

Multi Enzyme Complex for the Management of Delayed Onset Muscle Soreness after Eccentric Exercise: A Randomized, Double Blind, Placebo Controlled Study

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Abstract

Background: Delayed onset muscle soreness (DOMS) results from muscle overload or strenuous exercise that goes beyond the intensity or duration for which the muscle is accustomed to perform. It is accompanied with the sensation of pain, tenderness, deep ache, and stiffness in muscles that usually begins several hours after the exercise. The aim of this study was to evaluate the effect of multi enzyme complex capsule (50 mg) thrice a day for a period of 3 days compared to placebo in reducing pain associated with DOMS induced by standardized eccentric exercise.

Methods: Twenty healthy males (10 pairs) were randomized in this double blind, placebo controlled trial to receive a placebo or multi enzyme complex capsule (50 mg) thrice a day for a period of 3 days. Mean differences within the group and between groups were assessed at each data collection time-point using Analysis of Covariance (ANCOVA) and Wilcoxon signed rank sum test for all outcome measures.

Results: In this controlled clinical study, intake of multi enzyme complex for 3 days resulted in no statistically significant differences in pain, tenderness, deep ache, and stiffness in muscles compared to placebo. Multi enzyme complex supplementation improved the outcome measures related to DOMS induced by standardized eccentric exercise.

Conclusion: The study results suggest that compared to placebo, Multi enzyme complex supplementation improves the outcome measures related to DOMS induced by standardized eccentric exercise.

Keywords: Delayed onset muscle soreness (DOMS); Muscle soreness questionnaire (MSQ); Pressure pain threshold (PPT); Hand held dynamometer; Illinois agility run test; Multi-enzyme complex

There is some evidence that ibuprofen, naproxen, and massage may accelerate the resolution of DOMS [12]. In addition, several dietary supplements have been tested in the treatment of DOMS including protein, vitamin C, proteases (enzymes), phosphatidylserine, chondroitin sulphate, and fish oil, all with variable success [4,12-18].

Introduction

Delayed onset muscle soreness is related to muscle damage occurring several hours after unaccustomed exercise, particularly when eccentric muscle activity is involved [1,2]. Contracting muscles are forcibly lengthened with eccentric exercise like downhill running which limits physical function for several days [3,4]. This triggers an inflammatory response and the production of reactive oxygen species (ROS) that sustain inflammation and oxidative stress by promoting the activation of transcription factors like the nuclear factor- κ B (NF- κ B), a pro-inflammatory master switch that controls the production of inflammatory markers and mediators [5]. Inflammation ensures musculoskeletal injury; uncontrolled inflammation may prolong skeletal muscle recovery [4].

Non-steroidal anti-inflammatory drugs (NSAIDs) like ibuprofen are used widely as anti-DOMS recourse. NSAIDs are known to interfere with chemotaxis of monocytes as well as inhibit neutrophil aggregation [19]. Monocytes produce cytokines, which are responsible for most of the physiological responses accompanying injury, and neutrophils produce elastase and collagenase, which increase vascular permeability via degradation of the vasculature and healthy tissue near the injury site [20]. It is possible that the use of NSAIDs may impair and lengthen the healing process.

Delayed onset muscle soreness (DOMS) is a well-documented phenomenon, often occurring as the result of the unaccustomed or high intensity eccentric exercise. Associated symptoms include muscle shortening, increased passive stiffness, swelling, decreases in strength and power, localized soreness and disturbed proprioception. Symptoms will often occur within 24 h post-exercise and typically subside after 3-4 days. The severity of damage and soreness varies as a function of several factors [6].

In spite of inconsistencies, dose and timing of various NSAIDs also in different studies there are side effects such as gastrointestinal distress and hypertension. Hence NSAIDs are not an optimal choice for treating DOMS [12]. Using enzymes to combat DOMS is also well established.

Considerable amount of research on the treatment of DOMS has been carried out till date but no single treatment has been proven successful in consistently preventing or treating DOMS. Treatment strategies have often integrated multiple therapeutic approaches such as cryo therapy, ultrasound, compression therapy, stretching and deep

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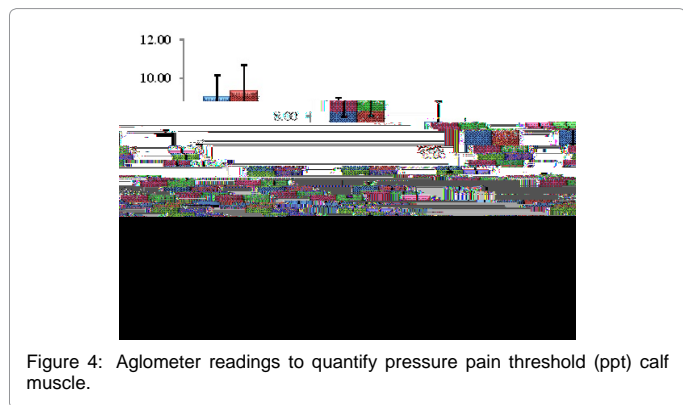
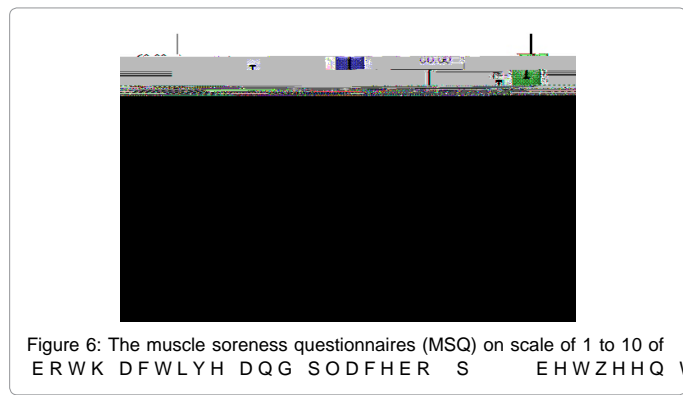
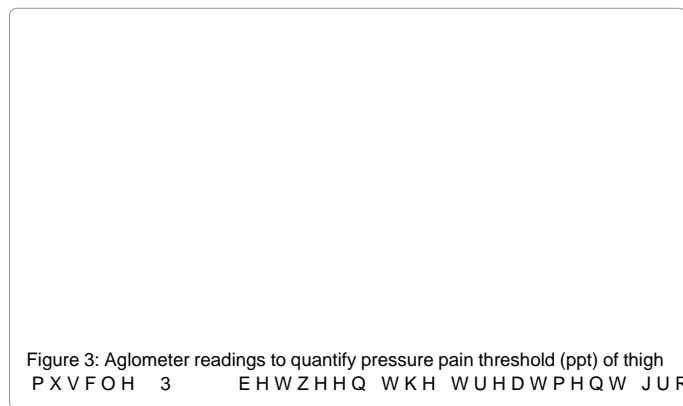
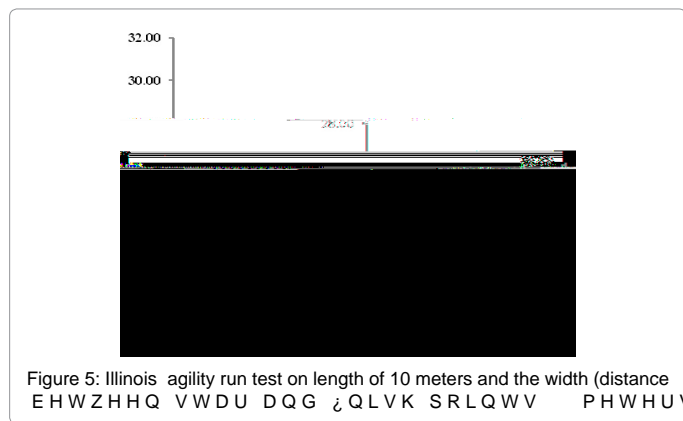
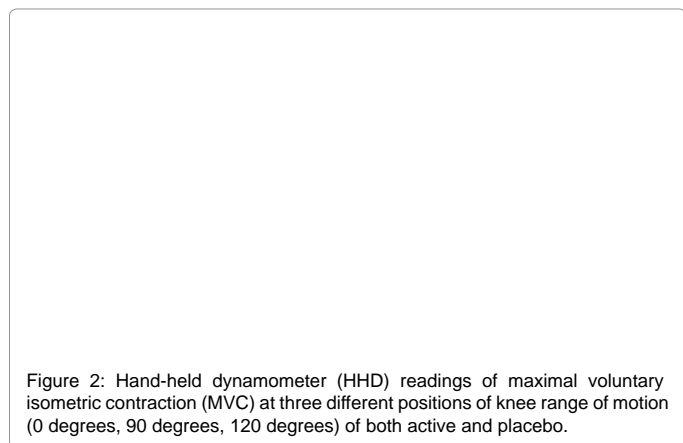
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blindness of the study and concealment of allocations. Computer generated random allocation software (version 2.0) was used for the allocation of concealment. Block randomization (only one block) was followed wherein the subjects were randomized to receive either active or placebo. The randomization codes were kept strictly confidential and were accessible only to authorized persons on an emergency basis as per the Sponsor standard operating procedures until the time of unblinding.

Blinding

The study was double blinded wherein neither the Investigator nor the trial participants knew whether they would receive the active or the placebo. The investigational products were provided in pre-labelled containers to avoid bias.



24 hours post exercise, subjects on the placebo group showed trend towards a higher level of CK than the multi enzyme complex group. This trend continued through the 72 hour assessment. Difference between the multi enzyme complex group and placebo in CK values was not statistically significant. Lactate dehydrogenase also showed a similar phenomenon, which trended higher at 24 and 72 hours post-exercise in the placebo group (Figures 7-8).

Flexion and extension measurements

On analysing the pre exercise leg flexion measurements, they were found to be equal between the groups for the left leg. Whereas the extension measurement was found to be significantly greater ($p=0.049$) for the right leg in the placebo group.

When the post exercise flexion measurements were analysed, only the 24-hour right leg extension measurement was found to be significant ($p=0.004$) in the multi enzyme complex group.

Tenderness assessment

On the tenderness quotient, subjects taking multi enzyme complex demonstrated significantly less tenderness, 72 hours after exercise ($p=0.042$).

Muscle damage assessments

Liberation of biochemical substances such as creatine kinase, lactate dehydrogenase, protein metabolites and myoglobin occurs from muscle cells approximately 24 hours post exercise and have been found in plasma up to 48 hours [29]. Creatine kinase being a surrogate index of muscle damages more indicative of damage or gaps in the sarcolemma [30]. The CK response was less in the multi enzyme complex group suggesting the membrane integrity was maintained to a greater extent than the placebo group.

Safety evaluations

Vital signs such as Blood Pressure, Respiratory Rate, Pulse Rate and any abnormal laboratory parameters were considered for safety evaluations. No clinically significant changes were recorded for descriptive physical examination in both the groups (Multi enzyme complex and placebo). The safety of multi enzyme complex was assessed using adverse event data (occurrence, intensity, and relationship to study drug). No adverse events were noticed in the study.

Discussion

Multi enzyme complex capsules contain alpha-amylase, neutral protease, lipase, lactase and cellulase. The capsule contains free broad acting enzymes obtained from the fermentation process

In the present study multi-enzyme complex capsules demonstrated significant improvement in subjective pain and tenderness, with no significant improvement in levels of markers of inflammation, muscle damage or muscle exertion. Multi-enzyme complex contains a multiple enzymes that are indicated for relieving the symptoms of DOMS.

Findings of this study suggest that multi enzyme complex can have several potential clinical applications. Protease supplementation when coupled with a well-managed training programme can result in more rapid recovery of the damage caused to contractile mechanism by DOMS.

Registration

The trial was registered on the Clinical Trial Registry of India with the registration number CTR/19/2016 demonstrated

with AS capsules
manufacturing technique ensures that the gastric enzymes from AS capsules
small intestine, respectively. Various studies have shown protease supplementation may attenuate muscle soreness after downhill running [31].

A subsequent series of four studies have evaluated papain, in combination with other proteases, in small samples of male athletes, especially with regard to its effectiveness in attenuating DOMS post eccentric exercise. Two of the studies were able to show better exertion in the tested limb post eccentric load which was hypothesised to be mediated by regulation of leukocyte activity and inflammation. Two further studies showed an improvement in contractile function and subjective pain and tenderness ratings but not in biochemical measures of DOMS. Further interpretation of these studies is difficult as all four used a combination of papain with other proteolytic enzymes (e.g. bromelain, amylase, lysozyme, and trypsin) [8].

In the present study we sought to investigate the effects of multi enzyme complex on delayed onset muscle soreness induced by eccentric exercise.

Delayed onset muscle soreness (DOMS) due to eccentric muscle activity is associated with inflammatory responses and production of reactive oxygen species (ROS) that sustain both inflammation and oxidative stress. After eccentric exercise, damage to the contractile element of the muscle leads to the occurrence of DOMS. The results of this study suggest that supplementation with Multi enzyme complex supplementation helps in the recovery of this contractile fraction of the muscles.

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