Effects of Somadril Compound Drug on Testicular Trace Element Levels and Hormonal Parameters of Male Albino Rats.

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Background: Somadril compound is a frequently prescribed muscle relaxant. In recent years, this drug has been increasingly abused. However, little is known about the reproductive toxicity of somadril compound in male albino rats. **Aim of the work**: the present study aims to evaluate the toxic effect induced by somadril compound drug on testicular trace element levels and serum hormonal parameters on male reproduction. **Materials and Methods**: Adult male Sprague Dawley rats were orally administrated (21.6mg and 43.2mg/100g rat body weight) of somadril compound tablets in corn oil (corresponding to therapeutic dose and supratherapeutic doses in human) by gastric gavage for 15,30 and 45 days. The 45-days treatment was followed by 15 days of withdrawal (w15). The changes in the levels of copper (Cu), iron (Fe), zinc (Zn), and calcium (Ca) in testis were determined. Hormonal parameters were evaluated including the levels of total testosterone (T), luteinizing hormone (LH), follicle-stimulating hormone(FSH), thyroid-stimulating hormone (TSH),cortisol, triiodothyronine (T3), and thyroxine (T4) in the serum. The results showed that somadril compound significantly decreased the level of Cu, Fe, Zn, and Ca by daily oral administration. Chronic administration of somadril compound significantly lowered the level of cortisol, T, LH and FSH. Levels of T3 and T4 appeared with a decreased tendency, and TSH presented no obvious regularity. It indicated that somadril compound administration resulted in the

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disbalance of testicular trace elements and influenced hormone levels, which may be possible underlying reproductive toxicity mechanism.
Keywords: Somadril compound. Rats. Testis. Trace element. Hormones.

Introduction

The use of psychoactive prescription drugs (PPDs) by young people is part of a broader worldwide trend towards the consumption of pharmaceuticals to improve social, emotional, and sexual performance. This study focus on one potent painkiller, Somadril compound, which is freely available over the counter in pharmacies. The flow of information on somadril's harmful effects, however, was less evident [1,2].

Carisoprodol (*N*-isopropylmeprobamate, Soma) is one of the main component of somadril compound . It is a centrally acting skeletal muscle relaxant frequently prescribed for the alleviation of lower back pain [3,4]. Although evidence of carisoprodol abuse has been reported for several years [5,6] , its abuse is on the rise [7]. In Egypt, carisoprodol is available as somadril compound contains carisoprodol 200 mg, paracetamol 160 mg and caffeine 32 mg. It is a prescribed drug produced by Mina Pharm for pharmaceutical and chemical industries. It is classified schedule 2 pharmaceutical regulations by the decision of the Minister of health and population No. 172 of the year 2011, while, meprobamate the active metabolite of carisoprodol [8] is a schedule III controlled substance on Anti-drug law No.182 of the year 1960. Carisoprodol may be a contributing factor in death, even when present at therapeutic concentrations. Once ingested, carisoprodol is metabolized to hydroxycarisoprodol, hydroxymeprobamate, and meprobamate [9,10,11].

Paracetamol (acetaminophen), is one of the component of somadril compound and is a widely used over-the-counter drug for analgesic and antipyretic effects[12,13]. However, paracetamol and other mild analgesic are often mis- or over-consumed, including in population subgroups, such as elite athletes, to prevent pain and treat injuries[14]. The risks associated with the misuse of mild analgesics, such as hepatotoxicity[15], cardiovascular side effects[16] or inducing asthma[17] are well known. Recent findings indicate that paracetamol and NSAIDs have endocrine disruptive potential during fetal life[18].

Indeed, several independent epidemiological studies indicate the existence of a significant association between the intake of paracetamol alone or combined with NSAIDs during pregnancy, and an increased risk of cryptorchidism in newborn boys[19]. Mild analgesics were also found to display anti-androgenic effects in the rat fetal testis both *in utero* and *in vitro*[20]. In mice, administration of 600 mg/kg body weight paracetamol caused degeneration of spermatids as early as 6-h post-treatment[21]. High doses of acetaminophen (400 mg/kg) given intraperitoneally daily for 5 d caused reduction in relative testicular weight in mice[22]. Significant decreases in the incorporation of thymidine into the testis were observed during the first 3 h following a single treatment with acetaminophen (100 to 400 mg/kg). In mice treated with acetaminophen (400 mg/kg) daily for 5 d, flow cytometric analysis revealed large reductions in one of the tetraploid populations of testicular cells (mostly early pachytene spermatocytes) on days 5 and 10. Fetal exposure to mild analgesics exerts an anti-androgenic action in the male[23].

Caffeine is one of the somadril compound and is a central nervous system and metabolic stimulant and is used both recreationally and medically to reduce physical fatigue and to restore alertness when drowsiness occurs[24]. Severe bilateral testicular atrophy with aspermatogenesis or oligospermatogenesis in 85-100 percent of the rats fed caffeine[25].

Therefore, this research aimed to investigate testicular toxicity induced by somadril compound using the male rat as a model. The changes in the levels of Cu, iron (Fe), Zn, and Ca in testis were determined. Evaluation also included levels of total testosterone(T), LH, FSH, thyroid-stimulating hormone (TSH), triiodothyronine(T3), and thyroxine (T4),cortisol in the serum. Histopathological examination of testis was examined.

Materials and Methods:

Chemicals and Kits: All chemical used in the present study were purchased from BDH. Chemical Ltd., Pools (England). All utilized kits were obtained from BioMerieux laboratory reagents and products (France) and Boehringer, Mannheim GmbH (Germany).

Somadril compound: Somadril compound drug was obtained as tablets of a combination product containing carisoprodol 200 mg, paracetamol 160 mg and caffeine 32 mg from Mina Pharm for pharmaceuticals and Chemical industries, Cairo, A.R.E.

Animals:

100 male Sprague Dawley rats weighed about (100-150 g body weight.) were obtained from experimental animal house, Helwan, Egypt. Animals were maintained on a normal rat chows *ad libitum* during the experimental period. They were allowed free access to water. The animals were divided into three groups, one group served as control (20 rats) and administered oral doses of corn oil for 45 days. The other two groups served as treated (40 rats in each group) and administered oral daily doses of somadril compound suspended in corn oil equal to 21.6 mg and 43.2 mg/100 g body weight of rat respectively for 15, 30 and 45 days. These doses represented the low and high therapeutic doses and were calculated for rats according to Paget and Barnes ,1964[26] tables for species inter-conversion of dosage. The 45-days treatment was followed by 15 days of withdrawal (w15)[27]. All animals were sacrificed after 30 minutes from the last administration, the blood and testis tissue samples were immediately collected.

The blood samples were collected in dry clean centrifuge tubes and allowed to clot at 37°C for 30 minutes. These blood samples were centrifuged at 3000 rpm for 10 min. The serum was then separated and stored at -20 °C to be thawed once on demand.

Testis were excised; the same testis was chosen and divided into two parts. One part kept in formalin for histological examination and the other part homogenized using cold 0.9% NaCl solution for biochemical analysis determination and kept at -20^{0}C till analysis.

Biochemical Analysis

Determination of the Concentrations of Cu, Fe, Zn, and Ca in Testis Tissue.

The contents of Cu, Fe, Zn, and Ca in testis tissue were determined using flame atomic absorption spectrometry(FAAS)[28].

Determination of T, LH, FSH, TSH, T3, T4and cortisol in serum:
Rat serum T, LH, FSH, TSH, T3, T4 and cortisol were measured by ELISA kits, according to the manufacturer's protocol.

- Rat T (Total testeosterone) ELISA Kit (Cat. No: 55-TESMS-E01).
- Rat LH (luteinizing hormone) ELISA Kit (Cat. No: CSB-E12654r).
- Rat FSH (Follicle Stimulating Hormone) ELISA Kit (Cat. No: AER004).
- Rat TSH (Thyroid Stimulating Hormone) ELISA Kit (Cat. No: RSHAKRTS010R).
- Rat T3 (Triiodothyronine) ELISA Kit (Cat. No: T3043T-100).
- Rat T4 (Thyroxine) ELISA Kit (Cat. No: T4105T-100).
- Rat (Cortisol) ELISA Kit (Cat. No: K7430-100).

Histopathological Studies
For microscopic evaluation tissues were fixed in a fixative (absolute alcohol 60 percent, formaldehyde 30 percent, glacial acetic acid 10 percent) and embedded in paraffin, sectioned at 4μm, and subsequently stained with hematoxylin and eosin. Sections were studied under light microscope (DIALUX 20 EB) at 10x magnifications. Slides of all the treated groups were studied and photographed[29].

Statistical Analysis
Statistical analysis of all data was performed by SPSS procedures. When a significant value ($p<0.05$) was obtained by one-way ANOVA, Data are expressed as mean ± SD.

Results:
1 - The Contents of Cu, Fe, Zn, and Ca in Testis: The effects of different concentrations of somadril compound on Cu, Fe, Zn, and Ca in testis are shown in (Fig. 1). The results showed that the Cu content in the testis appeared in a dose and time-dependent fashion. There was a non significant decrease of Cu in the 1st experimental group (21.6mg/100g rat body weight) compared to that of controls. The Cu

content in the higher dose group (43.2mg/100g rat body weight) on the 30th day and 45th day decrease significantly ($p< 0.01$ and 0.001 respectively) compared with the control group. Besides, the variances within the different somadril groups were high ($p<0.05$ or $p<0.01$, Fig. 1a).

There was a decrease in the Fe level in all experimental groups compared to that of the control group. There was a non significant decrease of Fe in the 1st experimental group compared to that of controls. However, the Fe level in the 2nd group on the 30th day and 45th day had decreased significantly by 10.31 % and 19.72 %, respectively, compared with control (Fig. 1b).

The **Zn level** in different experiment groups showed a decrease in tendency, except for that in the1st group. Notably, the Zn content in the 2nd group on the 45th day decreased significantly by 21.16 % compared with control ($p<0.01$; Fig. 1c).

Compared with the control group, the Ca level in the 1st group on the 45th day showed no statistical difference ($p>0.05$). However, the Ca content in 2nd experiment group was decreased significantly compared with control ($p<0.05$ or $p<0.01$). Typically, the Ca level in the 2nd group on the 45th day was decreased obviously by 25.145 % compared with control ($p<0.01$; Fig. 1d).

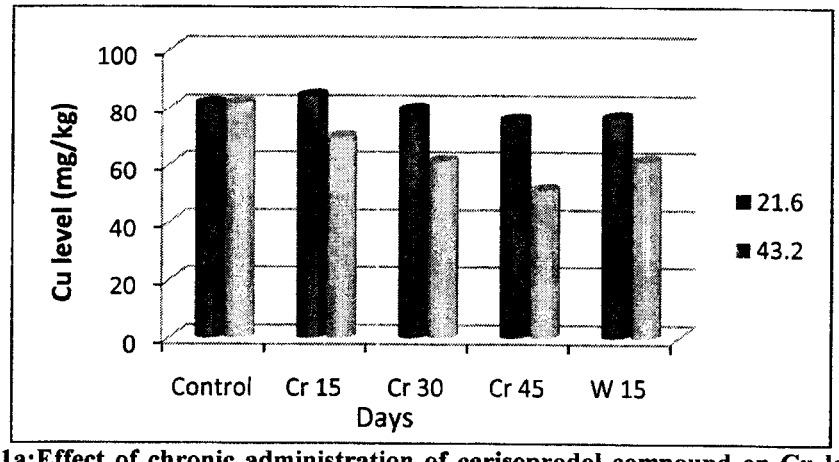

Fig1a:Effect of chronic administration of carisoprodol compound on Cu level (mg/Kg) in adult rat testis.

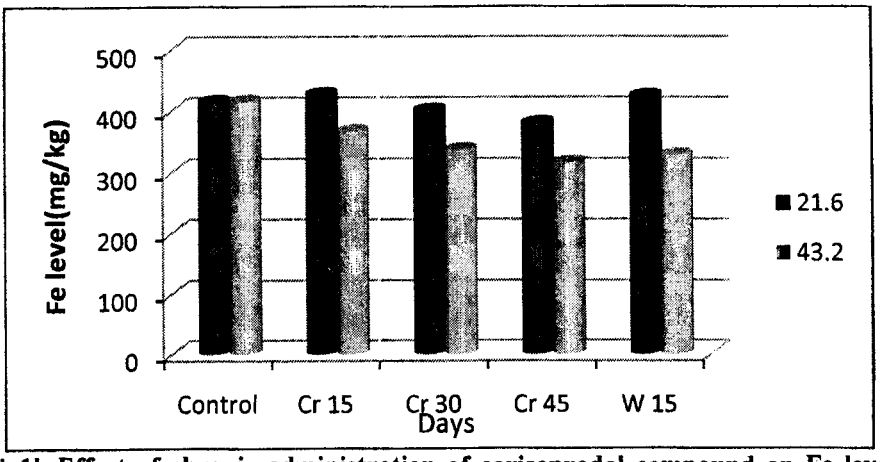

Fig1b:Effect of chronic administration of carisoprodol compound on Fe level (mg/Kg) in adult rat testis.

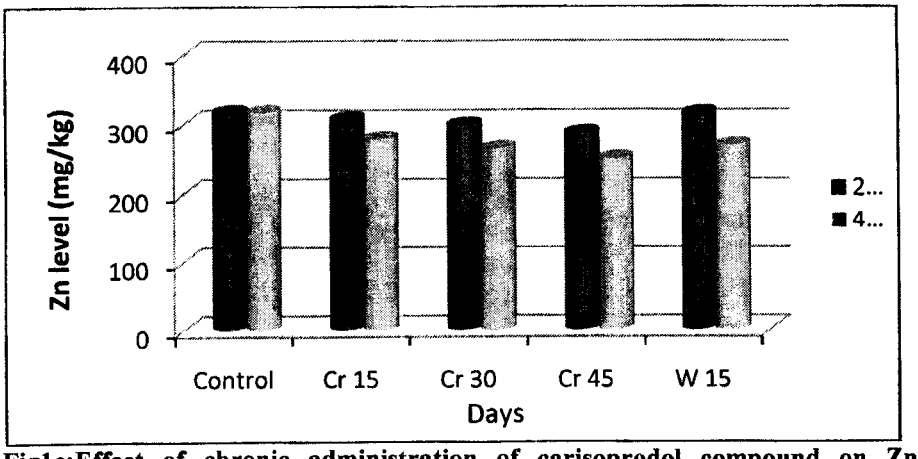

Fig1c:Effect of chronic administration of carisoprodol compound on Zn element in adult rat testis.

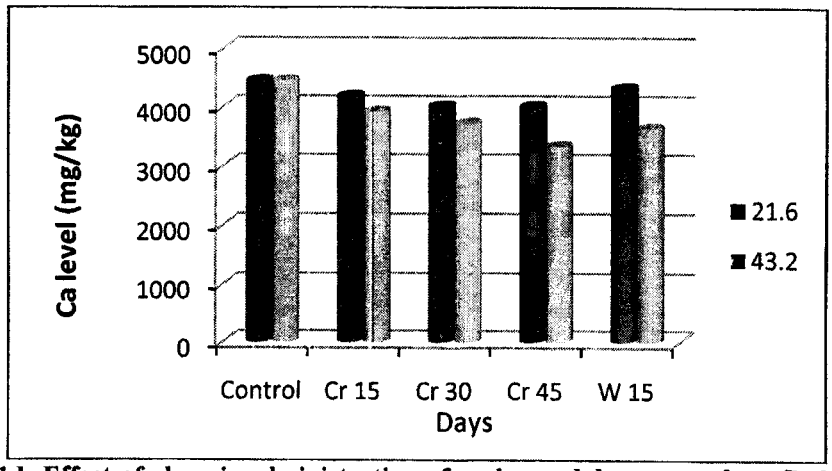

Fig1d: Effect of chronic administration of carisoprodol compound on Ca level (mg/Kg) in adult rat testis.

2-The Contents of T, LH, FSH, TSH, T3, and T4 in Serum:

The effects of carisoprodol compound chronic doses against hormonal concentration of testosterone, luteinizing hormone (LH), follicle stimulating hormone (FSH), are summarized in Table(1).

The effects of excessive administration of somadril compound on total testosterone (T) levels in serum are presented(in table 1). There was a dose-dependent decrease of T at each time point of the 1st dose(21.6mg/100g rat body weight) with no significant difference except on 45 days ($p<0.05$) compared to that of the control group. Compared with the control group, the T levels in the higher dose group (43.2 mg/100g rat body weight) on the 15,30, 45th and crw (carisoprodol withdrawal dose) day were decreased significantly ($p<0.05$-$p<0.001$).

Chronic administration of (21.6mg/100g rat body weight), the LH and FSH levels on the 15th day and 30th day showed no significant effect, but showed a decreased tendency on the 45th day ($p<0.05$). On the other hand, the LH and FSH levels in the second group dose(43.2 mg//100g rat body weight) decreased significantly, all experimental

groups had significant differences compared with control ($p<0.05$ - $p<0.001$; Table 1).

Table (1): Effect of chronic administration of carisoprodol compound on serum hormonal profile in adult rat.

groups / Parameter	21.6mg/100g rat body weight			43.2mg/100g rat body weight		
	FSH	LH	Testosterone	FSH	LH	Testosterone
	mg/dl	mg/dl	mg/dl	mg/dl	mg/dl	mg/dl
Control Mean +S.D	21.5±0.95	25.34±1.11	47.45±1.43	21.5±0.95	25.34±1.11	47.45±1.43
cr15 Mean +S.D	24.1±2.23	27.8±1.35	44.23±.1.12	16.1±3.15	19.8±2.63	39.23±.3.18
%change	12.09	9.71	-6.79	-22.32	-21.86	-17.09
P<	N.S.	N.S.	N.S.	0.01	0.01	0.05
cr30 Mean +S.D	19.34±3.22	27.11±1.47	40.9±2.78	14.33±1.52	17.19±3.52	34.9±2.38
%change	-10.047	6.985	-13.8	-33.3	-32.16	35.95
P<	N.S.	N.S.	N.S.	0.001	0.001	0.001
cr45 Mean +S.D	17.45±3.46	20.97±2.98	38.32±3.98	14.15±2.36	17.07±3.48	29.12±3.08
%change	-18.84	-17.25	-19.24	-34.19	-32.64	-38.6
P<	0.05	0.05	0.05	0.001	0.001	0.001
crW Mean +S.D	22.34±2.11	24.56±1.23	44.57±1.45	16.21±3.61	18.41±3.63	33.17±3.15
%change	3.91	-3.08	-6.07	-24.6	-27.35	-30.09
P<	N.S.	N.S.	N.S.	0.01	0.01	0.01

P-value <0.05 statistically significant, D_{15}, D_{30}, D_{45} and W_{15} = duration of time taken 15, 30, 45 and with 15 days, n=(10)

The effects of chronic administration of somadril compound on the TSH levels in serum were shown in table (2). Compared with the control group, the TSH levels in the first dose experiment group (21.6mg/100g rat body weight) presented no differences along with experiment on15 and 30day, except for that on the 45th day ($p<0.05$). The TSH levels at 2nd higher dose on the 15,30,45 and crW day decreased significantly ($p<0.001$), compared with control.

The T3 levels in serum were shown in table (2). By contrast, the T3 levels on each time point were decreased significantly along with the increase in carisoprodol compound dose ($p<0.001$), except for that in the 1st dose group (21.6/100g rat body weight) on the 30th and 45 day increased significantly ($p<0.05$).

The T4 levels in serum were shown in table 2 .There was a dose-dependent decrease of T4 at each time point compared with the control group. The significant differences in the T4 levels were observed in all experimental groups compared with control ($p<0.01$). It could be observed from the result obtained in this study that a high dose of 43.2mg/100g rat bodyweight of carisoprodol compound gradually produced an abnormal cortisol level in serum .

Table (2): Effect of chronic administration of carisoprodol compound on serum cortisol and thyroid hormones in serum of adult rat.

Groups	21.6mg/100g rat body weight				43.2mg/100g rat body weight			
Parameter	CORTISOl [µg/100 ml]	TSH [µIU/ml]	T3 [pg/ml]	T4[pg/dl]	CORTISOl [µg/100 ml]	TSH [µIU/ml]	T3 [pg/ml]	T4 [pg/dl
Control Mean +S.D	7.03 ± 0.31	0.18 ± 0.01	2.38 ± 0.10	2.62 ± 0.11	7.03 ± 0.31	0.18 ± 0.01	2.38 ± 0.10	2.62 ± 0.11
Cr15 Mean +S.D	7.12±0.58	0.184±0.03	2.42 ± 0.25	2.65±0.13	6.10 ± 0.53	0.148 ± 0.03	1.92 ± 0.11	2.11 ± 0.06
% change	1.28	0.02	1.68	1.15	-13.23	-17.78	23.96	-24.17
P<	N.S.	N.S.	N.S.	N.S.	0.01	0.001	0.001	0.001
Cr30 Mean +S.D	6.99± 0.72	0.178±0.05	2.50 ± 0.11	2.41±0.21	5.33 ± 0.43	0.115 ± 0.02	1.76 ± 0.24	1.76 ± 0.08
% change	-0.569	-1.11	5.04	-8	-24.18	-36.11	42.02	-48.86
P<	N.S.	N.S.	0.05	0.05	0.001	0.001	0.001	0.001
Cr45 Mean +S.D	6.97±0.63	0.166±0.09	2.57±0.12	2.29±0.14	3.93 ± 0.35	0.103±0.07	1.04±0.27	0.96±0.07
% change	-0.853	-7.78	7.98	-12.6	-44.09	-42.78	56.30	-63.36
P<	N.S.	0.05	0.05	0.01	0.001	0.001	0.001	0.001
CrW Mean +S.D	7.15±0.56	0.181±0.07	2.33±0.17	2.53±0.18	5.41±0.44	0.14 ± 0.05	1.36 ± 0.09	1.93±0. 35
% change	1.71	0.56	-2.1	-3.44	-23.04	-22.22	-42.86	-38.17
P<	N.S.	N.S.	N.S.	N.S.	0.001	0.001	0.001	0.001

P-value <0.05 statistically significant, D_{15}, D_{30}, D_{45} and W_{15} = duration of time taken 15, 30, 45 and with 15 days, n=(10).

3-Toxic Effect of Somadril Compound on Histopathology of Testis:

In this study, it was found that high doses of somadril compound(43.2mg/100g rat body weight) could influence the seminiferous epithelium by histopathological examination. The arrangement of cells in the higher dose groups was irregular and disordered, and intercellular connections, e.g. gap junctions, were not compact, which indicated that somadril compound could pass blood-

testis barrier and disturb the junction between sertoli cells and germ cells.

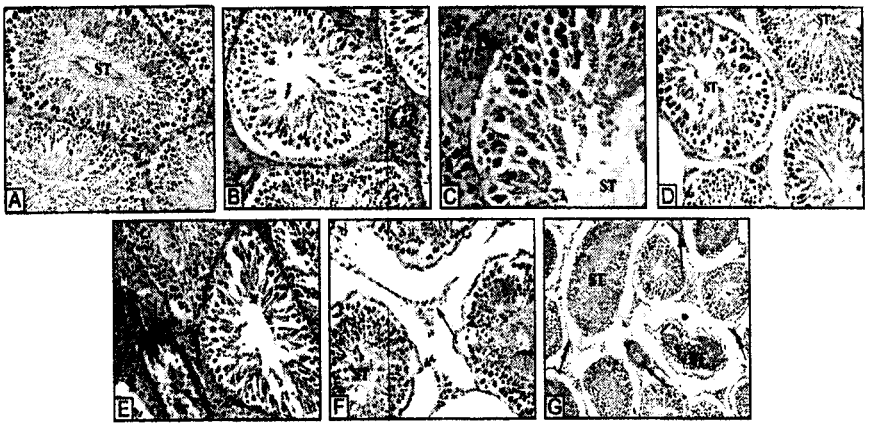

Figure 1. Histopathologic changes in testicular tissue after somadril compound administration for 15,30, 45 d. The testicular tissue was sectioned with a thickness of 5 μm and stained with H&E. Magnification, 400X. (A) Control, (B) Cr15, (C) Cr30, (D,E) Cr45 and (F,G) withdrawal group for 15 days.

Discussion:

Usages of somadril compound tablets have increased in past few years owing to its rapid metabolism to meprobamate[30]. Widespread use of somadril compound have increased the risk of toxicity in humans [31]. Owing to the lipophilic nature of testicular tissue, somadril compound may have accumulated in this tissue resulting in excessive production of ROS and tissue damage. Previous study showed that carisoprodol drug depresses spermatogenesis in mammals by causing death of developing germ cells in the seminiferous tubules[32].

Chronic administration of high levels of drug leads to its accumulation in testis, resulting in the inbalance of trace elements such as Cu, Fe, Zn, and Ca being disturbed in testis, as shown in (Fig. 1). Trace elements can adversely affect animal health and reproductive system and its functions, through either direct or indirect effects on numerous organs and systems [33]. In the present study, trace elements

such as Cu, Fe, Zn, and Ca were determined after daily administration of the drug(21.6mg and43.2mg/**100g** rat body weight) for 15, 30 and 45 days . These elements often act as the cofactors of many enzymes, play an important role in the process of normal spermatogenesis and testicular development, and are indispensable elements in semen of male animals[34].

Cu is a vital trace element required for normal growth and development of many organisms and acts as an electron transfer agent because of its ability to donate or accept electrons through redox reactions[35]. Eybl *et al.*, 2006[36] demonstrated that Cu could help to reduce drug metabolites accumulation to weaken its toxicity. In the present study, the level of Cu in testis decreased while drug increased, which may indicate that Cu was used to prevent carisoprodol free radicle accumulation.

Fe is an essential element for many cellular activities like oxygen transport, electron transfer, and gene regulation[37,38]. Zheng *et al.*, 1999[39] reported that chronic drug administration altered Fe homeostasis possibly by expediting unidirectional influx of Fe from the systemic circulation to cerebral compartment. In this study, the Fe content decreased along with the increase of drug in testis. These results suggest that carisoprodol compound treated rats may be more susceptible to lipid peroxidation in the presence of promoters like Fe. The enhanced lipid peroxidation in testis may decrease testis membrane fluidity, increase the negative surface charge distribution and alter membrane ionic permeability including proton permeability[40].

Zinc is indispensable element for growth, reproduction, development, differentiation, immune and antioxidant functions, gene expression, DNA synthesis, hormone synthesis, storage and release of neurotransmitters, memory, visual processes and apoptosis[41]. Zn has close relationship with endocrine system being essential for testosterone synthesis and spermatogenesis. Its deficiency causes atrophy of seminiferous tubules and failure of spermatogenesis[42,43].

In this study, the Zn content decreased along with increase of drug in testis. Oxidative stress has been suggested to be an early effect of zinc deficiency. Reactive oxygen species (ROS) or free oxygen

radical (FOR) are normally generated by Sertoli cells that cause alteration in cellular structures and induces morphological changes in spermatids during spermiogenesis[44].

Ca is one of the most important and abundant minerals in the body. Ca had the role in limiting the reproductive performance of avian species[45]. However, in this study, Ca content had no significant differences in low-dosed group , whereas it decreased gradually along with the increase of using drug. Carisoprodol compound acts as a toxicant to organisms when the concentrations are elevated and starts affecting neuromuscular transmission by interacting with mitochondrial Ca2+ and disturbing the ion balance in testes membrane[46].

Spermatogenesis is a complex process by which the spermatogonia mature gradually to spermatozoa through a series of events involving mitoses, meiosis and cellular differentiation. The spermatogenesis process was considered critically dependent on the high intratesticular testosterone levels induced by the two pituitary gonadotropins, LH and FSH[47]. LH stimulates testosterone production by Leydig cells whereas FSH stimulates the Sertoli cells to regulate spermatogenesis by secreting INH-B that will affect Leydig cell function. The exposure to many toxicants lead directly to a remarkable decline in spermatogenesis function and fertility of animals and humans.

In this study, it was found that high doses of somadril compound could influence the seminiferous epithelium by histopathological examination. The arrangement of cells in the higher dose groups was irregular and disordered, and intercellular connections, e.g. gap junctions, were not compact, which indicated that carisoprodol compound could pass blood-testis barrier and disturb the junction between Sertoli cells and germ cells. Furthermore, these impairments might be related to reduction of testosterone production of Leydig cells, because it is well understood that testosterone affects and controls the physiological functions of Sertoli cells and histological integrity[48].

Thus it might be concluded that following administration of carisoprodol compound , Leydig cells would degenerate and decline in number per mm2 of the interstitial tissue, and their ability for synthesis of testosterone also decreased. Lebda *et al.*,2014[49] explained

the reduction in serum testosterone ,LH and FSH as follow , rat's Leydig cells utilize both serum uptake and Denovo synthesis of cholesterol from acetate to produce testosterone. Cytoskeletal inhibition by drug could result in diminished uptake of cholesterol and consequent reduced testosterone levels. In addition, putative drug-induced cytoskeletal dysfunction could inhibit the synthesis and/or transport of LH receptors to the cell membrane of Leydig cells, thereby indirectly decreasing testosterone biosynthesis.

The major novel finding of this study is that, to our knowledge, it provides the first evidence that carisoprodol compound disrupts the hypothalamic-pituitary-gonadal axis (HPG) of adult male rats, and even more specifically, that the mechanism for this effect involves the targeting of the hypothalamic-preoptic GnRH system. Our results are consistent with observations that environmental or pharmaceutical substances that disrupt monoaminergic neurotransmitter functions in the hypothalamus, including pesticides[50] and polychlorinated biphenyls (PCBs)[51], affect GnRH and LH release.

The dose-dependent toxicity of carisoprodol compound was also confirmed by histological studies. In testis, degeneration of the seminiferous tubules and vacuole formation was observed. The degree of degeneration and vacuolization was more pronounced at 43.2 mg/100gbw as compared to lower dose. induced system toxicity in male Wistar rats in a dose-dependent manner. The higher dose produced more deleterious effect as compared to lower dose. Repeated administration of rats for 15,30,and 45 day at 21.6mg or 43.2 mg/100g rat body weight of the drug produced significant toxicity in testis.

A sensitive TSH assay is now an accepted initial screening test of thyroid function. T3 and T4 circulate in the blood as equilibrium mixtures of free and protein-bound hormones. Low levels of T4 and T3 are related with delayed puberty and reproductive disorders, so the levels of thyroid hormones are important in the reproductive activity of the animals[52]. Parchwani *et al.*, 2012[53] had found that though men with abnormal semen profile had higher total T3, T4 concentrations, and lower TSH concentrations compared to those with normal semen profile. However, in this study, TSH levels presented

no obvious regularity on different carisoprodol compound days in different groups, and T3 and T4 levels presented descending trends in serum. It indicated that carisoprodol compound could also affect testis system of rats through influencing levels of thyroid hormones.

In conclusion, the present study demonstrated that excessive carisoprodol compound administration accumulated largely in testis of rats disturbed the imbalance of the microelement metabolism and influenced hormone levels. Moreover, the reproductive system of rats was injured and the reproductive functions were probably also suppressed in the same manner. However, the mechanism of this effect in the developmental toxicity of carisoprodol compound remains to be further studied.

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تأثير عقار مركب السومادريل على مستوى العناصر النادرة فى الخصيتين وتتابع الهرمونات فى ذكور الجرذان البيضاء

ليلى عبد القوى

يستخدم مركب السومادريل كباسط للعضلات، ولكن يتم اساءة استخدامه فى كثير من الأحيان فى السنوات الأخيرة. ومع ذلك، لا يعرف إلا القليل عن السمية الإنجابية لهذا العقار فى ذكور الجرذان البيضاء.

الهدف من العمل:

تهدف هذه الدراسة إلى تقييم التأثير السام الناتج عن تناول عقار مركب السومادريل على مستوى العناصر النادرة فى الخصيتين وتتابع الهرمونات الذكرية فى الدم فى الجرذان البيضاء.

المواد والطرق:

تحقن ذكور الجرذان البالغة عن طريق الفم ((21.6mg and 43.2mg/100g rat body weight) بأقراص مركب السومادريل فى زيت الذرة (الجرعة العلاجية والجرعات فوق العلاجية فى الإنسان) من خلال أنبوب التغذية فى المعدة لمدة ١٥ و ٣٠ و ٤٥ يومًا. ويعقب الحقن لمدة ٤٥ يومًا، الانسحاب لمدة ١٥ يومًا (W15).

تم تحديد التغيرات فى مستويات النحاس (Cu) والحديد (Fe) والزنك (Zn)، والكالسيوم (Ca) فى الخصية. كما تم تقييم الهرمونات الذكرية فى الدم بما فى ذلك مستويات هرمون التستوستيرون الكلى (T)، هرمون (LH)، هرمون (FSH)، هرمون الغدة الدرقية (TSH)، الكورتيزول، ثلاثى يودوثيرونين (T3)، وهرمون الغدة الدرقية (T4) فى مصل الدم.

وأظهرت النتائج أن تناول مركب السومادريل يوميًا عن طريق الفم يؤدى إلى انخفاض مستوى النحاس، والحديد، والزنك، والكالسيوم بشكل ملحوظ، وأن الجرعات المزمنة من مركب السومادريل تؤدى إلى الانخفاض بشكل كبير فى مستوى الكورتيزول، T، LH و FSH. كما أظهرت مستويات T3 و T4 ميل إلى الانخفاض، وعدم انتظام واضح فى TSH. وأشارت النتائج إلى أن مركب السومادريل ينتج عنه عدم الاتزان فى العناصر النادرة فى الخصية ومستويات الهرمون والتى قد تكون مفسرة لآلية السمية الإنجابية.