

## **Estrogen receptor modulatory effects of germinated brown rice bioactives in the uterus of rats through the regulation of estrogen-induced genes**

### **ABSTRACT**

**PURPOSE:** The expression of genes regulated by estrogen in the uterus was studied in ovariectomized (OVX) rats treated with germinated brown rice (GBR) bioactives, and compared to Remifemin or estrogen at different doses to identify the regulation of these genes in the uterus and their molecular mechanisms. **METHODS:** Rats were treated orally with GBR bioactives (phenolics), acylated sterol glucosides (ASG),  $\gamma$ -amino butyric acid (GABA), and  $\gamma$ -oryzanol (ORZ) at 100 and 200 mg/kg, Remifemin (REM) at 10 mg/kg and 20 mg/kg, or estrogen (EST) at 0.2 mg/kg. Ribonucleic acid (RNA) was extracted from the uterus, and messenger (m)RNA expression of selected genes encoding estrogen receptor-beta (ER- $\beta$ ), calcium-binding protein (CaBP9k), complement protein (C3), heat shock protein 70 kDa (HSP70), and interleukin (IL)-4 receptor were quantified. Similarly, serum steroid hormone concentration was monitored at 2, 4, and 8 weeks after treatments. ER- $\beta$  antibody binding to the uterus sections was also studied using immunohistochemistry. **RESULTS:** The group treated with EST (0.2 mg/kg) upregulated ER- $\beta$ , C3, and IL-4 receptor genes compared to other groups ( $P < 0.001$ ). GBR phenolics (200 mg/kg) treatment upregulated the ER- $\beta$  gene almost to the level of the sham non-treated group. The CaBP9k gene showed upregulation in groups treated with ASG (200 mg/kg), EST (0.2 mg/kg), and ORZ (200 mg/kg) ( $P < 0.05$ ). Estrogen levels increased in groups treated with EST, ASG, and ORZ (200 mg/kg) compared to the OVX untreated group ( $P < 0.05$ ), and there was a slight non-significant decrease ( $P > 0.05$ ) in the progesterone levels in the OVX untreated group compared to the sham and other treated groups. There was a significant increase at 8 weeks in the level of FSH ( $P < 0.05$ ) in the treated groups compared to the OVX untreated group. There was no significant difference ( $P > 0.05$ ) in serum luteinizing hormone (LH) between the OVX untreated group and other groups. The sham and GBR phenolics treated group showed ER- $\beta$  reactivity at the glandular epithelium, while the group treated with EST showed immunoreactivity at the glandular, luminal, and stromal epithelium. **CONCLUSION:** GBR phenolics moderately regulate the expression of ER- $\beta$ , HSP70, and IL-4 receptor genes, and gave a positive immunoreaction to ER- $\beta$  antigen in the uterus. ASG regulates the expression of CaBP9k and IL-4 receptor genes, and ORZ regulates the expression of the CaBP9k gene, while GABA at 100 mg/kg regulates the expression of the HSP70 gene. GBR and its bioactives might have an effect on estrogen-regulated genes in the uterus of rats.

**Keyword:** Estrogen receptor- $\beta$  gene; GBR-bioactives; Serum hormonal level; Uterine tissue