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Testicular Energy Metabolism Impairment and Dyslipidemia Induced by Cadmium Chloride in Rats: Ameliorative Effect of Polyherbal Remedies, STC30 and PurXcel.

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KEYWORDS

Testicular, metabolism, dyslipidemia, Cadmium, STC30, PurXcel, impairment.

ABSTRACT:

Introduction: Exposure to Cadmium is associated with oxidative stress. PurXcel and STC30 are polyherbal remedies rich in antioxidants. Their effects on Cadmium-induced dyslipidemia and impaired testicular energy metabolism are unknown.

Objectives: To achieve our aim, testicular energy metabolism ((lactate, pyruvate, fructose) and serum lipid profile were assayed.

Methods: Thirty five male wistar rats were randomly assigned into seven groups of five rats each, control, Cadmium-only, PurXcel-only, STC30-only, Cadmium+PurXcel, Cadmium+STC30 and Cadmium+PurXcel+STC30. The duration of daily administrations was 28 days.

Results: Testicular concentrations of fructose, pyruvate and lactate were significantly reduced in the Cadmium-only group compared with the control but which was higher in all PurXcel or STC30-treated groups whether singly or in combination with Cadmium than in the Cadmium-only group. Serum total cholesterol and triglyceride were increased in the Cadmium-only group compared with the control but lower in the PurXcel-only, STC30-only and in the Cadmium+PurXcel+STC30 than in the Cadmium-only groups. The high density lipoprotein cholesterol in the Cadmium-only group was decreased compared with the control but higher in all PurXcel or STC30-treated groups than in the Cadmium-only groups. Low density lipoprotein cholesterol was increased in the Cadmium-only group compared with the control though lower in all PurXcel or STC30-treatment groups, singly or in combination with Cadmium in the Cadmium-only group.

Conclusion: Cadmium-impaired testicular energy and lipid metabolisms are ameliorated by PurXcel or STC30, which if administered singly to normal rats have no significant effects on testicular energy or lipid metabolism.

Introduction:

Cadmium (Cd) is a soft malleable bluish white metal found especially in zinc ores, zinc by-products and to a much lesser extent, in the Cadmium mineral greenokite. It is a toxic non-essential metal that posses a health risk to both humans and animals [1]. Cadmium is naturally occurring in the environment as a pollutant derived from industrial and agricultural sources [2].

Cadmium has a wide range of applications. It is used in making of battery, plastics, paints, antirust coatings glass, fertilizers, solar panel semiconductors Led television, photocopier drums, cigarette as well as in electroplating [3,4,5], electronic and plastic recycling, waste collectors, municipal incinerators, welders and painters are frequently exposed to Cadmium [2]. It can therefore be seen that Cadmium

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exposure and its possible effects are major issues.

Exposure to Cd occurs primarily by ingestions of contaminated water sources and food as well as by inhalation. It is easily transported from soil unto plants consumed by animals and humans. Exposure occurs also by consuming plants grown in soils contaminated with Cadmium. Exposure to Cd has been associated with several detrimental effects on health [6]. Such exposures have been associated with nephropathies [7], female reproductive impairment [8], male reproductive toxicity [9,10] as well as dyslipidemia [11,12].

Dyslipidemia is an increases in total cholesterol, triglycerides, low density lipoprotein and a decreased HDL. In a cross-sectional study, exposure to Cadmium was associated with dyslipidaemia in a dose-dependent manner [11,13]. Dyslipidemia has been implicated as a major factor in cardiovascular diseases [14]. Dyslipidemia is not only a consequence of impaired glucose metabolism but also a cause of it [15]. It has also been linked with alteration in semen and testicular quality and infertility [16,17]. Dyslipidemia is connected with reduced pyruvate, lactate dehydrogenase and citrate synthase activities as well as reduction in sperm content of ATP and increase in sperm oxidative damage [16,18].

Cadmium cytotoxicity is associated with imbalances in redox status of tissues like increased malondialdehyde concentration and reduced gluuthathione peroxidase levels [19]. This is strengthened by the observed improvement in redox status in experimental animal models with Cadmium-induced toxicity treated with various antioxidant [9,10,20].

There has been growing interest and patronage in natural or polyherbal remedies as they are believed to be natural, have fewer side effects and very often within reach of the ordinary man [21,22]. These remedies which are usually enriched with antioxidants are used to treat a wide range of diseases as well as supplementing body stores of some essential ingredients [23,24]. Antioxidants play critical role in maintaining the Redox status of tissues [25]. Their patronage is increasing with all sort of claims about their efficacies, most of which have not been scientifically authenticated [20,26,27,28]. PurXcel and STC30 are examples of such polyherbal formulations.

PurXcel is a proprietary product of LivePure, Frisco, Texas, USA. It is a polyherbal product that is said to contain about 18 conplementary ingredients like glutathione. Aloe acemannan, superoxide dismutase, vitamin C, Selenium, alpha lipoic acid, turmeric, broccoli, moringa oleifera, blueberry, schisandra, grape seed extract, pomegranate and black pepper extract [29], PurXcel is claimed to be hepatoprotective, anti-aging, immune boaster, as well as improves redox status and reproductive health [29]. There is however, paucity of information on these claims scientifically.

Superlife Total Care 30 (STC30) is another polyherbal remedy, a proprietary product of Superlife World, Kualar Lumpur, Malaysia. The ingredients in STC30 include blackcuriant, juice powder (which is rich in antioxidants, anthocyanins and polyphenolic substances), bilberry extract, vitis vinifera etc [30]. This product is claimed to rejuvenate, detoxifies and helps regenerate damaged cells and tissues by activating stem cells in the body. It is also said to combat aging, supports healthy immune system and improves the redox status of the body [30]. Although most of these claims are yet to be substantiated scientifically, few studies have been done on STC30. A significant improvement in renal function impairment (urea, creatinine, glumenular filtration rate and electrolytes) and elevated serum C- Reactive protein induced by carbon tetrachloride was observed by [31,32]. In another study, improvement in liver function indices in animal model of CCl4-induced hepatocellular carcinoma was observed [33]. In their toxicological studies, [34] found the LD50 of STC30 to be greater than 5000.

From the fore-going, it may be seen that most of the beneficial health claims of STC30 and PurXcel have not been substantiated despite their wide popularity and patronage. It therefore became necessary to evaluate the possible effects of these remedies on lipid profile and testicular energy metabolism in rats following administration of Cadmium.

Materials and Methods:

Ethical approval

The approval for this study (Approval No. 256PHY2103) was issued by the Animal Research Ethics Committee of the Faculty of Basic Medical Sciences, University of Calabar Calabar Nigeria.

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Chemicals

The chemicals included PurXcel (LivePure, Frisco, Texas, USA) purchased from Puregen African Nigeria Limited, Lagos, Nigeria, Cadmium Chloride, (Sigma-Aldrich, Chemical Company, St Louis, MO, USA) and STC30 (Superlife World, Malaysia).

Acute toxicity studies

The acute toxicity studies of PurXcel and STC30 were determined using Lorke's method [35] with a follow-up using the Up-and-down method described by [36].

Laboratory animals

Thirty five male Wistar rats weighing 250 to 300 g were purchased and housed in plastic cages in the Animal House of the Department of Physiology, University of Calabar. They were given free access to drinking water and rat chow. The rats were handled in line with international guidelines.

Experimental design

The thirty five rats were randomly assigned to 7 groups of five rats each. Group 1 served as the control, group 2 was Cadmium-only group (administered with 5mg/kg of Cadmium Chloride) as used by [37] while group 3 was PurXcel-only group. Group 4 was STC30-only, group 5 was Cadmium+Purxcel, group 6 Cadmium+STC3 group while group 7 was the Cadmium+PurXcel+STC30 group. PurXcel was given at a dose of 38.4mg/kg while STC30 was administered at 132.7mg/kg. All drugs were administered daily by gavaging for 28 days The animals were weighed regularly and the amount of their drugs adjusted accordingly.

Sample collection

At the end of the experimentation period, the rats were anaesthetized and blood samples collected from them via cardiac puncture into prelabelled plain sample bottles for determination of lipid profile. They were then sacrificed and their testicles extracted for evaluation of testicular energy metabolism.

Preparation of testicular homogenate: The left testis of each rat was homogenized separately in 50mm Tris-Hcl buffer (pH 7.4) which contains 1.15% KCl to prepare 20% (15 w/v) tissue homogenate. Homogenization was carried out using Potter Elvelyen Homogenizer (BEE International, Apion Company, USA). The homogenized tissue was then centrifuged in a cool centrifuge (USCF0424AR Multipurpose Centrifuge, Guanghzhon, China) at 10000g for 10 minutes. The supernatant was then obtained for the determination of parameters.

Determination of testicular energy metabolism

Testicular fructose

This was done in testicular homogenate by colorimetric method using Fructose Assay Kits (BioAssay systems Hayward, CA, USA). The reagent systems react directly and specifically with fructose to form a coloured product whose optical density was read at 565nm with a microplate. The manufactuer's protocol was followed and the concentration of fructose calculated using the formula :

$$[\text{Fructose}] = \frac{\text{OD sample} - \text{OD } H_2O}{\text{Slope } (\mu M^{-1})} \times n\ (\mu M)$$

Where n is the dilution factor

Testicular pyruvate

This was done in testicular homogenate using pyruvate kit (BioAssay systems, Hayward, CA, USA) and following the manufacturer's protocols. The procedure involved addition of a single working reagent to 10µl of homogenate and incubating the mixture for 30 minutes at 100m temperature. The optical density was read at 570 nm.

Testicular lactate

This was done with lactate kit (BioAssay systems Hayward, CA, USA) according to manufacturer's protocol. This is based on lactate dehydrogenase-catalysed oxidation of lactate. The optical density at time zero was read at 568nm and after 20 minutes of incubation at room temperature

Serum lipid profile estimation

Total cholesterol (TC)

This was done using enzymatic colorimetric test kit method of [38] and used by [39]. In this method, the degree of cholesterol ester cleavage through catalytic hydrolysis by cholesterol esterase is achieved. The free cholesterol is then oxidized to cholestene-3-one and hydrogen peroxide in a reaction catalyzed by cholesterol oxidase. The released hydrogen peroxide combines with phenol and 4-amino-antipyrine to form a coloured quinonemine whose optical density is read at 540nm.

Triglycerides (TG)

The serum TG concentration was evaluated as described by [40] using commercially available kits.

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Triglycerides are hydrolyzed enzymatically to fatty acids and glycerol which is phosphorylated by a glycerol kinase to glycerol-3-phosphate. The final product of these reactions is a coloured quinoneinine dye and its optical density read colorimetrically at 540nm.

High density lipoprotein cholesterol (HDL-C)

This was assayed as described by [38] using commercially acquired reagents. The samples were mixed thoroughly and allowed to stand for 10 minutes in a water bath (37^0c) all at room temperature. The optical density of the precipitate/product formed from these reactions was read and HDL-c computed as:

$$\text{HDL-c} = \frac{\text{Absorbance of test}}{\text{Absorbance of standard}} \times \text{concentration of standard (2.3 mmolL}^{-1}\text{)}$$

The result was then multiplied by 3.0 dilution factor:

Very low density lipoprotein (VLDL) and low density lipoprotein (LDL)

These were computed based on Friedewald formula [41] or relationship thus:

LDL-c = TC – (HDL-c + VLDL-c)

VLDL-c (mg/dL) = serum total Triglyceride /5

Results::

Comparison of testicular energy metabolism in different experimental groups

Fructose Concentration (ng/mg protein)

The fructose concentration in the Cadmium-only group (0.50±0.16) was significantly reduced ($p<0.05$) compared with the control (1.42±0.15) but higher ($p<0.05$) in the PurXcel-only (1.64±0.31), STC30-only (1.76±0.30), Cd+PurXcel (1.12±0.40), Cadmium+STC30 (1.18±0.29) and Cd+PurXcel+STC30 (1.32±0.19) groups than in the Cadmium-only group as shown in Fig. 1.

Lactate concentration (ng/mg protein)

Testicular concentrations of lactate in the control, Cadmium-only, PurXcel-only, STC30-only, Cadmium+ PurXcel, Cadmium+STC-30 and Cadmium+PurXcel+Cadmium groups were 1.96± 0.24, 0.80±0.34, 2.02± 0.40, 2.06±0.38, 1.42±0.18, 1.38±0.28 and 1.62±0.24 respectively. Lactate concentration was significantly reduced ($p<0.05$) in the Cadmium-only group compared with the control ($p<0.05$) but increased in all STC30 or PurXcel administered groups compared with the Cadmium-only group ($p<0.05$). It was higher in the PurXcel-only and STC30-only groups than in the Cadmium+PurXcel or Cadmium+STC30 groups as shown in Fig. 2.

Pyruvate Concentration (ng/mg protein)

The concentration of pyruvate was significantly reduced ($p<0.05$) in the Cadmium-only (0.76±0.28) compared with the control (2.50±0.46), but higher in the PurXcel-only (2.44¥0.23), STC30-only (2.52±0.28), Cadmium+PurXcel (1.72±0.29), Cadmium+STC30 (1.86±0.32) and Cadmium+PurXcel+STC30 groups than in the Cadmium-only group. It was significantly lower in the Cd+STC30 and Cadmium+STC30 groups than in the PurXcel-only and STC30-only groups as shown in Fig. 3.

Comparison of serum lipid profile

Total cholestorol (mmol/l)

The total cholestorol was significantly increased ($p<0.05$) in the Cadmium-only group (1.78±0.08) compared with control (1.38±0.22) but lower ($p<0.05$) in PurXcel-only (1.30±0.16), STC30-only (1.42±0.15) and Cd+PurXcel+STC30 (1.32±0.13) groups than in the Cadmium–only group. No significant differences were found in the Cadmium+PurXcel (1.44±0.23) and Cadmium+STC30 (1.54±0.21) compared with other groups as shown in Table 1.

Triglycerides (mmol/L)

The triglyceride concentration was significantly increased ($p<0.05$) in the Cadmium-only group (1.38±0.15) compared with the control (0.80¥0.10) but lower ($p<0.05$) in the PurXcel-only (0.54±0.21), STC30-only (o.64±0.19) and Cd+PurXcel+STC30 groups than in the Cadmium-only group. There were no significant differnces between the Cadmium+PurXcel (0.62±0.19) and Cadmium+STC30 (0.72±0.15) groups as shown in Table 1.

High density lipoprotein cholesterol (mmol/L)

High density lipoprotein cholesterol was significantly decreased ($p<0.05$) in the Cadmium-only group (0.20±0.12) compared with the control (0.54±0.18) but significantly higher ($p<0.05$) in the PurXcel-only (0.78±0.11), STC30-only (0.76±0.17), Cadmium+PurXcel (0.62±0.19), Cadmium+STC30 (0.66±0.18) and Cadmium+PurXcel+STC30 (0.70±0.16) groups than in the Cadmium-only group as

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shown in Table 1.

Low density lipoprotein cholesterol (mmol/L)

Serum concentration of LDL-C in the Cadmium-only group (1.24±0.23) was significantly increased ($p<0.05$) compared with the control (0.70±0.16) but significantly lower ($p<0.05$) in the PurXcel-only (0.52±0.19), STC30-only (0.40±0.18), Cadmium+PurXcel (0.66±0.11), Cadmium+STC30 (0.72±0.15) and Cadmium+PurXcel+STC30 (0.54±0.11) groups than in the Cadmium-only group as shown in Table 1.

Very low density lipoprotein cholesterol (mmol/L)

Serum VLDL-C was significantly increased ($p<0.05$) in the Cadmium-only group (1.12±0.26) compared with control (0.36±0.11) but lower (p,0.05) in the PurXcel-only (0.24±0.09), STC30-only (0.32±0.18), Cadmium+PurXcel (6.44±0.21), Cadmium+STC30 (0.58±0.16) and Cadmium+PurXcel+STC30 (0.46± 0.19) groups than in the Cadmium-only group as shown in Table 1

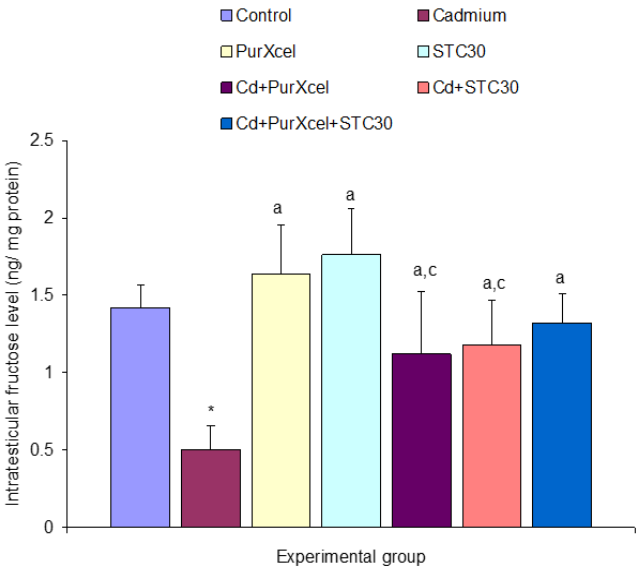

Fig. 1: Intratesticular fructose level in the different experimental groups.

Values are expressed as mean +SEM, n = 5.
* = p<0.05 vs Control
a = p<0.05 vs Cadmium
c = p<0.05 vs STC30

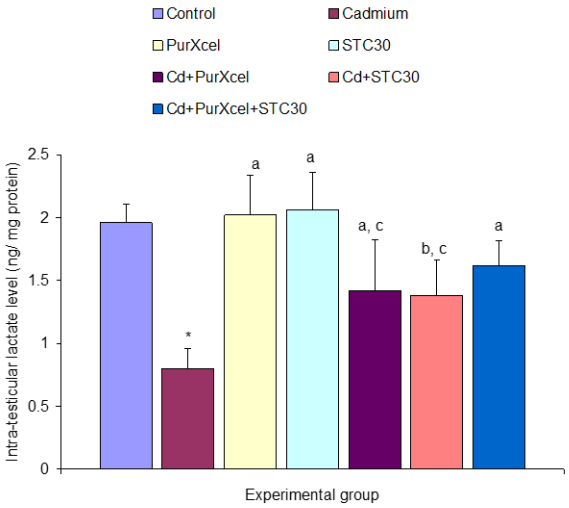

FIG. 2: Intra-testicular lactate level in the different experimental groups.

Values are expressed as mean +SEM, n = 5.
* = p<0.05 vs Control
a = p<0.05 vs Cadmium
b = p<0.05 vs PurXcel
c = p<0.05 vs STC30

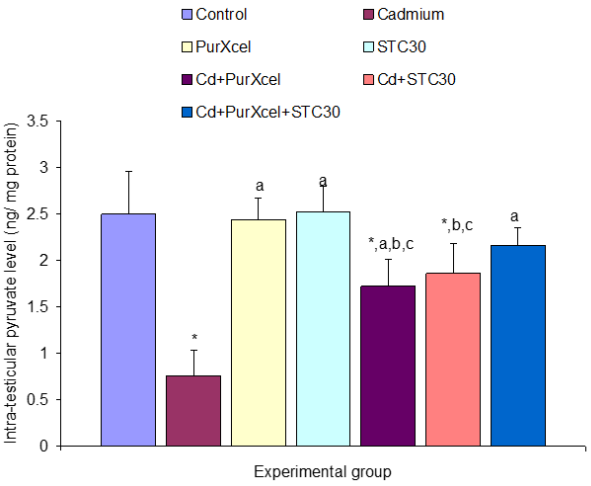

Fig. 3: Intra-testicular pyruvate level in the different experimental group.

Values are expressed as mean +SEM, n = 5.
* = p<0.05 vs Control
a = p<0.05 vs Cadmium
b = p<0.05 vs PurXcel
c = p<0.05 vs STC30

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TABLE 1: Serum lipids concentration of the different experimental groups

Variable	TC (mmol/L)	TG (mmol/L)	HDL-c (mmol/L)	LDL-c (mmol/L)	VLDL-c (mmol/L)
Control	1.38 ±0.22	0.80 ±0.10	0.54 ±0.18	0.70 ±0.16	0.36 ±0.11
Cadmium	1.78 ±0.08*	1.38 ±0.15*	0.20 ±0.12*	1.24 ±0.23*	1.12 ±0.26*
PurXcel	1.30 ±0.16[a]	0.54 ±0.21[a]	0.78 ±0.11[a]	0.52 ±0.19[a]	0.24 ±0.09[a]
STC30	1.42 ±0.15[a]	0.64 ±0.19[a]	0.76 ±0.17[a]	0.40 ±0.16[a]	0.32 ±0.18[a]
Cd+PurXcel	1.44 ±0.23	0.62 ±0.19[a]	0.62 ±0.19[a]	0.66 ±0.11[a]	0.44 ±0.21[a]
Cd+STC30	1.54 ±0.21	0.72 ±0.15[a]	0.66 ±0.18[a]	0.72 ±0.15[a]	0.58 ±0.16[a]
Cd+PurXcel+STC30	1.32 ±0.13[a]	0.52 ±0.19[a]	0.70 ±0.16[a]	0.54 ±0.11[a]	0.46 ±0.19[a]

Values are expressed as mean ±SEM, n = 5.
* = $p<0.05$ vs Control
a = $p<0.05$ vs Cadmium

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Discussion:

There is an increasing preparation and patronage of polyherbal remedies including STC30 and PurXcel with many, but scientifically unsubstantiated claims. In this study, we evaluated the effects of PurXcel and STC30 on testicular energy metabolism, and serum lipid profile in male wistar rats exposed to Cadmium.

The decrease in the concentration of fructose in the Cadmium-only rats compared with the control noted in this study suggests that Cadmium impairs fructose availability to testicular cells by yet to be identified mechanisms. This could impair sperm function as fructose is necessary for testicular energy need [42]. This was however prevented in all the groups administered PurXcel, STC30 or both. This might have been due to possible antioxidant effect of PurXcel and STC30. One of the mechanisms of the cytotoxicity from Cadmium is oxidative stress [10]. Antioxidants have been known to ameliorate oxidative stress damage to tissues [43], Optimal energy metabolism is essential for the maintenance of spermatogenesis.

Lactate concentration in testicular tissue was significantly reduced in the Cadmium-only group compared with the control which suggests that Cadmium impairs testicular energy metabolism which could in part be due to interference with processes that affect normal availability of lactate to testicular cells. Energy metabolism in testis exhibits some specificity in that lactate is the central energy metabolite used by germ cells [44]. The significantly higher concentration of lactate in all groups where Cadmium was co-administered with STC30, PurXcel or both compared with the Cadmium-only group suggests the ability of these polyherbals to interfere with the mechanism by

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which Cadmium causes the impaired lactate metabolism.

The observed reduction in testicular pyruvate in the Cadmium-only group compared with the control was prevented in all PurXcel or STC30-treated groups. It was however lower in the Cadmium-administered groups treated with either PurXcel or STC30 than in normal rats given PurXcel or STC30. This suggests that STC30 and PurXcel administered alone or in combination ameliorate the pyruvate-reducing effect of Cadmium in the testis. Pyruvate plays a key role in testicular energy metabolism [45].

The increase in total cholesterol observed in the Cadmium-only administered group compared with the control is similar to the findings by [11]. The synergistic effect of STC30 and PurXcel to ameliorate Cadmium-induced hypercholesterolaemia is seen in the Cadmium-administered group treated with both PurXcel and STC30.

The observed increase in triglyceride concentration in the Cadmium-only group compared with the control is similar to the findings by [11]. When administered alone, neither STC30 nor PurXcel could prevent the Cadmium-induced hypertriglyceridemia. The reduction in triglyceride concentration in the Cadmium+STC30+PurXcel group compared with the Cadmium-only, Cadmium+PurXcel and Cadmium+STC30 points to the synergistic effect of STC30 and PurXcel to prevent Cadmium-induced hypertriglyceridemia.

The Cadmium-induced decrease in HDL-c concentration and the increases in the concentration of LDH and VLDL-C seen in this study are comparable to findings reported by [11,26]. The coadministration of PurXcel or STC30 with Cadmium prevented these alterations in lipid profile. Dyslipidemia has negative impacts on cardiovascular function, testicular parameters and energy metabolism [26,46,47].

Conclusion

PurXcel or STC30 ameliorate Cadmium-induced derangement in testicular energy metabolism and dyslipidemia but have no significant effect on testicular metabolism and serum lipid profile if given to normal rats.

References

1. Marrow, H. Cadmium and Cadmium alloys. Kirk-Othmar Encyclopedia of Chemical Technology. John Wiley and Sons, New Jersey, 2005.
2. Genchi G., Sinicroppi M.S, Lauria G., Carosi A. and Catalano A. 2020. The effects of Cadmium toxicity. Int J Environ Res and Publ Health, 17(11):3782. Doi:10.3390/ijerph1711378
3. Scoullos M.J., Vonkeman G.H., Thorten L. and Mackuch Z. Mercury, Cadmium, Lead: Handbook for Sustainable Heavy Metals Policy and Regulation. Springer. New York, 2001.
4. Unsal V., Dalkiran T, Cicek M. 2020. The role of natural antioxidants against reactive oxygen species produced by Cadmium toxicity: a review. Adv Pharmaceut Bull. 10(2)184-202.
5. Lee C. and Hsi C.S. 2002. Recycling of scrap cathode ray tubes. Environ SciTechnol. 36(1)69-75. Doi:10:1021/es010517q
6. Godt J., Scheidig F., Grosse-Siestrup C., Esche V., Brandenburg P., Reich A., Groneberg D.A. 2006. The toxicity of Cadmium and resulting hazards for human health. J. Occup Med Toxicol. 1:22 Doi:10.1186/1745-6673-1-22
7. Jarup L., Berglund M., Elinder C.G., Nordberg G. and Vahtwr M. 1998. Health effects of Cadmium exposure -a review of literature and a risk estimate. Scand J Work, Environ Health, 24(1)1-51
8. Plasek M. and Laskey J.W. 1999. Effects of in vitro Cadmium exposure on ovarian steroidogenesis in rats. J Applied Toxicol. 19(3)211-217
9. El-Neweshy M.S., El- Madawy Z.K., El-Sayed Y.S. 2012. Therapeutic effect of date palm (Phoenix dactylifera L) pollen extract on Cadmium-induced testicular toxicity. Andrologia. 1-10 Doi: 10.1111/and.12025
10. Abarikwu S.O., Obafemi P.D., Lawrence C.J., Wekere F.C., Ochulor A.C. and Barikuma A.M. 2016. Ratin, an antioxidant flavonoid induces gluthathione peroxidase activities to protect against ethanol effect in Cadmium-induced oxidative stress in the testis of adult rats. Andrologia. 49(7).
11. Zhou Z., Lu Y., Pi H., Gao P., Li M., Zhang I., Pei L., Moi X., Liu L., Zhoa Q., Qin Q., Chen Y., Jiang Y., Zhang F. and Yu Z. 2016. Cadmium exposure is associated with the prevalence of dyslipidemia. Cell Physiol Biochem40:633-643
12. Gu J., Kong A., Guo C., Liu J., Li K., Ren Z.,

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(5), 689-697 | ISSN:2251-6727

Zhou Y., Tanh M. and Shi H. 2022. Cadmium perturbed lipid profile and induced liver dysfunction in mice through phosphotidylcholine remodelling and promoting arachidonic acid synthesis and metabolism. Endocrinol Environ Safety, 247:114252

13. Tangvarasitichai S., Niyomtam S., Pringmuangkaew P., Nunthawarasilp P. 2015. Dyslipidemia in the elevated cadmium exposure population. Int J Toxicol Pharmacoll Res 7(2): 92-98. www.researchgets.net.
14. Hedayantnia Asadi Z., Zane-Feyzabadi R., Yaghooti-Khorasani M., Ghazizadeh H., Ghaffarian-Zirak R., Nosrati-Tinkani A., Mohamadi-Bajgiran M., Rohban M., Sadabadi F., Rahimi H., Ghalandari M., Ghaffari M., Yousefi A., Pouresmaeili E., Besharatlou M., Moohebati M., Ferns G.A., Esmaily H., and Ghayour-Mobarhan M. 2020. Dyslipidemia and cardiovascular disease risk among the MASHAD study population. Lipids in Health and Dis 19(42). www.link.srpinger.com
15. Parhofer K.G. 2015. Interaction between glucose and lipid metabolism: More than diabetic dyslipidemia. Diabetes and Metabolism J. 39(5): 353-362. Doi.10.4093/dmj.2015.39.
16. Ferramosca A., Conte A., Moscatelli N., Zara V. 2016. A high-fat diet negatively affects rats sperm mitochondrial respiratory. Andrology 4(3): 520-525. https://doi.org/10.1111/andr.12182.
17. Semir B.A. 2007. Effect of fixed oil of nigella sativa on male fertility in normal and hyperlipidemic rats. Int J Pharmacol 3(1): 27-33.
18. Ergun A., Kose S K., Aydos K., Ata A. and Avci A. 2007. Correlation of seminal parameters with serum lipid profile and sex hormones. J Reproductive Systems, 53(1): 23-25.
19. El-Demerdash F.M., Yousef M.I., Kedwany F.S, Baghdadi H.H. 2004. Cadmium-induced changes in lipid peroxidation, blood hematology, biochemicals parameters and semen quality of male rats: protective role of vitamin E and beta carotene. Food Chem Technol, 42(10):1563-1571
20. Olaniyan O.T., Ojewale A.O., Eweoya O.O., Adedoyin A.A., Adesanya O.A., Adeoye A.O., Okeniran O.S. 2021. Modulatory role of vitamin E on proton pump (ATPase) activity of Cadmium Chloride-induced testicular damage in Wistar rats. BioMed Res Int. htpps://doi.org/10.1155/2021/4615384
21. Ogbonnia S.O., Nkemehule E.E., Anyika E N. 2009. Evaluation of acute and subchronic toxicity of starchyarpheta angustifolia (mill) vahl (fam. Verbanaceae) extract in animals. J Biotech. 8:1793-1799.
22. Ekor M. 2004. The growing use of herbal medicines: Issues related to adverse reactions and challenges in monitoring safety. Frontiers in Pharmacoogy, 4:77. Doi.3389/fphar.2013.00177.
23. Lambardo F., Sansone A., Ramannel F., Paoli D., Loredana D., Andrea L. 2011. The role of antioxidants therapy in the treatment of male infertility: an overview. Asian Journal of Andrology.13(5)690-697
24. Zhai Q., Narbad A. and Chen W. 2015. Dietary strategies for the treatment of Cadmium and Lead toxicity. Nutrients. 7(1)552-571
25. Aribo E.O, Uquetan S.U, Philip A.E and Uduak A.O. 2024. Ameliorative effect of Quercetin and Omega-3 fatty acids on hematological and liver function impairment induced by Mosquito coils smoke in male Wistar rats. Nigerian journal of Parasitology 45(1)126-134
26. Kafuor G., Abruguah A.A., Audu R., Moah J. 2016. Patronage and perceived efficacy of herbal anti-typhoid preparations and antisalmonella activity of a herbal preparation used in Ghana. J Applied Pharmaceut Sci 6(3): 001-007. Doi: 107324/JAPs.2011.60301
27. World Health Organization. WHO global atlas of traditional, complementary and alternative medicine. Eds. Bodeker G., Burford G., Grundy C., Ong C.K., Bodeker G., Burford G. and Shein K. 2005. World Health Organization, Geneva. www.who.int.
28. Rana S., Badola A. and Agarwal B. 2022. Polyherbal formulations, New emerging technology in herbal rememdies. International J Adv Eng Magt. 4(9): 728-732. www.ijaem.net.
29. Life Pure. www.lifepure.com
30. Super Life World. www.superlifeworld.com
31. Ekpo G.I and Johnson J.T. 2021[a]. Effects of Ganoderma lucidum, astaxanthin, Liv, STC30 and 52HB on Renal function parameters of Animal Model with CCl4-induced hepatocellular carcinoma. J Adv Med Medical Res, 33(31): 175-

182.

32. Ekpo G.I. and Johnson J.T. 2021[b]. Effect of ganoderma lucidum, astaxanthin, Liv, 52HB and STC30 on CRP concentrations of animal model with CCl4-induced hepatocellular carcinoma. Annals Pharma Res. 9(2): 411-416. Doi 1033425/2689-1050.1022.
33. Johnson J.T., Modo and E.U. 2024. Effect of Liv, 52HB ganoderma lucidum, STC30 and Astaxanthin on serum TNF and liver function indcies following CCl4-induced hepatocelloar carcinoma in albino rats. Achieves Clin Res Studies 2(1): 25-36. www.journalserpublications.com.
34. Erhirhie O.E., Okafor N.J., Nwafor C.M., Agaegbo O.C. and Akunne T.H. 2023. Toxicological evaluation of a popular polyherbal remedy: STC30 in wistar rats. Iranian J Toxicol. 17(3):1-9.
35. Lorke D. 1983 A new approach to practical acute toxicity testing. Archives of Toxicol. 54:275-287
36. Erhirhie E.O., Ihekwerem C.P., Ilodigwe E.E. 2018. Advances in acute toxicity testing: strength, weakness and regulatory acceptance. InterdiscToxicol. 11(1)5-12
37. Da- Costa R., Botana D., Pinero S., Proverbio F., Marin R. 2016. Cadmium inhibits motility, activities of plasma membrane Ca^{2+} - ATPase and axodemal ATPase of human spermatozoa. Andrologia 48(4):464-9. Doi.10.9734/jammr/2021/v3312131146.
38. Siedel J, Hagele E.O., Ziegenhom J., Wahlefeld A.W. 1983. Reagent for the enzymatic determination of serum total cholesterol with improved lipolytic efficiency Clin Chem 29(6) 1075-80.
39. Nku C.O, Ikpi D.E, Nna V.U and Agiande G.U 2014. Altered serum lipid profile in albino wistar rats following the consumption of cola nitida rubra (kola nut). Australian J Basic Applied Sci 8 (13) 82-89.
40. Hegele R. Lipoprotein and lipid metabolism: in Emery and Rimoin's Principles and Practice of Medical Genetics. eds Rimon D, Pyertilz R and Korf B. Elsevier Ltd, New York, 2013. http://doi.org/10.1080/01485010600888961
41. Friedewald W.T., Levy R.I and Fredrickson D.S 1972. Estimation of the concentration of low density lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge. Clin Chem 18(6)499-502
42. Van de Hoek, M., Richard J.P and de Graaf S. 2022. Motility assessment of ram spermatozoa. Biology (Basel). 11(12): 1715. Doi:w.3390/biology11/21715.
43. Aribo E.O., Udokang N.E, Sunday V.E and Urom S.E. 2023, Selenium and Omega-3 fatty acids ameliorate HAART-induced Reproductive Impairment in Male Wistar Rats. Nigerian Journal of Physiological Sciences. 38(1)29-35. https://doi.org/10.54548/Njps.v38i1.6
44. Oliveira P.H., Alves M.G., Rate L., Silva J., Sa R., Barros A., Sousa M., Carvalho R.A., Cavaco J.E and Sacorro S. 2011. Influence of S. alpha dehydratestosterone and 17-beta-estradoil human sertole cells metabolism. Int J Andrology. 34:612-620.
45. Girgis S.M, el-Rahman Y., Awad H., Elsa I., Younan N., Mittawy B. and El-Sale Q.A. 1981. Lactate and pyruvate levels in the testicular vein of sub-fertile males with varicocele as test for the theory of underlying hypoxia. Andrologia, 13:1): 16-19.
46. Samarghandian S., Azini-Nezhad M., Shabestani M.M., Azadi F.J., Farkhondeh T. and Bafandeh F. 2015. Effect of chronic exposure to cadmium on serum lipid, lipoprotein and oxidative stress indices in male rats. Interdisc Toxicol 8(3): 151-154. Doi:w.1515/intox-2015-0023
47. Pappas N. and Rehman A. Dyslipidemia. Stat Pearls. Treasure Island, 2023. http://www.ncbi.mil.nih.com