Evaluating the Efficiency of Yohimbe, Horny goat weed and Maca Powder against Testicular Damage Induced by Cadmium Chloride in Male Rats

and

BasmaR.Khateib
Department of Nutrition and Food Science, Faculty of Home Economics , Menoufia University, Shebin El-kom , Egypt
Basmaelkhateeb9@gmail.com

LamiaaA.Diab
Department of Nutrition and Food Science, Faculty of Home Economics , Menoufia University, Shebin El-kom , Egypt
lamiadiab2017@gmail.com

Abstract :

The purpose of this study is to determine the effectiveness of some plants against testicular damage caused by cadmium chloride in male rats. Thirty-six adult male albino rats weighing 150 ± 20 g were split into two major groups at random. The first main group consisted of six rats and was considered as negative control group, as they were fed on basal diet only. The second main group (30 rats) received an intra-peritoneal injection of two milligrams of cadmium chloride per kilogram of body weight to injure their testicles. Five groups were then created from this second main group, each containing six rats. One of the five groups was designated as a positive control group, while the other four groups were fed on yohimbe, horny goat weed, maca powder and their mixture at 5% of the diet for 28 days, respectively. The testes were extracted for histopathological examination and evaluation of antioxidant enzyme activity. The findings indicated that, when compared to the positive control group, consuming 5% of yohimbe, horny goat weed, maca powder and their mixture for 28 days led to significant increases in the levels of the serum sex hormones (luteinizing hormone (LH), testosterone (T) and follicle-stimulating hormone (FSH)), in addition to increasing the activity of antioxidant enzymes in testicular tissue. However, there were significant decreases in the indicators for kidney and liver function, lipid profiles and serum glucose level. It can be recommended that the consumption of yohimbe , horny goat weed and maca in the diet has anti-testicular toxicity and antioxidant effects that play significant safer role in fertility and inhibit of complications .

Key words: *Fertility, Medicinal plants, Oxidative stress, Experimental animals and Masculinity*

Introduction :

Infertility is the incapacity of a couple to conceive after a year without the use of contraceptive measures **(Ho *et al.*, 2020)**. According to **Gerrits *et al.*, (2017),** 15% of women who are of reproductive age are infertile.Worldwide, infertility is predicted to affect 10% of people , 15% of couples, 13% of women and 10% of men **(De *et al.*, 2020 and Doryanizadeh *et al.*, 2021)** . For the majority of infertile people, infertility impacts not just their health but also every aspect of their personal and social lives. Anxiety, depression, and stress are psychological issues that infertile couples are more likely to experience. These issues can lead to marital misery, social dysfunction (social exclusion, stigma and feelings of failure), and a lower quality of life **(Rooney and Domar, 2018).**

Numerous positive findings support the use of dietary supplements to increase the likelihood of conception in males who are sub fertile. An effective substitute treatment for male infertility or subfertility is nutritional therapy. Unlike other advanced invasive treatments, these are affordable and simple to apply **(Zafar *et al.*, 2023).** Male infertility may be prevented or treated by increasing dietary nutrients according to observations by **Almujaydil, (2023)**. It is crucial to determine which food components may affect a man's ability to become fertile **(Pecora *et al.*, 2023).**

Pausinystalia yohimbe is a commonly used medicinal plant with aphrodisiac properties **(Okwakpam *et al.*, 2023)**. Up to 6% of the total alkaloids in authentic yohimbe bark, of which 10%–15% is yohimbine, may be present. According to **Zanolari *et al.*, (2003)**, corynantheidine, beta-yohimbine, pseudoyohimbine, rauwolscine, coryanthine, and allo-yohimbine are other minor indole alkaloids. Yohimbine hydrochloride is primarily prescribed for the treatment of male impotence. Its α2-adrenergic receptor antagonist action is responsible for several of its effects, including elevated blood pressure, heart rate, norepinephrine levels, and central sympathetic outflow. Yohimbine raises norepinephrine release, which makes blood pressure regulation in patients taking diuretics and antihypertensives unsatisfactory **(Jabir *et al.*, 2022)**.

Various herb species belonging to the genus *Epimedium* are referred to as "horny goat weed". It is a dried aerial part. The species used as a dietary supplement is *Epimedium grandiflorum*. It is pungent and sweet in flavor **(Shi *et al.*, 2022 and Salinas-Arellano *et al.*, 2023)**. Several phytochemical components, including alkaloids, flavonoids, glycosides, saponins, tannins and triterpenoids, were investigated qualitatively in the hydroethanolic extract of *E. grandiflorum* leaves.

Because flavonoids and phenolic compounds are their main secondary metabolites, their large quantities may have contributed to the good antioxidant activities shown by their scavenging capability. Gallic acid, catechin, ferulic acid, sinapic acid, caffeic acid, and chlorogenic acid are among the several phenolic chemicals that may be in charge of horny goat weed significant antioxidant activity **(Munir *et al.*, 2020)**.

Because of its pro-fertility properties, horny goat weed is known to improve spermatogenesis and raise testosterone levels **(Erasmus and Leisegang, 2021)**. The primary flavonoid active component in horny goat weed is icaridin, also known as Ica **(Seyedi *et al.*, 2023).** The biological activities of horny goat weed are multifaceted and include antirheumatic, antioxidant, and anticancer properties. According to earlier research, leaf flavonoids, particularly Ica, are responsible for the majority of these therapeutic benefits **(Yu *et al.*, 2023).**

The health benefits of maca *(Lepidium meyenii Walpers)* have made it a widely used practical plant food. It is a nutrient-rich, tasty, useful plant **(Wang and Zhu, 2019)**. Maca extracts have been shown to exhibit a variety of biological characteristics, such as immunomodulatory, anti-inflammatory, and antidepressant effects. Maca extracts include glucosinolates, alkaloids, polysaccharides, flavonoids, fatty acids, and macamides, among other chemical compounds that have already been found **(Carvalho *et al.*, 2023)**.

Macamides are a unique class of chemicals found only in maca extracts, and they are primarily responsible for the extracts' pharmacological qualities. There are currently 32 known macamides, which are made up of fatty acids and benzylamine. Macamides have demonstrated biological properties such as antifatigue, antitumoral, and neuroprotective effects **(Zhu *et al.*,2020)** As a result, maca and its separated components, known as macamides, have the potential to be used as therapeutic targets to treat a range of illnesses **(Minich *et al.*,2024).**

Maca may enhance human sexual function and boost sperm count and motility. Maca has been shown to have a number of benefits, including reducing the vacuolation of spermatogenic tubules and testicular lesions, encouraging spermatogenic epithelium recovery, preventing stromal cell proliferation, considerably raising serum testosterone levels, and enhancing sperm quantity and quality **(Zhou *et al.*, 2023).**

Therefore, this study was carried out to investigate and compare the possible modifying effects of yohimbe , horny goat weed and maca powder against cadmium chloride induced testicular damage in male rats

Material and methods:

Rats: The Medical Insects Research Institute, Doki, Cairo, Egypt, provided us with 36 adult male albino rats weighing 150 ± 20 g. Menoufia University's Institutional Animal Care and Use Committee (IACUC) granted ethical approval for this investigation (**Reg. No., MUFHE /F/NFS/4/24).**

Plants used: El-Misryia Company for Trading Herbs and Medical Plants (Haraz), Bab ElKhalk, Cairo, Egypt is the source purchase of both dried yohimbe, horny goat weed and maca powders. The Menoufia University, Shebin El-Kom, Egypt's Agricultural Plant Department conducted taxonomic confirmation on powdered yohimbe, horny goat weed and maca**.**

Chemicals: Sigma Chemical Company, Cairo, Egypt, was the supplier of cadmium chloride and chemical kits.

Diet : The basal diet prepared according to **Reeves *et al*., (1993)**. While the salt mixture used was prepared in accordance with **Hegsted *et al*., (1941)**, the vitamin mixture component utilized was that advised by **Campbell (1963)**. Basal diet(casein, cellulose, vitamins and minerals) were purchased from the El-Gomhoriya Company for Trading Drugs, Chemicals, and Medical Instruments.

Sterility induction: Thirty male albino rats in good health received intraperitoneal injections of cadmium chloride ($CdCl_2$) at a dose of two milligrams per kilogram BW. Six rats in the negative control group received the same volume of 0.9% saline intraperitoneal injections (ip) **(Kini *et al*., 2009)**. To be sure that sterility markers were developing, the testosterone level was measured both before and 72 hours after the $CdCl_2$ injection**.**

Experiment design: Following the introduction of 36 adult male albinos, they were kept in normal, healthy conditions and separately housed in wire cages in a room kept at $25 \pm 2\ ^0$C. Prior to the experiment, all rats were given a basic diet for one week in order to allow them to become acclimated. Thirty-six adult male albino rats were split into two major groups at random. The first main group consisted of six rats and was considered as negative control group, as they were fed on basal diet only. The second main group (30 rats) received an injection of two milligrams of cadmium chloride per kilogram of body weight to injure their testicles. Five groups were then created from this second main group, each containing six rats. One of the five groups was designated as a positive control

group, while the other four groups were fed on yohimbe, horny goat weed, maca powder and their mixture at 5% of the diet, respectively.

Rats were starved for an entire night and given diethyl ether anesthesia at the conclusion of the 28 -day experiment. Glass centrifuge tubes that were dry and clean were used to collect blood samples. The serum was separated using centrifugation for 15 minutes at room temperature and 4000 rpm (**Schermer , 1967)**. The serum was meticulously extracted and then placed into sterile, noise-free polypropylene tubes, which were then frozen at -20°C awaiting further examination. To check for testicular tissue lipid peroxidation and antioxidant enzymes, the right testis was excised. The left testis was preserved in 10% formalin solution for histopathological analysis.

Biochemical analysis:

Methods described by **Tietz and Berger (1976), Henry (1974)** and **Moss (1982)** were used to estimate alkaline phosphatase (ALP), aspartate aminotransferase (AST) and alanine aminotransferase (ALT). Serum creatinine, urea and uric acid were measured using the techniques described by **Schirmeister (1964), Patton and Crouch (1977)** and **While *et al.*, (1970)**. Serum high-density lipoprotein cholesterol (HDL-c), triglycerides (T.G.) and cholesterol were measured in accordance with **Fossati and Principe (1982), Richmond (1973),** and **Cc (1974),** respectively. Serum low density lipoprotein cholesterol (LDL-c) as mg/dl was calculated by **Castelli *et al.*, (1977).**

LDL Concentration (mg/dl) = Total Cholesterol - (HDL + VLDL)

According to **Lee and Nieman (1996),** serum very low density lipoprotein cholesterol (VLDLc) was measured as

VLDL-C (mg/dl) =TG/5

Catalase (CAT), Superoxide dismutase (SOD) were assessed in testicular tissue in accordance with **Aebi (1984), Masayasu and Hiroshi (1979)** in that order. Malonaldehyde (MDA) was determined according to **Ohkawa *et al.*, (1979).** The method used to assess serum testosterone (T) was by **McCann and Kirkish (1985)**. Serum levels of luteinizing hormone (LH) and follicle stimulating hormone (FSH) were determined in accordance with **Ballester *et al.*, (2004)**.

Histopathological examination :

The testicular specimens were cut, cleaned, and dried in increasing alcohol concentrations according to **Carleton (1978),** these specimens were cleaned in

xylene, embedded in paraffin, sectioned at a thickness of 4-6 microns, and stained with hematoxylin and eosin (HandE). They were then studied under a microscope.

Statistical Analysis :

A one-way ANOVA computer program was used to statistically evaluate the data. The findings are shown as mean ± SD. Treatment differences were deemed significant when they reached the P value of 0.05 or higher **(Steel and Torrie, 1960)**.

Results and discussion:

Table (1): Effect of yohimbe, maca, horny goat weed and their mixture on sexual organs weight in rats with testicular damage

Groups	Prostate weight (g /100 g BW)	Vesicle weight (g /100 g BW)	Testes weight (g /100 g BW)
(G1):Control negative	$0.51^{a} \pm 0.10$	$1.83^{a} \pm 0.10$	$1.86^{a} \pm 0.15$
(G2):Control positive	$0.21^{a} \pm 0.10$	$1.33^{b} \pm 0.20$	$1.53^{b} \pm 0.12$
(G3) : Yohimbe (5% of diet)	$0.46^{a} \pm 0.15$	$1.65^{ab} \pm 0.14$	$1.7^{ab} \pm 0.10$
(G4) : Maca (5% of diet)	$0.43^{a} \pm 0.12$	$1.57^{ab} \pm 0.13$	$1.63^{ab} \pm 0.15$
(G5): Horny goat weed (5% of diet)	$0.32^{a} \pm 0.17$	$1.39^{b} \pm 0.2$	$1.56^{ab} \pm 0.06$
(G6): Mixture (5% of diet)	$0.48^{a} \pm 0.37$	$1.78^{a} \pm 0.10$	$1.80^{ab} \pm 1.0$
LSD	0.340	0.276	0.214

Each value is expressed as mean ± SD. Means under the same column with different superscript letters are significantly different (p≤ 0.05).

Data in Table (1) show that there is a significant decrease in the weight of testes, prostate, and vesicle in the group with infertility caused by cadmium chloride. These results are consistent with **Bhardwaj *et al.*, (2024)**, they reported that cadmium has a tendency to build up and have harmful effects on a variety of body organs, including the liver, kidney, testicle and ovary in both people and animals. However, upon treatment with yohimbe, maca, horny goat weed and their mixture, there was an improvement in the weight of the aforementioned organs. The best results were recorded for the mixture group. Although **Ajonuma *et al.*, (2017)** examined the effects of yohimbe on sperm and reproductive organs in rats, but they found no appreciable changes in the relative organs weight. The improving effect of yohimbe, maca, and horny goat weed may be due to their rich content of antioxidants, especially ellagic acid, which is well-known for its ability to improve testicular, epididymal, seminal vesicle, and prostate weight reductions as well as epididymal sperm motility and concentration, which can be brought on by certain drugs like cisplatin **(Türk *et al.*, 2008).**

Table (2): Effect of yohimbe, maca, horny goat weed and their mixture on liver function markers in rats with testicular damage

Groups	ALP (U/L)	AST (U/L)	ALT (U/L)
(G1):Control negative	193.70 ± _2.10	70.36^{f} ± 1.58	17.20^{f} ± 1.05
(G2):Control positive	262.63^{a} ± 3.19	117.90^{a} ± 2.1	$36..93^{a}$ ± 1.15
(G3) :Yohimbe (5% of diet)	217.10^{d} ± 2.57	90.96^{c} ± 1.76	23.63^{d} ± 1. 40
(G4) : Maca (5% of diet)	241.43^{c} ± 1.71	82.93^{d} ± 2.31	28.46^{c} ± 1.65
(G5): Horny goat weed (5% of diet)	252^{b} ± 1.95	110.53^{b}± 1.62	33.46^{b} ± 2.08
(G6): Mixture (5% of diet)	197.76^{e} ± 2.47	77.90^{e} ± 2. 1	20.13^{e} ± 1.20
LSD	4.145	3.438	2.612

Each value is expressed as mean ± SD. Means under the same column with different superscript letters are significantly different (p≤ 0.05). ALP: Alkaline phosphatase; AST: Aspartate transaminase; ALT: Alanine aminotransferase.

Data in Table (2) show the effect of yohimbe, maca, horny goat weed and their mixture on liver function markers in rats with testicular damage. It is noted that there is an increase in liver enzymes in rats with poor fertility compared to the healthy group. The accumulation of cadmium in the liver and kidney has been linked to poisoning. The development of oxidative stress is the primary potentially harmful process. In addition to increasing the liver's generation of free radicals, $CdCl_2$ disrupts the body's defense system against oxidative stress. Rat liver enzyme levels can become unbalanced as a result of exposure to $CdCl_2$ **(Goodarzi *et al.*, 2020** and **Chen *et al.*, 2023)**. The oxidation state in which Cd might replace zinc in metallothionein, preventing it from functioning as a free radical scavenger inside the cell, is one potential cause of hepatotoxicity **(Hasan *et al.*, 2019).**

However, treatment with yohimbe, maca, horny goat weed, and their mixture, caused anoticeable improvement in liver enzymes, and the mixture group recorded the best results. yohimbine therapy considerably reduced inflammation and fibrosis by decreasing differentiation, oxidative stress, and collagen deposition.These findings could provide support for the suggestion that yohimbine is a promising lead chemical for liver fibrosis **(Sharma *et al.*, 2024).**

Also, previous studies have also confirmed the effective role that maca plays in improving fertility levels, **Ybañez-Julca *et al.*, (2022)** confirmed that by lowering liver levels of ALT and AST in a dose dependent way, maca therapy reduced MDA levels in erythrocytes, the brain, and the liver, thus mitigating the oxidative stress caused by acrylamide. It is likely that carbolines, alkamides, fatty acids, and macamides contribute to their antioxidant defense.

In the same context, the results in the table showed positive effects of the horny goat plant, which is completely consistent with **Jin *et al.*, (2005) and Munir *et al.*, (2020),** they demonstrated that the treatment of various doses of horny goat weed following CCl_4 intoxication in albino male rats significantly restored the selected parameters, such as renal profiles and liver enzymes. Horney goat weed scavenges the free radicals that CCl_4 produces, hence having a hepatoprotective effect. The existence of many phenolic compounds and functional groups is what causes this action.

Table (3): Effect of yohimbe, maca, horny goat weed and their mixture on kidney function markers in rats with testicular damage

Groups	Urea (mg /dl)	Uric acid (mg /dl)	Creatinine (mg /dl)
(G1):Control negative	$35.2^{e} \pm 0.9$	$1.06^{d} \pm 0.152$	$0.51^{c} \pm 0.072$
(G2):Control positive	$55.83^{a} \pm 2.02$	$2.83^{a} \pm 0.305$	$0.88^{a} \pm 0.077$
(G3) : Yohimbe (5% of diet)	$40.76^{d} \pm 1.17$	$1.76^{bc} \pm 0.208$	$0.66^{bc} \pm 0.026$
(G4) : Maca (5% of diet)	$51.96^{b} \pm 1.85$	$2.63^{a} \pm 0.305$	$0.77^{ab} \pm 0.144$
(G5): Horny goat weed (5% of diet)	$44.2^{c} \pm 1.57$	$2.1^{b} \pm 0.2$	$0.73^{ab} \pm 0.110$
(G6): Mixture (5% of diet)	$37.26^{e} \pm 1.10$	$1.36^{cd} \pm 0.152$	$0.53^{c} \pm 0.015$
LSD	2.659	0.408	0.154

Each value is expressed as mean ± SD. Means under the same column with different superscript letters are significantly different (p≤ 0.05).

Data in Table 3 show the effect of yohimbe, maca, horny goat weed and their mixture on kidney function markers in rats with testicular damage. It is observed that the value of kidney enzymes (urea, creatinine and uric acid) increased in the group affected by impaired fertility due to cadmium chloride, compared to the healthy group.

These results are consistent with **Farag *et al.*, (2023)** who reported that cadmium induces oxidative stress in hepatic and renal cells through the up-regulation of lipid peroxidation, which raises IgG levels as a protective innate immune response and triggers the production of pro-inflammatory cytokines (TNF-α and IL-1β) that cause localized glomeruli enlargement, proximal tubular degeneration in the kidney, hepatic bleeding, and irregular hepatocytes in the liver.Treatment with yohimbe, maca, horny goat weed and their mixture led to an improvement in the level of those aforementioned indicators and the mixture group achieved the best results. In the same context as the previous results**, Tsutsui *et al.*, (2018**) showed that yohimbine, an α2-adrenoceptor antagonist, inhibited cytokine expression via α2C-adrenoceptors, preventing renal ischaemia and reperfusion damage in rats. On the other hand, **Okwakpam *et al.*, (2023)** demonstrated that when *Pausinystalia yohimbe* was

administered to rats at a dosage of 800 mg/kg body weight, the levels of sodium significantly increased while those of urea, creatinine, potassium, chloride, and bicarbonate did not change significantly in comparison to the control group.

While **Smarta (2023)** supported the positive effect of maca, he demonstrated that the presence of macaenes and macamides in maca has an impact on maintaining a balanced and abundant level of renal hormone secretion in humans. The kidney is fully capable of absorbing the trace elements included in maca. Consequently, the maca can satisfy people's actual needs for renal tonification.

Additionally, **Su *et al.*, (2022)** demonstrated how a high concentration of icariin (ICA), the primary active ingredient in horny goat weed, can inhibit the response of the endoplasmic reticulum stress in diabetic kidney disease (DKD) tissues via encouraging the G protein-coupled estrogen receptor's (GPER) expression , decreasing the increase of diabetic kidney disease, and speeding up tissue apoptosis.

Table (4): Effect of yohimbe, maca, horny goat weed and their mixture on serum glucose level in rats with testicular damage

Groups	glucose (mg /dl)
(G1):Control negative	$62.96^{f} \pm 1.76$
(G2):Control positive	$126.96^{a} \pm 2.05$
(G3) :Yohimbe (5% of diet)	$92.93^{d} \pm 2.150$
(G4) : Maca (5% of diet)	$112.73^{b} \pm 2.08$
(G5): Horny goat weed (5% of diet)	$102.66^{c} \pm 1.15$
(G6): Mixture (5% of diet)	$72.5^{e} \pm 2.5$
LSD	3.548

Each value is expressed as mean ± SD. Means under the same column with different superscript letters are significantly different ($p \leq 0.05$).

Data in the previous table (Table 4) showed that the glucose level increased in the positive control group that was injected with cadmium chloride compared to the negative control group. Studies in epidemiology and experimentation indicate that hyperglycemia associated with diabetes and cadmium may exacerbate metabolic control. Hyperglycemia is a result of cadmium chloride exposure. Its consequences could result from long-term exposure through insulin resistance in various peripheral organs and pancreatic damage **(Hasan *et al.*, 2019 and Iqbal *et al.*, 2022).** Treatment with yohimbe, maca, goat horn and their mixture led to a decrease in the glucose level.

Sudhakar *et al.*, (2023) reported that yohimbine may be useful as a therapy to repair pancreatic damage caused by diabetes and to restore the balance between fat

and carbohydrates. Yohimbine, an antagonist of alpha-2adrenoceptors, improved glucose tolerance in the diabetic population. The pancreatic cells had seen remarkable regeneration and had grown in size and density.

According to **Mohamed *et al.*, (2024)**, feeding rats on maca roots reduced the elevation of blood glucose and lipids, enhanced insulin resistance and liver function, and successfully restored the state of oxidative stress and inflammation. This effect might be brought about by the ballast chemicals found in maca; dietary fiber, particularly insoluble fiber, retains water and gels. They are essentially not absorbed by the circulatory system since they are not broken down by the body. They affect the glycemic response, lower cholesterol, increase satiety, and increase faecal bulk. Thus, fiber can be used to treat diseases like diabetes.

In reference to the favorable outcomes generated by goat horny, **Bourebaba *et al.*, (2024)** expounded that icariian derived from *Epimedium* have shown significant promise in enhancing the anti-diabetic potential of mesenchymal stromal cells (MSCs). This is primarily achieved by enhancing the MSCs' immunomodulatory, migratory, survival, regenerative, and angiogenic capabilities as well as their overall metabolic homeostasis, which includes insulin signaling pathways.

Table (5): Effect of yohimbe, maca, horny goat weed and their mixture on lipid profile in rats with testicular damage

Groups	TG (mg /dl)	TC (mg /dl)	VLDL (mg /dl)	HDL (mg /dl)	LDL (mg /dl)
(G1):Control negative	$42.23^{d} \pm 2.11$	$47^{f} \pm 1.21$	$8.44^{d} \pm 0.42$	$32.5^{a} \pm 2.26$	$6.05^{e} \pm 3.51$
(G2):Control positive	$67.43^{a} \pm 1.60$	$94.26^{a} \pm 1.18$	$13.48^{a} \pm 0.32$	$12.66^{d} \pm 1.45$	$68.11^{a} \pm 1.70$
(G3) : Yohimbe (5% of diet)	$53.1^{c} \pm 2.71$	$57.23^{d} \pm 1.70$	$10.62^{c} \pm 0.54$	$26.1^{b} \pm 1.74$	$20.51^{d} \pm 2.57$
(G4) :Maca (5% of diet)	$63.8^{b} \pm 1.75$	$82.76^{b} \pm 1.89$	$12.76^{b} \pm 0.35$	$15.16^{d} \pm 1.15$	$54.50^{b} \pm 3.50$
(G5): Horny goat weed (5% of diet)	$60.9^{b} \pm 2.02$	$76.03^{c} \pm 1.87$	$12.18^{b} \pm 0.40$	$22.33^{c} \pm 1.56$	$41.52^{c} \pm 0.77$
(G6): Mixture (5% of diet)	$45.4^{d} \pm 1.70$	$50.7^{e} \pm 1.96$	$9.08^{d} \pm 0.341$	$31.63^{a} \pm 1.48$	$9.98^{e} \pm 1.79$
LSD	3.598	2.971	0.719	2.927	4.476

Each value is expressed as mean ± SD. Means under the same column with different superscript letters are significantly different ($p \leq 0.05$). TG: Triglyceride; TC: Total Cholesterol; LDL: Low-Density Lipoprotein; HDL: High-Density Lipoprotein; VLDL: Very Low-Density Lipoprotein.

Table (5) shows the impact of yohimbe, maca, horn goat weed and their combination on the lipid profile in rats with reduced fertility. The findings showed that the positive control group's levels of triglycerides, total cholesterol, LDL, and

VLDL were greater than those of the normal control rats. These results are consistent with previous studies that confirm that exposure to Cd disrupts the heart's lipid metabolism . By controlling linoleic acid, sphingolipid, and glycerolipid, cadmium caused abnormalities related to lipid metabolism **(Chen *et al.*, 2023)**. According to **Lin *et al.*, (2023),** a higher body burden of cadmium raises the risk of dyslipidemia mostly because of the increased likelihood of low HDL-C and a high ratio of triglycerides to LDL-C. While treatment with yohimbe , maca , horn goat wood and their mixture significantly caused decreases in triglyceride, total cholesterol and LDL of treated groups as compared to positive group. Conversely, when compared to the positive control group, the HDL value increased in all treatment groups.

According to **Sudhakar *et al.*, (2023),** yohimbine improved lipid profiles by increasing HDL-c levels and decreasing triglyceride and LDL-c values. Yohimbine has been shown to promote lipolysis, or the burning of fat, by making more of the hormone and neurotransmitter norepinephrine accessible to fat cells and by preventing alpha-2 receptor activation, which causes an increase in norepinephrine release **(Caruso *et al.*, 2008 and Petrie *et al.*, 2000).**

Maca's biological action could be attributed to contents, which contains free fatty acids like oleic, linoleic, and palmitic. The lipid profile is influenced by it **(Khalifa *et al.*, 2023)**. **Mohamed *et al.*, (2024)** noted that dietary fiber, particularly insoluble fiber, lowers cholesterol levels and is one of the ballast components found in maca. Therefore, fiber can be used to treat disorders like obesity and asthma, as well as to lower the risk of hypertension, coronary heart disease, colon cancer, hemorrhoids, gallstones, and kidney stones.

Cui *et al.* (2023) reported that the icariin pro-glycymicelles demonstrated increased in vitro activities, such as those related to antioxidant, α-glucosidase, lipase, and cholesterol esterase inhibition. Also, **Nasef and El-Sheikh (2023)** clarified that the use of horn goat weed in therapy contributed to a decrease in LDL, TG and TC as well as an increase in the quantity of good fats (HDL).

Table (6): Effect of yohimbe, maca, horny goat weed and their mixture on MDA, CAT and SOD in rats with testicular damage

Groups	MDA (nmol /mg)	CAT (ng /mg)	SOD (U /mg)
(G1):Control negative	$0.540^{f} \pm 0.07$	$12.71^{a} \pm 2.49$	$209.9^{a} \pm 2.15$
(G2):Control positive	$20.87^{a} \pm 1.53$	$0.548^{d} \pm 0.23$	$32.12^{f} \pm 2.1$
(G3) : Yohimbe (5% of diet)	$10.2^{d} \pm 1.05$	$10.16^{ab} \pm 0.76$	$163.23^{c} \pm 2.95$
(G4) : Maca (5% of diet)	$17.66^{b} \pm 1.80$	$4.13^{c} \pm 0.90$	$52.9^{e} \pm 2.6$
(G5): Horny goat weed (5% of diet)	$13.76^{c} \pm 1.40$	$7.96^{b} \pm 0.45$	$119.6^{d} \pm 2.09$
(G6): Mixture (5% of diet)	$6.40^{e} \pm 1.34$	$12.4^{a} \pm 1.44$	$201^{b} \pm 1.41$
LSD	2.351	2.289	4.191

Each value is expressed as mean ± SD. Means under the same column with different superscript letters are significantly different (p≤ 0.05).). SOD: Superoxide dismutase; CAT: Catalase; MDA: Malonaldehyde.

Table (6) lists the antioxidant (SOD, CAT) and oxidant (MDA) indicators that were examined in the test tissue. The findings showed that in the testicular tissue, Cd reduced the activities of enzyme antioxidants including SOD and CAT. Furthermore, it was shown that the application of Cd led to an increase in MDA levels, a significant marker of lipid peroxidation. These results agree with **Yesildag *et al.*, (2022)** they emphasized that through the removal of cations from the active sites of several antioxidant enzymes, Cd leads to the degradation of redox equilibrium. Additionally, it inhibits antioxidant enzymes by binding to their sulfhydryl groups **(Al Omairi *et al.*, 2018)**. These factors result in a build-up of reactive oxygen species and a breakdown of the equilibrium between oxidants and antioxidants **(Refaie *et al.*, 2018**). However, it has been noted that certain antioxidant substances used to combat Cd also shield against toxicity by lowering oxidative stress **(Park *et al.*, 2021).** It was noted that SOD and CAT activities increased with the administration of yohimbe , maca , goat horn , and their mixture because they contain many antioxidants.

These outcomes are entirely in line with the findings of **Keumedjio *et al.*, (2023)** who stated that numerous active secondary metabolites, including glycosides, alkaloids, phenols, flavonoids, and saponins were found during the phytochemical screening of yohimbe extract. It demonstrated antioxidant properties and androgenic effects without appreciable cytotoxicity, so confirming traditional healers' use of yohimbe extract to treat male infertility.

According to **Gencoglu (2023),** maca polysaccharide (MP) is the active ingredient in maca, which is an organic dietary supplement with strong antioxidant and energy metabolism-improving qualities. Serum transaminase elevations were dramatically suppressed by MP, which also improved pathological alterations,

decreased oxidative stress, and raised the amounts of enzymes involved in energy metabolism. MP prevented hepatocyte death by resolving issues with lipid metabolism and controlling the pentose phosphate pathway and acid metabolism. Additionally, Maca has been shown by **Mohamed *et al.*, (2024)** to enhance insulin resistance and liver function in addition to effectively reversing oxidative stress and inflammation.

Nasef and El-Sheikh (2023) reported that the testicular tissue of rats supplemented with horny goat weed showed lower levels of MDA and higher levels of antioxidant enzymes. When compared to positive control rats, rats treated with 10% horny goat weed had the greatest levels of SOD and CAT activity. These findings could be explained by both an increase in the antioxidant-defense system's activity and a decrease in the generation of lipid peroxidation.

Table (7): Effect of yohimbe, maca, horny goat weed and their mixture on T, FSH and LH hormones in rats with testicular damage

Groups	T (ng/ml)	FSH (ng/ml)	LH (ng/ml)
(G1):Control negative	$2.75^{a} \pm 0.278$	$9.17^{a} \pm 0.645$	$2.86^{a} \pm 0.513$
(G2):Control positive	$1.2^{d} \pm 0.1$	$4.3^{b} \pm 0.4$	$0.8^{c} \pm 0.115$
(G3) :Yohimbe (5% of diet)	$2.06^{bc} \pm 0.251$	$6.83^{c} \pm 0.763$	$1.93^{b} \pm 0.321$
(G4) :Maca (5% of diet)	$1.6^{cd} \pm 0.264$	$5.56^{d} \pm 0.404$	$0.96^{c} \pm 0.152$
(G5): Horny goat weed (5% of diet)	$1.9^{bc} \pm 0.360$	$6.23^{cd} \pm 0.251$	$1.26^{c} \pm 0.251$
(G6): Mixture (5% of diet)	$2.46^{ab} \pm 0.251$	$8^{b} \pm 0.5$	$2.3^{b} \pm 0.360$
LSD	0.467	0.929	0.560

Each value is expressed as mean ± SD. Means under the same column with different superscript letters are significantly different (p≤ 0.05). T: Testosterone H; LH: luteinizing hormone; FSH: Follicle-stimulating hormone.

Table (7) demonstrated that T, LH and FSH decreased significantly (P≤0.05) in positive control groups (+ve) compared to (-ve) groups after $CdCl_2$ infestation. The testis has a high sensitivity to the toxicity of $CdCl_2$. These outcomes agree with the conclusions made by **Marini *et al.*, (2022)** and **Antar *et al.*, (2023),** they demonstrated how testicular injury from Cd exposure has been linked to poor spermatogenesis and lower fertility in both humans and animals. It is believed that this damage results from inflammation and oxidative stress brought on by Cd, which can cause apoptosis and damage to cells. It has also been demonstrated that cadmium can damage the blood-testis barrier, changing the testicular microenvironment and increasing permeability. Furthermore, alterations in gonadotropin secretion and reduced testosterone synthesis have been connected to Cd exposure.

Hormone levels rose rather considerably when yohimbe, maca, horny goat weed and their combination were used in contrast to the positive group. Testicular tissue hormone levels were more effectively raised by a 5% combination treatment.

Methanol extract of *P. yohimbe* root has been shown to improve sexual behavior in male rats, according to studies by **Ojatula *et al.*, (2020) and Keumedjio *et al.*, (2023)**. The elevated blood testosterone concentrations brought on by the bioactive chemicals in the plant extract, which work through a variety of central and peripheral pathways, may be connected to the aphrodisiac effects of the extract.

As for the appropriate doses of yohimbe that stimulate sexual activity, The results of **Eweka *et al.*, (2010)** study on the impact of yohimbe aqueous extract on testicular activity indicate that, at low dosages, the extract may promote spermatogenesis; however, at higher levels, spermatogenic activity was significantly reduced.

Zhang *et al.*, (2023) reported that maca enhanced overall health and decreased interleukin-6 levels. By functioning as an antioxidant, maca has an impact on male reproductive health, including post-ejaculatory latency, premature ejaculation and libido, and increased sperm count in the epididymis. **Shin *et al.*, (2023)** also observed that rats' sexual performance was more effectively enhanced by maca, and they attributed this to glucocinolates. Fatty acid amide hydrolase inhibitors, which are lipophilic components of maca, may have an impact on central nervous system neurotransmissions.

The results of the group treated with horn goat weed also showed the positive and stimulating role of goat in raising the level of fertility hormones. This may be due to the Icariin compound, which is one of the most important active ingredients found in it. Icariin has been demonstrated to naturally mimic testosterone, which is one of the reasons it enhances strength, libido, and even athletic ability. In one study, researchers discovered that, in comparison to rats that did not get the extract, the rats treated with icariin had better overall reproductive organ conditions and higher levels of testosterone in their blood **(Ganapathy *et al.*, 2021)**.

Histopathological examination of testes

Under a microscope, the testes of the rats in group 1 displayed a normal seminiferous tubule histological structure, complete spermatogenesis, and normal spermatogoneal cells **(Photos 1and 2).** On the other hand, group 2's analyzed sections showed severe interstitial edema and necrosis of Leydig cells **(Photo 4)** , as well as vacuolar degeneration and necrosis of spermatogoneal cells lining seminiferous tubules **(Photos 3 and 4)** . While other sections from group 3 revealed no histopathological alterations, normal seminiferous tubules, and full spermatogenesis **(Photo 6)** , certain analyzed sections from group 3 showed interstitial edema and necrosis of spermatogoneal cells lining some seminiferous tubules **(Photo 5)** . Additionally, the testes of the rats in groups 4,5 and 6 showed normal seminiferous tubules and no histological changes **(Photos 7, 8, 9 and10) .**

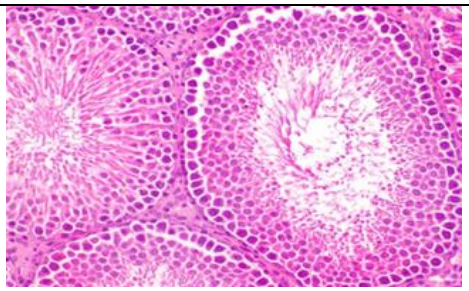


Photo (1) : A photomicrograph of a rat's testis from group 1 (negative group) demonstrates the seminiferous tubule's normal histological structure, complete spermatogenesis, and normal spermatogoneal cells. (HandE X 400).

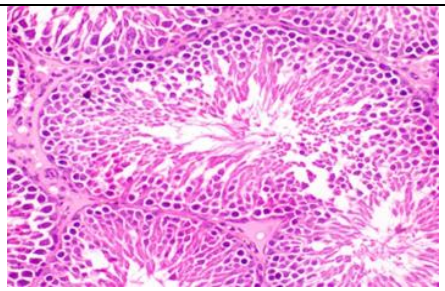


Photo (2): A photomicrograph of a rat's testis from group 1 (negative group) demonstrates the seminiferous tubule's typical histological structure, complete spermatogenesis, and normal spermatogoneal cells (HandE X 400).

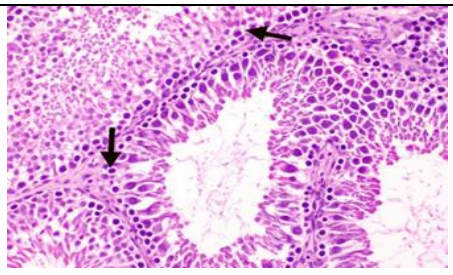


Photo (3) : Photomicrograph of rat testis from group 2 (positive group) demonstrating necrosis of spermatogoneal cells lining seminiferous tubules and vacuolar degeneration (HandE X 400).

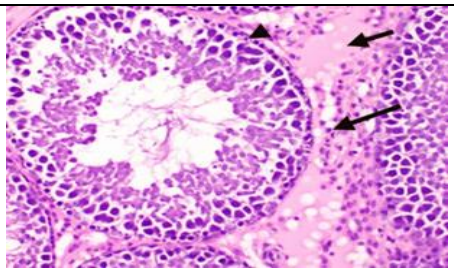
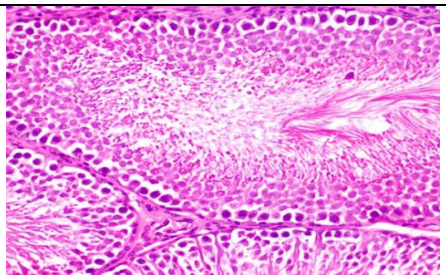
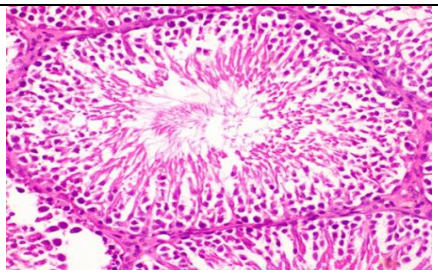
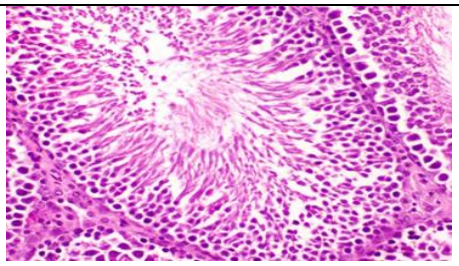
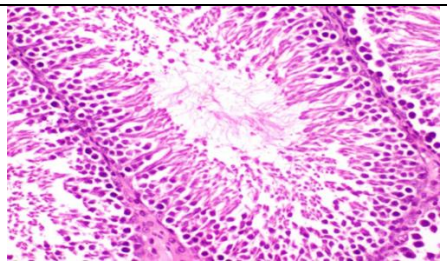


Photo (4): Rat from group 2's testis (positive group) was photographed under a microscope, revealing significant interstitial edema, Leydig cell necrosis, and spermatogoneal cell necrosis lining seminiferous tubules. (HandE X 400)

 **Photo (7):** Testis of rat from group 4 (Maca 5% of diet) photomicrograph displaying normal seminiferous tubules and no histological changes (HandE X 400).	 **Photo (8):** Photomicrograph of rat testis from group 4 (Maca 5% of diet) demonstrating normal seminiferous tubules and no histological changes (HandE X 400).
 **Photo (9):** Rat testis from group 5 (Horny goat weed 5% of diet) photomicrograph demonstrating normal seminiferous tubules and no histopathological changes (HandE X 400).	 **Photo (10):** Photomicrograph of testis of rat from group 6 (Mixture 5% of diet) showing no histopathological alterations with normal seminiferous tubules (HandE X 400).

The histopathological findings are consistent with theory that exposure to Cd increases oxidative stress injury, which in turn causes pyro ptosis in testicular tissue, activating the AIM2 pathway. This puts the testicular damage brought on by exposure to Cd into perspective **(Zhou *et al.*, 2022).** Exposure to cadmium may promote the growth of blood vessel endothelial cells and mural cells, which could result in aberrant testicular function **(Yang *et al.*, 2022)**. Based on the level of fatty acids (primary metabolites) and macamides (secondary metabolites) in the sperm composition, numerous investigations have demonstrated that *Lepidium meyenii* enhances sperm quality and concentration. Their impact on testicular histopathology is evidenced by their direct action on the reproductive tract and their influence on oxidative stress **(Dzhakova *et al.*, 2023).** According to **Zhou *et al.*, (2023),** maca may help reduce the vacuolation of spermatogenic tubules and testicular lesions, encourage spermatogenic epithelium healing, stop stromal cell growth, considerably raise serum testosterone levels, and enhance sperm quantity and quality.

Treatments with horny goat weed enhanced testicular tissue and markedly decreased testicular toxicity **(Nasef and El-Sheikh, 2023).**

Conclusion :

Based on the current study's findings, male infertile individuals can improve their sexual function by using yohimbe , maca and horny goat weed and their mixture, as they improved fertility indicators , lipid profile, kidney function, serum glucose and liver enzymes as well as biological indicators and histopathology of the testicles, without experiencing any negative side effects when used in male rats at a dose of 5% of the diet **.**

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تقييم فاعلية مسحوق نبات اليوهمبي و العنزة والماكا ضد تلف الخصية الناجم عن كلوريد الكادميوم في ذكور الفئران

بسمة رمضان خطيب
قسم التغذية وعلوم الاطعمة – كلية الاقتصاد المنزلى
جامعة المنوفية

لمياء عبدالحميد دياب
قسم التغذية وعلوم الاطعمة – كلية الاقتصاد المنزلى
جامعة المنوفية

ملخص البحث :

الغرض من هذه الدراسة هو تحديد مدى فاعلية بعض الأجزاء النباتية ضد تلف الخصية الناتج عن كلوريد الكادميوم في ذكور الفئران . تم تقسيم 36 فأر بالغ إلى مجموعتين رئيسيتين بشكل عشوائي . تكونت المجموعة الرئيسية الأولى من ستة فئران ، واعتبرت كمجموعة ضابطة سالبة حيث تغذت على الوجبة الأساسية فقط . تم حقن المجموعة الرئيسية الثانية (30 فأر) بكلوريد الكادميوم بجرعة 2 ملجم/كجم من وزن الجسم لإصابة الخصيتين بالتلف. تم عمل خمس مجموعات من المجموعة الرئيسية الثانية تحتوى كل مجموعه منها على ست فئران.تم تحديد إحدى المجموعات الخمس كمجموعة ضابطة موجبة ، بينما تم تغذية المجموعات الأربع الأخرى على مسحوق نبات اليوهمبي والعنزة والماكا وخليطهم على التوالى وذلك بنسبة 5٪ من الوجبة. تم استخراج الخصيتين لإجراء الفحص الهستوباثولوجى وتقييم نشاط الانزيمات المضادة للأكسدة . أشارت النتائج إلى أنه عند المقارنة بالمجموعة الضابطة الموجبة ، فإن تناول 5% من مسحوق اليوهمبي، العنزة ، الماكا وخليطهم لمدة 28 يوم أدى إلى زيادة كبيرة في مستوى الهرمونات الجنسية (الهرمون اللوتينى والتستوسيترون والهرمون المنبه للجريب) في الدم بالإضافة إلى زيادة نشاط الإنزيمات المضادة للأكسدة في أنسجة الخصية. ومع ذلك، كانت هناك انخفاضات كبيرة في مؤشرات وظائف الكلى والكبد، وصورة الدهون ومستوى الجلوكوز في الدم. يمكن التوصية بأن استهلاك مسحوق اليوهمبي والعنزة والماكا في النظام الغذائي له تأثيرات مضادة للسمية على الخصية وتأثيرات مضادة للأكسدة والتى تلعب دورًا أكثر أمانًا في الخصوبة وتمنع المضاعفات.

الكلمات المفتاحية: *الخصوبة ،النباتات الطبية، الاجهاد التأكسدي، حيوانات التجارب ، الذكورة.*