TOXICOLOGICAL EFFECT OF COPPER SULPHATE AND COBALT CHLORIDE AS FEED ADDITIVES ON FERTILITY IN MALE ALBINO RATS.

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A B S T R A C T

This study is designed to investigate the effect of copper sulphate and cobalt chloride, which are used as additives in feed on fertility of male white albino rats. One hundred rats classified to five groups. First group used as control; second and third group were given 1/10 and 1/5 LD_{50} of $CuSo_4$ respectively, fourth and fifth groups were given 1/10 and 1/5 LD_{50} of $CoCl_2$ respectively (orally via stomach tube). Testis and epididymis were dissected and used for detection of sperm motility and counts. Histopathological examination was performed on testis. Results showed significant decrease in testis and epididymis weight and significant increase on sperm abnormalities while sperm numbers were significantly decreased. It can be concluded that ingestion of copper sulphate and cobalt chloride in high doses decrease fertility in male albino rats.

Key words: cobalt toxicity- copper toxicity – spermatogenesis- heavy metals.

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1. INTRODUCTION

Copper is an essential trace element as an integral component of many enzymes and protein, and is needed in a wide range of metabolic processes. It is one of the key trace minerals required for an effective immune response. The biological functions of copper include electron- transfer catalysis by means of its two accessible oxidation states (Georgopoulos et al., 2001). Copper is a normal constituent of semen, where bound to the tail mid piece of spermatozoa and present in seminal plasma, (Valsa et al., 1994). High doses of copper ions have a toxic effect on the epididymis, testes, and scrotum of mammals, which may ultimately lead to reduced fertility (Pesch et al., 2006). Cobalt is an essential dietary trace element as a component of vitamin B12 (cyanocobalamin), each molecule of the vitamin containing one atom of cobalt (Lahaye et al., 1984). Male rats exhibited reduced testicular sperm counts and daily sperm production, the testes displayed severe abnormalities, including hypertrophy of the interstitial leyding cells, congested blood vessels, degeneration of the spermatogonial cells, and necrosis of seminiferous tubules and interstitial tissue at dose of 400-800 mg/L cobalt chloride (Elbetieha et al., 2004).

In light of these facts, the main goal of the present study was to evaluate the effect of copper sulphate and cobalt chloride **on** fertility of male white albino rats after chronic exposure for six months.

2. MATERIAL AND METHODS

2.1. Experimental animals:

One hundred apparently healthy male albino rats (western strain) weighted 175-182 g were obtained from Veterinary Serum and Vaccine Research Institute, Abbasia, Cairo, Egypt. The animals housed in stainless steel wire bottom cages and kept under constant environmental conditions and fed on fresh standard pellet and given tap water throughout the study. All animals

were acclimatized for 1 week before the beginning of the experiment.

2.2. Tested substance:

Copper in the form of copper sulphate pentahydrate (Cu $SO_4.5H_2O$) crystals from El gomhoria company and cobalt in the form of cobalt chloride hexahydrate ($CoCl_2 \cdot 6H_2O$), crystals from El gomhoria company, were used in thus experiment .

2.3. Experimental design:

In this study 100 male albino rats (western strain) were divided into five groups each one contain 20 rats. First group was kept as control; while second and third groups were given 1/10 and 1/50 LD_{50} of $CuSo_4$ (Abu-Zinadah and Hussein 2010) respectively. Fourth and fifth groups were given 1/10 and 1/50 LD_{50} of $CoCl_2$ (National Institute for Occupational Safety and Health (NIOSH) 2003). Respectively (orally by stomach tube) 3 days per week for 6 months.

2.4. haematological studies:

-Erythrogram and leucogram performed by using Celly 70 (automatic blood cell counter performing 18 parameters): *4, Rueb galvani 91745 Massy Cedex.*

2.5. Sperm counts: - sperm counts was done according to (Wook et al., 2004), where caudate epididymis was chopped with a sharp scissor and then homogenized with a low speed in 10 ml distilled water for 1.5-2 minutes at 4-6 c°. The number of homogenization resistant spermatids was enumerated using a hemocytometer.

2.6. Analysis of sperm:-

Sperm suspension (40 ml) was placed on dry and clean glass slide then stained by eosin and nigrosin stains then spread as film and leave to dry then examined under oil immersion lens.

2.7. Copper and cobalt residue in liver and kidney:

Determination of copper and cobalt residues were performed according to (Iwegbue 2008).

2.8. Statistical analysis:

Data were analyzed for obtaining mean, standard deviation (SD) and statistical comparisons between means of different groups. The statistical analyses were done by one way ANOVA and DUNCAN test using SPSS program version 11. *P* value < 0.05 was assumed for statistical significance.

3. RESULTS

3.1. Effect of administrated copper sulphate and cobalt chloride on erythrogram of male white albino rats for 6 months :

The data of erythrogram (red blood cells count (RBCs), hemoglobin (Hb), packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular hemoglobin(MCH) and mean corpuscular hemoglobin concentration (MCHC) of rats in different experimental groups were cleared in table (1). RBCs counts, Hb concentration, PCV and MCH in different groups statistically different at 2nd, 4th and 6th, months of experiment. RBCs count, Hb concentration and PCV of rats received copper sulphate showed significant decrease compared with control group. While the MCV revealed significant increase in treated groups compared with control group. However, the MCHC showed no statistical differences throughout the experimental period. These results more clear on group received high dose (1/5 LD_{50}) of copper sulphate. RBCs count, showed significant increase in cobalt chloride treated groups in compared with control groups. On the other hand, the Hb concentration, MCV and PCV in cobalt chloride treated groups showed significant decrease in compared with control groups. While MCHC showed no statistical differences throughout the experimental period. These results more clear on group received high dose (1/5 LD_{50}) of cobalt chloride (Table 1).

Table (1) Effect of administrated of copper sulphate and cobalt chloride on Erythrogram (RBCs, Hb, PCV, MCV, MCH and MCHC) of white albino rats for 6 months (mean± SD):-

Items	2nd month					4th month					6th month				
Groups	GI control	GII 1\10 LD50 cuso4	GIII 1\5 LD50 cuso4	GIV 1\10 LD50 cocl2	GV 1\5 LD50 cocl2	GI control	GII 1\10 LD50 cuso4	GIII 1\5 LD50 cuso4	GIV 1\10 LD50 cocl2	GV 1\5 LD50 cocl2	GI control	GII 1\10 LD50 cuso4	GIII 1\5 LD50 cuso4	GIV 1\10 LD50 cocl2	GV 1\5 LD50 cocl2
RBCs M/µl	7.58 ± 0.6 b	6.95 ± 0.9 c	6.12 ± 0.7 c	8.12 ± 0.1a	8.94 ± 0.2 a,	7.64 ± 0.24 b	5.80 ± 0.24 c	4.95 ± 0.3 c	9.34 ± 0.4 a,	9.85 ± 0.38 a,	7.65 ± 0.9 b	4.90 ± 0.21 c	3.63 ± 0.23 d	10.13 ± 0.43 a	10.61 ± 1.01 a
Hb g/dL	14.85 ± 0.2 a,	13.56 ± 0.4 b	11.8 ± 1.16 c	13.9 ± 0.23 b	13.62 ± 0.3 b	14.88 ± 0.24 a,	12.72 ± 0.61 b	10.00 ± 0.45 c	13.30 ± 0.6 b	12.90 ± 0.34 b	14.89 ± 1.34 a	11.80 ± 1.3 c	8.90 ± 1.2d	12.70 ± 0.51 b	11.30 ± 0.6 c
PCV %	45.74 ± 0.9 a,	42.46 ± 0.2 b	41.21 ± 0.7 b	44.71 ± 0.9 a	44.14 ± 0.32a,	45.24 ± 0.12 a,	42.21 ± 0.26 d	40.93 ± 0.51 e	44.13 ± 0.81b	43.79 ± 1.31c	45.01 ± 0.38 a	36.00 ± 0.9 c	31.00 ± 0.17 d	42.60 ± 0.38 b	40.40 ± 0.51 b
MCV fL	60.34 ± 0.4 b	61.09 ± 0.3 b	67.33 ± 0.5 a,	55.06 ± 0.4c	49.37 ± 0.27 d	59.21 ± 0.57 c	72.77 ± 0.3 b	82.68 ± 0.43 a,	47.25 ± 0.52d	44.46 ± 0.37 e	58.83 ± 0.9 c	73.46 ± 0.37 b	85.39 ± 0.35 a	42.05 ± 0.41 d	37.61 ± 0.16 e
MCH Pg	1.96 ± 0.03 a	1.95 ± 0.98 a	1.93 ± 2.9 a	1.71 ± 0.5 b	1.52 ± 1.o5 c	1.95 ± 0.17 b	2.19 ± 0.35 a	2.02 ± 0.42 a	1.42 ± 0.32 c	1.31 ± 1.03 c	1.94 ± 0.3 b	2.41 ± 0.71 a	2.45 ± 0.87 a	1.25 ± 0.47 c	1.07 ± 0.73 d
MCHC g/dL	32.47 ± 1.34 a	31.93 ± 0.91 a	28.63 ± 0.7 c	31.08 ± 0.61 a	30.85 ± 0.32 b	32.89 ± 0.23 a	30.14 ± 0.51 b	24.43 ± 0.59 d	30.14 ± 0.57 b	29.46 ± 0.31 c	33.08 ± 0.91 a	32.77 ± 0.85 b	28.71 ± 0.93 c	29.81 ± 0.37 c	27.97 ± 0.43 d

Mean with different letters at the same row differ significant ($P < 0.05$).

Table (2) Effect of administration of copper sulphate and cobalt chloride on sperm gram of white albino rats for 6 months (mean± SD):

Groups	2nd month				4th month				6th month			
	Testis Wt. (gm) (R&L)	Epididymis Wt. (gm) (R&L)	Sperm No/ ml (million)	Abnormalities %	Testis Wt (gm) (R&L)	Epididymis Wt (gm) (R&L)	Sperm No/ ml (million)	Abnormalities %	Testis Wt (gm) (R&L)	Epididymis Wt (gm) (R&L)	Sperm No/ ml (million)	Abnormalities %
Group I control	2.10 ±0.52[a]	0.18 ±1.6[a]	132 ±0.58[a]	5.20 ±2.5[c]	2.80 ±0.19[a]	0.19 ±0.3[a]	137 ±0.6[a]	7.30 ±0.15[c]	3.20 ±0.25[a]	0.25 ±0.8[a]	140 ±0.17[a]	8.10 ±0.13[c]
Group II 1\10 LD50	1.62 ±0.21[b]	0.17 ±1.2[b]	93 ±0.21[b]	15.60 ±0.12[b]	1.40 ±0.53[b]	0.15 ±1.35[b]	68 ±0.83[b]	31.20 ±0.56[b]	1.00 ±0.59[b]	0.14 ±1.75[b]	24 ±0.4[b]	39.70 ±0.19[b]
Group III 1\5 LD50	1.30 ±0.62[b]	0.16 ±0.22[b]	89 ±0.66[b]	31.20 ±0.69[a]	0.99 ±0.47[c]	0.14 ±0.51[c]	36 ±0.65[d]	42.10 ±0.7[a]	0.79 ±0.10[c]	0.13 ±0.3[c]	9.60 ±0.03[c]	52.90 ±0.2[a]
Group IV 1\10 LD50	1.84 ±0.01[b]	0.17 ±1.35[b]	96 ±1.03[b]	15.20 ±0.76[b]	1.54 ±0.03[b]	0.15 ±0.16[b]	75 ±0.06[b]	27.90 ±0.26[b]	1.42 ±0.01[b]	0.13 ±0.09[b]	29 ±1.03[b]	36.10 ±0.12[b]
Group V 1\5 LD50	1.52 ±0.33[b]	0.16 ±0.32[b]	91 ±0.58[b]	29.80 ±0.81[a]	1.24 ±0.02[c]	0.14 ±0.14[c]	49 ±0.22[c]	38.70 ±0.21[a]	1.08 ±0.19[c]	0.13 ±0.26[c]	11.50 ±0.24[c]	47.50 ±1.35[a]

Mean with different letters at the same column differ significant ($P < 0.05$

Table (3) the residues of copper and cobalt in liver and kidneys tissues (µg/g) of white albino rats administrated by copper sulphate and cobalt chloride for 6 months (mean± SD):

organ / Group		2nd month		4th month		6th month	
		Liver ppm	Kidney ppm	Liver ppm	Kidney ppm	Liver ppm	Kidney ppm
Group I Control	copper	6.11 ±2.1	0.55 ±0.05	6.15 ±1.1	0.58 ±0.26	6.18 ±0.8	0.62 ±0.7
	Cobalt	8.20 ±0.1 d	1.6 ±0.2 d	8.4 ±0.8 c	1.8 ±0.3 d	8.9 ±0.6 c	2.1 ±0.4 d
Copper	Group II 1\10 LD50	27,00 ±3.44 c	2.6 ± 1.3c	38.00 ±1.21b	5.4 ±2.5c	61.00 ±1.2 b	7.3 ±2.5 c
	Group III 1\5 LD50	46.00 ±0.7 a	6.8 ±2.1 b	78.00 ±1.3 a	11.7 ±3.2 b	102.00 ±0.8 a	15.9 ±0.93 b
Cobalt	Group IV1\10 LD50	33.2 ±1.4 b	5.7 ±0.73 b	40.1 ±0.87 b	12.4 ±1.6 b	72.6 ±2.3 b	16.2 ±1.8 b
	Group V 1\5 LD50	45.2 ±2.1 a	11.7 ±2.5 a	81.3 ±0.93 a	17.5 ±0.51 a	108.1 ±0.1 a	29.8 ±0.6 a

Mean with different letters at the same column differ significant ($P < 0.05$).

3.2. Effect of administration of copper sulphate and cobalt chloride on Sperm gram of white albino rats for 6 months

Table (2) illustrated the effect of copper sulphate and cobalt chloride on testis and epididymis weight and the sperm number; where a significant decrease in treated groups (copper sulphate and cobalt chloride) were detected compared to control group. Abnormalities percent were significantly increased in treated groups (copper sulphate and cobalt chloride) in compared to control group. These results were pronounced at groups received large dose of copper sulphate and cobalt chloride (1/5 LD_{50}) compared with control group.

3.3. Residues of copper and cobalt in liver and kidneys tissues of white albino rats administrated copper sulphate and cobalt chloride for 6 months:

The residues level of copper and cobalt were significant increased in liver and kidney tissues of rat received copper sulphate and cobalt chloride for 6 months in compared to control. (Table 3).

1. DISCUSSION

Copper one of the key trace minerals required for an effective immune response. The biological functions of copper include electron- transfer catalysis by means of its two accessible oxidation states (Georgopoulos et al., 2001). Cobalt is an essential metal for human and is part of the enzyme cyanocobalamin (vit B12) but high exposure levels has serious effect. Regarding to the effect of copper sulphate on the erythrogram during experimental period Table (1) revealed red blood cell

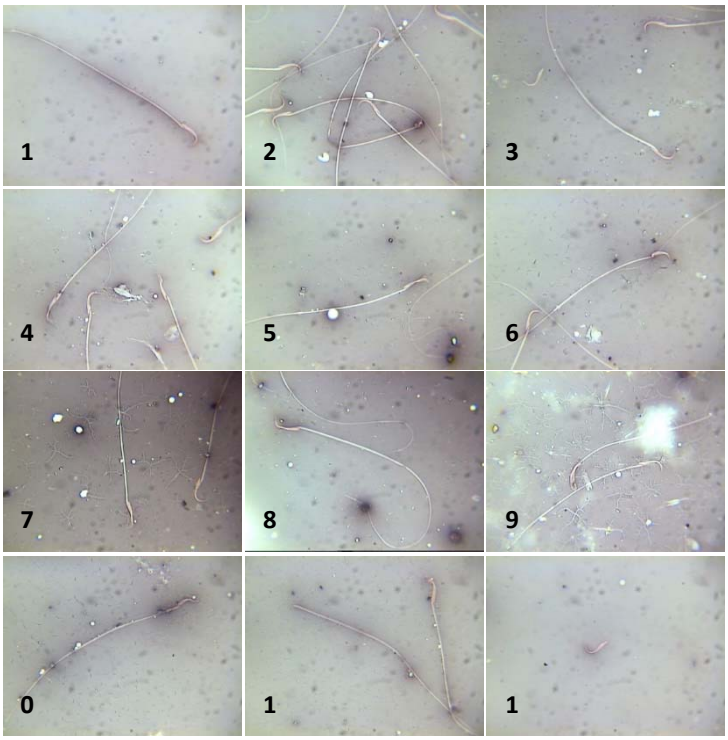

Fig (2):A representative rat epididymal sperm head abnormalities in control (1-3), copper (4-9) and cobalt groups (10-12) stained with eosin-nigrosin stain and examined under light microscopy; magnification x100 oil-immersion objective. Arrows referred to sperm heads. (1) normal head. (2) amorphos head. (3, 12) detached head. (4-8) flattened head. (9) knobbed hock. (10-11) banana head.

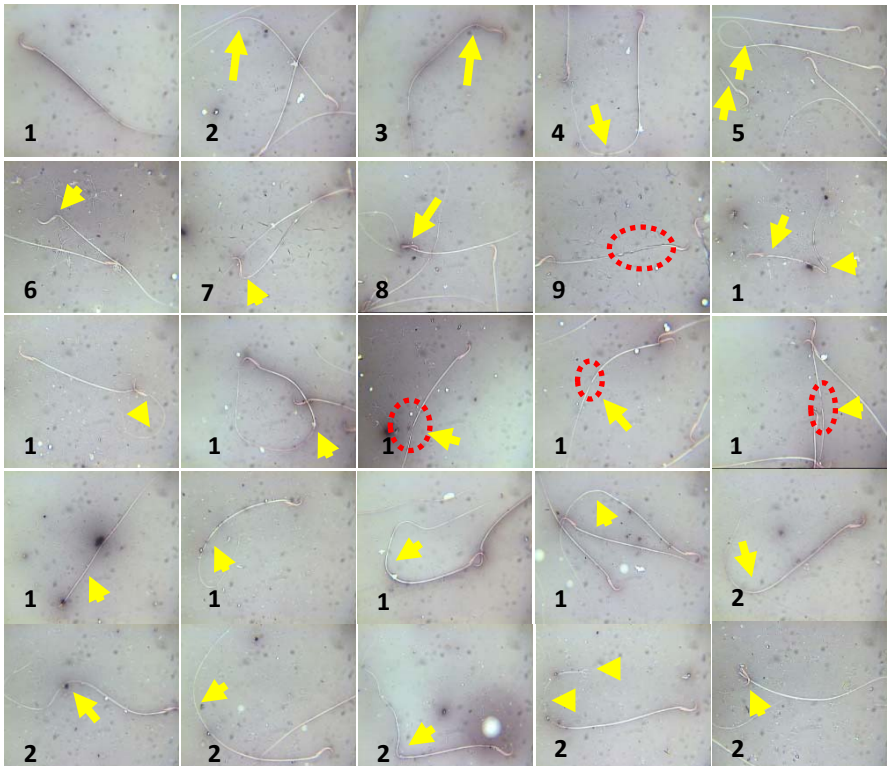

Fig (1):A representative rat epididymal sperm tail abnormalities in control (1-5), cadmium (6-16) and chromium groups (16-25) stained with eosin-nigrosin stain and examined under light microscopy; magnification x100 oil-immersion objective. Arrows referred to sperm tail abnormalities and dashed circle indicated the detached sperm sheath.

counts (RBCs), hemoglobin (Hb) and Packed cell volume % (PCV %) level in rats of treated groups showed significant decrease at 2nd ,4th & 6th month of experiment if compared with control group. Our result agreed with the result obtained by (Jezierska et al., 2009, Wilson, 2010). These results may be due to the malfunctioning of hemopoietic system or destruction of circulating cells caused by morphological alterations in renal interstitium (Singh et al., 2008). Or due to free radicals and lipid perioxidation process due to copper sulphate enhanced degradation of erythrocytes, which associated with release iron (Mori and Hirayama 2000).Or may be attributed to that copper was able to penetrate the erythrocytes and inhibit glycolysis, and promoting denaturation of hemoglobin due to inhibition of erythrocytes glucose- 6-phosphate dehydrogenase activity (ACGIH, 1986). Or hemolytic anemia may be caused either by direct red cell membrane damage or indirectly as a result of the inactivation of enzymes (including glutathione reductase) which protect against oxidative stress, copper ions can oxidize heme iron to form methaemoglobin (Ashish et al., 2012). Or may be due to heavy metals exposure also decrease RBCs, Hb, and hematocrite concentration due to impaired intestinal absorption of iron (Joshi et al., 2002). Hemolysis occurred and was attributed to the accumulation of copper in erythrocytes resulting in precipitation of hemoglobin (Singh and Singh, 1968), or hemolysis was due to entry of excessive copper into erythrocytes lead to reduction of superoxide radicals that cause erythrocytes membrane damage (Howell and Gooneratne 1987). Or may be due to high copper/ molybdenum ratio may contribute to iron deficiency anemias and possibly cause iron- storage disease. Several anemias which don't respond to iron therapy have been found to be associated with biounavailable copper, copper is required to convert iron from ferric to ferrous form so it can be utilized. Copper is also required to incorporate iron into hemoglobin molecules. High tissue copper levels can cause a relative manganese deficiency, manganese is necessary to stimulate hemoglobin formation this anemia can result from a copper- induced deficiency of manganese (Blundell et al., 2003). These result disagreed with (Tavares-Dias et al.,2002) which may be due to the different concentration and times used in the treatments and the species sensitivity to copper sulphate. Mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) showed significant decrease at 6th month of experiment in treated groups if compared with control group. The results are similar to that of **(**Carvalho and Fernandes 2006). Result disagreed with (Tavares-Dias et al., 2002) which may be due to larger erythrocyte volume caused by hypoxia situation.

Concerning our results of blood parameters as recorded in table (1) due to the effect of cobalt chloride , a highly significant increase in red blood cells count (RBCs) which more prominent in highly dose group. These results were agreed with those recorded by (Di Giulio et al., 1991,Alippi et al., 1992). The significant increase of RBCs may be attributed to cobalt acts through a mechanism believed to involve a heme containing proteins to increase erythropoietin which stimulate the production of RBCs causing polycythaemia (Di Giulio et al., 1991) , which is considered one of the toxic end points of cobalt **(**Maxwell and Salnikow 2004 and lippi et al., 2005). Or increase RBCs may be due to early decomposition of both old and newly formed erythrocytes under the action of hypoxia at higher levels of cobalt exposure, which elicits the haemopoietic effect on bone marrow (Carson et al., 1986). The significant decreases in MCHC may be attributed to that cobalt chloride may interfere with the normal physiology of RBCs (Atamanalp et al., 2002), decrease MCHC level are indicative of hypochromic

anemia. The significant decrease in Hb, PCV, MCV and MCH in group treated with high dose of cobalt especially at the end of experiment. These results agreed with Ahmad et al., (1995), Atamanalp and Yanik (2003). The decrease in Hb concentration may be attributed to the fact that oxygen carrying capacity was affected by cobalt chloride which interfere with the ability to bind Hb to oxygen during respiration (Atamanalp and Yanik 2003)**.** Or may be due to cobalt stimulate heme oxidation in many organs by inducing heme- oxygenase and causing a reduction in the levels of hemoglobin and other hemoprotein like cytochrome p450 (Elbirt and Bonkosky 1999)**.** This result disagreed with Atamanalp et al., (2002) may be due to increased erythropoiesis and Hb synthesis. The MCV reduction shows that cobalt chloride may interfere with normal physiology of RBCs (Yanik and Atamanalp 2001).

Concerning to the effect of copper sulphate on spermogram table (2) recorded a significant decrease in sperm cell count either per ml or per gm of epididmal suspension and a significant increase in the percentage of morphological abnormal spermatozoa in the examined rats as a result of dose and time of administration. These results very clear in group of high dose of copper sulphate compared with control one. These results were agreed with CCOHS (1999). The significant effect of copper in treated male rats may be attributed to the direct cytotoxic effect of copper on the tissue of testis of exposed animal to copper (CCOHS 1999). Also may be due to copper has damaging effect of spermatogonial cells specially late stage of sperm maturation (Dent 2007).

Regarding to the effect of cobalt chloride on spermgram of rats, there were significant increase in sperm abnormality and significant decrease in sperm count of treated group as shown in table (2). These results are in agreement with (Clyne et al .,2001, El betieha et al., 2004). These results may be attributed to cobalt chloride may be toxic to testicular histological structure.

Regarding to the effect of copper sulphate residues in the kidneys and liver of treated rats table (3) . The amount of copper residues were increased gradually in higher dosed group and through long time. These results agreed with those obtained by (Marta, et al., 2005, Sani, 2011). The cumulative effect of copper sulphate in liver may be attributed to direct transfere of these compound after oral adminisration from the intestine to the liver via the portal vein. Lower hepatic metabolism of copper sulphate leading to more cumulative effect in hepatic tissue with poor excretion, this showed that liver acts as a store house for toxic and heavy metals (Oguntola 2008). Or residues increased due to increased hepatic synthesis and release of ceruloplasmin (Linder 1991).

The conclusion we draw from the results is that, copper sulphate and cobalt chloride most likely have a risk on fertility. For this reason, it is necessary to be careful when using it in food as food additives.

2. REFERENCES

Abu- Zinadah ,O., Hussein, H. 2010. The potential of stem cells to correct the lost tissue mass in liver and kidney of rat after copper toxicity. Insight stem cell Res. 1(1) :1- 5.

ACGIH (American Conference of Governmental Industrial Hygienists,) Inc, 1986. Documentation of the threshold limit values and Biological exosure Indices, 5th ed., 146.

Ahmad, F., Ali, S.S., Shakoori, A.R. 1995. Sublethal effects of danitol (fenpropathrin), a synthetic pyrethroid, on fresh water chinese grass carp, ctenopharyngodon-idella. Folia. Biol. 43:151-159.

Alippi, R.M., Boyer, P., Leal, T., Barcelo, A.C., Martinez, M.P., Bozzini, C.E. 1992. Higher erythropoietin secretion in response to cobaltous chloride in post- hypoxic than in hypertransfused

polycythemic mice. Haematologica, 77: 446-449.

Ashish, B., Neeti, K., Himanshu, KH. 2012. Copper toxicity: A comprehensive study.Research Journal of Recent Science, 2:58-67.

Atamanalp. M., Yanlk, T., Halloglu, H. , Aras, M. 2002. Alterations in the haematological parameters of rainbow trout, *oncorhynchus mykiss*, exposed to cypermethrin. Tst. J. Aquacult. Bamidgeh, 54(3):99-103.

Atamanalp. M., Yanik, T. 2003. Alterations in the haematological parameters of rainbow trout, *oncorhynchus mykiss*, exposed to Mancozeb. Turk J Vet Anim Sci, 27:1213-1217.

Blundell, S., Curtin, J., Fitzgerald, D. 2003. Blue lips, coma and haemolysis. J Paediatr Child Health. 39(1): 67-8.

Carson, B.L., Ellis, H.V., McCann, J.L. 1986. Toxicology and Biological Monitoring of Metals in Humans. Lewis publishers Inc. Michigan, USA, pp. 65,71,97,133,165,297.

Carvalho, C.S. , Fernandes, M.N. 2006. Effectof temperature on copper toxicity and hematological responses in the Neotropical fish, Prochilodus scrofa at low and high PH. Aquaculture, Amsterdam, 251:109-117.

CCOHS (Canadian Centre for Occupational Health and Safety) 1999. Copper sulphate CHEMINFO record. International programme on chemical safety , ontario canada.Issue 98-2.

Clyne, N, Hofman- Bang, C., Haga, Y., Hatori, N., Marklund, S., Pehnssons, K., Wibom, R. 2001. Chronic cobalt exposure affects antioxidants and ATP production in rats myocardium Scandina- vian Journal of clinical and Laboratory Investigation, 61 (8): 609-614.

Dent, M. 2007. Strengths and limitations of using repeated dose toxicity studies on predict effects fertility. Regul toxical pharmacol 48(3): 241-258.

Di Giulio, C., Data, P.G. , Lahiri, S. 1991. Chronic cobalt causes hypertrophy of glomus cells in the rat corotid body. American Journal of physiology. 261: 102- 105.

Elbetieha, A., Al- Thani, A., Al- Thani, R., Darmani, H., Owais, W. 2004. Chronic exposure to cobaltous chloride caused adverse effects on fertility of male mice. Toxicology and applied pharmacology, 197(3) :351.

Elbirt, K.K., Bonkovsky, H.L. 1999. Heme oxygenase: recent advances in understanding its regulation and role proc. Assoc. Am. Phys. 111: 438-447.

Georgopoulos, P.G., Roy, A., Yonone-Lioy, M.J. , 2001. Environmental copper: its dynamics and human exposure issues. J. Toxicol Environ Health B, 4:341-394.

Howell, J.M., Gooneratne, S.R. 1987. The pathology of copper toxicity in animals. 53-78 in copper in Animals and Man.

Iwegbue, C.M.A. 2008. Heavy metal composition of livers and kidneys of cattle from southern Nigeria. Department of Chemistry, Delta State University, Abraka, Nigeria. Vet. Arhiv 78(5), 401-410.

Jezierska, B., Lugowska, K. ,Witeska, M. 2009. The effects of heavy metals on embryonic development of fish. Fish physiol. Biochem., 35:625-640.

Joshi, P.K., Bose, M., Harish, D. 2002. Hematological changes in blood of Clarias battrachus exposed to mercuric chloride. Ecotoxicology and Environmental Monitoring, 12:119-122.

Lahaye, D., Demedts, M., Vanden Oever, R., Roosels, D. 1984. Lung diseases among diamond polishers due to cobalt. Lancet , 1:156-7.

Linder, M.C. 1991. Nutritional Biochemistry and Metabolism with clinical Application. 2nd lange, Nor walk, ed. Plenum , Press, New York. 37: 233-236.

Lippi, G., Franchini, M., Guidi, G.G. 2005. Cobalt chloride administration in athletes. A new perspective in blood doping? Br. J. Sports Med. 39: 872-873.

Marta, M., Marta, L.A. , Jose, L.B. 2005. Copper, zinc, iron and manganese accumulation in cattle from Asturias. Biological trace elements, 109: 134-135.

Maxwell, P. ,Salnikow, K. 2004. HIF-1: an oxygen and metal responsive transcription factor. Cancer Biol. Ther. 3:29-35.

Mori, N., Hirayama, K. 2000. Long term consumption of methionine supplemented diet increase iron and lipid peroxide levels in rat liver. J. Nutr. 130: 2349-2355.

National Institute For Occupational Safety and Health (NIOSH) . 2003. The Registry of toxic effects of chemical substances Nickel(II) sulphate hexahydrate and cobalt (II) chloride hexahydrate.

Oguntola, S. 2008. National Health. Nigeria Tribune. 3:41-42.

Pesch, S., Bergmann, M. , Bostedt, H. 2006. Determination of some enzymes and macro and microelements in stallion seminal plasma and their correlations to semen quality. In Theriogenology, 66: 307-313.

Sani, U. 2011. Determination of some heavy metals concentration in the tissues of Tilapia and Cat fish. Determination of pure and industrial chemistry, Bayero university, Kano. P.M.B. Nigeria. Biochemistri, 23(2): 73-80.

Singh, M. , Singh, G. 1968. Biochemical changes in blood in cases of acute copper sulphate poisoning. J. Ind. Med. Assoc. 50:549-554.

Singh, D., Nath, K., Trivedi, S.P., Sharma, Y.K. 2008. Impact of copper on hematological profile of freshwater fish, Channa punctatus. The Journal of Environmental Biology, Lucknow, 29: 253-257.

Tavares- Dias, M., Martines, SM., Schaleh, S., Onaka, E., Quintana, C., Moraes, J. , Moraes, F. 2002. Alteracoes hematologicas, histopatologicas em pacu, Piaractus mesopotamicus, Holmberg, tratadocom culfato de cobre (cuso4), Aeta Scientiarum, Maringa, 24: 547-554.

Valsa, J., Gusani, P.H., Skanhan, K.P. , Modi, H.T. 1994. Copper in split and daily ejaculates. In the Journal of Reproductive Medicine. 39: 725-728.

Wilson, L., 2010. Copper toxicity syndrome, the center for development. J. Rheumatol. 35: 445-447.

Wook, Y., Beom, L., Sang, N., Byeongwoo, A., Jin, H., Jae, D., Young, K. , Young, L. ,Young, Y. 2004. Reproductive disorder in pubertal and adult phase of the male rats exposed to viclozolin during pubert. J. Vet. Med. Sci. 66(7): 847-853.

Yanik, T ., Atamanalp, M . 2001. Introduction to water pollution in fish farming. The publication of Agricultural College, 322, Erzurum, Turkey.

التأثير السمي لكبريتات النحاس وكلوريد الكوبلت كإضافات اعلاف على الخصوبة في ذكور الفئران البيضاء

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الملخص العربي

في هذه الدراسة تم تقييم تأثير كبريتات النحاس وكلوريد الكوبلت على الخصوبة في ذكور الفئران البيضاء حيث تم معرفة عدد الحيوانات المنوية واشكالها ومعدل التشوهات بها. هذا وقد استخدم لإجراء هذه الدراسة عدد 100 من ذكور الفئران البيضاء اعمارها حوالي اربعة اسابيع واوزانها من 175–182 جرام وقد قسمت الى خمس مجموعات متساوية اشتملت كل مجموعة على عدد عشرون فأر وتم توزيعها كالاتي: المجموعة الاولى: (المجموعة الضابطة): اشتملت على عشرون فأر لم تعطى أي ادوية واستخدمت كمجموعة ضابطة للمجموعات الاخرى. – المجموعة الثانية: تكونت من عشرون فأر تم اعطاؤها 10/1 من الجرعة نصف المميتة لكبريتات النحاس لمدة ستة أشهر. المجموعة الثالثة: تكونت من عشرون فأر تم اعطاؤها 5/1 من الجرعة نصف المميتة لكبريتات النحاس لمدة ستة أشهر. المجموعة الرابعة: تكونت من عشرون فأر تم اعطاؤها 10/1 من الجرعة نصف المميتة لكلوريد الكوبلت لمدة ستة أشهر. المجموعة الخامسة تكونت من عشرون فأر تم اعطاؤها 5/1 من الجرعة نصف المميتة لكلوريد الكوبلت لمدة ستة أشهر عن طريق الفم. وقد تم تجميع الخصية في الشهر الثاني والرابع والسادس من التجربة. وقد اسفرت النتائج تأثير كبريتات النحاس وكلوريد الكوبلت على عدد الحيوانات المنوية واشكالها حيث يقل عدد الحيوانات المنوية معنويا في كل المجموعات المعاملة خاصة المعاملة بجرعات عالية كما تظهر النتائج وجود تشوهات بالحيوانات المنوية وكانت أكثر وضوحا مع المجموعات العالية.

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