

Can Soy Change Serum Estradiol Concentration in Neonate Ovariectomized Rat?

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Abstract: Problem statement: Phytoestrogens are plant derived compound found in a wide variety of foods, most notably soy. The purpose of this study was to assess the effect of soy isoflavones on circulating 17- β estradiol in neonate ovariectomized rat. **Approach:** Thirty, one day olds rats were used. Blood sample were collected after two months. 17- β estradiol was assayed by radioimmuno assay method. Data were analyzed by one way ANOVA and Duncan as post-hoc test. The level of significance was considered $p < 0.05$. **Results:** Our data showed that ovariectomy significantly ($p < 0.05$) reduced serum 17- β estradiol. Application of soy in doses 0.75 and 1.5 mL kg⁻¹ day⁻¹ following ovariectomy had not significant effect relative to ovariectomy without application of soy, but application of soy in dose 3 mL kg⁻¹ day⁻¹ significantly ($p < 0.05$) increased 17- β estradiol relative to ovariectomy without application of soy. There was no significant difference between dose 3 mL kg⁻¹ day⁻¹ and control and sham group. **Conclusion/Recommendation:** Our results indicated that soy milk isoflavone can compensate the 17- β estradiol decrease in ovariectomized rat.

Key words: Soy milk, 17- β estradiol, neonate ovariectomized, ovariectomized rat

INTRODUCTION

Soy isoflavones, Known as Phytoestrogens, have estrogenic and anti-estrogenic properties (Cohen *et al.*, 2007), they have structural similarities with mammalian estrogens and may interact with pathways of estrogen activity in the body (Wood *et al.*, 2007). Soy isoflavones have been characterized as natural selective estrogen receptor modulators (Wood *et al.*, 2006). The three soy isoflavones are genistein, daidzein and glycitein.

These isoflavone are diphenolic compounds that bond to both Estrogen Receptors alpha (ER $_{\alpha}$) and beta (ER $_{\beta}$) and for this reason, are commonly referred to as phytoestrogens (Messina and Wood, 2008). Genistein, which is the main circulating and best studied isoflavone transactivates ER $_{\alpha}$ and induces estrogenic effect with $\sim 10^3$ - 10^4 less potency than that 17- β estradiol (Messina and Wood, 2008).

Low estrogen level in menopause often result in vasomotor symptoms, atrophy of the vaginal epithelium and bone loss (Levis and Griebeler, 2010). Isoflavone are currently used extensively as an alternative to traditional hormone replacement therapy (Cohen *et al.*,

2007). Between dietary phytoestrogens, isoflavones of soy seem to have the most beneficial effects (Chiechi *et al.*, 2003). There is some evidence suggesting that soy or its isoflavones, while suppressing the rate of bone resorption, concomitantly enhance the rate of bone formation. Soy or its isoflavones enhance bone formation based on at least two lines of evidence: (1) Soy isoflavone stimulate osteblastic activity through activation of estrogen receptor and (2) Soy isoflavone promote insulin-like growth factor-I Production (Arjmandi and Smith, 2002).

It seems that soy isoflavone can change the serum concentration of 17- β estradiol, so the aim of present investigation was to study of the effect of soy milk on the serum 17- β estradiol in neonate ovariectomized rat.

MATERIALS AND METHODS

Thirty neonate one day olds rats and 6 mothers were obtained from Shiraz University of medical. Animals were maintained on 12h light/dark cycles and standard temperature 20-24°C.

Animals were divided into 6 groups of five rats each. No operation was done on the first group (control), the rats in the group 2 were served as the

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sham group which underwent laparotomy and abdominal manipulation. The rest of the rats were underwent ovariectomy operation. Group 3 received no treatment at all. The rats in group 4, 5 and 6 received soy in doses of 0.75, 1.5 and 3 mL kg⁻¹ day⁻¹ respectively. Blood sample were collected after two months. The soy milk contained 2.5% (2.5 g 100 mL⁻¹) of soy protein.

Ovariectomy was done on 7th day of birth. They were anesthetized by xylazine and ketamine combination. The rats restrained on their back, the abdominal wall was prepared for an aseptic surgery. The linea alba incised and both ovaries were located, excised and removed. The abdominal wall was closed routinely. Application of soy milk was done after ovariectomy for two months.

Data were analyzed by SPSS (version 18). The data was analysis by one way ANOVA and Duncan as post-hoc test and the level of significance was considered p<0.05. The Data were presented in Mean ± SEM.

RESULTS

The data in group 3 (negative ovariectomized rats) show that the serum 17-β estradiol concentration was significantly (p<0.05) lower than control and sham groups and the three positive ovariectomized group (Fig. 1). In positive ovariectomized groups with soy milk doses of 0.75 and 1.5 mL kg⁻¹ day⁻¹ the serum 17-β estradiol was significantly (p<0.05) lower than control and sham groups; but in positive ovariectomized group which received soy milk dose 3 mL kg⁻¹ day⁻¹, 17-β estradiol significantly (p<0.05) increased relative to negative ovariectomized and positive ovariectomized (0.75 and 1.5 mL kg⁻¹ day⁻¹). There was no significant difference between positive ovariectomized group (3 mL kg⁻¹ day⁻¹) compared to control and sham groups (Fig. 1).

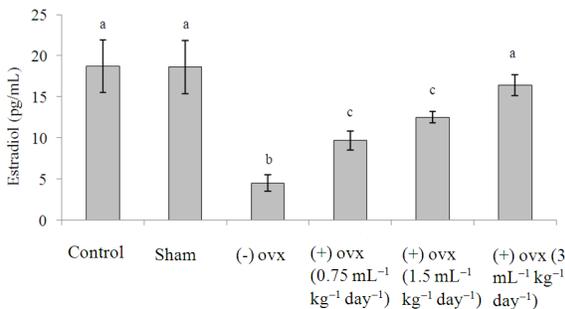


Fig. 1: Effect of soy milk on serum 17-β estradiol in neonate ovariectomized rat. Character represent significance between groups (P<0.05)

DISCUSSION

Phytoestrogens are plant substances that have effects similar to those of estrogens. Since the first discovery of the estrogenic activity of plant compounds, over 300 plants have been found to have phytoestrogenic activity. Preparations vary from enriched foods such as bread or drinks (soy milk) to more concentrated tablets (Panay and Rees, 2005). Soy products have been actively sought by menopausal women because of their isoflavone content (Levis *et al.*, 2010).

In the present investigation soy milk in low doses of 0.75 and 1.5 mL kg⁻¹ day⁻¹ during two months had no effect on ovariectomized reduced of 17-β estradiol rats. Chiechi *et al.* (2002a) reported that soy rich diet, containing high levels of active phytoestrogens, can provide some protection against postmenopausal osteoporosis. They also found that diet is not as effective as hormone replacement therapy (Chiechi *et al.*, 2002a). Imhof *et al.* (2008) findings showed safety improvement of the conventional hormonal replacement therapy by boosting the clinical combination of estrogens and soy isoflavones, especially regarding the risk of breast cancer (Imhof *et al.*, 2008). Wood *et al.* (2007) reported that diet containing isoflavones lead to reduction of catabolism of estradiol by 21-26%, since the estrogens circulate predominately as inactive sulfate which are deconjugated within peripheral tissues, selectively catabolized and excreted. As estrogen-like phytochemicals, soy isoflavonoids are metabolized in similar enzymatic pathways. They suggest that exposure to certain isoflavones may modulate pathway of estrogen catabolism (Wood *et al.*, 2007).

Nahas *et al.* (2007) showed that regular consumption of soy isoflavone extract (100 mg) produces a significantly higher reduction in the number of hot flushes than placebo. Chiechi *et al.* (2003) reported that dietary phytoestrogens may modulate the consequences of the postmenopausal estrogen deficiency state (Chiechi *et al.*, 2002b). Pop *et al.* (2008) suggested that unconjugated soy isoflavones are safe and well tolerated in healthy postmenopausal women at dose of 900 mg day⁻¹. Very few adverse events occurred and the only drug-related adverse events were mild in severity (Pop *et al.*, 2008).

CONCLUSION

Present investigation proved that soy milk in high dose 3 mL kg⁻¹ day⁻¹ can compensated the low estradiol following ovariectomy. It may be due to diminished catabolism of β estradiol (Wood *et al.*, 2007), or by the

increasing the levels of 17- β estradiol production in other sites. Also, in the present study by determining the level of the 17- β estradiol in soy milk samples proved that the 17- β estradiol was $\sim 143.1 \mu\text{g mL}^{-1}$. Therefore, it seems that soy isoflavone are 17- β estradiol agonist (Messina and Wood, 2008) and in high dose can compensate the absence of ovarian hormone.

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Conflict of interest: All the authors can confirm that there is no financial or other relationship that would cause a conflict of interest.

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