

RESEARCH ARTICLE

PROTECTIVE EFFECTS OF *PLUKENETIA CONOPHORA* EXTRACT ON CADMIUM-INDUCED REPRODUCTIVE TOXICITY IN MALE WISTAR RATS: A BIOCHEMICAL AND PHYTOCHEMICAL INVESTIGATION

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ABSTRACT

Infertility is defined as the medical condition which prevents a woman from becoming pregnant after she has experienced 12 months of unprotected sexual intercourse. Male infertility is a major factor which accounts for 50 percent of infertility cases that affect couples. Male infertility happens when men experience medical conditions and infectious diseases and when they encounter environmental pollutants such as cadmium. This research study tests whether *Plukenetia conophora* ethanol seed extract provides protection against cadmium-induced male infertility in Wistar rats. The study aimed to evaluate the protective role of *Plukenetia conophora* extract against cadmium-induced reproductive toxicity and its effects on body weight, hormone levels and the phytochemical constituents of *Plukenetia conophora*. The research study used thirty-six adult male Wistar Rats and divided them into six groups to receive various treatments. Group A served as the control group, Group B and C received 250mg/kg and 500mg/kg of ethanolic seed extract of *Plukenetia conophora* only respectively, group D and E received 250mg/kg and 500mg/kg of *Plukenetia conophora* + 10mg/kg of cadmium chloride respectively, and group F received 10mg/kg of cadmium chloride only, followed by assessment of hormonal profiling assay over a 56-day period. The study showed that Cadmium chloride caused body weight and testosterone level decreases while FSH level showed a minor increase. The higher dose of *Plukenetia conophora* extract showed better results for reducing these negative effects. The phytochemical analysis of the extract showed beneficial compounds which included saponins and steroids and terpenoids. *Plukenetia conophora* extract protected male Wistar rats from reproductive toxicity which was caused by cadmium. The extract's phytochemicals helped to maintain body weight and hormonal levels and testicular health. The research needs to investigate how *Plukenetia conophora* might function as a treatment for male infertility.

KEYWORDS

Male infertility, Cadmium toxicity, *Plukenetia conophora*, Reproductive health, Phytochemical Analysis

1. INTRODUCTION

Infertility is a medical condition that affects both men and women and is described as the inability to conceive following at least 12 months of frequent unprotected sexual intercourse (World Health Organization, 2023). The worldwide problem of infertility affects one in six people who will experience this condition at some time during their life (World Health Organization, 2023). The global population who experience infertility problems is estimated to be 180 million people (World Health Organization, 2023). As a study report that male infertility constitutes 20-30% of all infertility cases yet male-related factors cause 50% of all infertility cases which means that 50% of couples who cannot conceive face problems related to their male partner (Vander Borgh and Wyns, 2018). The World Health Organization estimates that male infertility currently affects 8 to 12% of all couples who are of reproductive age around the globe. Infertility can have a wide range of intricate causes. Male infertility can occur when men experience diabetes together with genetic disorders and undescended testicles as well as hormone imbalances and any medical condition that affects their ability to produce or create healthy sperm (Vander Borgh and Wyns, 2018). Sperm production and quality can be disrupted by various infections such as gonorrhoea, mumps, HIV, and chlamydia (Vander Borgh and Wyns, 2018). Ovulatory problems,

endometriosis, or anomalies in the uterus can all lead to infertility in women (World Health Organization, 2021).

The good news for people who suffer from infertility results from the existence of multiple treatment options. According to Mascarenhas et al. (2012) (4), they can include hormone-related drugs, minor surgeries, and assisted reproductive technologies (ART) including intrauterine insemination and vitro fertilisation (IVF). The couple's age together with their health status and the reason for their infertility condition determine which treatment option they should select according to (Mascarenhas et al., 2012). It is essential to understand that infertility affects many people and you need not feel isolated in your battle with this condition. The available treatments together with the existing resources will provide you with necessary assistance. Your specific situation requires you to consult a healthcare expert for tailored advice (Mascarenhas et al., 2012).

2. MATERIALS AND METHODS

2.1 Experimental rats

The experiment used thirty-six adult male Wistar rats who had body weights between 180 grammes and 200 grammes. The rats required a two-week period to acclimatize before the research team initiated their treatment procedures. The subjects received unlimited access to standard

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rat food and drinking water. The College of Medicine at the University of Benin implemented all Research Ethics Committee guidelines for animal

welfare together with the ethical approval which received the identifier CMS/REC/2024/626.

Table 1: Experimental Protocol

Groups	Treatments;
Group A	Served as the control group.
Group B	Received 250mg/kg of ethanol seed extract of <i>Plukenetia conophora</i> only for 56 days
Group C	Received 500mg/kg of ethanol seed extract of <i>Plukenetia conophora</i> only for 56 days.
Group D	Received 250mg/kg of ethanol seed extract of <i>Plukenetia conophora</i> + 10mg/kg Cadmium Chloride for 56 days
Group E	Received 500mg/kg of ethanol seed extract of <i>Plukenetia conophora</i> + 10mg/kg Cadmium Chloride for 56 days.
Group F	Received 10mg/kg of Cadmium chloride only daily for 56 days.

All administrations were done by gavage and lasted for fourteen (56) days.

2.2 Administration

The *Plukenetia conophora* and cadmium were given using a gavage with an orogastric tube. The rats were carefully handled to minimize oral or oesophageal injuries.

2.3 Sacrifice of animals.

The researchers conducted weekly weight assessments of the rats throughout the experimental period to observe weight changes which occurred during the study. The researchers used a compact electric weighing scale which had grams as its calibration unit to take the final weight measurements of the rats at the moment of their sacrifice. The researchers used 30 milliliters of chloroform which they enclosed in a container to soak cotton wools which they used as an anaesthetic for the animals. The researchers placed the rat in a supine position on the dissection trolley after they had anaesthetized it and they performed a

ventral abdomino-thoracic incision to expose the rat's internal organs. Blood samples were taken from the inferior vena cava using 5 milliliter syringes and they processed the samples through centrifugation before storing the serum in sterile plain bottles for hormone analysis.

Statistical analysis

The researchers presented their results as Mean \pm SEM (standard error of mean) measurements. The researchers used one-way analysis of variance (ANOVA) to compare the different means of measurements. The researchers considered the results as statistically significant when the P value reached a threshold of 0.05 or lower.

The researchers used LSD Post Hoc test to identify the specific locations of statistical significance. The research team used GraphPad Prism version 9.0 (GraphPad Software Inc.) for Windows to analyze their study data.

3. RESULTS

Table 2: Body And Testicular Weight Analysis

	initial body weight	final body weight	body weight change	Testicular weight	Testiculosomatic index
Control	167.00 \pm 3.62 ^a	206.00 \pm 3.69 ^{a*}	39.00 \pm 1.05 ^a	2.38 \pm 0.11 ^a	1.16 \pm 0.04 ^a
LD only	177.80 \pm 6.83 ^a	212.80 \pm 2.87 ^{a*}	35.00 \pm 4.67 ^a	2.56 \pm 0.07 ^a	1.20 \pm 0.03 ^{ab}
HD only	171.75 \pm 3.79 ^a	207.25 \pm 4.92 ^{a*}	35.50 \pm 5.36 ^a	2.60 \pm 0.07 ^a	1.28 \pm 0.03 ^b
LD \pm CdCl	179.33 \pm 4.06 ^a	167.67 \pm 2.96 ^b	-11.67 \pm 2.73 ^b	1.90 \pm 0.06 ^b	1.17 \pm 0.03 ^{ab}
HD \pm CdCl	180.33 \pm 7.26 ^a	153.67 \pm 2.33 ^{bc*}	-26.67 \pm 5.21 ^{bc}	1.73 \pm 0.07 ^b	1.17 \pm 0.03 ^{ab}
CdCl	176.00 \pm 10.00 ^a	143.00 \pm 15.31 ^{c*}	-33.00 \pm 10.21 ^c	1.20 \pm 0.20 ^c	0.80 \pm 0.06 ^c

Unlike superscripts down a row means statistically significant (P<0.05) across the group while like superscripts down a row means not

statistically significant (P>0.05) across the group. *means statistically significant comparing initial and final body weight within a group.

TABLE 3: Hormone Profile

	Testosterone	LH	FSH
Control	3.73 \pm 0.50 ^a	11.43 \pm 0.85 ^a	7.53 \pm 0.55 ^a
LD only	3.40 \pm 0.36 ^a	10.53 \pm 1.46 ^a	6.93 \pm 0.95 ^a
HD only	3.33 \pm 0.33 ^a	12.83 \pm 1.89 ^a	8.43 \pm 1.24 ^a
LD \pm CdCl	2.30 \pm 0.23 ^a	19.20 \pm 3.52 ^a	12.67 \pm 2.34 ^a
HD \pm CdCl	3.43 \pm 0.19 ^a	13.10 \pm 1.73 ^a	8.63 \pm 1.13 ^a
CdCl	2.97 \pm 0.24 ^a	12.67 \pm 1.40 ^a	8.33 \pm 0.93 ^a

Unlike superscripts down a row means statistically significant (P<0.05) across the group while like

superscripts down a row means not statistically significant (P>0.05) across the group.

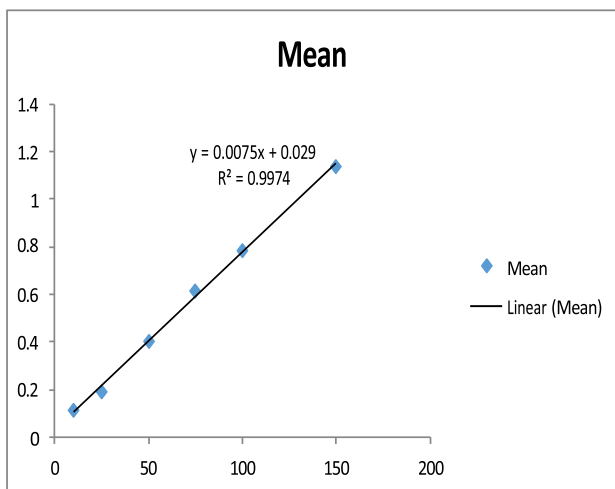
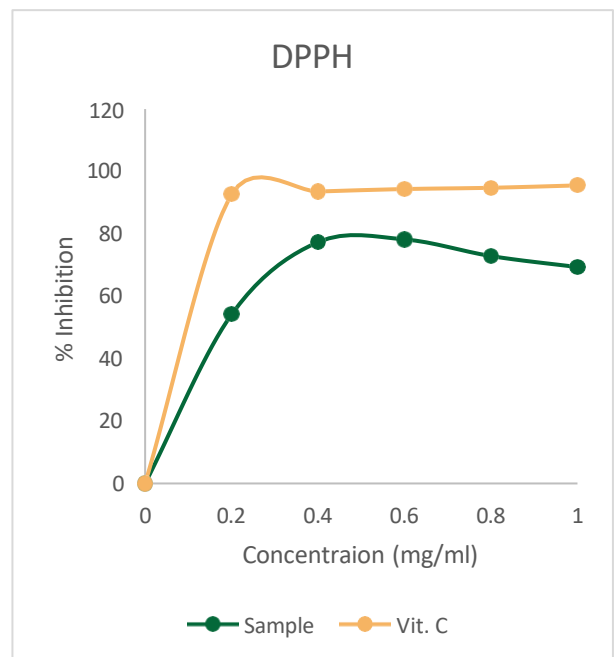
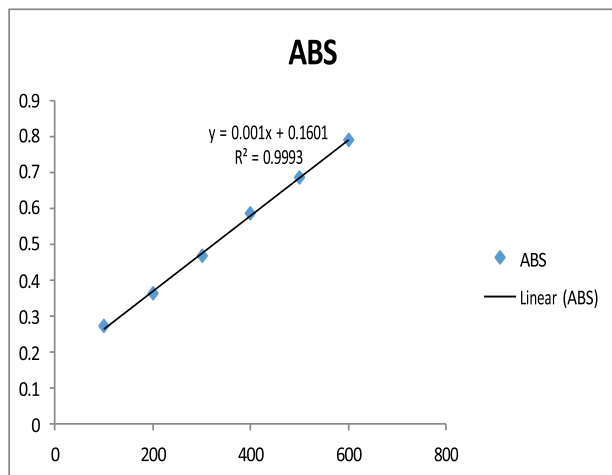
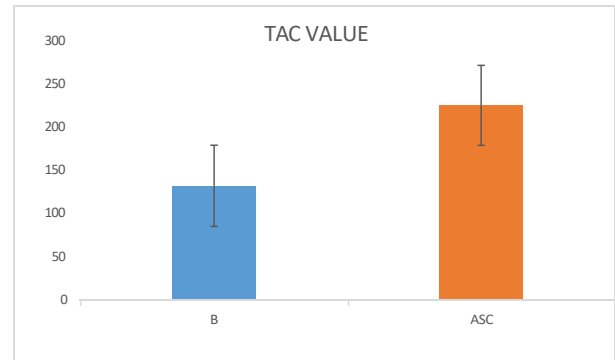
Table 4.1: Phytochemical screening

FLAVONOIDS	-
TANNINS	-
CARDIAC GLYCOSIDES	++
SAPONINS	++
STEROIDS	++
TERPENOIDS	++

Table 4.1 (Cont): Phytochemical screening	
PHENOLS	-
PHLABOTANNINS	-
COUMARIN	+
ALKALOIDS	+
ANTHRAQUINONE	-

Present (Mild +) Present (Abundant ++) Absent (-)

Table 4.2: Showing Proximate Analysis					
Moisture Content	ASH Content	Crude fibre Content	Crude Fat Content	Crude Protein	Carbohydrate
%	%	%	%	%	%
9.133333	6.133333	17.86667	4.8	9.243333	52.82333



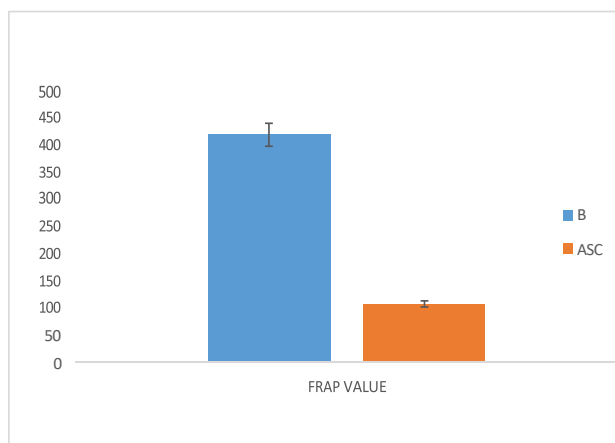
Graph comparing the DPPH's radical scavenging activity of different concentrations of Vitamins C and extracts from the walnut seeds.

4. DISCUSSION

The biological half-life of cadmium establishes a hazardous metal that accumulates in human bodies while its toxic effects impact various body tissues and organs (Renu et al., 2021). Human beings face unavoidable cadmium exposure because the metal exists in nearly all food items which it transfers from soil to plants (Franz et al., 2008). The pathophysiology of high-dose cadmium poisoning that occurs over a short period of time remains unknown while public awareness of poisoning from long-term chronic deposition of cadmium continues to grow (Li and Shen, 2023).

The initial body weight measurements showed that all groups began with the same weight. The cadmium-only treatment group showed a significant body weight reduction when compared to the control group which demonstrates that cadmium treatment produces harmful effects on body weight. The toxic heavy metal cadmium which damages the body's systems and organs has been shown to cause weight loss (Rhman et al., 2011). conducted a study in which they fed Wistar rats a zinc and cadmium chloride mixture for 12 weeks after which they measured the rats' growth rate which resulted in the lowest growth rate. The evidence demonstrates that cadmium chloride produces effects which lead to weight loss.

Results of this study show that cadmium chloride treatment caused FSH serum levels to rise in rats yet the increase remained statistically insignificant. Although the rise in plasma FSH levels reached statistical



insignificance, it exists because this peptide functions as the primary inhibitory mechanism which controls FSH secretion (de Souza Predes et al., 2010).

Cadmium has been recognized as a major environmental endocrine disrupting chemical which causes changes in plasma LH levels through its hypothalamic effects on LH secretion from the pituitary gland (Zhang et al., 2008; Wood and Loudon, 2016).

The research did not find significant results but study showed a significant increase (Al-Ani et al., 2015). The current experiment used 10mg/kg of Cadmium chloride but (Al-Ani et al., 2015). Study used 20mg/kg of Cadmium chloride which means that higher doses or extended experiment time would have shown significant results.

The research studies demonstrated that Cadmium chloride decreases plasma gonadotropin levels (Mahmood et al., 2015). The study showed a testosterone level decrease which resulted from changes in FSH and LH plasma levels (Lafuente et al., 2000). The study found that severe hyalinization and calcification of the testes caused a decrease in testosterone levels. Testicular tubule obstruction occurs because hyalinization and calcification create narrow passages which lead to total blockage of the tubules that prevent sperm from being transported out of the testicles and into the epididymis where they develop into mature sperm (Kapadia and Walsh, 2020).

Result of the phytochemical present in Walnut (*T. conophora*) extract shows presence of Coumarins and alkaloids and these phytochemicals where mildly present. Alkaloids are a diverse group of nitrogen-containing compounds found in plants (Gutiérrez-Grijalva et al., 2020). They have a wide range of pharmacological activities and have been used traditionally in medicine (Bhambhani et al., 2021). The mild presence of alkaloids in African Walnut suggests its potential as a natural source of these bioactive compounds, which may contribute to its medicinal properties. This is in agreement with previous study by who reported the presence of alkaloids in African walnut seed (Chikezie, 2017).

The results demonstrated that the tested sample contained significant amounts of cardiac glycosides saponins and steroids together with terpenoids. Cardiac glycosides are a group of compounds known for their ability to increase the force of contraction of the heart muscle (El-Mallakh et al., 2019). People have used the medicinal herb since ancient times to treat heart conditions that include both congestive heart failure and atrial fibrillation. The presence of Cardiac glycosides is in contrast with the report who reported that African walnut seed showed a complete absence of cardiac glycoside (Chikezie, 2017). Saponins are amphipathic glycosides that exist in multiple plant species (Nguyen et al., 2020). The researchers investigated the biological activities of the substance which demonstrated capabilities to lower cholesterol levels and reduce inflammation while enhancing immune system functions (Ribeiro et al., 2019). This result also contrasted that's of (Chikezie, 2017). Steroids are a class of lipids characterized by a four-ring structure (Talapatra and Talapatra, 2014). In plants, steroids play various roles, including structural components of cell membranes and precursors to other bioactive compounds (Moreau et al., 2018). Some plant steroids have been investigated for their potential pharmacological activities, such as anti-inflammatory and anti-cancer effects (Chen et al., 2021). The presence of Steroids in abundant quality was also reported by (Chikezie, 2017). Terpenoids, also known as isoprenoids, are a large and diverse class of organic compounds produced by plants (Tetali, 2018). They have a wide range of biological activities, including antioxidant, anti-inflammatory, and antimicrobial properties (Yang et al., 2020). Terpenoids are also responsible for the characteristic aromas and flavors of many plants (Tetali, 2018). This result also showed different outcomes compared to Chikezie's research from 2017 (Chikezie, 2017). Which reached its 18th conclusion. Steroids belong to the lipid category which displays a distinctive four-ring structure (Talapatra and Talapatra, 2014). Steroids function in plants through different pathways which include their usage as building materials for cell membranes and their function as biological active substance precursors (Moreau et al., 2018).

Researchers have studied certain plant steroids because they may have medical properties including the ability to reduce inflammation and fight cancer (Chen et al., 2021). The study reported that Steroids appeared in his research work in substantial amounts (Chikezie, 2017). Terpenoids represent a major category of organic substances that plants produce which scientists also call isoprenoids.

The biological activities of these compounds extend to three main functions which include antioxidant capacity and their ability to combat inflammation and bacterial infections (Yang et al., 2020). Plants produce terpenoids as their natural substances which create specific smells and tastes that define their identity (Tetali, 2018).The phytochemical

screening of African Walnut indicates that its samples lack all five tested compounds which include flavonoids, tannins and phenols together with phlobatannins and anthraquinones. The study found two compounds which include flavonoids that provide antioxidant and anti-inflammatory effects and tannins which deliver astringent and antimicrobial properties. The study found that phenols which deliver antioxidant effects and potential anti-cancer properties were not present. The study found that phlobatannins which have received less research demonstrate multiple bioactive effects across different plant species and the study found that anthraquinones which provide laxative effects were not present (Choe et al., 2020; Lombardi et al., 2022). The study results showed that African Walnut does not contain specific health advantages which come from those particular compounds. The study results showed different results because previous research discovered that both flavonoids and tannins existed in the tested samples (Oriakhi et al., 2018). The study results differ because the research team chose different solvent extraction methods, while used methanol as their preferred solvent for extraction (Oriakhi et al., 2018).

The proximate analysis of African Walnut shows that the walnut contains 9.00% moisture content which represents the total water content in the walnut. The moderate percentage (9%) indicates a balance that helps maintain freshness and shelf life while preventing microbial growth and spoilage (De Corato, 2019).

The total mineral content of the sample shows 6.40% ash content as its measurement. Minerals perform essential functions in the human body to support bone development, nerve system operations and metabolic activities (Al Ali, 2023). The African Walnut tree displays moderate ash content which functions as a mineral source that improves its nutritional value (Chijioke et al., 2015).

The crude fiber content reached 17.80% of the total material. The high amount of crude fiber in the food product helps people digest food better because it helps maintain regular bowel movements and stops constipation and makes people feel full, which helps them control their weight (Ioniță-Mîndrican et al., 2022). The high fiber content in African Walnut makes it a great dietary fiber source which helps maintain proper digestion and healthy gut function (Youness et al., 2022).

The crude fat content reached 5.40% while fat serves as a vital component for energy production and absorption of fat-soluble vitamins (A, D, E, K) and preservation of cell membrane structure (Youness et al., 2022). The African Walnut exhibits a moderate level of crude fat content which enables it to deliver essential fatty acids without excessive calorie production thus serving as a healthy choice for people who aim to keep their lipid levels in check (Vannice and Rasmussen, 2014).

Crude protein content was present at 8.97%. Proteins are essential because they help with body tissue development and repair work and maintenance of body tissues and enzymes and hormones (Akande, 2015). The moderate protein content in African Walnut shows that it can help people meet their daily protein needs, which supports their muscle development and immune system health and body maintenance needs (Wen et al., 2023).

The carbohydrate content of African Walnut was measured at 52.53%. The body uses carbohydrates as its main energy source (Chandel, 2021). The African Walnut contains a high carbohydrate content which makes it an exceptional energy source that supplies essential fuel for both daily activities and metabolic functions (Sharma et al., 2022). People who require sustained energy throughout their day will find this high energy content especially useful (Sato et al., 2022).

African Walnut with its balanced nutritional composition provides multiple health advantages (Khair and Pan, 2019).The high carbohydrate and fiber content of the food item serves as a vital energy source which also aids in digestive health (Adetunji et al., 2021).The protein and fat content of the food item supports vital body processes while helping to absorb nutrients from food (Ekwe and IHEMEJE, 2013).Essential minerals present in African Walnut increase its nutritional content which makes it a healthful food choice for people who want to eat better (Adetunji et al., 2021).The food product requires proper storage to keep its freshness and maintain its nutritional value (Chatrabnous et al., 2018).The in-vitro study showed that Sample B from FRAP testing showed a lower capacity to scavenge than Standard Ascorbic acid at 107uM according to their ferric reducing antioxidant power results (Benzie et al., 1996). The Total Antioxidant Capacity (TAC) measurement depends on the ability of the extract to convert molybdenum (IV) into molybdenum (V) which creates a green phosphate/molybdenum(V) complex at acidic PH conditions. TAC result shows that the extract (132mg/mL) form less Phosphate/molybdenum (V) complex compare to standard Ascorbic acid with 225.30mg/mL.

Conflict of Interests

The authors declare that there is no conflict of interest in this experimental study.

Ethical Approval

Ethical considerations in this study included obtaining permission from the College Ethics Committee of the College of Medical Sciences, University of Benin with approval number CMS/REC/2024/626 assigned.

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