables	Stage 1 M±SD	Stage 2 M±SD	Stage 3 M±SD	Pillai's Trace	F	Sig.
White Blood Cells (W.B.C) ($10^3/\mu L$)	6.78±1.48	6.72±1.20	6.77±1.18	0.234	1.220	0.345
Neutrophil ($10^3/\mu L$)	4.43±1.44	3.96±0.76	3.95±0.83	0.346	2.118	0.183
Lymphocyte ($10^3/\mu L$)	2.16±0.26	2.38±0.50	2.38±0.35	0.300	1.715	0.240
Monocyte ($10^3/\mu L$)	0.09±0.03	0.20±0.04	0.18±0.06	0.280	1.555	0.269
Eosinophil ($10^3/\mu L$)	0.10±0.04	0.19±0.09	0.26±0.13	0.425	2.962	0.109
IL-6 (pg/ml)	26.42±11.20	0.596±0.022	27.75±10.53	0.841	21.150	0.001*
LDH (iu/l)	294.91±32.61	255.64±21.8	276.73±31.68	0.217	1.110	0.375

Stage 1: supermaximal training, Stage 2: Bromelain supplementation + supermaximal training, Stage 3: Pharmacokinetics + supermaximal training; M: Mean; SD: Standard Deviation.
*: P<0.05

According to Table 3, four weeks of bromelain supplementation had a significant decreasing effect on serum IL-6 levels following supermaximal weightlifting exercises (P<0.05).

4. Discussion

In explaining the findings, it can be stated that there is a general agreement that supermaximal exercise causes changes in haematological parameters. However, there are conflicting findings regarding the direction of these changes. For example, while Brun et al. (16) reported an increase in red blood cells, haematocrit values, and haemoglobin concentration after exercise, Mirbaiurel (21) showed a decrease in haemoglobin and haematocrit. Additionally, Lambert et al. (22) and Moaz et al. (23) reported an increase in leukocyte count, whereas Ramos-Campo et al. (24) reported a decrease in absolute lymphocyte count alongside an increase in neutrophil and monocyte counts. Similarly, Natal et al. (25) found that total white blood cell (WBC) counts increased during and immediately after exercise, while Pitsaus et al. (5) reported lower WBC counts. However, different patterns of cellular accumulation were observed in the circulation after 5 minutes of intense exercise. Blood samples collected from individuals who exercised at high intensity showed increased numbers of cell types, including segmented and banded neutrophils, lymphocytes, monocytes, and eosinophils. This increase could be attributed to the enhanced net blood flow that occurs during supermaximal exercise (22). It may also be due to the release of catecholamines, which have been reported to increase in plasma after short-term intense exercise (26).

In one study, it was shown that taking bromelain supplements increases WBC counts. However, in the present study, no changes were observed in the white blood cell count. In line with the justification of the findings, it can be stated that previous studies have indicated that white blood cell counts increase immediately after supermaximal exercise. In the present study, the duration of the blood test may have affected the results. On one hand, the increase in WBC from bromelain supplementation was noted in individuals with cancer or illness (10). In this study, bromelain supplementation was administered to semi-professional athletes who have a different physiological response compared to the aforementioned individuals.

LDH is an enzyme that plays a role in various metabolic processes, particularly in the conversion of lactate to pyruvate and vice versa. In supermaximal exercise, an increase in LDH is usually due to muscle damage and metabolic stress. If bromelain cannot effectively reduce muscle damage, it may not have an impact on LDH levels.

Bromelain is best known as a proteolytic enzyme that helps reduce inflammation and facilitate tissue repair; however, it may not have a direct effect on LDH activity, as LDH is more dependent on metabolic status and muscle damage. LDH levels may be influenced by a variety of factors, such as exercise intensity, type of exercise, and the individual's physiological state. If the exercise is not intense enough or if the athlete is well-conditioned, significant changes in LDH levels may not be observed. Furthermore, the duration of bromelain use may not have been sufficient to observe its effects on LDH, as supplements usually take time to manifest their effects in the body. On the other hand, inconsistencies with other studies may be attributed to the type of supplement used or the sample size. Bromelain was significantly effective in reducing IL-6 concentrations. As a proteolytic enzyme, bromelain may help decrease interleukin-6 (IL-6) levels through several mechanisms. It may facilitate the repair of damaged tissues and possesses anti-inflammatory properties that can aid in the recovery of injured tissues in athletes, potentially leading to a reduction in IL-6 production. Another beneficial property of bromelain is its positive effect on the immune system, which may also contribute to a decrease in IL-6 levels. Furthermore, bromelain may influence cell signalling pathways associated with the production of IL-6, thereby helping to reduce the production of this cytokine.

5. Conclusion

Based on the conducted review, it can be concluded that four weeks of bromelain supplementation has a significant effect on serum IL-6 levels following maximal weightlifting exercises, leading to a reduction ($p<0.05$). However, it does not have a significant effect on white blood cell counts or serum LDH levels ($p>0.05$).

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Conflict of interests: The authors declare that they have no conflict of interest relating to the publication of this manuscript.

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