

## Effects of High-Dose Isoflavones on Rat Uterus

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**Objective:** To evaluate the effect of high concentration of isoflavones in castrated rat uterus.

**Design:** All: ovariectomized virgin rats (n = 40) were treated for 30 consecutive days: vehicle (GCtrl) and different concentrations of genistein 42 (GES42), 125 (GES125) and 250 (GES250) µg/g body weight per day. The soybean extract, and vehicle (propyleneglycol) were administered by gavage for 30 consecutive days. At the end of the experiment, we had regular vaginal smear and measured the animal and uterine weight. Also, we removed the middle third of uterine horns and fixed them in 10% formaldehyde and processed for paraffin inclusion and histological study. Histological sections of 5 µm were stained by HE and analyzed under light microscopy. We assessed the morphology of endometrium, as well as the endometrial area, number and area of glands and, number of eosinophils in propria laminae were calculated through the Axiovison Rel 4.6 (Carl Zeiss) program. The data are evaluated through the ANOVA and Tukey-Kramer test (p <0.05).

**Results:** The uterine weight, endometrial glandular area, number of glands and eosinophils of GES250 and G125 were superior than other groups (GES250 > GES125 > GES42 = GCtrl = p <0.05). The morphological data showed signs of endometrial proliferation with genistein treatment, mainly in animals of GES125 and GES250 that were more developed than other groups (Fig. 1 and 2). In all animals of GES250 we found signs of squamous metaplasia (Fig. 2D).

**Conclusion:** The high-dose isoflavone administrate may promote squamous metaplasia in ovariectomized rat endometrium.

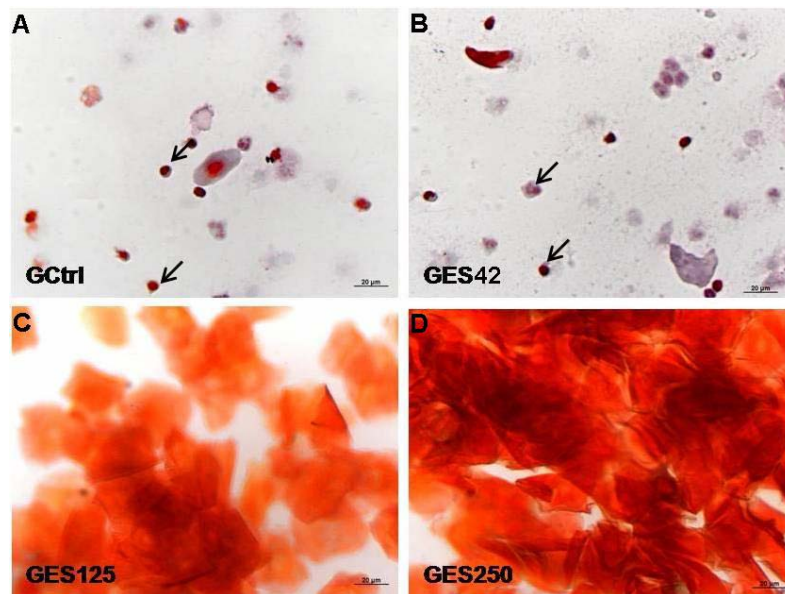


Fig. 1 - Photomicrographs showing female rats colposcytologic treated with different concentrations of isoflavones. A and B note the scarcity of cells from vaginal epithelium and numerous leukocytes (arrows). C and D can be observed epithelial acidophilic cells originated from the superficial layers of vaginal epithelium. Harris-Shorr - 400 X. Scale bar = 20 µm.

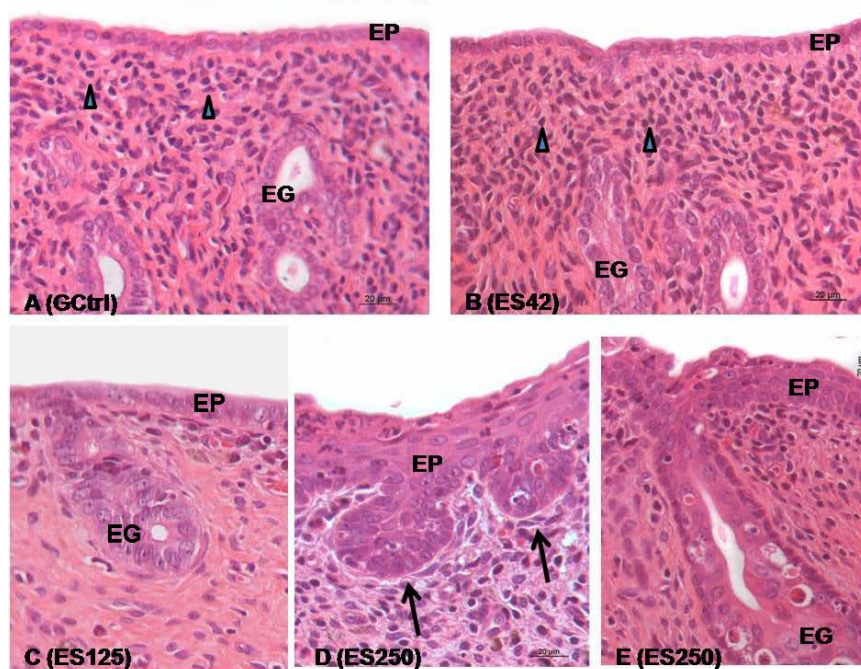


Fig. 2 - Photomicrographs showing the endometrium of rats treated with different concentrations of isoflavones. A and B note the surface of the coated endometrium's cylindrical type epithelium (SE) and glandular (GE) with simple lamina propria, showing a large cell concentration with heterochromatic nuclei (arrowheads). C note in the superficial epithelium (EP) and glandular (EG) and propria laminae cells with large nuclei and euchromatin (arrows). D and E observe the surface epithelium (SE) and glandular (GE) stratified squamous non keratinized (EP). Note D in the superficial epithelium buds into the propria laminae (arrows). H.E - 400 X. Scale bar = 20 µm.