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File: ■ Lemon Verbena (*Aloysia citriodora*)
■ Chronic Exercise
■ Muscular Damage Markers

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RE: Effect of Lemon Verbena Supplementation on Muscular Damage Markers in Chronic Exercise

Funes L, Carrera-Quintanar L, Cerdán-Calero M, et al. Effect of lemon verbena supplementation on muscular damage markers, proinflammatory cytokines release and neutrophils' oxidative stress in chronic exercise. *Eur J Appl Physiol.* April 2011;111(4):695-705.

Moderate exercise has many positive health benefits, but prolonged intense exercise may impair immune function and is associated with acute increases in oxidative stress. Additionally, recent research indicates that antioxidant supplementation in humans blunts the adaptive antioxidant and metabolic (insulin sensitivity) response to exercise. Lemon verbena (*Aloysia citriodora*) extracts contain flavones, iridoids, and phenylpropanoids, including verbascoside. Verbascoside has demonstrated anti-inflammatory and antioxidant effects in pre-clinical studies. In this double-blind, placebo-controlled clinical trial, researchers examined the effect of a lemon verbena extract standardized to 10% (w/w) verbascoside "on neutrophils' antioxidant response, muscular damage markers and cytokines' profile of healthy male volunteers subjected to intense training sessions."

Enrolled were young, healthy, "moderately trained" men (n=15) seeking Sports Sciences degrees at Miguel Hernandez University, Elche, Spain. The subjects' diets and exercise routines were monitored at meetings conducted twice a week. The subjects avoided using dietary supplements or medications during the study and followed a diet designed with Dietsource Novartis to include 60% carbohydrates, 25% lipids, and 15% protein. Subjects were randomized to take 3 capsules/day lemon verbena extract (1,800 mg/day; n=8) or a placebo (n=7) for 21 days following a 3-week wash-out period intended "to homogenize food habits and trained status." Notably, no mention of unblinding was made, or of a lemon scent being added to the placebo, nor if the subjects were able to correctly determine to which group they were assigned (given the distinctive odor of the active material).

The lemon verbena capsules were manufactured by Monteloeder S.L. (Elche, Spain) and standardized to contain 10% (w/w) verbascoside. The subjects performed more

intense exercise than normal during the trial: 3 sessions per week of 90-minute eccentric (presumably downhill) running (which is known to induce intense muscle damage and inflammation). The researchers collected blood samples before and after the training and supplementation period. Measured were creatine phosphokinase (CK), myoglobin (Mgb), aspartate aminotransferase (AST), alanine aminotransferase (ALT), γ -glutamyltransferase (GGT), malondialdehyde (MDA), protein carbonyl derivatives, catalase (CAT), glutathione peroxidase (GPx), glutathione reductase (GRed), superoxide dismutase (SOD), interleukin-1 β (IL-1 β), IL-6, myeloperoxidase (MPO), and tumor necrosis factor- α (TNF- α).

High performance liquid chromatography (HPLC) analysis showed that the lemon verbena extract contained verbascoside (10% w/w), along with isoverbascoside, martynoside, and diglucuronidated flavones. At baseline, there were no significant differences between the groups in age, body characteristics, or performance. After 21 days, levels of the non-specific cell damage markers CK and Mgb did not change significantly. ALT activity did not change significantly compared to pre-treatment levels in the extract group, but increased in the placebo group ($P < 0.05$). Only AST displayed a significant decrease between groups, seen in the extract group after 21 days of supplementation. Activity of GGT decreased significantly compared to baseline in the extract group ($P < 0.05$), but not in the placebo group. After treatment, CAT and GPx activity increased significantly in both groups as compared to baseline levels ($P < 0.05$ for all), but the increases were greater in the placebo group (placebo: 67% and 110%, respectively; extract: 32% and 57%, respectively), but not significantly greater between groups. MPO activity was the only neutrophil marker that showed a significant difference between groups after supplementation, increasing by over twofold in the placebo group compared to baseline values ($P < 0.05$), while decreasing by over a third in the extract group.

The neutrophil oxidative stress marker MDA increased significantly greater in the placebo group at day 21, while neutrophil protein carbonyl derivatives were increased compared to baseline values in the placebo group (carbonyl derivatives: $P = 0.08$), but not significantly greater than observed in the extract group. Cytokine release of IL-6 and IL-1 β in whole blood decreased significantly compared to baseline values in both groups ($P < 0.05$). IL-6 was significantly lower after treatment in the extract group compared to the placebo group ($P < 0.05$ for all). No significant effects were observed for TNF- α release or GRed expression.

The authors conclude, "Moderate antioxidant supplementation with lemon verbena extract protects neutrophils against oxidative damage, decreases the signs of muscular damage and acute inflammation in chronic running exercise and do not block the cellular adaptation to exercise." However, a more thorough examination of the adaptive antioxidant and metabolic responses to exercise as influenced by lemon verbena extract is warranted, especially using untrained subjects (as the current study employed trained subjects).

—*Marissa Opel-Sutter, MS*

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