Soy isoflavones reduce adiposity via increasing estrogen receptor beta expression in ovariectomized female rats.

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ABSTRACT

Soy phytoestrogens have estrogenic activity and are used as a natural substitute for estrogen as a replacement therapy in case of estrogen deficiency. They have many useful activities in vitro and in vivo. However, Evidence is emerging that dietary phytoestrogens play a beneficial role in obesity and metabolic syndrome. The objectives of this study was to determine the effect of soy phytoestrogens on some metabolic parameters including energetic status (weekly food intake and body weight gain), abdominal and brown fat masses, adipocyte size, estradiol receptor beta (ERβ) expression in adipocytes, liver fatty changes, plasma high density lipoproteins (HDL), low density lipoproteins (LDL), triglycerides (TG), total cholesterol (TC) and oral glucose tolerance test (OGTT), insulin tolerance test (ITT), plasma leptin and adiponectin levels. A total of 30 ovariectomized female Albino rats were divided into two groups (15 females / group). Control group (C) received phytoestrogen-free casein-based diet and high soy phytoestrogens (HF) group received high phytoestrogens diet containing (27% soybeans) for 7 weeks. The results revealed that high phytoestrogens in diet decreased food intake and body weight gain significantly (P<0.05) than control group starting from 4th week and 5th week, respectively. Abdominal fat mass, brown fat masses and adipocytes size were significantly (P<0.05) lower in HF group than control. Adipocytes ERβ expression of in HF group was significantly (P<0.05) higher than control. The histopathological studies showed fatty infiltration in control group. The expression values of ERβ in adipocytes was significantly higher (P<0.05) in HF group than control. Levels of HDL was significantly (P<0.05) increased in HF group while LDL, TC and TG were significantly (P<0.05) decreased than control. Oral glucose tolerance showed non significant change while insulin sensitivity was significantly improved in HF group. Plasma leptin levels were significantly (P<0.05) decreased, while adiponectin levels were increase in HF group than control group. These findings show the high dietary phytoestrogens interfere with adiposity and metabolic syndrome via increasing adipose ERβ expression with consequent reduction in leptin production and increase in adiponectin level that improves insulin sensitivity in ovariectomized female rats.

Keywords: Phytoestrogens , lipid profile, ERβ, leptin, adiponectin, overiectomized rats.

INTRODUCTION

Recently, adipose tissue was shown to be a major endocrine system that produce soluble mediators (adipokines) that play a role in energy homeostasis, lipid metabolism, immune response, and reproduction (Badman & Flier 2005 and Kershaw & Flier 2004 and Tolba, 2013). From these adipokines, leptin which plays a key role in regulating energy intake and expenditure, including appetite and hunger,
metabolism, and behavior. It is one of the most important adipose-derived hormones (Brennan and Mantzoros 2006) it acts on the brain and peripheral organs to regulate energy homeostasis and the neuroendocrine axis (Ahima and Osei, 2008). Adiponectin, Another adipokine, which has been postulated to be an important mediator of the interaction between adiposity and insulin sensitivity (Cnop et al., 2003) through regulation of glucose and lipid metabolism by targeting the liver and skeletal muscle. (Ahima and Osei, 2008). This hormone plays a role in the suppression of the metabolic derangements that may result in type 2 diabetes (Ukkola and Santaniemi 2002), obesity and atherosclerosis, (Díez and Iglesias 2003), non-alcoholic fatty liver disease (NAFLD) and an independent risk factor for metabolic syndrome (Renaldi et al., 2009).

Estrogens promote, maintain, and control the typical distribution of body fat and adipose tissue metabolism, through a still unknown mechanism. These steroids are known to regulate fat mass by increasing lipolysis through the modulation of the expression of genes that regulate adipose deposition (lipogenesis) and differentiation and adipocyte metabolism (Cooke et al., 2001; Cooke & Naaz, 2004). This regulatory mechanism occurs mainly through estrogen receptors (ERα and ERβ), which also mediate the action of several nutritional compounds such as phytoestrogens.

Phytoestrogens are bioactive molecules present as nutritional constituents of commonly consumed vegetables. Their name derives from the fact that they can bind to estrogen receptors and induce an estrogenic/antiestrogenic response in target tissues (Kuiper et al., 1998). The isoflavones genistein and daidzein are among the most abundant phytoestrogens in human and animal diets and are found predominantly in legumes like soy. Goodman-Gruen and Kritz-Silverstein (2001) revealed that the consumption of isoflavones – genistein and daidzein were known by their ability to reduce body mass indexes, fasting insulin concentration, increased HDL cholesterol (Nogowski, et al., 1998; Potter et al., 1998 and Sanders et al., 2002) lower total cholesterol, LDL cholesterol (Potter et al., 1998; Merz-Demlow et al., 2000; Teede et al., 2001; Wangen et al., 2001; Jayagopal et al., 2002; Lemay et al., 2002).

The estrogenic activity of phytoestrogens was depending on its concentration (Wilson et al., 2004), endogenous estrogen levels (Ratna 2002), and gender (Faughnan et al., 2004). In vitro studies showed that, at low doses, genistein efficiently binds both estrogen receptors, with high affinity to ERβ (Kuiper et al., 1998). However, high doses genistein was reported to act as a tyrosine kinase inhibitor (Huang et al., 1992 ; Hong et al., 2005), an antioxidant (Hwang et al., 2003), and a steroid-metabolizing enzyme modulator (Atkinson et al., 2003). In addition, it may inhibit the action of estrogen receptors by acting through nuclear receptors such as the peroxisome proliferator-activated receptors (PPARs) (Dang and Lowik 2004). Furthermore, recent studies on adipose tissue in women (Goodman-Gruen, 2003; Kritz-Silverstein 2003) and female mice (Naaz et al., 2003) indicate that genistein inhibits adipose deposition and decreases adipose mass, through regulation of the expression of specific genes (Penza et al, 2006). Genistein and daidzein were also found to inhibit lipogenesis and stimulate lipolysis in rat adipocytes. The previous studies on the influence of genistein and daidzein on metabolism of fat cells suggests the possibility of its effect on leptin and adiponectin secretion (Yanagisawa et al., 2012). Accordingly the aim of this study was to put an insight view on the effect of dietary phytoestrogens in estrogen deprived status on energy balance through determination of food intake, weight gain, lipid profile, abdominal fat mass %, brown fat mass% and adipocytes size. In addition to their relation to expression of ERβ in adipocytes, oral glucose tolerance test (OGTT),
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insulin levels and insulin tolerance test (ITT) and plasma leptin and adiponectin hormone levels as factor regulating the energy status at high doses.

**MATERIALS AND METHODS**

**Animal care:**
Thirty female Albino rats aged 13 weeks old and mean weight 130.9±10.8 g were used in this study and housed in cages (4 females in each) under standard laboratory conditions. They were kept at room temperature (28±2°C) under natural day light rhythm two weeks prior surgical interference to ovariectomy. The animals were accessed to casein based diet and tap water freely. They received humane care and experiments were carried out according to the criteria outlined by Faculty of Veterinary Medicine, Suez Canal University.

**Ovariectomy**
Thirty female Albino rats (5 month) weighing approximately 180.9±11.4 g were anaesthesiaed by an intraperitoneal injection of thiopental sodium 50 mg/kg. Ovariectomy was preceded by a midline dorsal skin incision, 3 cm long, approximately half way between the middle of the back and the base of the tail after placing the animal on its ventral surface. Incision of the muscles was made at linea Alba. The ovary was found, surrounded by a variable amount of fat after accessing to peritoneal cavity. The blood vessels were ligated at the connection between the Fallopian tube and the uterine horn was cut and the ovary moved out. Suturing to muscle layer then to skin was performed by simple continuous suture using vicryl 4/0 (Lasota and Danowska-Klonowska 2004). Animals were given broad spectrum antibiotic (amoxicillin, 10 mg/kg) for 3 successive days after ovariectomy and continued on casein based diet.

**Experimental groups**
After 3 weeks from ovariectomy, the ovariectomized female rats were divided randomly into two groups: Control group (C), n= 15, they were fed on casein based diet and high phytoestrogens group (HF), received high phytoestrogens diet. All diets were formulated to fulfill all the nutritional requirements of adult rat (Table 1) according to NRC (1995) and were offered for 49 days. Weekly food intake and weekly body weight gain were recorded.

Table 1: Diet composition

<table>
<thead>
<tr>
<th>INGREDIENTS</th>
<th>CONTROL %</th>
<th>HIGH PYTOESTROGEN %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yellow corn</td>
<td>40.59</td>
<td>35.04</td>
</tr>
<tr>
<td>Corn gluten</td>
<td>15.00</td>
<td>-</td>
</tr>
<tr>
<td>Soybean*</td>
<td>-</td>
<td>26.41</td>
</tr>
<tr>
<td>Casein</td>
<td>5.00</td>
<td>5.00</td>
</tr>
<tr>
<td>Sucrose</td>
<td>22.43</td>
<td>22.32</td>
</tr>
<tr>
<td>Starch</td>
<td>7.63</td>
<td>4.16</td>
</tr>
<tr>
<td>Cellulose</td>
<td>1.30</td>
<td>0.17</td>
</tr>
<tr>
<td>Corn oil</td>
<td>5.00</td>
<td>-</td>
</tr>
<tr>
<td>Soybean oil</td>
<td>-</td>
<td>5.00</td>
</tr>
<tr>
<td>Ground limestone</td>
<td>1.02</td>
<td>1.04</td>
</tr>
<tr>
<td>Dicalcium phosphate</td>
<td>0.34</td>
<td>-</td>
</tr>
<tr>
<td>Common salt</td>
<td>0.13</td>
<td>0.13</td>
</tr>
<tr>
<td>Premix</td>
<td>0.30</td>
<td>0.30</td>
</tr>
<tr>
<td>Methionine</td>
<td>0.30</td>
<td>0.43</td>
</tr>
<tr>
<td>Lysine</td>
<td>0.26</td>
<td>-</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>0.70</td>
<td>-</td>
</tr>
</tbody>
</table>

Total 100.00 100.00

*Soybean was autoclaved at 110°C for 30 minutes according to (Westfall and Hauge, 1948) to inactivate trypsin inhibitor, tannins, saponins, phytate, protease inhibitors, lectins and goitrogens.
**Blood and tissue sampling**

At the end of experiment, the rats were fasted overnight and weighed then sacrificed under effect of light anaesthesia for obtaining blood. Whole blood was collected on EDTA tubes then centrifuged at 3000 g for 20 min for obtaining plasma then stored at -20°C for determination of lipid profile, leptin and adiponectin levels. Visceral fat was collected from the superficial area covering the alimentary tract and the uterus, was removed and weighed, immediately after blood sample collection. Brown fat also was dissected and weighed. Samples from liver and abdominal fat will kept in 10% formalin saline for histopathology and immunohistochemistry.

**Lipid profile**

Plasma levels of high-density lipoprotein cholesterol (HDL), total cholesterol (TC) and triglycerides (TG) were measured using enzymatic calorimetric kits (Cat. No. 0599, Stanbio Laboratory, USA, Cat. No. 304710050, ELITech Diagnostic, France and (Cat. No. 303113050, ELITech Diagnostic, France), respectively according to (Treitz, 1990). Plasma low density lipoprotein cholesterol LDL-C was calculated by Friedwald formula described by Davidson et al., 2009.

\[
LDL-C = Total\; Cholesterol - (Triglycerides/5 + HDL-Cholesterol).
\]

**Immunohistochemistry**

The paraffin embedded livers and adipose tissues, fixed in formalin saline 10%, were cut into 5 µm sections and mounted on positively charged slides for ERβ immunohistochemistry. Sections were dewaxed, rehydrated and autoclaved at 120°C for 10 minutes in 10 Mm citrate buffer (PH 6). After washing with PBS endogenous peroxidase was blocked using 0.3% H2O2 in methanol (15 minutes). Slides were washed in PBS again and blocking was performed by adding blocking buffer and incubated for 30 minutes at room temperature. Primary antibody for ERβ (Cat. No. RB- 10658-R7, Thermo Scientific Co., UK) was added after dilution by PBS in a rate 1:10 and incubated for 30 minutes. Biotinylated polyvalent secondary antibody (Cat. No. 32230, Thermo Scientific Co., UK) was applied to tissue sections and co-incubated for 30 minutes after washing. The reaction was visualized by adding Metal Enhanced DAB Substrate according to (Bancroft and Cook, 1994).

**Histopathology**

Sections of 5μ thickness of livers that were fixed in 10% neutral buffered formalin were stained with haematoxylin and eosin and examined under light microscope according to (Bancroft and Gamble, 2007).

**Quantification of IHC and adipocyte size**

For quantitative analysis, the intensity of immunoreactive parts was used as a criterion of cellular activity after subtracting background noise. Measurement was done using an image analyzer (Image J program). From each slide of both experimental groups, 9 fields were randomly selected. The total field and immunohistochemical (IHC) stained areas were calculated then the %IHC stained area calculated as follow:

\[
%\; IHC\; stained\; area = (IHC\; stained\; area)/(Total\; area) \times 100%.
\]

Adipocyte size in each experimental group was determined by the same program from 9 fields were randomly selected from each animal.

**Oral glucose tolerance test**

After overnight fasting, blood glucose levels of ovariectomized female rats were determined via glucometer (Accu-Chek Active, Germany). Then they were administered oral glucose solution (40%) 1g/ kg using gavage tube (Pederson et al., 1998), then glucose levels were estimated by glucometer at 0 , 30 , 60 , 90, 120, 150 and 180 minutes.
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**Insulin tolerance test**

Insulin tolerance test was performed 4 days after OGTT, using 0.75 U/kg human insulin (humulin) in 0.9% saline injected i.p after 30 min from oral glucose administration by same dose of OGTT. Blood glucose levels were estimated by glucometer at 0, 30, 60, 90 and 120 minutes.

**Determination of plasma leptin and adiponectin levels**

Plasma leptin and adiponectin concentrations were determined using commercial enzyme linked immunoassay rat assay kit (Code No. 27295, IBL, Japan and Cat. No. 22-ADPRT-E01, ALPCO diagnostics, USA), respectively according to manufacturer instruction.

**Statistical analysis**

All values were expressed as the mean ± SE. Differences among groups were determined by T test using SPSS program version 16.0. A value of $P < 0.05$ was considered to be statistically significant (Field, 2000).

**RESULTS**

The performed experiment demonstrated that dietary phytoestrogens significantly ($P<0.05$) lower the food intake in high dose group starting from 4th week of treatment 112.17±3.57 g/ week versus 126.33±3.8 g/ week in control group and till the end of experiment (Fig.1). Body weight gain was significantly ($P<0.05$) lower in high phytoestrogens-fed group starting from 5th week 0.87±0.38 g/week than control one 5.28±1.26 g/ week till the end of experiment.

![Food intake](image)

**Fig. 1:** Effect of dietary phytoestrogens on food intake g/ week of ovariectomized female rats

The abdominal, brown fat masses % and adipocytes diameter showed a significant ($p<0.05$) reduction in HF group than control group with values (Table 2). The values of lipid profile shown in Table (2) revealed that HDL was significantly ($P<0.05$) higher in treated group than control. While TG, TC and LDL showed significant decrease in its value in HF group than control. Adipocytes diameters showed the same trend while the expression of ERβ in adipocytes were significantly higher ($P<0.05$) in HF group than those of control one (Fig. 2 and Plate 1). Liver histopathological sections showed fatty infiltrations and steatosis in control group with sinusoidal dilatation while high phytoestrogens fed rats livers showed normal architecture without fat infiltration (Plate 2).
Table 2: Effect of dietary phytoestrogens on lipid profile mg/ dl, abdominal fat mass%, brown fat mass% adipocytes diameter (µm), plasma leptin levels and plasma adiponectin levels.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control group</th>
<th>Phytoestrogen-treated group</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDL mg/dl</td>
<td>10.42 ± 0.42</td>
<td>12.12 ± 0.48 *</td>
</tr>
<tr>
<td>TG mg/dl</td>
<td>115.21 ± 6.82</td>
<td>83.65 ± 8.49 *</td>
</tr>
<tr>
<td>TC mg/dl</td>
<td>66.74 ± 2.09</td>
<td>60.29 ± 1.88 *</td>
</tr>
<tr>
<td>LDL mg/dl</td>
<td>33.27 ± 2.88</td>
<td>31.36 ± 2.25 *</td>
</tr>
<tr>
<td>Abdominal fat masses %</td>
<td>6.12 ± 0.45</td>
<td>4.29 ± 0.28 *</td>
</tr>
<tr>
<td>Brown fat masses %</td>
<td>0.80 ± 0.15</td>
<td>0.36 ± 0.04 *</td>
</tr>
<tr>
<td>Adipocytes diameter/ µm</td>
<td>74.16 ± 15.94</td>
<td>32.45 ± 3.452</td>
</tr>
<tr>
<td>Leptin levels ng/ml</td>
<td>200.6 ± 3.06</td>
<td>162.72 ± 3.015 *</td>
</tr>
<tr>
<td>Adiponectin levels ng/ml</td>
<td>4.005 ± 0.05</td>
<td>6.24 ± 0.17 *</td>
</tr>
</tbody>
</table>

(*) represents a significant difference between the control and treated groups, using Student Unpaired t-test (p< 0.05).

Fig. 2: Effect of dietary phytoestrogens on body weight gain g/ week of ovariectomized female rats

Plate 1: Immunostaining of abdominal fat masses A: Control, B: phytoestrogen-treated group. The plate showed that ERβ were localized predominantly within the cytoplasm. Phytoestrogen treatments produced a significant up regulation of ERβ expression and decrease in size in abdominal adipocytes relative to control.

Fig. 3: Effects of phytoestrogens on ERβ expression in adipose tissue Change in adipocytes size compared with normal control group (p< 0.05).

Concerning blood glucose levels in oral glucose tolerance test (OGTT) no significant difference was observed between two tested groups However, it was
noticed from the curve it was noticed that phytoestrogens fed rats showed return to basal fasting glucose level after oral glucose tolerance while control group showed elevated glucose level than fasting one (Fig. 4). Insulin tolerance test (ITT) showed significant decrease in glucose level in phytoestrogens fed rats than control (Fig. 4).

Plasma leptin levels showed a significant (P<0.05) decrease in HF group than control while plasma adiponectin levels showed significant increase in HF group than control as shown in (Table 2).

Fig. 4: Effect of phytoestrogens on OGTT (A) and ITT (B) of ovariectomized female rats.

Plate 2: Representative photomicrographs showing liver histopathology of control group (A) and phytoesrogen-treated group (B) rats. Steatosis and dilatation of sinusoids were noted in control group [hematoxylin and eosin (H&E) stain; original magnification: ×20]

DISCUSSION

The metabolic syndrome is characterized by obesity, insulin resistance, and a predisposition to hypertension, dyslipidemia, and type 2 diabetes. A common feature linking these metabolic abnormalities is the dysregulation of ERs expression in estrogen deprived condition and its consequent changes in energetic status, some adipokines (leptin and adiponectin), lipid profile, OGTT and ITT. The present study demonstrated the protective effects of soy phytoestrogens against the risks of obesity and metabolic syndrome in ovariectomized female rats under estrogen-deprivation conditions. Dietary soy phytoestrogens administered to ovariectomized female albino
rats affect food intake and substantially diminished the body weight gain in high phytoestrogens fed rats than control. These results are consistent with previous records (Kim et al., 2005 and Tolba 2013). Phytoestrogens are structurally similar to endogenous estrogens, they can act as a weak estrogen and bind to the ERs in various tissues (Naaz et al. 2003), thus reduction in feed intake may be due to the appetite repressing action of estrogen (Roy and Wade, 1975) as dietary phytoestrogens decreased food intake and hence decreased body weight. The decrease implies that the estrogenic action of phytoestrogens is beneficial to body fat regulation due to the decreased level of leptin as observed in the current study that is produced from adipose tissue and influences hypothalamic neuropeptide Y (NPY) levels which regulates feeding behaviour and energy loss (Szkudelska et al., 2000 and Naaz et al., 2003). In the current study, the effect of soy phytoestrogens was manifested as decrease in abdominal, brown fat masses % and adipocytes diameter that could be attributed to apoptotic effect of phytoestrogens on adipocytes, suggesting that at least part of the weight loss is due to ablation of fat cells, which could result in better maintenance of weight loss (Kim et al., 2005). These results, are coincide with those recorded by Cederroth et al., (2007) and Cederroth et al., (2008) who found that mice fed dietary phytoestrogens were leaner due to increase their locomotor activity as observed in this study which may be due to preferential use of lipids as fuel source. These in vivo data are further supported by in vitro studies showing that genistein induced lipolysis and inhibited de novo lipid synthesis in 3T3-L1 adipocytes (Harmon & Harp 2001 and Harmon et al., 2002) and in rat adipocytes (Szkudelska et al., 2000). Phytoestrogens also affect fat growth and development, which is the main source of leptin, through peroxisome proliferator-activated receptors (PPARs) (Anderson et al., 2004) which is a major factor involved in de novo fatty acid synthesis, adipocyte differentiation, lipid accumulation, and adipocyte survival/maintenance (Jump et al., 2005).

Dietary phytoestrogens was also shown to have direct effects on lipid metabolism as it decreased TC, TG & LDL and increased HDL significantly (P<0.05) which are consistent with previous record of Kirk et al., 1998; Nogowski et al., 1998; Wangen et al., 2001, Uesugi et al., 2002 and Tolba, 2013. Because they affect lipid metabolism in liver and adipose tissue, decreasing triglycerides (Nogowski et al., 1998) that reflected by decrease in adipocytes diameter and decrease in liver fatty changes in treated group. These results suggests the hypolipidemic effect of phytoestrogens that are ascribed to their structural similarities to estradiol (E2) which acts predominantly via two distinct nuclear ERs, ERα and ERβ, defined as ligand-inducible transcription factors (Rosen et al., 2000). Dietary phytoestrogens increased adipocytes expression of ERβ that inhibits lipogenesis is primarily through decreasing expression levels and activity of lipoprotein lipase (LPL), an enzyme that regulates lipid uptake and filling of adipocytes (Misso et al., 2003, Naaz et al., 2003 and Heim et al., 2004). Phytoestrogens might lower cholesterol levels by increasing LDL receptor activity, and the reduction in cholesterol may offer some protection against atherosclerosis (Kirk et al., 1998). Another explanation is that soy phytoestrogens decrease intestinal cholesterol absorption increase in bile acid excretion that mediate the lipid-lowering effect of soy protein (Greaves et al., 2000).

The observation that dietary phytoestrogens depressed significantly (p<0.05) plasma leptin levels, which is a mediator of long-term regulation of energy balance (Klok et al., 2007) than control group in combination with the depression in abdominal fat mass, brown fat mass% and adipocytes diameter allowed us to believe that this effect of phytoestrogens was due to its direct influence on adipocytes which
are the main source of leptin (Szkudelski et al., 2005). The effect of phytoestrogens especially genistein inhibit some enzymes in adipocytes substantially abates leptin secretion (Bradley and Cheatham 1999) in spite of unchanged expression of its gene (Szkudelski et al., 2005).

- In the present study dietary phytoestrogens doesn’t affect OGTT significantly but it was noticed that glucose levels returned to its fasting level at the end of OGTT while in control the glucose levels were elevated above the fasting level at the end of OGTT. The significant improvement of ITT in treated group could be attributed to the elevated levels of plasma adiponectin that have receptors in liver and skeletal muscle, and the signaling through these receptors increases insulin sensitivity (Karastergiou and Mohamed- Ali 2010) and improves glucose tolerance (Wasim et al, 2006) by decreasing triglyceride content in muscle and liver (Yamauchi et al., 2001). Since genistein and daidzein have both been shown to bind to and activate PPARγ (Dang et al. 2003, Mezei et al, 2003 and Dang et al., 2004), it is likely that changes in insulin sensitivity could then be modified by adiponectin, which is increased in response to PPARγ agonists (Lihn et al., 2005 and Kadowaki et al., 2005). Moreover, adiponectin stimulates decreased gluconeogenesis, increased glucose uptake (Diez and Iglesias 2003 and Nedvidková et al., 2005), lipid catabolism (Vasseur et al., 2003), β-oxidation of fatty acids and triglyceride clearance (Nedvidková et al., 2005). The reduction of adiposity accompanied by decreased leptin and increased adipocytes expression of ERβ and ectopic fat deposition in liver with absence of steatosis in HF group that occurs with the elevated levels of adiponectin are in coincidence with the concept of Kadowaki et al., 2005 that exist the relationship between dietary phytoestrogens and ERs especially ERβ expression due to the preferential affinity of these compounds to ERβ (Kuiper et al., 1998) in regulation of body fat mass and glucose metabolism.

CONCLUSION

This study brought a new knowledge in understanding of the role of soy and its component phytoestrogens in the regulation of energy balance and obesity, it was appeared that these compounds may have more potent effects in prevention of some metabolic abnormalities that are part of the metabolic syndrome in estrogen depriving condition. The results of the current study showed that high dietary phytoestrogens interfere with adiposity by decreasing energy intake, increasing energy expenditure, reduction of lipid parameters (abdominal, brown fat mass, adipocytes diameter and lipid profile) with consequent reduction in plasma leptin levels while plasma adiponectin levels increased with improvement in insulin sensitivity and all this seem to follow the upregulation of ERβ expression in ovariectomized female rats.

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