DIETARY ESTROGENS INTERACTIONS WITH THE ESTROGEN RECEPTOR AND THEIR EFFECT ON THE ESTROGEN RECEPTOR SIGNALING PATHWAYS

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Plants such as soya and clover produce dietary estrogens which are known to have estrogenic activities in mammals and are suspected to have cancer-protective effects mediated by the estrogen receptor (ER). In this study fluorescence polarization binding assay was developed to compare the relative binding affinities (IC_{50}) of the phytoestrogens genistein, daidzein, and coumestrol; the phytoalexin glyceollin; and the mucoestrogen zearalenone for human ER? ? and ER? . Expressed, purified ER ? and ER? ? (PanVera Inc., Madison, WI) were preincubated with an optimal concentration of fluorescein-labeled 17? ? Estradiol and then concentrations of the test compound were added to the ER-fluorescein labeled 17? ? Estradiol complex. Competitive binding of the phytochemicals was measured as a decrease in polarized fluorescence on Beacon 2000 fluorescence polarization instrument (PanVera Inc., Madison, WI). Similar fluorescence polarization experiments were performed in order to establish the binding affinities of ER? ? and ER? , liganded with the dietary estrogens under study, and an estrogen response element (ERE). Fluorescein-labeled Xenopus vit A2 ERE (Oligos etc., Wilsonville, OR), was incubated with concentrations of ER? ? and ER? in the presence of saturation amounts of the dietary estrogens and the binding affinities were determined using Beacon 2000. Genistein, coumestrol, and zearalenone displaced 17? ? Estradiol from ER in the range of 12-50M while daidzein and glyceollin 17? ? Estradiol from ER in the range of 1-20M. Similar trend was observed in the affinity of ER? ? and ER? to bind the ERE.
The dietary estrogens genistein, coumestrol, and zearalenone show high affinity for both ER? ? and ER? ? ? and can successfully compete with the natural estrogens in physiological conditions.