ISSN: 2754-477X

Journal of Food Technology & Nutrition Sciences

SCIENTIFIC Research and Community

Research Article

Open Access

Effect of Dual Polyphenolic Ingredient on Muscle Injury and Performance: A Prospective, Double-Blind, Placebo-Controlled, Randomized, Interventional Study in Healthy Volunteers

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ABSTRACT

Background: Eccentric exercise is a regular part of rehabilitation and sports training and to the unaccustomed, can cause muscle damage that presents as delayed soreness, strength and range of motion loss, swelling, and increased passive stiffness. These symptoms reduce exercise ability and might be harmful if exercise is further continued. In this study, we sought to test the efficacy of a proprietary dietary supplement, Gremin®, contains green coffee bean extract and curcumin in alleviating the severity of muscle damage and injury after standardized eccentric exercise. This study was a prospective, double-blind, placebo-controlled, randomized, interventional study. Sixteen healthy, moderately active, non-smoking volunteers with no known musculoskeletal pathology were enrolled. Mean differences within and between groups were assessed inferentially at each data collection point using t-tests for all outcome measures.

Results: In this controlled study, the intake of Gremin® for 10 days resulted in a significant reduction in standardized measures of pain and tenderness at several post-eccentric exercise points compared to the placebo group. The Gremin® group had significantly reduced levels of plasma indicators of inflammation (C-reactive protein) and muscle damage (creatine kinase and lactate dehydrogenase), as well as standardized measures of pain and tenderness at several post-eccentric exercise time points, than the placebo group.

Conclusions: Gremin® appears to be beneficial in accelerating the healing of acute muscle injury. Further studies with a larger sample size are warranted based on the current results.

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Received: February 23, 2022; **Accepted:** February 28, 2022; **Published:** March 07, 2022

Keywords: Dietary Supplement, Eccentric Exercise, Muscle Damage, Sports Injuries, Muscle Injuries, Endurance

Background

One of the common challenges faced by athletes, joggers, brisk walkers, and people doing regular exercise is muscle injuries. These are painful, lead to muscle function changes, and require a long time to recover, thereby affecting return to exercise, practice, or sports events of those suffering from these injuries. Several hours of unaccustomed high-intensity eccentric exercise can lead to a combination of muscle pain and stiffness, commonly referred to as delayed onset muscle soreness [1]. Muscle damage or injury may generate reactive oxygen species (ROS) causing sustained oxidative stress and inflammatory response, leading to the expression of pro-inflammatory cytokines [2]. Hence, the recovery and healing process associated with muscle injury and stiffness may play an important role in sports or exercise-induced muscle damage. In this context, several approaches have been utilized, including pre-and post-exercise stretching, light exercise, ultrasound, topical analgesics, and pharmacologic agents, in mitigating muscle damage or injury [3]. Nevertheless, there is a lack of effective and natural interventions or treatment regimens that lessen the severity of exercise and sports-related muscle damage.

Furthermore, athletes or sportspersons endure long training sessions; hence, endurance plays a significant role in improving health and physical fitness. In particular, it could increase tolerance to physical exhaustion, thereby allowing prolonged workouts or effective tackling of day-to-day activities. Therefore, to reduce the risk of muscle injury, it is important to improve muscle strength and endurance. To do so, nutritional intervention could be regarded as one of the most effective strategies in quenching ROS and reducing inflammation, leading to quick recovery from muscle injury and boosting endurance levels [4].

Keeping this in mind, we conducted our study with Gremin® a natural ingredient manufactured using proprietary technology. Gremin® is infused with herbal actives with synergistic anti-inflammatory and antioxidant properties and constituents that

improve stamina and increase endurance levels. This unique product contains two different polyphenolic compounds with varying physicochemical properties embedded in a matrix system to ensure better efficacy and therapeutic benefits. Moreover, it contains pharmacologic active moieties proven to burn excess body fat, increase energy levels, regulate blood glucose levels, and improve metabolic rate. For this reason, Gremin® can be considered an appropriate choice for mobility and sports segments [5,6]. In sum, Gremin® is a combination of poly phenolic extracts with excellent antioxidant, anti-inflammatory, weight management, and pain management features, which is a standalone product that possibly addresses overall muscular strength, stamina, and endurance [7].

The objective of this study was to evaluate the role of Gremin® in improving exercise-induced muscle injury or damage in sportspersons. In this study, we recruited 16 Asian volunteers and administered either Gremin® or the placebo control at different visits. At each visit, we assessed and estimated different biomarkers, including creatine kinase, myoglobin, blood urea nitrogen, lactate dehydrogenase (LDH), serum ferritin, total iron, transferrin, sodium levels, visual analog scale (VAS) score for muscle damage, physical tests, maximal oxygen consumption (VO2 max) for endurance, and complete blood count (CBC), C-reactive protein (CRP), and tumor necrosis factor (TNF) alpha for inflammatory response.

Methods

Subjects and General Procedures

Sixteen subjects in a ratio of 8:8 (test product: placebo) were enrolled for this study. The inclusion criteria were healthy, moderately active (regular aerobic exercise for at least 4 hours per week), non-smoking male volunteers aged 18-40 years with no known musculoskeletal pathology. Candidates must have maximal oxygen consumption (VO2 max) of at least 35 ml/kg, as assessed by the maximal treadmill exercise test. The candidates were identified as healthy per the clinical judgment of a certified clinician. The qualified volunteers who were willing to comply with the study procedure signed written informed consent. The exclusion criteria were the following: intake of anti-inflammatory agents, analgesics, or antioxidants in the previous month; a history of abnormal liver or renal function tests; laboratory findings suggestive of an active inflammatory or infectious process; the presence of any known disease in the last three months; any current alcoholism or drug abuse; allergy to at least one of the component in the trial; participation in other clinical trials in the last six months; presence of open wounds and injuries involving the skeletal system or deep soft tissue injury in the last three months; presence of neurological disorders; uncontrolled systemic disease; and steroid or ergogenic users in the last three months. Among the 16 men enrolled, mean age ± standard deviation (SD) was 22.25 ± 4.187 years, mean height ± SD was 1.71 ± 0.05 m, and mean weight ± SD was 68.22 ± 8.163 kg. A detailed demographic summary is provided in Table 1.

Table 1: Summary of Demographics Characteristics – Full Analysis Set population

	Test (N=8)	Placebo (N=8)	Overall (N=16)
Gender, n (%)			
Male	8 (100)	8 (100)	16 (100)
Female	0 (0.0)	0 (0.0)	0 (0.0)
Age			
n	8	8	16
Mean ± SD	22.13 ± 1.73	22.38 ± 5.88	22.25 ± 4.187
Median	22.50	20	21.5
Race, n (%)			
Asian	8 (100)	8 (100)	16 (100)
Other	0 (0.0)	0 (0.0)	0 (0.0)
Ethnicity			
Indian	8 (100)	8 (100)	16 (100)
Other	0 (0.0)	0 (0.0)	0 (0.0)
Height (m)			
n	8	8	16
Mean ± SD	1.70 ± 0.03	1.72 ± 0.07	1.71 ± 0.05
Median	1.71	1.72	1.71
Min, Max	1.65, 1.73	1.60, 1.81	1.60, 1.81
Weight (kg)			
n	8	8	16
Mean ± SD	66.55 ± 8.80	69.79 ± 7.69	68.22 ± 8.163
Median	70.30	67.93	69.90
Min, Max	49.25, 73.60	62.15, 85.90	49.25, 85.90
BMI (kg/m2)			
n	8	8	16

Mean ± SD	23.00 ± 3.23	23.81 ± 2.81	23.40 ± 2.955
Median	24.22	24.17	24.215
Min, Max	16.73, 25.62	19.57, 28.18	10=9.57, 28.18
Heart rate			
n	8	8	16
Mean ± SD	82.88 ± 7.55	79.25 ± 12.51	18.88 ± 1.02
Median	83.50	76	18
Min, Max	72, 107	68, 107	18, 20
Respiratory rate			
n	8	8	16
Mean ± SD	19.25 ± 1.04	18.50 ± 0.93	18.88 ± 1.02
Median	20	18	18
Min, Max	18, 20	18, 20	18, 20

*SD: Standard deviation

Supplementation

The details of investigational product (IP) , a co-processed nutraceutical ingredient containing curcumin and green coffee bean extract at optimal ratio (Gremin®) and placebo capsules (Micro crystalline cellulose) are presented in Table 2. The size, shape, color are identical for both IP and placebo capsules. According to their group, the subjects were administered with either Gremin® or 500 mg of the placebo capsule (IP/placebo) orally, 30 minutes after meals, from Days 0 to 10, as in the recommendation of Gremin®.

Table 2: Test Product and Placebo Information

Product	Test Products
IP	GreMin® Capsules; Placebo Capsules
Dosage form	Capsules
Strength	500 mg
Dosing regimen	Twice a day
Route of administration	Oral

Ethics

All volunteers provided written informed consent and completed a Health History Questionnaire and Physical Activity Readiness Questionnaire (PAR-Q) to assess their eligibility. The protocol and consent form were reviewed and approved by the Institutional Ethics Committee of Jehangir Clinical Development Center, Pune, Maharashtra, India, and were performed in compliance with ICH E6R2 "Guidance on Good Clinical Practice," Indian Good Clinical Practice Guidelines, National Ethical Guidelines for Biomedical and Health Research involving Human Participants, ICMR 2017, and the Declaration of Helsinki. This trial was registered in the Clinical Trial Registry of India under the registration number: CTRI/2020/11/029407. Written informed consent was obtained from each subject to participate in the trial after being informed about the nature and purpose of the study.

Study Design

The study design is summarized in Figure 1. We administered the IP/Placebo twice a day throughout a 10-day study protocol. At the screening Visit 1 (Day 0), the subjects were provided with a unique subject ID and randomized to one of the two study groups: the interventional and control arm, in a 1:1 ratio. On Visit 1 (Day 0), the subjects underwent screening and assessment based on demographics, medical history, prior medication use, and current/concomitant medication. General physical examinations, including vital signs and laboratory assessments, were recorded along with VO2 max. Laboratory assessment included CBC, CRP, TNF alpha, creatine kinase, myoglobin, blood urea nitrogen, LDH, serum ferritin, total iron concentration, transferrin, and sodium levels.

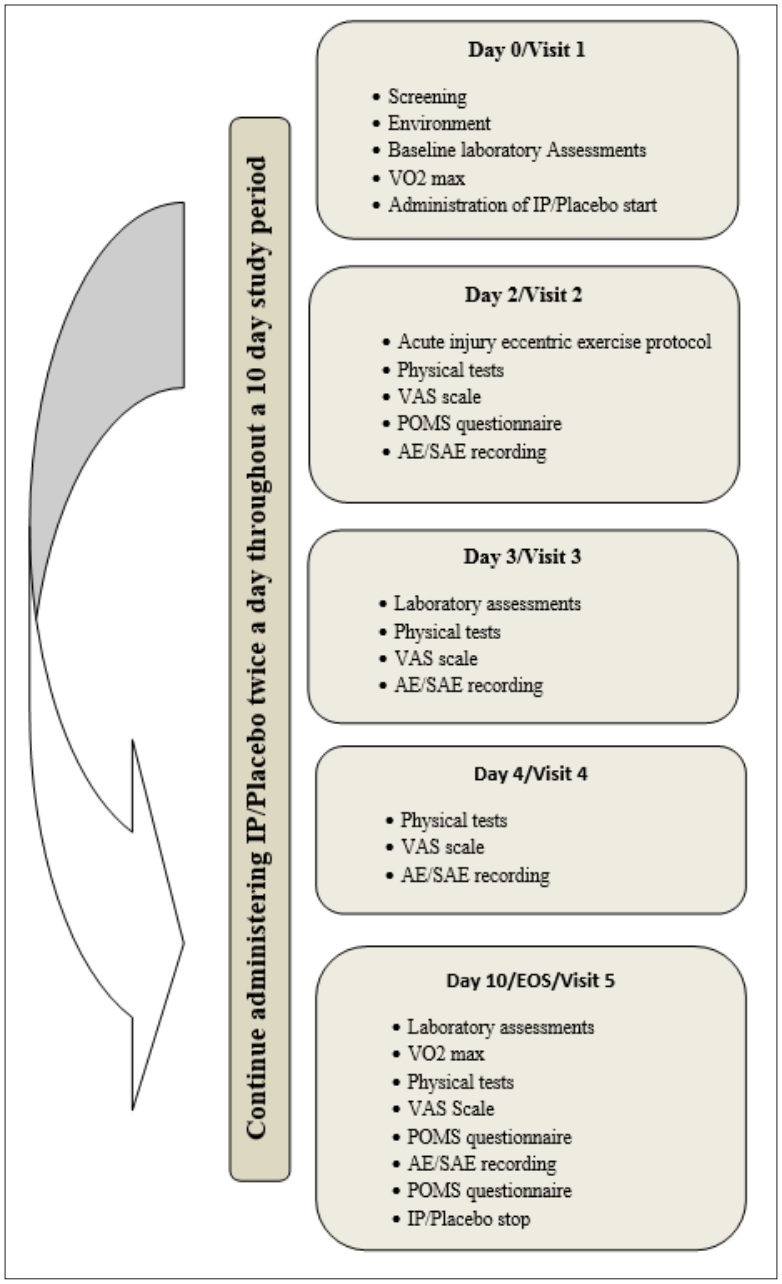

Figure 1: Study Design

At the subsequent scheduled study visit (Visit 2), all subjects were interviewed for compliance with the study procedure. The subjects were given diaries that were reviewed for documentation of episodes of illness and IP/placebo administration compliance. IP/placebo administration was performed along with laboratory assessments and physical tests. The acute injury protocol (eccentric exercise protocol) [8] was conducted on Day 2 (Visit 2) of this study. The protocol required the participants to perform a muscle-damaging exercise consisting of seven sets of 10 eccentric single-leg press repetitions on a leg press machine. Initially, the one-rep max (RM) weight lifted concentrically was determined for both legs in each participant. Afterward, 120% of the one RM was calculated and used for the eccentrically lowered weight. Each participant performed five sets of 10 repetitions at 120% of 1 RM and two sets of 10 repetitions at 100% of 1 RM. One RM was performed on each leg individually, and each participant completed all seven sets. During each eccentric contraction that lasted for 3-5 seconds, the load was resisted with the allocated leg from full knee extension to 90° angle of knee flexion. After each eccentric contraction, the load was raised by the subject using both legs concentrically. The participants were given 3 minutes of rest between sets.

On scheduled study Visit 3 (Day 3), all subjects were interviewed for compliance with the study procedure. The diaries of the subjects were reviewed for any episode of illness and documentation of IP/placebo administration compliance. The laboratory assessments were measured. Physical tests including doing squats and pushups in one set until failure, core stability, and walk tests were performed following the protocol.

On scheduled study Visit 4 (Day 4), all subjects were interviewed for compliance with the study procedure along with the diary review. Laboratory assessments and physical tests were conducted along with VAS score determination. At the subsequent scheduled study visit (Visit 5/Day 10), all subjects were interviewed for compliance with the study procedure. IP/placebo administration and laboratory assessments were conducted along with physical tests such as squats and pushups in one set until failure, core stability, VO2 max determination, and VAS score.

Treatment Compliance

Product administration was monitored using an IP compliance diary. Efficacy analysis was performed at the end of the study and summarized based on the recovery of muscle damage due to the eccentric injury protocol, increased endurance, and reduced inflammation. The effect of the 10-day supplementation with Gremin® was compared within groups and with the placebo group based on changes in biomarkers from baseline to the end of treatment.

Recovery from Muscle Damage Due to Sports Injuries

Creatine kinase, myoglobin, blood urea nitrogen, and LDH levels and the VAS score were determined for the recovery of muscle damage due to sports injury.

Increased Endurance

We analyzed the changes in laboratory assessments, (serum ferritin, total iron concentration, transferrin, sodium levels) and physical tests (number of squats and pushups in one set until failure, core stability, and VO2 max) to evaluate the changes in endurance.

Reduce Inflammation

To analyze reduction in inflammation, parameters such as CBC, CRP, and TNF-α were studied. For this purpose, laboratory assessments of these biomarkers were performed at predetermined visits as described in the schedule of assessments. These parameters for the primary endpoint are presented as n, mean, median, SD, minimum, and maximum and were analyzed using paired t-test for within-comparison and independent t-test for comparisons between the two treatment groups.

Statistical Analysis

Statistical analysis was performed using SPSS V.23 software. All available data were used for the analysis. Data not available were assessed as "missing values," and the observed population was evaluated.

Assessment of Safety

Safety evaluation included physical examination and periodic monitoring of vital signs and adverse events. Clinically significant changes in vital signs and physical examination findings were reported as appropriate and summarized. Adverse events were monitored using the information provided by the subjects and were not observed throughout the study.

Results

In this study, we recruited subjects based on the inclusion criteria with a mean height, weight, BMI, and age of 1.71 ± 0.05 m, 68.22 ± 8.163 kg, 23.40 ± 2.955 kg/m2, and 22.25 ± 4.187 years, respectively. Moreover, all subjects were of Asian origin, with mean heart and respiratory rates of 81.06 ± 10.16/min and 18.88 ± 1.02/min, respectively. The results showed no clinically significant abnormalities observed in any of the subjects in general, systemic, vital signs, or physical examinations during the entire study period. The safety profile demonstrated that Gremin® had no adverse effects and was favorable.

This study evaluated the efficacy of Gremin® in the healing process of exercise-induced muscle injury owing to its synergistic anti-inflammatory and antioxidant effects based on various endpoints such as recovery from muscle damage, increased endurance, and decreased inflammation. We evaluated different biomarkers, such as creatine kinase, myoglobin, blood urea nitrogen, LDH, and VAS score, for the recovery of muscle damage during the screening visit and visits 3 and 5. Our data demonstrated no significant increase in the mean levels of Creatine kinase (ng/ml) in the Gremin® group compared to the levels in their respective placebo control group during the screening visit and visits 3 and 5. A slightly higher creatine kinase level was observed in the Gremin® group than in the placebo control group at Visit 3 after the eccentric injury protocol; however, at Visit 5, a decrease in creatine kinase level was observed in the Gremin® group (Figure 2A). This indicates the positive effect of the test product, Gremin®, in decreasing creatine kinase levels from Visit 3 (Day 3) to Visit 5 (Day 10). This can possibly be manifested in the healing process of muscle injury caused by sports or exercise (Figure 2).

Similarly, at visits 3 and 5, the mean levels of myoglobin (ng/ml) (Figure 2B), blood urea nitrogen (mg/dl) (Figure 2C), and LDH (mg/dl) (Figure 2D) did not differ significantly between the Gremin® administered group and their respective placebo control group (Figure 2). Furthermore, when comparing the Gremin® administered test group at visits 3 and 5, there was no significant increase in mean levels of myoglobin (ng/ml) and blood urea nitrogen (mg/dl); however, the mean level of LDH (mg/dl) decreased during Visit 5 (208 mg/dl) compared to that during Visit 3 (215 mg/dl) (Figure 2), implying that Gremin® could have played a beneficial role in reducing the concentration of LDH at Visit 5 (Day 10). This decrease in LDH levels suggests the effect of Gremin® supplementation on muscle recovery. In addition, evaluation of the VAS scores at visits 2, 3, 4, and 5 revealed that no significant mean change in the test group in comparison to their respective placebo control groups (Figure 2E). Moreover, when comparing within groups of Gremin® administered subjects at various visits (2, 3 and 4), no significant difference was observed in the mean VAS score. Nevertheless, only at Visit 5 did we observed a significant reduction in the VAS score (1.00) from Visit 4 (2.5) ($P < 0.05$) in the test group, indicating the effectiveness of Gremin® in reducing pain generated by the eccentric exercise protocol.

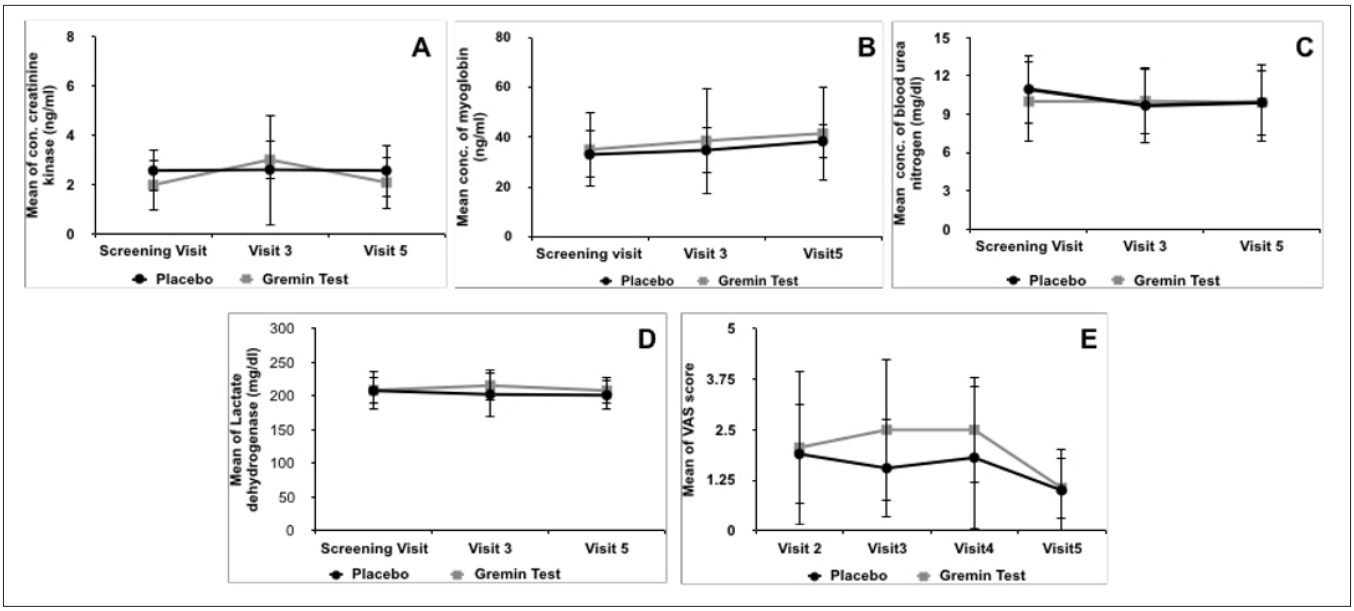

Figure 2: Expression of biomarkers for muscle damage due to sports injury after the administration of the test product, Gremin®, and placebo control. Images showing mean levels of (A) creatine kinase (ng/ml), (B) myoglobin (ng/ml), (C) blood urea nitrogen (mg/dl), (D) LDH (mg/dl), and (E) mean of the VAS score in the Gremin® and placebo control groups.
n=8. Data represented as mean ± S.D.

Moreover, we studied the effect of Gremin® in increasing the endurance of test subjects by estimating the levels of serum ferritin (Figure 3A), total iron (Figure 3B), transferrin (Figure 3C), sodium (Figure 3D) and in physical tests such as number of squats and pushups in one set until failure, core stability, and VO2 max (Figure 3E). The data indicated no significant difference in the mean levels of serum ferritin (ng/ml) between the Gremin® administered test group and their respective placebo control group at visits 3 and 5. Furthermore, the comparison within test groups at visits 3 and 5 did not show any significant difference (Figure 3). Nevertheless, we found a significant decrease ($P<0.05$) in the mean level of total iron (ug/dl) in the Gremin® administered test group compared to the placebo control group during Visit 3 (Figure 3B). There was a slight increase (9%) in total iron levels during Visit 5, suggesting that Gremin® could be involved in improving the iron levels during intense exercise regimen, although the changes were not significant (Figure 3B). Another endurance marker evaluated was transferrin (mg/ml), which did not reflect significant changes in the Gremin® administered test group compared to the placebo control group at visits 3 and 5. Comparison within the Gremin® administered test groups at visits 3 and 5 showed no change in the mean levels of transferrin (mg/ml) (Figure 3C).

Regulated blood sodium levels could be considered a factor indicating endurance during sports and exercise. This study revealed no significant difference between the mean levels of sodium in both the test and placebo control groups as well as in comparison within the test groups at visits 3 and 5 (Figure 3D), indicating that Gremin® was involved in boosting endurance without affecting sodium levels (Figure 3).

Similarly, we observed no significant difference in the mean change in VO2 max of the Gremin® administered test group compared to that of the placebo control group and also within the Gremin® administered test groups at Visit 5. Perhaps, chronic supplementation of Gremin® for a longer period may positively impact VO2 max levels in the test subjects. The physical test also demonstrated a similar trend with no significant difference in the mean change in the number of squats and sit-ups. However, at Visit 4, there was a significant difference within the Gremin® administered test groups but not in the placebo control groups ($P<0.05$) (Figure 3), indicating that the test product had prominent therapeutic benefits in improving stamina and endurance.

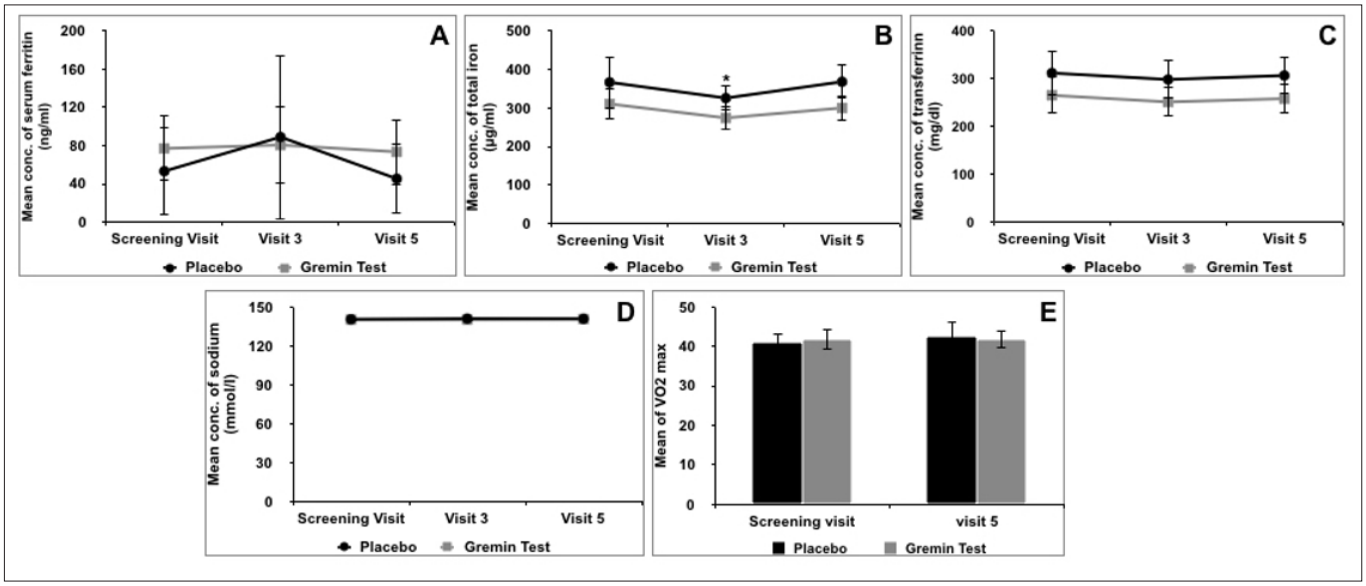

Figure 3: Expression of biomarkers for increased endurance in sports after the administration of the test product, Gremin®, and placebo control. Images showing mean levels of (A) serum ferritin (ng/ml), (B) total iron (ng/ml), (C) transferrin (mg/dl), (D) sodium (mg/dl), and (E) mean of VO2 score in the Gremin® and placebo control groups at Visit 3.
n=8, statistical significance: $p<0.05$, data represented as mean ± S.D.

The study also focused on the effect of Gremin® in reducing inflammation in sports-induced injury by estimating the levels of biomarkers such as CBC, CRP, and TNF alpha. We found no abnormalities in CBC values after Gremin® administration, indicating the importance of the test product in regulating essential CBC parameters. Furthermore, the data showed no significant difference in the mean levels of CRP (mg/l) in the Gremin® administered test group compared to those in the placebo control group at visits 2, 3, and 4 (Figure 4). However, there was a reduction in CRP value (1.46 mg/l) during Visit 4 compared to the screening visit (1.88 mg/l), although the change was not statistically significant (Figure 4A). This could possibly explain the role of Gremin® in muscle recovery, underlining its potential anti-inflammatory properties. The CRP value in the placebo control group (2.18 mg/l) during Visit 5 was higher than that at the respective screening visit (1.76 mg/l) (Figure 4A). There was a significant difference in the mean level of TNF alpha (pg/ml) in the Gremin® test group and placebo control group at Visit 5 ($P<0.05$); however, no significant change was observed within the Gremin® test or placebo control groups (Figure 4B). This reinforces the notion that the test product possesses potential anti-inflammatory properties.

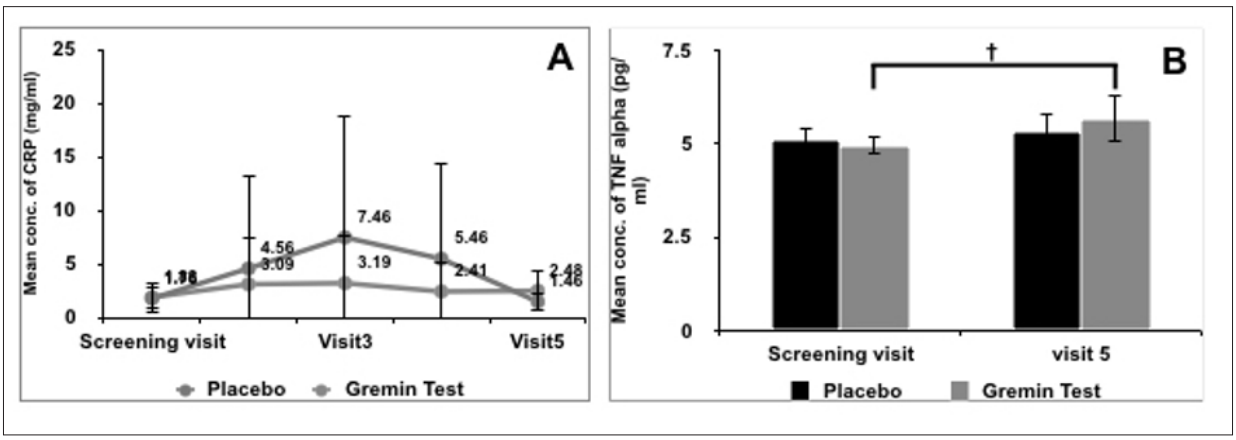

Figure 4: Expression of biomarkers for reduced inflammation in sports-induced injury after the administration of the test product, Gremin®, and placebo control. Images showing mean levels of (A) C-reactive protein (CRP) (pg/ml) and (B) tumor necrosis factor (TNF) alpha (ng/ml) in the Gremin® and placebo control groups at Visit 5.
n=8, statistical significance: $p<0.05$, data represented as mean ± S.D.

Discussion

This clinical study aimed to understand the efficacy of Gremin® in reducing muscle injury and improving stamina and endurance in participants who were subjected to an eccentric exercise protocol. Eccentric exercise can result in muscle lengthening or stretching, while in concentric exercises, muscle shortening can occur in response to the stimulation [9]. The unusual, high-intensity, and prolonged duration of eccentric exercise-induced muscle injury owing to the decreased rate of cross-bridge muscle detachments [10]. Moreover, muscle damage during unaccustomed exercise can result in the generation of reactive oxygen species (ROS), which would elicit inflammation or altered cellular functions and decreased endurance [11]. Moreover, it can lead to delayed onset muscle soreness (DOMS) with muscle pain and stiffness [1]. The complex physiological and cellular changes during this type of exercise by sportspersons can be estimated by studying the associated biomarkers for pain, muscle damage, endurance, and inflammatory responses. They have been widely used by several researchers to assess and monitor the health status, training, and performance of an individual [12-15]. Therefore, this study was designed with various biomarkers to evaluate the effects of Gremin® in muscle damage recovery, increase in endurance, and inflammation reduction.

High creatine kinase level in the blood is considered a prominent indicator of muscle damage [16]. We observed elevated creatine kinase levels after eccentric exercise in Gremin®-administered subjects at Visit 3 (Day 3 of exercise); thereafter, there was a gradual decrease in creatine kinase levels during Visit 5 (Day 10). In agreement, a single-blind, crossover, randomized controlled trial study revealed a reduction in creatine kinase activity after the intake of curcumin capsules (150 mg twice a day, 1 h before and 12 h post-exercise) by young men (n=14) [13]. This reduction could be attributed to the ability of curcumin to quench the ROS produced during physical exercise [17]. Furthermore, LDH, a potential biomarker of exercise-induced muscle damage [18], showed a similar trend during Visit 3. A decrease in LDH levels at Visit 5 might be because of Gremin®, which would result in the alleviation of muscle injury. In support of this, Córdova et al. showed a similar reduction in LDH levels in cyclists due to iron supplementation, which prevented muscle damage [18]. Furthermore, Gremin® supplementation in the participants relieved their muscular pain, as reflected by the decrease in the VAS score at Visit 5 compared to Visit 4. Likewise, some studies reported that curcumin supplementation also reduced muscle pain with a decrease in the VAS score after exercise, which could be related to its anti-inflammatory effect [19].

Gremin® also contributed to increasing endurance by regulating the total iron and sodium levels in the subjects, which could be attributed to its synergistic antioxidant and anti-inflammatory properties. In support of this, a study emphasized the role of increased iron stores by supplementation to enhance endurance capacity, thereby reducing fatigue and muscle damage [20]. Similarly, an investigation corroborated that the ingestion of sodium bicarbonate before exercise could possibly enhance muscular endurance by attenuating and delaying fatigue, while other reports indicated no effect of sodium on endurance levels [21,22]. Moreover, Gremin® improved stamina and endurance levels in volunteers during physical tests for the lower and upper body (squats, sit-ups, and press-ups), reinforcing its beneficial effect in the eccentric exercise protocol. A previous study has correlated increased endurance levels and supplementation with sodium bicarbonate in participants performing squats, leg press, and knee extension [21]. This supports our notion that Gremin® has the potential to regulate sodium levels in subjects, thereby influencing stamina and endurance.

In addition, Gremin® exhibited anti-inflammatory effects in treated subjects by modulating CRP and TNF alpha concentrations. Several investigations have also reported that curcumin supplementation to sportspersons has an immunomodulatory effect by regulating the cytokine and chemokine levels, which are involved in pro and anti-inflammatory effects [14,23,24]. In contrast to our assumption we understand that the study revelations were not statistically significant in many of the parameters. This may be because of the relatively smaller subject size, young study population and the acute supplementation protocol used. However, it is evident from the clinical data that Gremin® is effective in regulating the inflammation, muscle pain reduction, injury recovery and improving exercise endurance at the studied dose. This needs to be further investigated in a larger sample size in the future studies.

Conclusions

This clinical study tested the safety and efficacy of Gremin® in healthy volunteers for prospective human usage. Preliminary clinical data showed that Gremin® is safe and effective for human use and promotes a downward trend in creatine kinase and LDH levels. In addition, a reduction in the VAS score indicated muscle protection and pain management benefits. Furthermore, Gremin® showed the ability to regulate total iron and sodium levels, contributing to improved stamina and endurance. Moreover, Gremin® was shown to regulate CBC, CRP, and TNF alpha, suggesting its potential anti-inflammatory properties. This study further opens window of opportunities to decipher the mechanisms by which Gremin® could prove vital in alleviating muscle injury, improving endurance, and reducing inflammation.

Consent for Publication: Written informed consent was obtained from each subject to participate in the trial after being informed about the nature and purpose of the study.

Availability of Data and Material: The data presented in this study are available on request from the corresponding author

Competing Interests: The authors declare that they have no competing interests.

Funding: This project was funded by ZeusHygia LifeSciences Pvt Ltd, Hyderabad, India.

List of Abbreviations

CBC: complete blood count
CRP: C-reactive protein
IP: investigational product
LDH: lactate dehydrogenase
PAR-Q: Physical Activity Readiness Questionnaire
ROS: reactive oxygen species
RM: one-rep max
SD: standard deviation
TNF: tumor necrosis factor
VAS: visual analog scale
VO2 max: maximal oxygen consumption

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