The Egyptian Journal of Hospital Medicine (April 2019) Vol. 75 (4), Page 2550-2555

Comparison between Sesame Oil and Glycyrrhizaglabra Effect as Phytoestrogen on Male Albino Rats

Eman G.E. Helal[1], Mohamed A. El-Aleem[2], Shaimaa S. Ahmed[1]
Zoology Department, Faculty of Science, Al-Azhar University (Girls), Cairo, Egypt.[1]
Physiology Department, Faculty of Medicine, Al-Azhar University, Cairo, Egypt[2]
*Corresponding Author: Eman G.E. Helal, E-mail: emanhelal@hotmail.com, Mobile: 00201001025364,
Orchid.org/0000-0003-0527-7028

ABSTRACT

Background: Phytoestrogen is a plant-derived compound, which has estrogenic effect and it is found in liquorice root extract and sesame oil. **Aim of the work:** To investigate some biochemical effects of liquorice root extract and sesame oil on male albino rats.

Materials and methods: 18 animals were divided randomly into three groups. **Group A:** Control group, **group B:** rats treated with oral dose ofliquorice1 ml/kg body weight/day for one month, and **group C:** rats treated with oral dose of sesame oil 1 ml/kg body weight/day. At the end of the experiment, blood samples were collected for biochemical analysis.

Results: Liquorice and sesame oil induced highly significant decrease in TC, TG, LDL, VLDL, LDL/HDL($p<0.01$)and significant increase in HDL($p<0.05$). They also showed highly significantly decrease in FSH, testosterone and sperm count compared to control group ($p<0.02$).

Conclusion: The study supports that the high level intake of liquorice root extract or sesame oil caused hormonal disturbance and decreases sperm count.

Keywords: Liquorice root, Sesame oil, Lipid profile, Albino rats, Physiological parameters.

INTRODUCTION

Glycyrrhizaglabra, a family of Leguminosae, is a plant that grows in Egypt and other countries of the world. Its roots possess some nutritional value and medicinal properties. It is widely used as a cold drink and in the preparation of some pharmaceuticals such as hematinic pills [(1)].

Phytochemical analysis of *Glycyrrhizaglabra* (liquorice) root extract showedthat it contains saponintriterpenes (glycyrrhizin, glycyrrhetinic acid andliquirtic acid), flavonoids (liquiritin, isoflavonoids and formononetin) andother constituents such as coumarins, sugars, amino acids, tannins,starch, choline, phytosterols and bitter principles,which are most likely responsible for its therapeutic properties[(2)].

There are many phenols present in liquorice extracts such as liquiritigenin, liquiritin, isoliquiritigenin, isoliquiritin, glabridin and formononetin, which are responsible for the plant estrogen activity of this plant, extracts [(3)].

Medicinally its root is used widely either as tincture or fluid extract or ingredient in over the counter pharmaceutical products for cough, expectorant, asthma, peptic ulcers and hepatic-protective products. This is because of its anti-inflammatory, anti-ulcerative demulcent, antimicrobial and hepatic-protective activities[(4)].In Japan, intravenously, liquorice components are used for treating hepatitis B and C (National Center for Complementary and Integrative Health, 2016). Other indications still under research like different cancer conditions (Colon, Breast, Hepatic and Prostate), anti-diabetic, antiangiogenic, neuro-protective, rheumatoid arthritis and cardio-protective [(4)].

Sesame oil

Sesame belongs to the family Pedaliaceae. It is one of the richest food source oflignans, amajor type of phytoestrogens known to man since the dawn of civilization [(5)]and is increasingly incorporated into human diets because ofits health benefits[(6)]. Sesame lignans such as sesamin, episesamin, sesamolin, and sesamol isolated from *Sesamumindicum*seeds are implicated as having certain properties such as anti-tumorigenic[(7)]and antioxidant[(8)]. The proximate analysis of sesame seed indicates that it contains about 50-60 % oil, 8 % protein, 5.8 % water,3.2 % crude fiber, 18 % carbohydrate and 5.7 % ash. It is very rich in minerals such as calcium, phosphorus and vitamin E[(9)].The seed oil combats some health conditions like cold and chronic cough and in turn prevents bronchial lung disease. In addition, it helps in improving the blood glucose, glycosylated hemoglobin and lipid-peroxidation[(10)].Besides to its broad use in cooking, the oil is also used in the manufacture of margarine and some pharmaceuticals[(11)]. Sesamin, the most abundant lignan in sesame oil[(12)]is known to contain unique amounts of phytoestrogen, and has some effects on sex physiology[(12)].

MATERIALS AND METHODS

Roots of liquorice plant were purchased from market of Agricultural Seeds and Medicinal Plants, Cairo, Egypt. Clean roots (10gm) were soaked in cup

Received:30/1/2019
Accepted:2/3/2019

of water over night and then filtered. This extract was freshly prepared every day.

Sesame oil extracts were purchased from Cap Pharm for Extracting Natural Oils and Herbs, Cairo, Egypt.

Experimental animal

The experiment was carried out on 18 male albino rats ***Rattusrattus*** strain weighing (130-140gm) obtained from animal farm of El-Nile Company for Pharmaceutical Products, Cairo, Egypt. Animals were housed in metallic cages and maintained under standard condition of temperature, humidity and natural. light/dark cycle along the experimental period. Food and water were available throughout the experiment *ad libitum.* Rats were left to acclimatize for one week before starting the experiment.

Experimental design

Rats were divided into three equal groups (6 rats in each group) as the following:

Group I (control group): maintained on standard pellet diet and tap water *ad libitum* for 30 days.

Group 2: rats received orally sesame oil (1 ml/kg body weight/day) for 30 days.

Group 3: rats received orally liquorice (*Glycyrrhizaglabra)*root extract(1 ml/kg body weight/day) for 30 days.

Body weight measurement

Body weight was recorded onzero time and at the end of the experiment.

Blood sample collection

At the end of the experimental period, the blood samples were collected from the retro-orbital sinus after overnight fasting and the rats were anesthetized by ether. Serum was separatedby centrifugation at 2500 g for 15 minutes at room temperature to estimate biochemical parameters.

Biochemical analysis

Assessment of biochemical parameters:

In the present study, total protein (TP) and albumin concentration were estimated, then serum globulin concentrations were calculated according to the formula: Globulin (g/dl) = total protein (g/dl) – albumin (g/dl). Aspartate aminotransferase (AST), alanineaminotransferase (ALT), creatinine, BUN and blood glucose concentrations as well as lipid profile including total cholesterol, triglycerides and high-density lipoprotein cholesterol (HDL-C) were also determined. All parameters were estimated using BioMerieux SA kits, France.

Albumin/globulin ratio was determined. In addition, ratios of TC/HDL (risk factor1) and LDL/HDL (risk factor 2) were also calculated after calculation of serum LDL-C (low-density lipoprotein cholesterol) and VLDL (very low density lipoprotein cholesterol) using the Friedwald's[13] and Norbert [14]formulas, respectively as following:

Friedewald's equation:

LDL (mg/dl) = TC- {HDL +[TG/5]}.

Norbert equation: VLDL = TG/5.

TC/HDL (risk factor1)

LDL/HDL (risk factor 2)

Hormonal assay

Estimation of serum luteinizing hormone (LH), follicles-stimulating hormone (FSH) and testosterone (T) levels by following manufacture instructions of kit. All kits used for hormone assay were Monobind Inc.,lake forest CA 92630, USA).

Sperm collection and evaluation

The left caudal epididymis was separated and the total recovered sperm during 4 h of incubation in normal saline (volume=1 ml, 35∼37ºC) was calculated. The sperm concentration was determined by the conventional method using a hemocytometer chamber for the red blood cell count. The right epididymis was finely minced by anatomical scissors in 1 ml of warmed isotonic saline in a Petri dish. The sperm progressive motility (SPM) was estimated by evaluating 4 fields of asperm droplet under a cover-slip on a warm glass slide (35∼37ºC) under light microscopy (×40). The sperm vitality was assayed using a conventional procedure of eosin B-nigrosin stain (1.67% eosin, 10% nigrosin, and 0.1 M sodium citrate) under ×100 magnification and 100 sperm were counted. All of the sperm evaluation procedures were carried out based on the World Health Organization manual for human sperm analysis with some modifications [15].

Ethical approved

The study was approved by the Ethics Board of Al-Azhar University.

Statistical analysis

The results were expressed as mean ± SEM (stander error of the mean). Data were analyzed by T-test and were performed using the Statistical Package (SPSS) program, version 19. The Bonferroni test was used as a method to compare significance between groups.

RESULTS

Body weight and glucose level

Results of the present study showed a significant increase ($p<0.05$) in body weight in the treated groups and non-significant change in glucose level in the treated groups when compared to control rats (Table 1).

Table(1): Percentage changes in body weight and glucose level in control, sesame oil and liquorice groups.

Group / Parameters	Control	Liquorice	Sesame oil
Body weight	**137.6 ± 0.4**	**190.6±0.5* 38.5%**	**195.1±0.4* 41.8%**
FBS (mg/dl)	**94.0±2.8**	**88.3±2.0 -6.6%**	**90±1.9 -4.2%**

Values represent mean ±SEM. (p*<0.05, as compared to control group).

Kidney functions

The data in table (2) showed non-significant change in urea and serum creatinine in liquorice and sesame groups as compared to control (Table 2).

Table(2): Changes in the BUN and creatinine levels in the control, liquorice and sesame groups.

Groups / Parameters	Control	Liquorice extract	Sesame oil
BUN (mg/dl)	**20.3±0.2**	**16.6±0.4 -18.2%**	**20.1±0.2 -0.9%**
Creatinine (mg/dl)	**0.7±0.2**	**0.6±0.01 -28.5%**	**0.6±0.001 14.3%**

Values represent mean ±SEM.

Liver functions

Results of the present study showed non-significant change in ALAT and ASAT in the liquorice and sesame groups when compared to control rats (Table 3).

Table (3): Changes in ALAT and ASAT in the control, liquorice and sesame groups.

Groups / Parameters	Control	Liquorice extract	Sesame oil
ALAT(U/L)	**22.5±0.6**	**20.0±0.4 -11.1%**	**18.9±0.3 16%**
ASAT(U/L)	**33.5±0.5**	**29.1±0.3 -13.1%**	**32.1±0.2 4.2%**

Values represent mean ±SE (stander error).

Lipid profile

Results of the present study showed that liquoricea nd sesame produced highly significant decrease (p<0.01) in TC,TG, LDL, VLDL and LDL/HDL when compared to control group. While, there was highly significant increase (p<0.05) in HDL, as compared to control animals (Table 4).

Table (4): Changes in the lipid profile in the control, liquorice and sesame groups.

Groups / Parameters	Control	Liquorice extract	Sesame oil
T C(mg/dl)	**141.3±0.42**	**86.3±1.5** -38.9%**	**85±0.01** -39.8%**
T G(mg/dl)	**71.5±1.56**	**56.8±4.4* -20.5%**	**43.5±2.1** -39.1%**
HDL(mg/dl)	**50.3±0.33**	**61.3±0.33* 21.8%**	**60±0.01* 19.3%**
LDL(mg/dl)	**71.2±1.27**	**14.1±1.1** -80.1%**	**16.3±.58** -77.1%**
VLDL(mg/dl)	**14.3±0.31**	**11.0±0.9* -23.0%**	**8.7±0.58** -39.1%**
LDL/HDL(mg/dl)	**1.22±0.007**	**0.22±.01** -81.9%**	**0.27±0.01** -77.8%**
TC/HDL(mg/dl)	**2.4±0.008**	**1.4±.22** -41.6%**	**1.4±0.01** 41.6%**

Values represent mean ±SEM. (p*<0.05, p**<0.001as compared to control group).

Protein profile

In the present study, administration of liquorice and sesame to normal rats showed non-significant change in total protein, albumin, globulin and albumin/globulin ratio in the treated groups when compared to control rats (Table 5).

Table (5): Changes in the total protein, albumin, globulin and albumin/globulin levels in control and treated groups.

roups / Parameters	Control	Liquorice extract	Sesame oil
Total protein (g/dl) % of change	6.4±0.12	5.5±0.20 -14.0%	6.0±0.1 -6.25%
Albumin (g/dl) % of change	3.7±0.11	4.0±.15 8.1%	3.5±0.19 -5.4%
Globulin (g/dl) % of change	2.7±0.10	2.3±0.22 -14.8%	2.5±0.3 -7.4%
Albumin/Globulin(g/dl) % of change	1.3±0.1	1.7±0.06 30.7%	1.4±0.06 7.6%

Values represent mean ±SEM.

Hormones

The present study showed that administration of liquorice extract to normal rats showed a highly significant decreased FSH and testosterone($p<0.01$), while in sesame group there were a significantly decreased FSH and testosterone ($p<0.05$) when compared to control rats (Table 6).

Table(6): Changes in FSH, LH and Testosterone levels in control, sesame and liquorice groups.

Groups / Parameters	Control	Liquorice extract	Sesame oil
FSH(ng/ml) % of change	2.9±0.1	1.9±0.1** -34.4%	2.0±0.1* -31.0%
LH(ng/ml) % of change	1.9±0.1	1.7±0.1 -10.5%	1.8±0.1 -5.2%
Testosterone(µu /dl) % of change	3.9±0.2	2.8±0.2** -39.3%	2.9±0.2* -25.06%

Values represent mean ±SE (stander error). (p*<0.05, p**<0.001as compared to control group)

Sperm count

The data in table (7) showed decrease in sperm count in liquorice and sesame groups when compared to control rats.

Table (7): Sperm count in the control, sesame and liquorice group.

Groups / Parameters	Control	Liquorice extract	Sesame oil
Sperm count*10^6/ml % of change	100	38±0.01 -62%	63±0.01 -37%

DISCUSSION

Body weight

The findings in this study showed an increase in body weight in both experimental groups treated with *Glycyrrhizaglabra* (liquorice)and sesame oil. In *Glycyrrhizaglabra* the increase in body weight by *Glycyrrhizaglabra*root extract is in accordance with that reported by **Miller** [(16)]who demonstrated that *Glycyrrhizaglabra* inhibits 11 β-hydroxysteroid dehydrogenase and induces excess release of mineralocorticoids, which causes retention of sodium and water that leads to edema and increase in body weight. However, the increased body weight is explained by the improvement in feeding efficiency[(17)].

While in Sesame oil group the increase in body weight was due to unsaturated fatty acids such as oleic acid and linoleic acid, which increase the effectiveness of non-steroidal hormones such as thyroid and growth hormones which are important factors in increasing body weight by stimulating the basal metabolic rate[(18)].

Lipid profile

The decrease in serum total cholesterol and triglycerides reported in this study following oral administration of *Glycyrrhizaglabra (*(liquorice) root for 4 weeks is similar to that reported by **Khushbaktova *et al.*** [19] and **Fuhrman *et al*.**[20]**.** The studies of previously mentioned authors attributed the hypocholesterolemic effect of liquorice to the presence of certain isoflavones, which act as antioxidants via inhibition of LDL coxidation which inhibits the local mechanism of atherogenesis. Moreover, **Nikitina *et al.***[21] reported that the glycosides of *Glycyrrhizaglabra*prevent accumulation of cholesterol in cells as well as human blood serum. A significant decline in plasma LDL-cholesterol in treated groups could be correlated with saponin content of liquorice root, where saponin enhances the hepatic LDL-receptor levels, increase hepatic uptake of LDL-cholesterol and aids its catabolism to bile acid [22]. Saponinis known to lower triglyceride by inhibiting pancreatic lipase activity. While, the decline in VLDL cholesterol levels in the treated groups could be directly correlated to decline in triglyceride levels of these groups, as it is well established that VLDL particles are the main transporters of triglyceride in plasma[23]. Phytosterolsare reported to displace intestinal cholesterol and reduce cholesterol absorption from intestine [24]. Saponins are capable of precipitating cholesterol from micelles and interfere with enterohepatic circulation of bile acids, making it unavailable for intestinal absorption [25].

Insesame oil group, there was a significant decrease in lipid profile. Sesame lignans (sesamin and/or episesamin) reduced serum and liver cholesterol concentrations by inhibiting absorption and synthesis of cholesterol. **Ogawa *et al.*** [26] reported that daily oral intake of sesamin in hypercholesterolemic patients for 4 weeks significantly decreased total cholesterol and LDL-C concentrations. In rat, the mechanism for the hypocholesterolemic effect of sesaminis believed to be related to inhibition of intestinal absorption of cholesterol, increased excretion of cholesterol into bile and decreased activity of 3-hydroxy-3-methylglutaryl coenzyme A reductase.

Hormones

Change in hormonal levels in this study showed a significant reduction in follicle stimulating hormone and testosterone. Testosterone is a steroid hormone from androgen group, and is one of the major sex hormones produced by the body in both men and women. It plays key roles in health and well-being. FSH and testosterone are involved as synergistic in the process of spermatogenesis[27]. **Armanini *et al.*** [28] found that liquorice reduces serum testosterone in healthy men. Also liquorice inhibits 6 β-hydroxy steroid dehydrogenase and stimulating aromatase, resulting in reduced serum testosterone. Liquorice reduced the serum testosterone level and affected androgen metabolism by inhibiting the enzyme β-6 HSD and 17-βHSD hydroxysteroid dehydrogenase or by stimulating aromatase. Therefore, it was proposed that liquorice causes the deficiency in serum testosterone[29], glabridin, the major isoflavone in liquorice and many other phenols such as liquiritigenin, liquiritin, isoliquiritigenin, isoliquiritin, glabridin and formononetin that are responsible for phytoestrogen activity and estrogenic properties[30]**,** which cause hormonal disturbance and decrease the level of FSH and Testosterone, which lead to decrease in sperm count.

While in sesame oil group, the decrease in serum FSH and testosterone was approved by the study of **Brown and Chakraborty**[31] who showed that estrogen agonist like clomiphene has been found to decrease the synthesis and/or release of gonadotrophins with the implication of both low serum LH and testosterone concentration found in male rats. FSH concentration decreased in a high dose of sesame group compared to control group. **Shittu *et al.*** [32] found that sesame phytoestrogen lignanscan stimulate testosterone aromatization to estradiol, or convert it to Dihydrotestosterone.

CONCLUSION

Therefore, it can be concluded that the decrease in the concentrations of testosterone was due to its convers ionintoestradiol which is done by aromatase and reductase enzymes and sesame lignans. This study suppose that the decrease in FSH and testosterone level leads to decreasing in the sperm count.

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