Mediterranean Journal of Nutrition and Metabolism 10 (2017) 251–258
DOI:10.3233/MNM-17164
IOS Press

Effects of the date palm fruit (Phoenix dactylifera L.) on prolactin, IGF-1, and stress factors in lactating female rats and its impact on their litters' development

Saeed Ebrahimi F.[a], Mina Hemmati[b,*] and Mohammad Malekaneh[c]

[a]*Student Research Committee, Faculty of Medicine, Birjand University of Medical Sciences, Birjand, Iran*
[b]*Birjand Cardiovascular Disease Research Center, Birjand University of Medical Sciences, Birjand, Iran*
[c]*Department of Biochemistry, Faculty of Medicine, Birjand University of Medical Sciences, Birjand, Iran*

Received 16 June 2017
Accepted 20 August 2017

Abstract.
BACKGROUND: In the Middle East and North Africa, traditional medicine has labelled date palm fruit (Phoenix dactylifera L.) as milk-increasing fruit. The aim of this study was to evaluate the effects of dates on the amount of prolactin, insulin-like growth factor (IGF-1), Malondialdehyde (MDA) and glutathione (GSH) in mothers and their litters of Sprague Dawley rats.
METHODS: Fifteen lactating female rats were considered in this study. Each group consisted of five female rats and their litters. Suspension of palm fruit (Bam date) at doses of 1 g/kg and 2 g/kg was used for treatment. Bloodletting was conducted on the mothers on day 10 and day 22 of breastfeeding and on the litters from day 22. After measuring the analytes, the data were analysed using the SPSS software.
RESULTS: The serum prolactin in the palm-receiving mothers increased significantly compared to the control group. Date consumption dose-dependently increased the IGF-1 in the mothers and their litters. MDA, as a marker of lipid peroxidation, decreased and GSH increased due to date palm intake.
CONCLUSIONS: According to the results, Phoenix dactylifera L can be introduced as a diet supplement in breastfeeding females for improved the health and breastfeeding of mothers as well as for improved health, development, and the reduced stress conditions in litters.

Keywords: Phoenix dactilifera L, prolactin, IGF-1, stress factor

1. Background

The use of medicinal plants, especially in Asian countries, is increasingly growing [1]. The date palm fruit (with the scientific name Phoenix dactylifera L) is one of the most important medicinal plants in Southwest Asia and North Africa [2]. This plant had many medicinal uses in the past. In Morocco, this plant was used for the

*Corresponding author: Mina Hemmati, Ph.D., Associate Professor in Clinical Biochemistry, Birjand Cardiovascular Disease Research Center, Birjand University of Medical Sciences, Birjand, Iran. Tel.: +985632395418; Fax: +985632393004; E-mails: minahemmati@bums.ac.ir; mina1hemmati@yahoo.com.

ISSN 1973-798X/17/$35.00

treatment of diabetes and blood pressure [3]. The consumption of the pollen of palm trees to enhance the libido and fertility in men has been commonly observed [4]. In India, dates have been used alongside several other herbs as potions for pregnant and breastfeeding women [5, 6].

The most important chemical compounds in dates are phenols, steroids, carotenoids, anthocyanins, and flavonoids and procyanidins. The amount and concentration of these compounds depend on the date type, the stage of ripeness, the environment, and the soil conditions [4]. Several studies addressed the anti-inflammatory, immunity-stimulant, anti-fungal, anti-viral, liver-protective, anti-cancer, and renal-protective nature of the date palm fruits [4]. Another property of dates is their anti-diabetic activity; research has shown that the fruits of a palm tree and its leaves can reduce blood sugar, control fat, and increase insulin secretion [7, 8]. An aqueous extract of palm fruits can reduce the oxidant damage of atrazine on testicles with their antioxidant properties [9]. According to prior research, the use of pollen extract of date palm increases the hormonal secretion of oestrogen and progesterone in female rats [10], and the aqueous extract of Phoenix dactylifera L and its pollen increases the sperm count and enhances fertility in adult male rats [1, 9].

Breastfeeding is the best way to feed the litters, and it invigorates the health and the development of mothers and their new-borns [11, 12]. At least four factors are required for milk production; these include the prolactin, parathyroid, insulin, and glucocorticoid hormones, among which prolactin plays a major role in the production of milk [13, 14]. According to these studies, the date palm contains steroid alcohol or sterol compounds such as cholesterol, campesterol, stigmasterol, beta-Sitosterol, and isofucosterol [15]. Steroid alcohols, which are headed by cholesterol, are the production precursors of steroid glucocorticoids and oestrogen. Progesterone and oestrogen play a role in breastfeeding, evolution, and the proliferation of breast ducts and alveoli, and low doses stimulate prolactin secretion [14]. Based on previous studies, it is known that prolactin levels are directly related to IGF-1 [13].

IGF-1 is the most important growth factor that is responsible for the control and adjustment of growth in the postnatal and the embryonic period [16].

2. Objectives

According to the aim, this study was conducted to evaluate the suspension regime of palm fruits on the power of breastfeeding and litter growth by measuring factors such as prolactin, IGF-1 in mother's and litter serum. To evaluate the antioxidant power of the palm suspension and its relationship with the creation of better conditions for mothers and litters, two factors, GSH and MDA [17, 18], were measured, and the mothers and litters were weighed throughout the duration of this study.

3. Methods

3.1. Materials (reagents)

The rat MDA ELISA kit and the rat GSH ELISA kit were manufactured by Co. Zellbio, Germany; the kit for measuring IGF-1 (Rat IGF-1 ELISA) was manufactured by Co. Ray Biotech, USA; and the prolactin ELISA Kit was provided by Roche, Germany.

3.2. Provisions for and the preparation of Phoenix dactylifera L.

Fresh Mazafati or the Bam date was prepared in the city of Bam in the Kerman province of Iran. The peel and the core of the Phoenix dactylifera L were separated and they were completely homogenized by using a homogenizer, and then, they were mixed with normal saline and in a dilution of 1 g/kg and 2 g/kg; it was administered daily.

3.3. Animals

In this project, 15 adult female Sprague Dawley rats aged 8 weeks, which had an average weight of 195 ± 10 g, were considered; they were maintained under a condition of light (12 hours of light, 12 hours of darkness), temperature (22–25° C), and were given free access to food (commercial standard rat chow) and water at the Research Center of Experimental Medicine, Birjand University of Medical Sciences.

Each of the three female rats was mated with a male rat; then, after the pregnancy, each female rat was kept in a separate cage. After giving birth, four litters were randomly selected from each mother. The mother and her four litters were divided into three groups of rats, including a control group and two treatment groups. In each group, there were a total of 5 mothers and 20 litters. The phoenix dactylifera L suspension regime with two dilutions of 1 and 2 grams to a kilogram of body weight per day was set aside for the oral treatment of the groups. The control group only received normal saline.

The mother rats' blood was taken on day 10 and day 22 of lactation, and the litters' blood were taken on day 22, which was the last day of breastfeeding under full anaesthesia with ketamine and directly from the heart. Their serums were then isolated and kept aside at –20° C for the relevant tests. In all procedures laboratory animals were conducted in accordance to the institutes of ethics committee for care and use of laboratory animals and approved by the Ethics Committee of the Birjand University of Medical Sciences using the ir.bums.REC.1395.60 Code.

3.4. Statistical analysis

The data was analysed using One-Way ANOVA (Tukey's test). The significance of the differences between the control and the treated groups were evaluated using the student's *t*-test. *P*-values of 0.05 or lesser were considered significant. The SPSS version 22 software (SPSS Inc., Chicago, IL, USA) and Microsoft Excel were employed for performing statistical tests and drawing graphs, respectively.

4. Results

4.1. The effect of Phoenix dactylifera L on the prolactin levels

The reception of Phoenix dactylifera L showed a significant dose-dependent increase in the serum prolactin levels at day 10 and day 22 compared to the control group (Fig. 1).

4.2. The effect of Phoenix dactylifera L on the insulin-like growth hormone levels

The reception of Phoenix dactylifera L showed a significant dose-dependent increase in the serum insulin-like growth hormone levels compared to the control group (Fig. 2).

Figure 3 shows the effect of date palm consumption on the insulin-like growth hormone levels in mothers. According to the results presented in this graph, the use of Phoenix dactylifera L. dose-dependently increases the insulin-like growth hormone levels in mothers. These changes showed a significant difference in comparison with the control group ($P \leq 0.001$).

4.3. The effect of dates on the markers of oxidative stress

GSH and MDA, as markers of the oxidative stress status in the treated group, showed significant changes (Table 1). According to the results presented in Table 1, the dose-dependent palm fruit consumption for mothers and litters caused a significant decrease in MDA and an increase in glutathione. The MDA levels in the litters in which mothers received the date suspension did not show any difference in comparison to the control group.

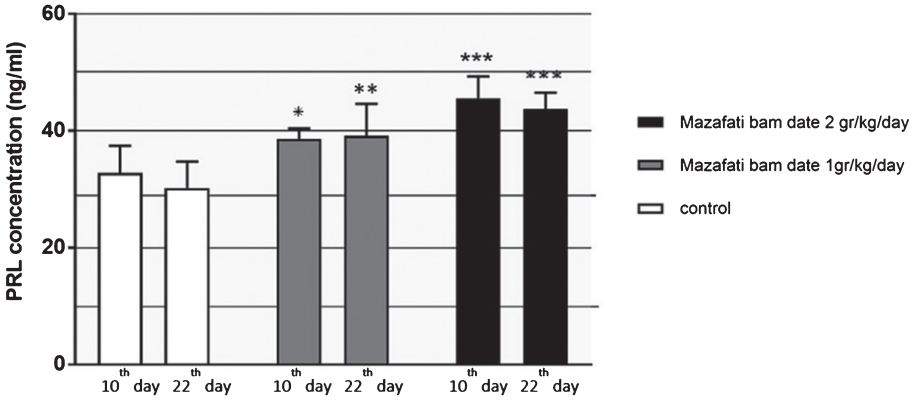

Fig. 1. Comparing the mean ± SD of the effect of date palm on the mother's prolactin between the control group and the treatment group with doses of 1 and 2 grams per kilogram of body weight on day 10 and day 22 of lactation (*: $P < 0.05$, **: $P < 0.01$ and ***: $P < 0.001$).

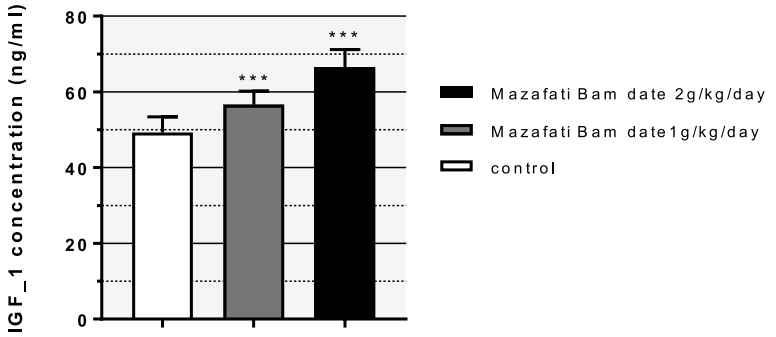

Fig. 2. The comparison of Mean ± SD of the effect of date palm on the IGF-1 of the litters between the control group and the treatment group with doses of 1 and 2 grams per kilogram of body weight on day 22 of lactation (***: $P \leq 0.001$).

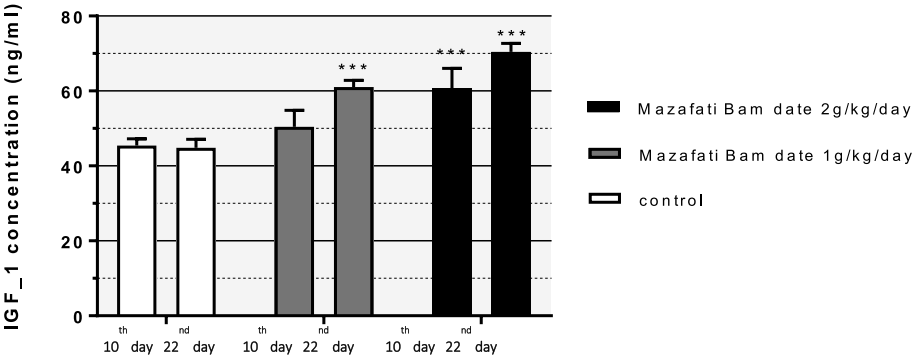

Fig. 3. Comparison of Mean ± SD of the effect of date palm on IGF-1 of the mothers between the control group and the treatment groups with doses of 1 and 2 grams per kilogram of body weight on day 10 and day 22 of lactation (***: $P \leq 0.001$).

Table 1
The comparison of changes in GSH and MDA in the groups in comparison to the control group (**: $P<0.01$ and ***: $P<0.001$)

Groups	GSH (mmol/g)	MDA (mmol/L)
Day 22 of Breastfeeding		
Mother (control)	48.0 ± 2.5	7.3 ± 0.4
Mother (case 1 g/kg/day)	$57.6 \pm 1.8^{**}$	$4.5 \pm 0.5^{***}$
Mother (case 2 g/Kg/day)	$64.4 \pm 5.3^{***}$	$4.0 \pm 0.9^{***}$
Litter (control)	48.2 ± 3.0	5.5 ± 0.4
Litter (case 1 g/kg/day)	$58.2 \pm 4.7^{***}$	5.5 ± 0.3
Litter (case 2 g/Kg/day)	$60.4 \pm 5.4^{***}$	5.1 ± 0.5

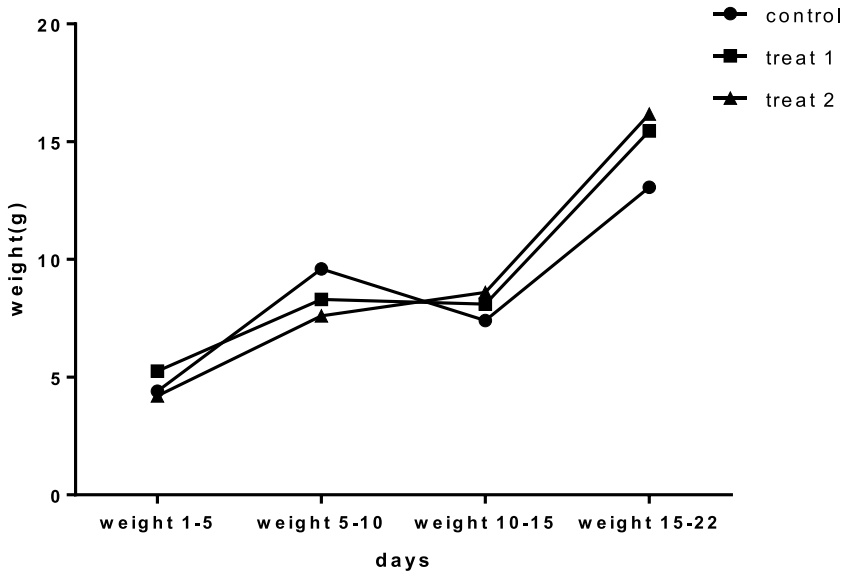

Fig. 4. Comparison of the average weight gain in the three groups during the breastfeeding period.

4.4. The effect of date palm consumption on the weight changes

The mothers' weight during the 22-day period of breastfeeding showed no significant change. Figure 4 shows the changes in birth weight in the different groups. Based on the results presented in Fig. 4, during the first 15 days, the litters in the different groups showed no significant weight changes; in the last week, however, the treatment Group 2 showed significant increase in comparison to the control group.

5. Discussions

The aim of this study was to evaluate the effects of the dietary supplement regime of Mazafati palm fruits in Sprague Dawley female rats; it was being designed to study the beneficial effects of the date fruit on the health and the breastfeeding of mothers, and the growth and the evolution of the litters.

The suspension of palm fruits in this study did increase prolactin in a dose-dependent manner during the breastfeeding period of the mothers. The hormone prolactin is released from the hypothalamus and imported into the anterior pituitary gland. Prolactin plays a role in lactation and pregnancy as well as steroid synthesis in the ovarian, testicular, and immune functions. Dopamine can be noted as one of its inhibitors, and suckling, oestrogen, and TRH are the stimulators [14, 19].

A study conducted by Amnouri et al. in 1970 showed that the changes in the levels of the hormone prolactin in the first days after birth in rats is about 65 ng/ml; this concentration stays constant for up to 8 days until the litters begin to get regularly breastfed, and on day 15 and day 23 after delivery, the concentration falls to half on the first day of the prolactin (25.7 ng/ml) [20], which is consistent with the control group of this study. In addition, dates have steroidal alcohols such as campesterol, stigmasterol, beta-Sitosterol, isofucosterol, and on top of these steroidal alcohols, cholesterol [15]; these alcohols are the production precursors of oestrogen [19]. Hiba et al. in 2014 showed that palm fruit increases the oestrogen hormone in the serum of rats [21]. Oestrogen (E2) itself plays a role in the preparation of the breast tissue for lactation during pregnancy in mammals [14]. As mentioned previously, in the traditional medicine of some countries, Phoenix dactylifera L. has been mentioned as a milk-increasing compound [5, 6], which can be approved by other studies.

The suspension of Phoenix dactylifera L. Increases the hormone IGF-1 in a dose-dependent manner in mothers and litters. IGF-1 in the liver is produced by the growth hormone (GH). IGF-1 is the most important growth factor in postnatal litters and also has a controlling and regulating role in embryonic growth [22]. There are many stimulators of growth hormones in the body; these include testosterone, oestrogen, thyroxin, exercise, stress, etc. [19]. On the other hand, prolactin could also induce the production of IGF-1 in the liver [13]. According to other studies and the results obtained in our experiments, it seems that PRL and IGF-1 increase the effect of dates in mothers and litters due to the increase of oestrogen.

The two-factor of GSH and MDA were measured to evaluate the conditions of oxidative stress in mothers and litters. The GSH significantly increased in mothers and litters through the consumption of dates with both doses. The MDA in mothers decreased in the treatment group, but there was no significant change in the litters being fed by the mothers' milk (Table 1).

The study conducted by Omana et al. in 2011 confirms the results of our studies on the use of palm and oxidative stress: the consumption of palm aqueous extract reduced the MDA induced by dimethoate [23]. Garcia et al. have demonstrated that IGF-1 decreased the MDA and oxidative damage [24], which can indirectly confirm our results.

There are many studies on the relationship between GSH and oestrogen metabolism [25, 26]. According to Baeza et al. in 2010, in a study conducted on Wistar rats that were ovariectomized, there was lower oestrogen and this reduction was also reduced to GSH. This study showed that the treatment of rats with soy phytoestrogens such as Ginestein have a similar therapeutic effect with oestrogen on increasing GSH [27]. According to the previous explanations about the effects of date palm on oestrogen and increased oestrogen, it can be said that they were indirectly consistent with our results.

Date consumption causes positive changes in the weight of litters receiving date palm in the last week, which showed the positive effects on weight gain. According to these results, it was likely for this gain to show an increasing trend if the study was elongated.

6. Conclusion

Based on the results of this study and the other studies cited, Phoenix dactylifera L. can be introduced as a food supplement regimen in the breastfeeding female, for the health and improvement of breastfeeding in mothers, and the health and the development of their litters. The results of this research show the beneficial effects of dates on prolactin, IGF-1, and the weight gain of that litters that has been performed for the first time. Considering the limitations of the related study, further studies are required to search for effective substances of this fruit.

Acknowledgment

This investigation was supported by Grant No. 455104 from the office of Vice Chancellor research, Birjand University of Medical Sciences.

Conflict of interest

None to report.

References

[1] Bahmanpour S, Talaei T, Vojdani Z, Panjehshahin M, Poostpasand A, Zareei S, et al. Effect of Phoenix dactylifera pollen on sperm parameters and reproductive system of adult male rats. Iranian Journal of Medical Sciences. 2015;31(4):208-212.

[2] Al-Farsi MA, Lee CY. Nutritional and functional properties of dates: A review. Critical Reviews in Food Science and Nutrition. 2008;48(10):877-87.

[3] Tahraoui A, El-Hilaly J, Israili ZH, Lyoussi B. Ethnopharmacological survey of plants used in the traditional treatment of hypertension and diabetes in south-eastern Morocco (Errachidia province). J Ethnopharmacol. 2007;110(1):105-17.

[4] Baliga MS, Baliga BRV, Kandathil SM, Bhat HP, Vayalil PK. A review of the chemistry and pharmacology of the date fruits (Phoenix dactylifera L.). Food Research International. 2011;44(7):1812-22.

[5] Chandra A, Chandra A, Gupta I. Datepalm research in Thar Desert: Scientific Publishers; 1992.

[6] Puri A, Sahai R, Singh KL, Saxena RP, Tandon JS, Saxena KC. Immunostimulant activity of dry fruits and plant materials used in Indian traditional medical system for mothers after child birth and invalids. Journal of Ethnopharmacology. 2000;71(1–2):89-92.

[7] Mard SA, Jalalvand K, Jafarinejad M, Balochi H, Naseri MK. Evaluation of the antidiabetic and antilipaemic activities of the hydroalcoholic extract of phoenix dactylifera palm leaves and its fractions in alloxan-induced diabetic rats. The Malaysian Journal of Medical Sciences: MJMS. 2010;17(4):4-13.

[8] Miller CJ, Dunn EV, Hashim IB. The glycaemic index of dates and date/yoghurt mixed meals. Are dates 'the candy that grows on trees'? European Journal of Clinical Nutrition. 2003;57(3):427-30.

[9] Akunna GG, Saalu CL, Ogunmodede OS, Ogunlade B, Bello AJ. Aqueous extract of date fruit (phoenix dactylifera) protects testis against atrazine-induced toxicity in rat. World Journal of Life Sciences and Medical Research. 2012;2(2):100.

[10] Moshtaghi A, Johari H, Shariati M, Amiri J. Effects of phoenix dactylifera on serum concentration of estrogen, progesterone and gonadotropins in adult female rats. Journal of Rafsanjan University of Medical Sciences. 2010;9(2):117-24.

[11] Jones G, Steketee RW, Black RE, Bhutta ZA, Morris SS. How many child deaths can we prevent this year? Lancet (London, England). 2003;362(9377):65-71.

[12] Organization WH. WHO traditional medicine strategy 2002-2005. 2002.

[13] Bole-Feysot C, Goffin V, Edery M, Binart N, Kelly PA. Prolactin (PRL) and its receptor: Actions, signal transduction pathways and phenotypes observed in PRL receptor knockout mice. Endocrine Reviews. 1998;19(3):225-68.

[14] Freeman ME, Kanyicska B, Lerant A, Nagy G. Prolactin: Structure, function, and regulation of secretion. Physiological Reviews. 2000;80(4):1523-631.

[15] Kikuchi N, Miki T. The separation of date (Phoenix dactylifera) sterols by liquid chromatography. Microchimica Acta. 1978;69(1-2):89-96.

[16] Baker J, Liu JP, Robertson EJ, Efstratiadis A. Role of insulin-like growth factors in embryonic and postnatal growth. Cell. 1993;75(1):73-82.

[17] Del Rio D, Stewart AJ, Pellegrini N. A review of recent studies on malondialdehyde as toxic molecule and biological marker of oxidative stress. Nutrition, Metabolism and Cardiovascular Diseases. 2005;15(4):316-28.

[18] Hayes JD, McLELLAN LI. Glutathione and GSH-dependent enzymes represent a co-ordinately regulated defence against oxidative stress. Free Radical Research. 1999;31(4):273-300.

[19] Burtis CA, Bruns DE. Tietz Fundamentals of Clinical Chemistry and Molecular Diagnostics. 7 ed. St. Louis, Missouri 63043: Elsevier Health Sciences; 2014. 1104 p.

[20] Amenomori Y, Chen CL, Meites J. Serum prolactin levels in rats during different reproductive states. Endocrinology. 1970;86(3):506-10.

[21] Al-Sayyed HF, Takruri HR, Shomaf MS, Al-Saleh A. The effect of date palm fruit (Phoenix dactylifera L.) on the hormone 17-β-estradiol in 7, 12-dimethylbenz (α) anthracene-induced mammary cancer in rats. Mediterranean Journal of Nutrition and Metabolism. 2014;7(1):5-10.

[22] Lupu F, Terwilliger JD, Lee K, Segre GV, Efstratiadis A. Roles of growth hormone and insulin-like growth factor 1 in mouse postnatal growth. Developmental Biology. 2001;229(1):141-62.

[23] Saafi-Ben Salah EB, El Arem A, Louedi M, Saoudi M, Elfeki A, Zakhama A, et al. Antioxidant-rich date palm fruit extract inhibits oxidative stress and nephrotoxicity induced by dimethoate in rat. Journal of Physiology and Biochemistry. 2012;68(1):47-58.

[24] Puche JE, Garcia-Fernandez M, Muntane J, Rioja J, Gonzalez-Baron S, Castilla Cortazar I. Low doses of insulin-like growth factor-I induce mitochondrial protection in aging rats. Endocrinology. 2008;149(5):2620-7.

[25] Lushchak VI. glutathione Homeostasis and functions: Potential targets for medical interventions. Journal of Amino Acids. 2012;2012.

[26] Urata Y, Ihara Y, Murata H, Goto S, Koji T, Yodoi J, et al. 17Beta-estradiol protects against oxidative stress-induced cell death through the glutathione/glutaredoxin-dependent redox regulation of Akt in myocardiac H9c2 cells. The Journal of Biological Chemistry. 2006;281(19):13092-102.

[27] Baeza I, Fdez-Tresguerres J, Ariznavarreta C, De la Fuente M. Effects of growth hormone, melatonin, oestrogens and phytoestrogens on the oxidized glutathione (GSSG)/reduced glutathione (GSH) ratio and lipid peroxidation in aged ovariectomized rats. Biogerontology. 2010;11(6):687-701.