

Study Coordinator: Ling Xin, MS

Title: The Effects of Two Botanical Supplements on Gene Expression Following Eccentric Exercise

Eccentric (muscle lengthening) actions typically cause transient muscle damage followed by a period of muscle regeneration. Symptoms of exertional muscle damage are muscle soreness, pain, swelling, and stiffness. The common indirect markers of exercise induced muscle damage include delayed onset muscle soreness, the blood level of creatine kinase (CK), and muscle strength loss. The initial insult from the exercise produces mechanical damage, which in turn results in generation of inflammatory cytokines that recruit neutrophils and macrophages into damaged muscle fibers. Neutrophils release reactive oxygen species (oxidative burst) to destroy necrotic tissue. This process also creates secondary damage to cells. Several studies have reported that antioxidant supplements attenuate exercise-induced muscle injury and oxidative stress and can reduce evidence of damage after eccentric exercise.

This study examined the effect of two independent botanical supplements containing mixtures of plant extracts with anti-inflammatory and antioxidant properties on changes in gene expression and muscle function following eccentric exercise.

41 healthy men aged 18-30 yrs were randomly assigned to receive a formula containing the placebo or 1 of 2 botanical supplements for 35 days; of these, 32 completed the study. The study period consisted of three stages: Stage 1 - subjects exercised one leg (knee extensors) and a muscle biopsy of both legs (vastus lateralis muscle) was taken at 3-4 hours post-exercise; Stage 2 - subjects took a dietary supplement or placebo for a 28-day period; Stage 3 - subjects repeated the exercise with the contralateral leg and a muscle biopsy of both legs was taken at 3-4 hours post-exercise. Serum CK activity, soreness and muscle strength were measured pre-exercise and each day for 5 days after exercise. Expression profiling was performed using Agilent Whole Genome Chips (Gene Logic, Gaithersburg, MD). Muscle strength, CK, and soreness were analyzed with a repeated measures analysis of variance (ANOVA). ANCOVA (Partek Genomics Suite; age and BMI covariates) was used to determine differentially expressed ( $p < 0.02$ ) genes. Up- and down-regulated genes for supplement 1 vs. placebo and supplement 2 vs. placebo were imported into Ingenuity Pathway Analysis software (IPA) for function and network analysis.

Preliminary analyses showed that the supplement results in less strength loss after eccentric exercise and IPA results suggest NF- $\kappa$ B as a key signaling pathway in response to the exercise and supplementation.

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