Phytochemical glyceollins, isolated from soy, mediate anti-hormonal effects through estrogen receptor alpha and beta.

Matthew E. Burow [1], Steve Boue [6] , Bridgette M. Collins-Burow [2], Lilia I. Melnik [2], Bich N. Duong [4], Tom Weiss [5], Ed Cleavland [6], John A. McLachlan [1].

[1]Environmental Endocrinology Project at the Tulane-Xavier Center for Bioenvironmental Research, [2]Molecular and Cellular Biology Program, [3]Department of Pharmacology, Tulane University Medical Center; [4]Department of Environmental Health Sciences, Tulane University School of Public Health and Tropical Medicine; [5]School of Pharmacy at Xavier University; [6]the Southern Research Center, United States Department of Agriculture, New Orleans, Louisiana 70112.

The flavonoid family of phytochemicals, which includes chalcones, coumestans, flavones and isoflavones, has received attention regarding their estrogenic activity as well as on human health and disease. The observation that soy phytochemicals can function as ER agonists is consistent with the observed health benefits of soy foods such as decreased incidence of osteoporosis and cardiovascular disease. However the similar decrease in risk of breast cancer would indicate a potential antiestrogenic activity of soy phytochemicals.In addition to these flavonoids other phytochemicals including phytostilbene, enterolactone, and lignans, also possess endocrine activity. The types and amounts of these compounds in soy are controlled by both constitutive expression and stress-induced biosynthesis. The health benefits of soy based food may be dependent upon the amounts of the various hormonally active phytochemicals within these foods. Given the knowledge that a soy diet as well as isolated flavonoids may function in an antiestrogenic manner, we examined the relative levels of phytochemicals derived from soy plants grown under different conditions. The aim was to identify unique soy phytochemicals that had not been previously assessed for estrogenic or antiestrogenic activity. Here we describe an increase biosynthesis of the flavonoid-related phytoallexin compounds, glyceollins, in soy plants grown under stressed conditions. In contrast to the observed estrogenic effects of coumestrol, daidzein and genistein, we observe a marked anti-estrogenic effect of glyceollins on ER signaling in the absence of any agonistic effect in MCF-7 cells. Further evaluation revealed antagonism towards both ER_ and ER_ in transiently transfected HEK 293 cells. Competition binding assays revealed a greater affinity of glyceollins for ER_ versus ER_ which correlated to the greater suppression of ER_ signaling with higher concentrations of glyceollin. In conclusion we describe the phytoallexin compounds known as glyceollins (1-3), that exhibit a unique antagonistic effects on ER in both HEK 293 and MCF-7 cells. The glyceollins as well as other phytoallexin compounds may represent an important component of the health benefits of soy based foods.