Glyceollin-Elicited Soy Protein Consumption Induces Distinct Transcriptional Effects As Compared to Standard Soy Protein

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ABSTRACT: Glyceollins are stress-induced compounds in soybeans with bioactive properties distinct from parent soy isoflavones. The goals of this study were to evaluate the effects of dietary glyceollin-enriched and standard soy protein isolates and identify candidate target pathways of glyceollins on transcriptional profiles within mammary gland tissue. Thirty female postmenopausal cynomolgus monkeys were randomized to diets containing one of three protein sources for 3 weeks: (1) control casein/lactalbumin (C/L), (2) standard soy protein containing 194 mg/day isoflavones (SOY), and (3) glyceollin-enriched soy protein containing 189 mg/day isoflavones + 134 mg/day glyceollins (GLY). All diets contained a physiologic dose of estradiol (E2) (1 mg/day). All doses are expressed in human equivalents scaled by caloric intake. Relative to the control C/L diet, the GLY diet resulted in greater numbers of differentially regulated genes, which showed minimal overlap with those of SOY. Effects of GLY related primarily to pathways involved in lipid and carbohydrate metabolism, including peroxisome proliferator-activated receptor (PPAR)-γ and AMP-activated protein kinase (AMPK) signaling, adipocytokine expression, triglyceride synthesis, and lipase activity. Notable genes upregulated by the GLY diet included PPAR-γ, adiponectin, leptin, lipin 1, and lipoprotein lipase. The GLY diet also resulted in lower serum total cholesterol, specifically non-high-density lipoprotein cholesterol, and increased serum triglycerides as compared to the C/L diet. No effects of GLY or SOY were seen on serum insulin, adipocytokines, or vascular and bone turnover markers. These preliminary findings suggest that glyceollin-enriched soy protein has divergent effects from standard soy with some specificity for adipocyte activity and nutrient metabolism.

KEYWORDS: glyceollin, soy, isoflavone, estrogen receptor, metabolism

INTRODUCTION

Diet is a key factor in the etiology of many chronic diseases, including cardiovascular disease, osteoporosis, diabetes, and cancer. Much recent interest has focused on the role of specific bioactive components, particularly from dietary plants, in the prevention and management of these conditions. Isoflavonoids are an important class of bioactive phytochemicals widely consumed as part of soy-based foods. Soy protein is rich in the glycosylated forms of the isoflavones genistein and daidzein, which have structural similarities to endogenous estrogens and exhibit a variety of biological functions relevant to human health.

Recent evidence indicates that isoflavone metabolites may also mediate certain health-related effects of soy foods. The best-studied example is equol, which is formed from daidzein by gut bacteria in a subset of human soy consumers and various nonhuman species. Under the influence of stressors such as trauma or infection, daidzein may also act as a precursor in soybeans to a unique class of defensive compounds called glyceollins. Prior studies have shown that glyceollins exhibit distinct properties as compared to genistein and daidzein, including inhibition of estrogen receptor (ER) signaling, which correlated with a comparable suppression of estrogen-induced proliferation of breast cancer cells. Glyceollins have also been characterized for their ability to inhibit fungal growth. More recently, glyceollins have been shown to help normalize glucose homeostasis in vitro by potentiating β-cell function and survival and to improve glucose utilization in 3T3-L1 adipocytes. Glyceollins have also demonstrated anti-inflammatory effects. These results suggest that the glyceollins have unique effects potentially relevant to human health.

Although much research has focused on the anticancer ability of the glyceollins, the effects of glyceollins on other biological pathways and systems are less known. Of particular importance is the in vivo activity of the glyceollins when consumed at dietary levels. In the current study, we evaluated the short-term effects of glyceollin-enriched soy protein on gene expression profiles in mammary gland adipose tissue. Also, serum lipids, vascular and bone markers, and metabolic markers were examined in each dietary group. Our goals were to identify candidate target pathways of glyceollins and to evaluate...