Soy Isoflavones Modulated Antioxidant Defense Systems and Decreased Lipid Peroxidation in Rats and Humans

By

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ABSTRACT

Isoflavones have antioxidant activities in vivo, however, their antioxidative potential against oxidative stress initiated by exercise was not explored. The first study investigated the effect of high-genistin isoflavone (HGI) supplementation on erythrocyte antioxidant enzymes and tissues' thiobarbituric reactive substances (TBARS) in acutely exercised one-year old rats. All tissue genistein concentrations increased after exercise. Ingestion of HGI seemingly enhanced running time to exhaustion, and maintained glutathione peroxidase (GPx) and catalase (CAT) activities decreased due to exercise. The second study investigated the dose effect of HGI supplementation. Genistein concentrations were significantly higher ($P<0.05$) in tissues of rats fed the 1045 PPM HGI diet than in rats fed 522 or 209 PPM HGI diets and increased the glutathione (GSH)/total glutathione (TGSH) ratio ($P<0.03$). Reductions of the in vivo MDA concentrations ($P<0.05$) were observed only in the plasma of rats fed 522 and 1045 PPM HGI diets compared to those fed 0 PPM (-1.08, -0.82, and 0.03 μM, respectively). Therefore, isoflavones at 522-1045 PPM HGI diet have antioxidative effects in rats.

The last two studies investigated the effect of isoflavone supplementation on the modulation of erythrocyte antioxidant enzyme activities, glutathione homeostasis, and other oxidative biomolecules in healthy young men undergoing 80%VO_2pk exercise. In Study 3 exercise at 80%VO_2pk increased oxidative stress which was best demonstrated by increased

superoxide dismutase (SOD) activity (16.5%), GSH/TGSH ratio, in vivo MDA (12.6%), plasma uric acid (4.9%) and ferric reducing/antioxidant ability (FRAP) (7.8%). Therefore, 30 minutes 80% VO_2pk exercise induced oxidative stress in moderately active college men. In study 4, four-week HGI supplementation produced plasma genistein and daidzein concentrations of 499 and 415 ng/ml, which were significantly increased to 633 and 539 ng/ml by exercise (P=0.04 and P=0.05). Isoflavones significantly decreased in vivo pre-exercise plasma MDA (P<0.05), increased pre-exercise blood TGSH (P=0.01) and pre-exercise erythrocyte SOD activity (P=0.0006), and maintained the decreased activities of GPx due to exercise at pre-exercise levels. Results demonstrated that isoflavones had antioxidant activity in vivo under normal physiological conditions in healthy young men. They also maintaining GPx activity which was decreased due to exercise, however, isoflavones may not overcome all oxidative stress initiated by intense exercise.

DEDICATION

To my parents Ma-Fu Chen and Huey-O Tsao.

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ABBREVIATIONS USED IN THE DISSERTATION

AA, ascorbic acid; AIN, American institute of nutrition; CAT, catalase; DHAA, dehydroascorbic acid; diff, difference as post-ex minus pre-ex; DMSO, dimethylsulfoxide; ELISA, enzyme-linked immunosorbent assay; FRAP, ferric reducing/antioxidant power; GPx, glutathione peroxidase; GR, glutathione reductase; GSH, glutathione; GSSG, oxidized glutathione; HGI, high-genistin isoflavone extract; H_2O_2, hydrogen peroxide; HPLC, high performance liquid chromatography; LDL, low-density lipoprotein; MDA, malondialdehyde; MPO, myeloperoxidase; $O_2^{\cdot -}$, superoxide; post-ex, post-exercise; pre-ex, pre-exercise; RBC, red blood cells; ROS, reactive oxygen species; SE, standard error; SOD, superoxide dismutase; SMC, smooth muscle cell; TAA, total ascorbic acid; TBA, thiobarbituric acid; TBARS, thiobarbituric acid reactive substances; TGSH, total glutathione; UA, uric acid; and VO_2pk, peak oxygen consumption.

PRELUDE

This dissertation is written in manuscript format where chapters 2-6 are complete papers each in its own right. Some redundancies are therefore inevitable, especially so in the introduction sections of closely topic related chapters.