The Curative Role of Taurine or Zinc and their Mixture on the Harmful Effects of Genistein Administration in Male Rats

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Abstract: The current study was designed to reveal the curative effects of taurine or zinc and their mixture against hazardous effects of genistein. Sixty male albino rats (160 ±10g) were divided into two main groups, the first group of rats (n=15 rats) acts as normal control. The second group of animals (n =45 rats) was daily injected with 500 mg genistein/ kg b.wt. for one month of injection. The last group (G. gr.) was divided into 3 subgroups each one 15 rats. The first subgroup of rats (genistein) was treated with 500 mg taurine while the second one was received 200 mg of $ZnSO_4$ was added to each Kg.diet for 60 days and the third subgroup was treated with both antioxidant agents for 30 and 60 days after one month of genistein administration. The blood samples and parts of testis were collected after 0, 30 and 60 days of treatment to estimate the physiological and biochemical parameters. Treatment animals with genistein led to a significantly elevation in the total number of abnormal sperms, sperm malformed head & tail, serum LH and FSH and serum malondialdehyde levels. On the other hand, the obtained data recorded a numerical decrease in total number of sperms associated with a remarkable reduction in the serum testosterone level. Moreover, significant decreases were pronounced in serum TAC level, testes GSH content and testes GP_x activity. Treatment of the rats with taurine or zinc showed a significant amelioration in all previous biochemical parameters which estimated in this study. The maximum correction was reached in rats which received the both antioxidants dependent on the time of treatment. These results my be due to the synergistic effects of both taurine and zinc.
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1. Introduction:

Phytoestrogens are estrogenic plant-derived non-steroidal compounds comprised of three classes: isoflavonoids, coumestans and lignans (Murkies, 1998; Tham *et al.,* 1998 and Davis *et al.,* 1999). Because many of these environmental estrogens are generally less potent than other estrogenic substances, exposure to them has been regarded as non-harmful, even beneficial. For instance, isoflavones, such as genistein, occur in high quantities in beans (such as the soy bean), and it is the ingestion of this soy meal, the staple diet of many Asian communities, that has been suggested by numerous epidemiological and experimental studies to cause a protective effect against hormone-dependent cancers (such as breast and prostate) in these populations (Whitten & Naftolin, 1998). Interestingly, feeding rats with a phytoestrogen or genistein rich diet resulted in lower serum testosterone levels, but had no obvious effect on testicular StAR protein levels when compared with those fed with a regular diet and they added that serum genistein levels were approximately 1.5 µM in rats (Weber *et al.,* 2001) and 10 µM in men (Joseph *et al.,* 2011) after consumption with a phytoestrogen-rich diet. However, it was not clear whether such concentrations of genistein are sufficient to suppress StAR gene expression.

The phytoestrogens, namely genistein and coumesterol, are able to bind to estrogen receptors, particularly the ERß isoform, in an agonistic fashion with high affinity (Strauss *et al.,* 1998). Given that both ER isoforms, but particularly ERß, are localized to sites important for male reproduction (Turner *et al.,* 2000), it is reasonable to speculate that these agonistic ligands may have direct effects on male reproductive function. It has been determined that virtually all natural rodent diets that include soy as a source of protein have detectable levels of estrogenic isoflavones (Atanassova *et al.,* 2000 and Mei *et al.,* 2011) and therefore, such diets may be capable of sustaining estrogen-like effects (Weber *et al.,* 2001 and Joseph *et al.,* 2011).

Taurine (2-aminoethane sulphonic acid) is a unique sulfur derivative that has a putative nutritional and osmo-regulatory effect possibly functioning by counteracting ion and water leakage of the membrane or by modulating intracellular calcium levels. Taurine is highly concentrated within the mammalian cells and its concentration is high in mammalian sperm and seminal fluid (Huxtable, 1992). Now, it has been shown to be involved in many important physiological functions e.g., as topic in the development of the CNS, maintaining the structural integrity of the cell membrane (Chesney *et al.,* 1998)

Several authors reported that taurine has the ability to protect the damage which occurred by different cytotoxic substances (Trachtman *et al.,* 1995). Moreover, taurine supplementation led to increase the activity and motility of human sperms and also prolong their life-span (El-Agouza *et al.,* 2009). Also, taurine can be applicable as therapeutic agent against adriamycin induced testicular damage although complete reversal to normal was not observed (Heibashy and Badie-Bakshwan, 1999).

Zinc is also involved in a number of functions of importance to sperm physiology (Riffo *et al.,*1992). In an *in vitro* study using rat testis tissues, the response of cyclic AMP and testosterone to human chorionic gonadotropin (hCG) was found to be augmented by zinc ion in the presence of calcium ion. This augmentation by zinc ion did not occur in the absence of calcium ion, indicating that zinc ion acts synergistically with calcium ion and plays an essential role in testicular function (kendall *et al.,* 2000). Moreover, zinc deficiency causes atrophy of the seminiferous tubules, failure of spermatogenesis and decreased testosterone secretion in the rat Hafiez *et al.* (1989), they observed appropriate responses of pituitary luteinizing hormone (LH) and follicle-stimulating hormone (FSH) to gonadotropin-releasing hormone (GnRH) administration and insufficient response of testosterone to hCG administration in zinc-deficient rats. They concluded that the hypogonadism in zinc-deficient rats resulted mainly from Leydig cell failure, but not from hypothalamo-pituitary dysfunction (Prasad, 2001).

The current study was conducted to demonstrate the chemoprevention efficacy of taurine or zinc and their possible amelioration effect on hazard effect of genistein which induced disturbance in the testis function and led to infertility in rats.

2. Material and Methods

Sixty male albino rats with ages 12 ± 1 weeks old and their weight averaged 160±10g were employed in this study. They were housed in a well ventilated vivarum of Zoology Department, Women's Collage, Ain Shams University. The animals were caged in wire bottom galvanized metal wall boxes under controlled environmental and nutritional conditions (25°C and 55-60 % relative humidity). They fed on a standard diet according to National Research Council (NRC, 1977). Feed and tap water were available *ad libitum*.

The study included two main categories; the first category was carried out on two main groups of rats to study the destructive properties of genistein on the genital system of male rats. To achieve this proposal, fifteen male rats were served as normal control rats group. The remaining rats (forty five of male rats) were daily injected (s.c) with 500 mg genistein / kg body weight for 30 days (Fritz *et al.,* 2002).

After one month of injection 500 mg genistein to rats, the animals were divided into three subgroups, the first subgroup of animals injected daily with 500 mg taurine / 100 g body weight for 30 and 60 days. The second subgroups of male rats, supplemented with 200 mg $ZnSO_4$ (Equal 81 ppm elemental zinc) , added to each kg diet (Bettger *et al.,* 1978) for 30 and 60 days. The third subgroup, male rats were treated with both antioxidants for the same intervals. All used drugs were purchased from Sigma Chem. Co., St. Louis, Mo, USA.

At the end of each experimental periods (zero, 30 & 60 days), the rats were slightly anaesthetized by diethyl ether (Sigma Chem. Co., St Louis, Mo. U.S.A.) and blood was collected from the heart in clean dry test tubes. Sera were separated and kept at -20°C until analysis. Testis of all rats groups were taken quickly on an ice cold plate for immediate estimation of glutathione and glutathione peroxidase.

Examination of semen:

A-Spermatic count and forms:

The scrotal sac was cut and code epididymis was removed and put in a drop of saline and cut into pieces to release the sperms. The sperms were smeared onto a clean glass slide. Then, the slides were stained with haematoxylin and eosin. one thousand sperms were examin under the oil immersion of research microscop to score the head morphology abnormality and the tail defromaties.

B-Microscopical examination

Smear of mature spermatozoa, collected from the cauda epididymis were stained with haematoxylin and eosin. Examination of normal and malformed sperms was carried out using light microscope fitted with oil immersion lenses.

Hormonal assay:

Serum testosterone, rat-luteinizing hormone (Rat-LH) and rat- follicle stimulating hormone (Rat-FSH) were estimated by radioimmunoassay (RIA) technique using solid phase component system (Diagnostic Product Corporation (DPC) USA).

Determination of oxidative and antioxidative status:

The lipid peroxidation (malondialdehyde) assay is based on the reaction of a chromogenic reagent (R1) with MDA at 45°C. One molecule of MDA reacts with two molecules of reagent (R1) to yield a stable chromphore with maximal absorbance at 586 nm. Analysis was performed with a colorimetric

commercial kit (Oxis, USA) according to Beom and Deloy (1995).

Serum total antioxidant capacity (TAC) was estimated according to the method which was described by Koracevic *et al.* (2001) and using ELISA commercial kit (Labor Diagnostika Nord GmbH & Co.). The determination of TAC was performed by the reaction of antioxidants in the sample with a defined amount of exogenously provided hydrogen peroxide (H_2O_2). The antioxidants in the sample eliminate a certain amount of the provided H_2O_2 and the residual H_2O_2 is determined colorimetrically by an enzymatic reaction which involves the conversion of 3,5,dicholoro-2-hydroxybenzensulphonate to a colored product.

Glutathione (GSH) content was determined according to Wafers & Sies (1983) using a commercial ELISA kit (IBL – Hamburg, Germany). Glutathione peroxidase activity (G_{px}) was determined by measuring the oxidized NADPH in the presence of glutathione reductase after addition of H_2O_2 substrate at 25°C for 1 min. The results were expressed as nmol of NADPH oxidized / min / mg protein (Zhang *et al.,* 1989).

Statistical analysis

Data were calculated with the aid of analysis of variance (ANOVA) followed by Duncan's multiple range test as described by Snedecor & Cochran (1989).

3. Results and Discussion

Phytoestrogens were first associated with adverse effects on mammalian development and fertility from observations of animals consuming phytoestrogen-rich plants (Adams, 1995). Limited studies completed in the male have suggested a role for these compounds in male reproductive processes (Carreau *et al.,* 1999; Ebling *et al.,* 2000 and O'Donnell *et al.,* 2001). The phytoestrogens, namely genistein and coumesterol, are able to bind to estrogen receptors, particularly the ERß isoform, in an agonistic fashion with high affinity (Strauss *et al.,* 1998).

The similarities, at molecular level of estrogen (estradiol-17β) and isoflavone (genistein and daidzein) allow them to mildly mimic and sometimes act as antagonists to estrogen (Yildiz, 2005). Isoflavones can also alter the pattern of synthesis and / or metabolism for the endogenous hormones (Sonnenschein and Soto, 1998; Yildiz, 2005). The soy isoflavones act by (1) Inhibiting the enzyme 17-hyroxysteroid oxidoreductase, type 1,which converts the relatively impotent estrone to the much more potent estradiol; (2)occupying the estrogen receptor, thus acting as antagonists to the naturally produced estradiol, inhibiting its effects (this behaviour is similar to that of another estrogen agonist-antagonist, tamoxifen) (Adlercreutz *et al.,* 1994) The consequent reduction in estrogenic action appears to have a useful prophylactic effect against many estrogen dependent disorders in adults, including mammary and prostatic tumours (Clarkson *et al.,* 1995). However, the same effect is deleterious in infants.

According to Yildiz (2005) the key structural elements crucial for the estradiol-like effects of soy isoflavones are : (1) The phenolic ring that is indispensable for binding to estrogen receptors; (2) The ring of isoflavones mimicking a ring of estrogens at the receptors binding site; (3) Low molecular weight similar to estrogens (MW=272). (4) Distance between two hydroxyl groups at the isoflavones nucleus similar to that occurring in estradiol and (5) Optimal hydroxylation pattern .

In addition to interaction with estrogen receptors (ERs), phytoestrogens isoflavones may also modulate the concentration of endogenous estrogens by binding or inactivating some enzymes and may affect the bioavailability of sex hormones by binding or stimulating the synthesis of sex hormone binding globulin (Johnston, 2004).

However, it must be remembered that isoflavones may exert biological activity by other mechanisms, for example, the isoflavone genistein is a potent selective inhibitor of tyrosine kinase in both man and rat myometrial cells (Palmier *et al.,* 1996).

The data which tabulated in table (1) were showed a numerical increase but not significant in the total number of sperms in the normal control rats. The total number of sperms was decreased ($P < 0.05$) significantly after the animals received 500mg genistein for 30 days. The percent of this decrease was 39.92.

On the other hand, a significant correction was occurred in the total number of sperms after treatment of rats with taurine or zinc and their mixture dependent on the time of treatment. The percent of these decreases were 7.90, 7.27 and 13.58 for taurine, zinc and mixture animal groups, respectively (Table 1).

Indeed, dietary phytoestrogen exposure in animals grazing estrogenic pastures has long been known to cause significant impairment of reproductive function (Adams, 1995).

Recent reports of the gradual decline in human semen quality have sparked much debate as to causes/risk factors. Some have suggested that spermatogenesis can be significantly affected by environmental and lifestyle factors that appear to have no other detrimental affect to the health of the

individual (Sharpe, 2000 and Sharpe & Franks 2002). Two such factors associated with adult exposure are seasonality, with demonstrably reduced sperm counts in summer months and dietary effects in adulthood have primarily been associated with women (Sharpe & Franks, 2002).

From tables (1 & 2), the administration of 500mg genistein for 30 days to rats led to increase in the total number of malformed sperms (Total, head, tail and head & tail). The animal groups which treated with taurine, zinc and their mixture led to a significant amelioration effect dependent on the time of treatment (30 & 60 days). These results may be attributed to the antioxidant powerful properties of taurine or zinc which acts as free radicals scavenger, decreases the lipid peroxidation production, elevates the immune system defense and their ability to correct the hypothalamus-pituitary-gondal axis (HPGA). The maximum correction was recorded in the animal group which treated with both antioxidants due to zinc administration which improve the physical and chemical properties of taurine. This improvement was dependent on the time (30 & 60 days) of treatment (Tables 1 & 2). These data are in harmony with those obtained by Heibashy & Badie-Bakshwan (1999) and El-Agouza *et al.* (2009). These authors attributed the elevation in the total number of sperms and correction in the number of malformed sperms (Total, head, tail and head & tail) after treated with taurine due to the correction in the levels of LH and FSH.

From table (3),a significant decline in the testosterone level while, a significant elevation was occurred in both LH and FSH levels after the rats received 500mg genistein for 30 days. The percent of these changes were -8.74 for testosterone and 163.64 and 35.70 LH and FSH, respectively. These results may be attributed to the estrogenic effects of genistein which led to the disturbance in the hypothalamus-pituitary-gonadal axis. These data were supported by Strauss *et al.* (1998); Tou and Thompson. (1999); Thigpen *et al.* (2001); Weber *et al.* (2001) and Chavarro *et al.* (2008).

Interestingly, experiments to examine the effects of phytoestrogens on human reproduction or sexual development are extremely difficult to conduct for both practical and ethical reasons (Murkies, 1998; Tham *et al.,* 1998 and Davis *et al.*, 1999). Most of the published work has been performed using laboratory animals, mainly rodent species. The extrapolation and interpretation of this research to humans is complicated by a number of species differences mostly notably in sexual development and reproductive function. A small number of studies has been conducted in non-human primates, which are of more relevance in terms of human risk assessment. However, there are ethical considerations that limit the use of these experimental models. Factors such as species, age, gender, diet, dose, route of administration, and metabolism, strongly influence the ultimate biological response to phytoestrogen exposure (Weber *et al.,* 2001).

The concentrations of testosterone, LH and FSH were corrected after the animals treated with taurine or/and zinc dependent on the time of treatment (Table 3). These results may be due to the antioxidant properties of taurine and zinc. These data are in harmony with those obtained by Whitten *et al.* (1995); Williams *et al.* (2001).

Table (1): The curative effects of taurine or zinc and their mixture on total count and abnormalities of sperm in normal and genistein treated rats.

Groups	No. of rats	Total no of sperm count					
		0 Days		30 Days		60 Days	
Control	15	881.47 ± 17.3 [a]		885.14 ± 17.9 [a]		912.22 ± 19.5 [a]	
Genistein	15	529.56 ± 14.3 [b]	- 39.92	719.18 ± 17.4 [c]	- 18.75	881.19 ± 19.1 [a]	- 3.40
Genistein + Tau	10			793.08 ± 17.7 [d]	- 10.40	984.25 ± 18.7 [e]	7.90
Genistein + Zn	10			797.15 ± 19.1 [d]	- 9.94	978.51 ± 20.5 [e]	7.27
Genistein + Mixture	10			814.44 ± 18.9 [a]	- 7.99	1036.11 ± 19.1 [f]	13.58
Total no of abnormal sperm count							
Control	15	92.17 ± 10.17 [a]		92.59 ± 11.07 [a]		91.11 ± 10.92 [a]	
Genistein	15	162.63 ± 12.12 [b]	76.45	137.42 ± 11.75 [c]	48.42	111.25 ± 10.56 [d]	22.11
Genistein + Tau	10			127.51 ± 11.31 [c]	37.71	95.62 ± 10.47 [a]	4.95
Genistein + Zn	10			133.81 ± 10.63 [c]	44.52	102.91 ± 9.51 [d]	12.95
Genistein + Mixture	10			100.67 ± 9.58 [d]	8.73	88.41 ± 9.69 [a]	- 2.96

- Values are expressed as means ± S.D.
- a, b, c, d, e, f means with a common superscript within a column are significant different at ($p<0.05$).

Table (2): The curative effects of taurine or zinc and their mixture on sperm abnormalities in normal and genistein treated rats.

Groups	No. of rats	Sperm malformed head					
		0 Days		30 Days		60 Days	
Control	15	50.42 ± 9.14 [a]		53.92 ± 10.12 [a]		50.84 ± 10.44 [a]	
Genistein	15	101.29 ± 13.17 [b]	100.89	79.43 ± 9.63 [c]	47.31	62.63 ± 10.07 [d]	23.19
Genistein + Tau	10			66.71 ± 11.91 [d]	23.72	57.98 ± 11.72 [e]	14.04
Genistein + Zn	10			69.83 ± 10.37 [d]	29.51	58.93 ± 9.92 [e]	15.91
Genistein + Mixture	10			62.27 ± 9.38 [d]	15.49	53.17 ± 8.82 [e]	4.58
Sperm malformed tail							
Control	15	20.14 ± 1.92 [a]		21.61 ± 1.83 [a]		19.52 ± 1.91 [a]	
Genistein	15	25.51 ± 2.04 [b]	26.66	23.88 ± 1.77 [c]	10.50	20.42 ± 1.75 [a]	4.61
Genistein + Tau	10			21.39 ± 1.88 [a]	- 1.02	20.55 ± 1.79 [a]	5.28
Genistein + Zn	10			20.54 ± 1.94 [a]	- 4.95	20.42 ± 1.82 [a]	4.61
Genistein + Mixture	10			20.83 ± 1.74 [a]	- 3.61	20.93 ± 1.75 [a]	7.22
Sperm malformed head & tail							
Control	15	21.16 ± 1.83 [a]		17.06 ± 1.91 [b]		20.75 ± 1.86 [a]	
Genistein	15	35.83 ± 2.19 [c]	65.80	34.11 ± 2.22 [c]	99.94	28.00 ± 1.98 [d]	34.94
Genistein + Tau	10			39.41 ± 2.38 [e]	131.01	17.09 ± 1.79 [b]	- 17.64
Genistein + Zn	10			43.44 ± 2.43 [f]	154.63	18.04 ± 1.82 [b]	- 13.06
Genistein + Mixture	10			17.57 ± 1.84 [b]	2.99	5.64 ± 0.92 [g]	- 72.82

- Values are expressed as means ± S.D.
- a, b, c, d, e, f means with a common superscript within a column are significant different at ($p<0.05$).

Table (3): The curative effects of taurine or zinc and their mixture on serum testosterone, LH and FSH in normal and genistein treated male rats.

Groups	**No. of rats**	**Serum testosterone (ng / ml)**					
		0 Days		**30 Days**		**60 Days**	
Control	15	1.83 ± 0.027 [a]		1.80 ± 0.031 [a]		1.90 ± 0.029 [a]	
Genistein	15	1.67 ± 0.031 [b]	- 8.74	1.69 ± 0.036 [b]	- 9.44	1.87 ± 0.033 [a]	- 1.58
Genistein + Tau	10			1.78 ± 0.034 [a]	- 1.11	1.97 ± 0.033 [a]	3.68
Genistein + Zn	10			1.69 ± 0.035 [b]	- 6.11	1.91 ± 0.032 [a]	0.53
Genistein + Mixture	10			1.92 ± 0.036 [a]	6.67	2.04 ± 0.034 [c]	7.37
Serum LH (ng/ml)							
Control	15	1.21 ± 0.017 [a]		1.26 ± 0.021 [a]		1.25 ± 0.022 [a]	
Genistein	15	3.19 ± 0.059 [b]	163.64	3.07 ± 0.069 [c]	143.65	2.88 ± 0.043 [d]	130.4
Genistein + Tau	10			2.58 ± 0.067 [e]	104.76	2.01 ± 0.059 [f]	60.8
Genistein + Zn	10			2.61 ± 0.079 [e]	107.14	2.24 ± 0.075 [g]	79.2
Genistein + Mixture	10			2.18 ± 0.077 [g]	73.01	1.63 ± 0.069 [h]	30.4
Serum FSH (ng/ml)							
Control	15	3.37 ± 0.037 [a]		3.45 ± 0.044 [a]		3.41 ± 0.041 [a]	
Genistein	15	5.18 ± 0.069 [b]	53.70	5.11 ± 0.074 [b]	48.11	4.95 ± 0.082 [c]	45.16
Genistein + Tau	10			4.48 ± 0.077 [d]	29.85	3.87 ± 0.088 [e]	13.48
Genistein + Zn	10			4.77 ± 0.078 [f]	38.26	4.06 ± 0.069 [g]	19.06
Genistein + Mixture	10			4.08 ± 0.086 [g]	18.26	3.52 ± 0.094 [a]	3.22

- Values are expressed as means ± S.D.
- a, b, c, d, e, f, g, h means with a common superscript within a column are significant different at ($p<0.05$).

The taurine-conjugate bile salt taurolithocholic acid 3-sulfate exerts a beneficial action in the prevention of sexually transmitted diseases (STD). By virtue of its detergent activity, taurolithocholic acid 3-sulfate demonstrates excellent anti-pathogen activity against chlamydia, herpes simplex (types 1 and 2), gonorrhea, and human immunodeficiency virus. It is also less cytotoxic than other agents used. Hence, taurolithocholic acid 3-sulfate may be a valuable topical STD microbiocidal agent *(Herold et al., 1999 and Schaffer et al., 2000)*.

Taurine regulates the most basic of cell functions genetic transcription Maar *et al.* (1998). The authors demonstrated in mice that taurine acts as both an osmoregulator (to balance cell volume) and neuromodulator (protecting against over-excitation that may lead to cell death). Taurine plays these roles in human cells likewise, from head to toe. Also, taurine is found abundantly in tissues that are excitable, rich in membranes, and that generate oxidants. Thus, it is the most prevalent of all the amino acids in the tissues comprising the skeletal and

cardiac muscles and the brain. It is critical to the proper function of the brain, heart, lungs, and blood. Because it performs key functions in cholesterol metabolism related to bile acids, it is essential to the role of the liver, pancreas and gall bladder. It also is a key in the renal function of the kidney (Heibashy, 2000).

Table (4): The curative effects of taurine or zinc and their mixture on serum malondialdehyde & total antioxidant capacity and testes GSH, Gpx in normal and genistein treated male rats.

Groups	No. of rats	Serum malondialdehyde (µM / 100 ml)					
		0 Days		30 Days		60 Days	
Control	15	0.187 ± 0.004 [a]		0.191 ± 0.004 [a]		0.188 ± 0.005 [a]	
Genistein	15	0.242 ± 0.007 [b]	29.41	0.231 ± 0.007 [b]	20.94	0.208 ± 0.009 [c]	10.64
Genistein + Tau	10			0.223 ± 0.008 [b]	16.75	0.197 ± 0.011 [a]	4.79
Genistein + Zn	10			0.228 ± 0.010 [b]	19.37	0.199 ± 0.012 [c]	5.85
Genistein + Mixture	10			0.211 ± 0.012 [c]	10.47	0.189 ± 0.011 [a]	0.53
Groups	No. of rats	Serum TAC (mmol/L)					
		0 Days		30 Days		60 Days	
Control	15	1.83 ± 0.027 [a]		1.80 ± 0.31 [a]		1.76 ± 0.029 [a]	
Genistein	15	1.11 ± 0.031 [b]		1.19 ± 0.36 [b]		1.36 ± 0.33 [c]	
Genistein + Tau	10			1.48 ± 0.34 [d]		1.81 ± 0.33 [a]	
Genistein + Zn	10			1.42 ± 0.35 [d]		1.76 ± 0.32 [a]	
Genistein + Mixture	10			1.62 ± 0.36 [e]		1.94 ± 0.34 [f]	
Testes GSH (mg / g tissue)							
Control	15	5.71 ± 0.031 [a]		5.74 ± 0.032 [a]		5.70 ± 0.032 [a]	
Genistein	15	3.69 ± 0.026 [b]	- 35.38	3.89 ± 0.027 [b]	- 32.23	4.42 ± 0.029 [c]	- 22.46
Genistein + Tau	10			4.12 ± 0.028 [c]	- 28.22	4.86 ± 0.029 [d]	- 14.74
Genistein + Zn	10			4.23 ± 0.027 [c]	- 26.31	4.97 ± 0.029 [d]	- 12.81
Genistein + Mixture	10			4.58 ± 0.028 [d]	- 20.21	5.23 ± 0.030 [e]	- 8.25
Testes Gp_X (µmol GSH oxidized / min / g tissue)							
Control	15	2.37 ± 0.020 [a]		2.45 ± 0.020 [a]		2.41 ± 0.021 [a]	
Genistein	15	1.18 ± 0.016 [b]	- 50.21	1.29 ± 0.017 [b]	- 47.35	1.32 ± 0.018 [b]	- 41.08
Genistein + Tau	10			1.39 ± 0.017 [b]	- 44.90	1.61 ± 0.018 [c]	- 33.20
Genistein + Zn	10			1.57 ± 0.017 [c]	- 40.00	1.83 ± 0.016 [d]	- 24.07
Genistein + Mixture	10			1.88 ± 0.018 [d]	- 35.92	2.14 ± 0.019 [e]	- 11.20

- Values are expressed as means ± S.D.
- a, b, c, d, e means with a common superscript within a column are significant different at ($p<0.05$).

Data presented in table (4) showed that harmful effect of genistein for one month. There is a significant increase in serum malondialdehyde where the increment percentage 29.41, while it was decreased gradually after stop the injection of 500mg. of genistein recorded 20.94 and 10.64 at the end of 30 and 60 days, respectively , on the other hand , a significant decreased was noticed in serum total antioxidant capacity TAC and testes GSH, GPx after treated the previous dose , respectively relative to control level These results may be , due to the increment of free radical production, decrease in the immune system defense and lowering in the β oxidation of lipid in the matrix of mitochondria .

The additional of taurine or zinc correct the levels of all previous parameters dependent on the time of treatment (Table 4). These data may be contributed to the antioxidant powerful of taurine and/or zinc. Moreover, the best correction was occurred in the animals group which treated with both them due to the synergistic effect However, the administration of zinc improve the biochemical and physical action of taurine (Trachtman *et al .,* 1995) .

More than 70 metalloenzymes are known to require zinc as a cofactor. One of these is the zinc- and copper-containing superoxide dismutase (SOD), which is important in the oxidative defense system. Zinc also induces metallothionein, a free radical scavenger. Metallothionein also binds other heavy metals, especially cadmium, and as such acts as a detoxifying agent. Although zinc levels in the body are regulated by homeostatic mechanisms and do not accumulate with continued exposure (Kendall *et al.,* 2000).

It could be concluded that the obtained data highlighted the general protection sustained by taurine and zinc against the oxidative damage induced by genistein. Pervious studies supported that taurine and zinc have a potential role in mediating the harmful effects of genistein, therefore their mixture manifested a great correction reached to near values of control levels in all previous parameters.

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