A TOXICOLOGICAL INVESTIGATION ON THE THERAPEUTIC EFFECT OF WATER MELON RINDS ON THE LIPID PROFILE OF WISTAR RATS EXPOSED TO CADMIUM

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(PHYSIOLOGY AND PHARMACOLOGY TECHNIQUES)

DEPARTMENT OF SCIENCE LABORATORY TECHNOLOGY

FACULTY OF LIFE SCIENCES, UNIVERSITY OF BENIN

BENIN CITY

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A PROJECT WORK SUBMITTED TO THE DEPARTMENT OF SCIENCE LABORATORY TECHNOLOGY ,FACULTY OF LIFE SCIENCES ,UNIVERSITY OF BENIN,BENIN CITY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FORTHE AWARD OF OF BACHELOR OF SCIENCE DEGREE (B.SC) IN SCIENCE LABORATORY TECHNOLOGY (PHYSIOLOGY AND PHARMACOLOGY TECHNIQUES)

OCTOBER, 2025

CERTIFICATION

This is to certify that the research seminar **A TOXICOLOGICAL INVESTIGATION ON THE THERAPEUTIC EFFECT OF WATER MELON RINDS ON THE LIPID PROFILE OF WISTAR RATS EXPOSED TO CADMIUM** was carried out by AMADIN LILABEL AISOSA **(Miss)** (MAT. No **LSC2009939**) of the department of Science Laboratory Technology (physiology and pharmacology techniques), Faculty of Life Sciences, University of Benin, Benin City,Edo State , Under the supervision of Mr O.C Ekhator.

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DEDICATION

I dedicate this work to God Almighty for His guidance and directions towards the successful completion of this work.

ACKNOWLEDGEMENTS

First and foremost, I give all glory, honor, and adoration to Almighty God for His divine guidance, wisdom, protection, and strength throughout the duration of this project. Without His grace, this work would not have been possible.

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ABSTRACT

This study investigated the protective effects of watermelon (*Citrullus lanatus*) rind extract against cadmium-induced toxicity,on lipid profiles in Wistar rats. Twenty rats were divided into five groups: a control, a cadmium-only group, a cadmium with vitamin C group, and two groups receiving cadmium along with watermelon rind extract at 250 mg/kg and 500 mg/kg body weight. The experiment lasted for 60 days. Results showed that cadmium exposure significantly suppressed weight gain and induced dyslipidemia, expressed by elevated cholesterol and triglycerides. Treatment with the hydroethanolic watermelon rind extract, particularly at the 500 mg/kg dose, ameliorated these effects, resulting in a significant increase in percentage weight gain and a normalization of the lipid profile, comparable to the protective effects of vitamin C. The extract did not significantly reduce blood cadmium levels, suggesting its mechanism is likely cytoprotection through antioxidant activity rather than metal chelation. The results show that watermelon rind phytowaste possesses bioactive compounds that can mitigate cadmium-induced metabolic disturbances.

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background of study

Heavy metals (the most toxic being cadmium, lead, arsenic, and mercury) are an integral part of the environment in which we live since they cannot be broken down or eliminated. Heavy metals are naturally occurring components of the Earth's crust, are persistent environmental pollutants, and have many unfavorable effects on ecosystems (Rice *et al*. 2014). Humans are also exposed to heavy metals through industrial operations such as foundries, smelters, oil refineries, petrochemical plants, pesticide manufacturing, and the chemical industry (Mitra *et al*. 2022). The toxicity of these pollutants is a growing concern due to ecological, nutritional, and environmental factors. Heavy metals such as arsenic, cadmium, chromium, copper, lead, nickel, and zinc are the most frequently detected heavy metals in wastewater and pose a threat to both human health and the environment (Lambert and Leven 2000).

Heavy metals can enter the body through several means, such as the intake of polluted food or liquids (water), inhalation of contaminated air, and dermal absorption, and may negatively affect a wide range of biological processes (Tchounwou *et al*. 2012). The risks associated with heavy metals usually outweigh the advantages. For example, even though trivalent chromium is beneficial to health, hexavalent chromium has been identified as a carcinogen, and if inhaled, it may cause lung cancer (Sun *et al*. 2015). Lead poisoning has been linked to intellectual impairments, predominantly in infants (Hou *et al*. 2013). In addition to their potential to cause harm to other parts of the human body, heavy metals often induce toxicity to the kidneys, brain, liver, skin, and heart. Even at lower exposure levels,

these metallic elements are known to cause damage to numerous organs and are classified as systemic toxicants. Both the International Agency for Research on Cancer and the U.S. Environmental Protection Agency classify several carcinogens as human carcinogens (known or probable).

Cadmium is a rare element in the Earth's crust and originates from the breakdown of rocks caused by physical and chemical forces (weathering) and volcanic action. Anthropogenic sources of cadmium result from the mining and processing of cadmium-containing sulfide ores of copper, zinc, and lead. Areas contaminated with cadmium represent a potential source of cadmium dust. The main route of Cd exposure is through the lungs and partly through the gastrointestinal tract. Many studies have confirmed that the half-life of cadmium in humans is approximately 15–20 years (Valko *et al*. 2005). Cadmium is blown into the air by the wind from natural and industrial processes such as the combustion of Cd-containing ores or volcanic activities. The origins of cadmium in water include water supplies close to mines, battery recycling facilities, landfills, hazardous waste sites, the burning of fossil fuels, excessive fertilizer use, waste incineration, and cadmium-using industrial activities. Aquatic organisms can absorb cadmium from contaminated water and accumulate it in their tissues (He *et al*. 2023). Relatively high amounts of cadmium in phosphorus fertilizers have a strong negative effect on the seed germination of crops. Thus, excessive anthropogenic activities due to the excessive use of chemical fertilizers may increase the concentration of cadmium in the food chain.

Watermelon (*Citrullus lanatus*), botanically considered as a fruit, belongs to the family *Cucurbitaceae* (Edwards *et al*., 2003).Watermelon is a valued source of natural antioxidants with special reference to lycopene, ascorbic acid and citruline. These

functional ingredients act as protection against chronic health problems like cancer insurgence and cardiovascular disorders (Zhang and Hamauzu, 2004).it contains almost U2 % water and 7.55 % of carbohydrates out of which 6.2 % are sugars and 0.4 % dietary fiber. It is enriched with carotenoid, vitamin C, citrulline, carotenoids and flavonoids and fat and cholesterol free, thus considered as low caloric fruit (Leskovar *et al*., 2004).Bruton *et al*., 200U).Additionally, watermelon is rich source of ß-carotene acts as an antioxidant and precursor of vitamin A.

1.2 Significance of the Study

This study aids in Investigating the potential of watermelon rind extract to mitigate cadmium- induced toxicity can provide valuable insights into natural protective agents.It also gives an insight into Understanding the effects of watermelon rind extract on lipid profiles in cadmium-exposed rats can contribute to the development of novel therapeutic strategies for managing lipid-related disorders.This study's findings can have implications for environmental health, particularly in regions where cadmium exposure is prevalent.

1.3 Aim of study

The aim of this research study is to investigate and evaluate the therapeutic effects of watermelon phytowaste(rinds) on the lipid profile of wistar rats exposed to cadmium.

1.4 Objective of study

1. Evaluate Cadmium-Induced Toxicity:Assess the impact of cadmium exposure on lipid profiles in Wistar rats.
2. Assess Protective Effects:Determine whether watermelon rind extract supplementation mitigates cadmium-induced lipid profile changes.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 CADMIUM

Cd, the malleable metal, highly reactive and is generally used in nickel–cadmium batteries, alloys, pigments, plastic stabilizers, dyes, paints, glass manufacturing, and the galvanic industry. Cd was discovered at Göttingen, Germany, by F. Stromeyer in 1817. It is also utilised in nuclear reactors to control uranium fission processes through electron capture. Cd produced as a byproduct when zinc is extracted from ZnS. The metallurgical sector is the primary source of Cd exposure, affecting approximately G00 million people annually through contaminated environments (Wang *et al*., 2021). Since Cd is categorised as a poisonous, carcinogenic, and stimulating element, its biological significance has been thoroughly studied over the past few decades. Location-specific variations in the amount of Cd present in the human body result in a biological half-life spanning 1G to 30 years. Chronic lung diseases, high blood pressure, and various cancers, such as prostate, bladder, pancreatic, kidney, and breast have been linked to Cd exposure (Lin *et al*., 2021; Niture *et al*., 2021; Parida and Patel, 2023). Cd exposure can also cause neurological diseases, such as Alzheimer's, Parkinson's, Huntington's, amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), deterioration of cognitive and behavioural functions. Chronic diseases like osteoporosis and osteomalacia, and conditions like itai-itai disease, cardiovascular disease, lung function abnormalities, and kidney damage, are also related to Cd exposure. It can also cross the placenta and affect fetal development, leading to teratogenic effects. The main target organ, the kidneys, have lower glomerular reabsorption rates and are extremely vulnerable to Cd pollution (Bakulski *et al*., 2020; Tarhonska *et al*., 2022). Even

though cadmium is a common environmental pollutant with a well- established toxicity, its entire effects on human health are still unclear. Due to its extensive distribution in industrial environments, as well as in food, water, and air, cadmium exposure continues to be a serious public health issue. With an emphasis on the impacts on important organs, the processes behind its toxicity, and the long-term health implications, the purpose of this study is to evaluate the body of current research on cadmium's harmful effects. The exposure path significantly affects cadmium absorption: inhalation, primarily through tobacco smoke, results in about 25 % absorption (range 5–50 %), meanwhile, oral ingestion of tainted food or water (such as offal and seafood) causes 5–10 % absorption. One cigarette smoking can raise blood cadmium levels by nearly 0.1–0.2 µg/L, as each one contains 1 to 2 µg of Cd, though Mexican cigarettes have been found to contain 2.5 to 2.8 µg each (Lee *et al*., 201U; Shariat *et al*., 201U). Newborns can be exposed to cadmium through breast milk, a concern highlighted by recent studies where mouse pups showed notable cadmium exposure via lactation after their mothers inhaled cadmium oxide (CdO) nanoparticles (Araujo-Padilla *et al*., 2022; Li *et al*., 2022). This study intensifies the clinical debate over nursing versus formula feeding in exposed populations and raises significant questions about breastfeeding as a key route of cadmium exposure.

2.1.1 Entry pathway of Cadmium into human body

Cadmium primarily absorbed by human body via ingestion. Cd accumulates in soil and is metabolised by plants. Edible plant components, such as fruits and seeds, accumulate Cd, which enters the food chain. Moreover, acid rain increases the amounts of Cd in plants. The main intake of cadmium is via leafy vegetables especially spinach, potatoes, legumes and nuts, stem/root vegetables and fruits. Fish and shellfish are the primary sources of Cd, followed by rice in eastern countries. The second cadmium pathway to human are via inhalation. Cd air levels can be hundreds of times higher at the workplace than elsewhere in the environment. Inhaled cadmium dust absorbs 10–50 % by body depending on particle size. Since very little cadmium is absorbed through skin, it is not regarded as a crucial exposure route. Following absorption, cadmium is primarily attached to the protein metallothionein, which has a sulfhydryl group, and is subsequently carried throughout the body in blood. The protein metallothionein binds to heavy metals and can guard against oxidative stress and heavy metal toxicity. Perhaps because of the kidneys' and liver's capacity to produce metallothionein, cadmium subsequently builds up in the human body, primarily in these cells. Cadmium lacks an effective excretory system in the body (Lin *et al*., 2021; Peana *et al*., 2022; Witkowska *et al*., 2021).

2.1.2 Effect of cadmium on cardiovascular system

Chronic renal disorders induced by cadmium significantly contribute to cardiovascular disease (CVD). Studies have indicated that the cardiovascular health is negatively impacted by even extremely low amounts of cadmium, despite the fact that its precise effects on the circulatory system are still up for debate. Data from the US National Health and Nutrition Examination Surveys (NHANES) showed a relationship between high blood

pressure and serum cadmium values.

Cardiovascular death in the US dropped in tandem with a decline in ambient cadmium exposure. According to these epidemiological studies, cadmium exposure has a negative impact on cardiovascular health (Obeng-Gyasi, 2020). Despite extensive documentation of cadmium-induced changes in cardiac biochemistry and physiology, it is unclear exactly which molecular pathways lead to cardiovascular damage when exposed to cadmium. To discover these pathways, a thorough grasp of the cellular changes in cardiomyocytes is necessary (Melila *et al*., 201U).

2.1.3 Effect of cadmium on lung function

Cadmium can irritate the nasal mucous membranes, which might disrupt the upper respiratory tract and cause a decrease in sense of smell. Workplace exposure, namely in the metallurgical sector, arises from breathing in fumes produced during joining, melting, or soldering materials that contain cadmium. Respiratory changes due to cadmium exposure can be identified through laryngological examinations, spirometry, and chest X-rays. Initial signs and symptoms, appearing within 24 h, resemble metal fume fever and pulmonary edema. Acute cadmium poisoning typically occurs at concentrations of 0.5 mg/m^3 from fumes and 3 mg/m^3 from inhalable dust particles, often leading to chronic bronchitis. Workers from metallurgical sector frequently conveys a reduced or lost sense of smell, drying, and ulceration of nasal mucous membranes, and a progression from a dry cough to expectorant symptoms indicative of chronic bronchitis. Emphysema, which is characterised by exertional dyspnea, lower exercise tolerance, and impaired lung ventilation efficiency, may arise after prolonged exposure to Cd. Exposure to airborne particles in occupational contexts is connected to diminished olfactory function, whereas chronic inhalation of cadmium particles is linked to anomalies in lung function and alterations on chest radiographs that resemble emphysema (Hossein-Khannazer *et al*., 2020; kadhim *et al*., 2023; Knoell and Wyatt, 2021; Satarug, 201U; Smith *et al*., 2023; Zuhra *et al*., 2024).

2.2 Watermelon

Watermelon (*Citrullus lanatus*) is a nutritious fruit rich in vitamins, minerals, and antioxidants, offering numerous health benefits. According to a comprehensive review by Nadeem *et al*., watermelon's phytochemical profile includes flavonoids, carotenoids, and saponins, which contribute to its therapeutic effects (Nadeem *et al*.,2021). The antioxidant properties of watermelon, attributed to its lycopene and β-carotene content, have been found to have anti-cancer effects. A study published in the Journal of Nutrition found that consumption of watermelon juice increased plasma concentrations of lycopene and β-carotene in humans (Edwards *et al*., 2003).

2.2.1 Biological Classification of Watermelon

Watermelon (*Citrullus lanatus*) is classified as follows:

1. Kingdom:Plantae (Plants)
2. Phylum:Magnoliophyta (Flowering plants)
3. Class:Magnoliopsida (Dicotyledons)
4. Order:Cucurbitales (Gourd-like plants)
5. Family:Cucurbitaceae (Gourd family)

G. Genus:Citrullus (Watermelon genus)

7. Species:C. lanatus (Watermelon)

2.2.2 Parts of *Citrullus lanatus*

2.2.2.1 Leaf

Leaves are ovate (oval but broader towards the base) to obovate (oval but broader at the apex), 8-20 cm long, scabrid (rough to touch) and deeply pinnatified. The lobes are pinnately divided inti three or four pairs of lobes.

2.2.2.2 Stem

The stems are hairy, rounded to angular in cross-section, and have branched tendrils at each node. The stems are highly branched and long (up to 400 cm). The tendrils are pinnately divided into three or four pairs of lobes.

2.2.2.3 Flowers and sex expression

Watermelons bear separate male and female flowers on the same plant (monoecious). The flowers are unisexual, solitary, axillary and pedicillate. The pedicel of male flower is slender and 12-30 cm long; the female flower pedicel is slightly stouter.

2.2.2.4 Female flower

Calyx and corolla as in male. Staminodes 3, tounge-shaped or represented by setae. Ovary is ovoid, pubescent, with 3 placentas and many ovules; style short, columnar; stigmas 3, thick and kidney- shaped (Dayer 1U75). Only female flowers set fruit. Bees are necessary for pollen transfer pollen.

2.2.2.5 Male flower

Calyx 5-lobed; tube campanulate; corolla 5-lobed; lobes ovate-oblong, glandular-hairy or setose outside. Stamen 3 or 4, one anther 1-thecous; thecae bent; connective flat and broad; inserted at base of calyx tube. Pistil is absent (Dayer 1U75).Watermelon flowers are small,

4-5 cm across, sulphur yellow in color, and less showy than other cucurbits. A few older varieties and accessions collected from the wild are andromonoecious, i.e having staminate and hermaphrodite flowers.

Flowering begins at about eight weeks after seeding, with the production of staminate flowers and later followed by the production of pistillate flowers. In some varieties hermaphrodite flowers develop after the production of staminate flowers.Most varieties have a ratio of 7:1 staminate to perfect or pistillate flower. There are some varieties with a ratio of 4:1. There is no advantage of andromonoecious sex expression because even the perfect flowers must be cross-pollinated to set fruit. For successful seedless watermelon production, bees are especially important as seedless varieties do not produce pollen. The pollinator variety is planted in alternate or every third row, or as every third plant in the row. Use a distinctly different variety as pollinator in order to easily distinguish seedless fruit. Icebox varieties used as pollinators result in early yields; picnic varieties used as pollinators result in greater total yields. Icebox varieties usually flower 7–10 days earlier than picnic varieties, so delay icebox pollinator planting.

2.2.2.6 Fruit

The fruit consists of a firm outer rind, a layer of white inner rind flesh of 0.5-1.4 cm thick, and an interior colored edible pulp embedded with seeds (seedy types). The fruit is round to oblong. The skin is smooth with color ranging from yellow, orange, light green to almost black, either solid or striped with a paler green or marbled. The flesh may be white, cream yellow, pale red, red or dark red. The edible part of the fruit is the endocarp (placenta), which contrasts with muskmelon (Cucumis melo), where the edible part of the fruit is the mesocarp. Fruit weight is usually 415 kg. But in Asia, smaller fruit in the range of 1-4 kg is popular. Fruit rind varies from thin to thick and from brittle to tough.

2.2.2.7 Seed

The seeds are embedded in the edible pulp, small in size (4-G cm), long and flattened (Stone 1U70). Seed color can be white, tan, brown, black, red, green, or mottled.

2.2.2.8 Watermelon rinds

These are also edible, and sometimes used as a fresh vegetable. In China, they are stir-fried, stewed, or more often pickled. When stir-fried, the de-skinned and de-fruited rind is cooked with olive oil, garlic, chili peppers, scallions, sugar and rum. Pickled watermelon rind is also commonly consumed in the Southern US, Russia, Ukraine, Romania and Bulgaria. In the Balkans, especially Serbia, watermelon slatko is also popular. It is a traditional food plant in Africa, since this fruit has potential to improve nutrition, boost food security, fosters rural development and support sustainable landcare.

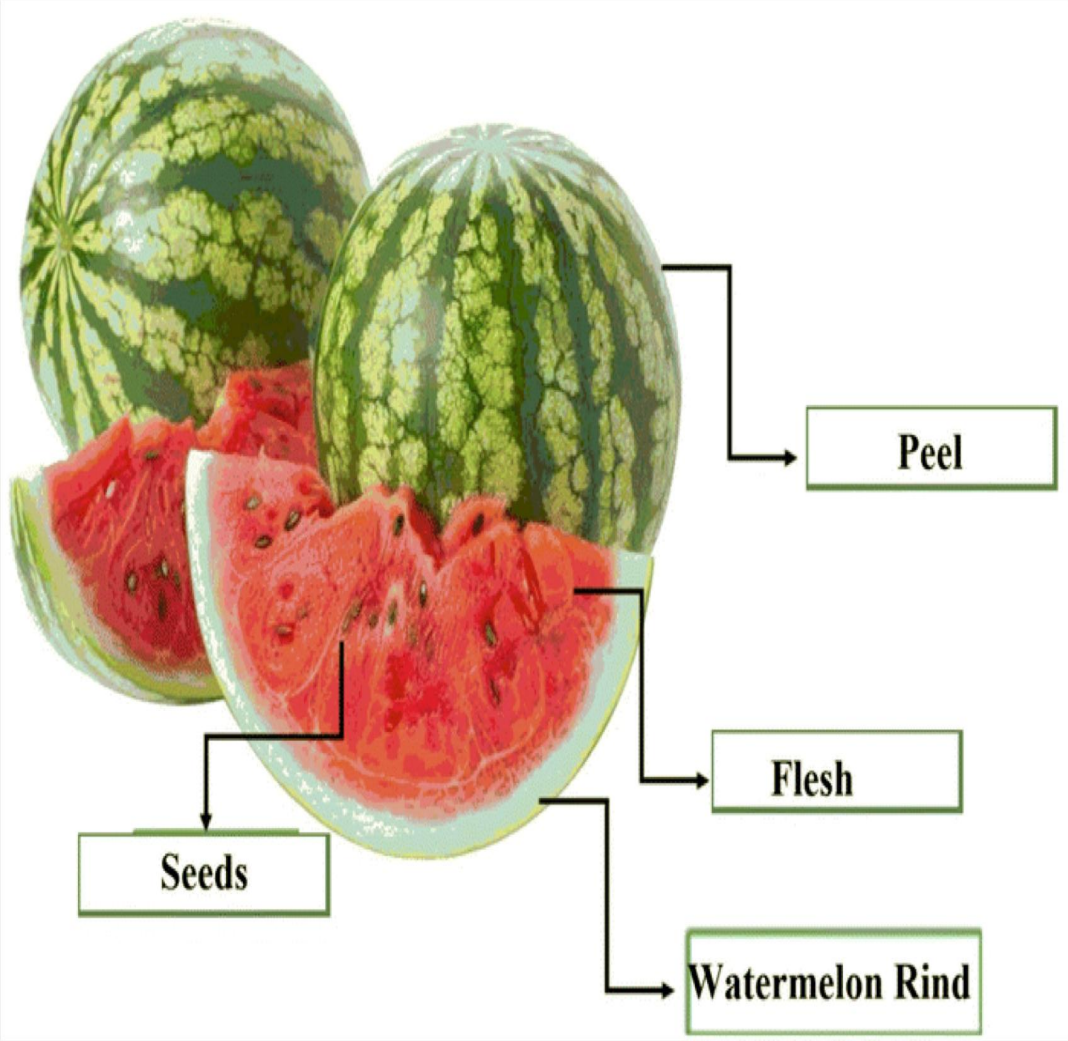

Plate 2.1: Zamuz *et al* 2021

2.2.3 Potential health benefits of *Citrullus lanatus*

2.2.3.1 Antioxidant activity

The antioxidant activity of melon by-products is due to specific compounds like flavonoids and polyphenols (Shan *et al*., 2012). Flavonoids are one of the most effective free radicle scavengers and antioxidants. Pulp and seed powder show antioxygenic solid activity (Ananthan Padmashree *et al*., 2011). The reactive oxygen species may react with biological molecules and result in severe cell damage, including oxidation of vital enzymes, DNA damage, and protein damage (Panda *et al*., 2015).

2.2.3.2 Anti-diabetic activity

The effect of WMR juice ingestion was studied in an experimentally induced type 2 diabetes female albino rat. WMR showed a significant decrease in blood glucose levels, ameliorating structural changes in the pancreas. The increased uptake of blood sugar into the tissue or the stimulation of pancreatic secretions by beta cells are the two main effects of WMR (Sorour *et al*., 201U)

2.2.3.3 Antibacterial activity

WMS includes bioactive components like phenol, flavonoids, saponins, glycosides, and tannins. In relation, it had shown potent antimicrobial activity against E. coli and decreased antibiotic-related side effects (Sola *et al*., 201U). Ethanolic extract of WMS can be used as a source of antimicrobial agents. Aqueous and methanolic extract of WMS powder had shown antibacterial effects against S. aureus, E. coli, S. Typhi, and B. subtilis (Hameed *et al*., 2020). Further, methanolic and hexane extract of the seeds of C. melo L was associated with excellent antimicrobial activity.

2.2.3.4 Antiulcer activity

The hydro methanolic extracts of WMR up to 500 mg/kg body weight had a healing effect on the stomach of albino rats after aspirin-induced gastric ulceration by lowering malondialdehyde (MDA), ROS and increasing the SOD and catalase activity (Elsayed *et al*., 2022).

2.2.3.5 Anti-cancer properties

Anticancer potential of melon by-products

Many polyphenols (hydrolyzable tannins, phenol acid, and flavonoids) have shown anti-proliferative effects. These substances also activate the xenobiotic detoxification system, modify carcinogens, protect DNA from oxidative stress and inhibit the emergence of mutant genes (Sabino *et al*., 2015). According to laboratory and clinical studies, oxidative stress and carcinogenesis are positively correlated (Sonia *et al*., 201G). Phototherapeutic products can prevent the growth of tumors and metastasis. MTT (diphenyl-2H-tetrazolium bromide) tests were used to assess the anti-proliferative capacity of melon residue extract in human cell lines, adenocarcinoma, cervical carcinoma, and cancer of the rectum. In all the

cancer lines, extracts significantly reduced the growth of cells.

Cucurbitacin B is an anticancer agent naturally isolated from the stems of C. melo. Cucurbitacin A and Cucurbitacin E also possess significant anticancer activity (Wright *et al*., 2007). Anticancer activity against leukemia, lymphoma, melanoma, breast cancer, and prostate cancer has been demonstrated by M. charantia extract (Grover and Yadav., 2004). The anti-proliferative potential of isolated polysaccharides from WMR was evaluated, and the results showed that they have substantial cytotoxic action against human laryngeal carcinoma Hep- 2 cells (Dammak *et al*., 201U).

2.2.3.6 Anti inflammatory and anti- pyretic activities

Anti-inflammatory and Anti-pyretic activity

Khalid *et al*. (2021) reported that WMS extract could be effectively used against inflammation and chronic pain.

CHAPTER THREE

MATERIALS AND METHODS

3.1 Materials and equipments

Beakers, 20 mL universal bottles, weighing balance, oven, funnels, plastic animal cages, UV spectrophotometer (Model T80+ UV), Whatman filter paper, knives, crucibles, micropipettes,syringes (1 mL, 2 mL, 5 mL), plastic jars, plain sample containers, EDTA sample bottles, bucket centrifuge, industrial blender, refrigerator, measuring cylinders, laboratory mortar and pestle, spatula, dissecting set,stirring rods, feed and water troughs, water bath, and microscope slides.

3.2 Fruit Purchase

A bag of fresh *Citrullus lanatus* fruits was purchased in February 2025 from the New Benin Market, located in Oredo Local Government Area, Edo State, Nigeria. The fruits were authenticated by a plant taxonomist in the Department of Plant Biology, University of Benin, Benin City, Edo State, Nigeria.

3.3 Chemicals and Reagents

The chemicals and reagents used in this study were of analytical grade and included the following: Cadmium chloride (.99.9 %), normal saline, chloroform, formaldehyde, ethanol (100%), distilled water, and vitamin C.

3.4 Experimental Animals

Healthy adult male and female albino Wistar rats weighing 104g-196g(initial weight)were used for the acute and sub-acute toxicity studies, respectively. The animals were procured from the animal house of the Department of Biochemistry, University of Benin, Benin City,

Nigeria. They were housed in clean plastic cages under standard laboratory conditions.The animals were acclimatized for two weeks prior to the experiment and were fed with standard rat pellets (Bendel Feeds, Nigeria) and water ad Libitum.

All experimental procedures were conducted in accordance with institutional ethical guidelines for the care and use of laboratory animals and were approved by the relevant ethical committee.

3.0 Methodology

3.5 Preparation of *Citrullus lanatus* Extract

The rinds of the Fresh fruits of *Citrullus lanatus* were peeled,then washed throughly to remove any dirt and sun-dried for 24 hours. The dried material was pulverized into fine powder using an industrial blender. The powdered sample was accurately weighed and macerated in a hydroethanolic solvent mixture comprising 50% ethanol and 50% distilled water (100% hydroethanol) for 72 hours in a plastic jar, with vigorous shaking every six hours to ensure maximum extraction of bioactive constituents.

After maceration, the mixture was filtered using Whatman No. 1 filter paper, and the residue (shaft) was discarded. The filtrate was concentrated to a semi-solid extract using a water bath at a controlled temperature to evaporate the solvent. The concentrated extract was transferred into properly labeled sample containers and stored in a refrigerator at 4°C until required for further analysis.

3.6 Experimental Design

After a 14-day acclimatization period, twenty-five (25) healthy Wistar albino rats were randomly divided into five (5) groups, with five (5) rats in each group. The treatment was carried out for sixty (G0) consecutive days as shown in Table 1 below.

Each group received specific treatments as follows:

Group I (Control): Received distilled water only.

Group II (Cd): Received water contaminated with cadmium chloride.

Group III (Cd + Vitamin C): Received cadmium-contaminated water and vitamin C.

Group IV (250 mg/kg of watermelon rinds extract+ Cd): Received cadmium-contaminated water and aqueous extract of *Citrullus lanatus* at 250 mg/kg body weight.

Group V (500 mg/kg of watermelon rinds extract + Cd): Received cadmium-contaminated water and aqueous extract of *Citrullus lanatus* at 500 mg/kg body weight.

All groups except the control (Group I) were given cadmium-contaminated water prepared by dissolving cadmium chloride at a concentration of 1 mg/mL in 300 mL of drinking water per cage daily.

Table 1: Experimental Design

Groups	**Treatment**	**Duration (Days)**
I	**Control (Distilled water only)**	**G0**
II	Cd (Cadmium-contaminated water)	G0
III	Cd + Vitamin C	G0
IV	AECLP (250 mg/kg) + Cd	G0
V	AECLP (500 mg/kg) + Cd	G0

Cd = Cadmium; AECLP = Aqueous Extract of *Citrullus lanatus* Phytowaste

3.6 Dose Calculation

At the commencement of the study, doses of the aqueous extract were calculated based on the average body weight of the rats. The appropriate amount of extract for each animal was determined using the formula:

Dose (mg) = Body Weight of Animal (kg) × Required Dose (mg/kg) 1Dose (mg)= 1

Body Weight of Animal (kg) × Required Dose (mg/kg)

The calculated doses were freshly prepared each day by dissolving the required amount of extract in a small volume of distilled water to facilitate oral administration.

3.8 Preparation of Cadmium Solution

Cadmium chloride ($CdCl_2$) was used to prepare the solution containing cadmium. A 1 mg/mL cadmium solution was prepared by dissolving 1 gram of cadmium chloride salt in 1 liter of distilled water. From this stock, 300 mL was measured daily for each cage and used as the contaminated drinking water throughout the G0-day experimental period.

3.9 Measurement of Food Intake (FI)

Food intake was monitored throughout the G0-day experimental period.During the first 30 days, each cage received 120 g of feed per day, while in the last 30 days, the feed quantity was adjusted to 80 g per day to correspond with changes in the rats' growth and appetite patterns.

Feed remnants were collected and weighed every morning before new feed was supplied. The amount of food consumed per cage was determined by subtracting the weight of the leftover feed from the weight of the feed provided the previous day. The mean daily feed intake per rat was then calculated by dividing the total feed consumed in each cage by the number of animals in that group. Feed Intake (g/rat/day) =

Feed Offered (g) —

Feed Leftover (g) Number of Rats per Cage Feed Intake (g/rat/day)=

Number of Rats per Cage

Feed Offered (g)−Feed Leftover (g)

This measurement provided an index of the animals' appetite, feeding behavior, and potential treatment-related effects on nutrient consumption.

CHAPTER FOUR

4.0 RESULTS

Table 4.1: Effect of the extract on the percentage weight change of the rat after 60 days of administration and cadmium exposure. The Negative control group administered cadmium showed the lowest percentage weight change (37.41%). The extract group (500mg/kg), had the highest percentage weight increase (84.66 %), followed by the 250mg/kg (83.66 %) extract group and Vitamin C (83.53%), and control group (47.31%) group respectively

Table 4.1: Effect of the extract on percentage weight change after cadmium exposure

GROUPS	% WEIGHT CHANGE
Control	47.31 %
Negative control (15mg/kg) $CaCl_2$	37.41 %
Vitamin C (50mg/kg)	85.53%
250mg/kg *Citrullus lanatus*	83.66 %
500mg/kg *Citrullus lanatus*	84.66 %

Table 4.2: Effect of Hydroethanolic extract of *Citrullus lanatus* on the Cadmium level in the blood

GROUPS	BLOOD
Control	0.13 ± 0.04
Negative control (15mg/kg) $CaCl_2$	0.21 ± 0.02
Vitamin C (50mg/kg)	0.17 ± 0.01
250mg/kg *Citrullus lanatus*	0.14 ± 0.05
500mg/kg *Citrullus lanatus*	0.32 ± 0.08

Data were represented as mean ± SEM. a represent a significant difference from control group, b represent a significant difference from Negative control group, c represent a significant difference from vitamin C group, d represent a significant difference from 250mg/kg extract group, e represent a significant difference from 500mg/kg extract group. No letter represent no significant difference from any group.

Table 4.3: Effect of the extract on the lipid profiles on the Wistar rat after exposure to cadmium

GROUPS	CHOL	TRI	HDL	LDL
Control	116.38 ± 35.85	96.92 ± 17.88	16.08 ± 6.00	89.64 ± 43.40
Negative control (15mg/kg) $CaCl_2$	150.28 ± 62.89	168.90 ± 21.36	28.29 ± 12.10	103.39 ± 68.44
Vitamin C (50mg/kg)	41.81 ± 12.02	160.96 ± 37.75	9.10 ± 1.08	5.44 ± 14.06
250mg/kg *Citrullus lanatus*	74.13 ± 6.73	130.80 ± 19.17	18.15 ± 5.40	29.81 ± 12.58
500mg/kg *Citrullus lanatus*	59.21 ± 7.73	127.46 ± 14.51	12.73 ± 1.97	20.98 ± 4.51

Data were represented as mean ± SEM. a represent a significant difference from control group, b represent a significant difference from Negative control group, c represent a significant difference from vitamin C group, d represent a significant difference from 250mg/kg extract group, e represent a significant difference from 500mg/kg extract group. No letter represent no significant difference from any group. There was no significant difference among the groups.

CHOL: Cholesterol, TRI: Triglyceride, HDL: High density lipoprotein, LDL: Low density lipoprotein

CHAPTER FIVE

5.0 DISCUSSION

The assessment of body weight change serves as a vital biomarker for understanding the overall health and metabolic status of experimental animals. In this study, the group exposed solely to cadmium chloride (Negative control) exhibited the lowest percentage weight gain (37.41%) over the 60-day experimental period. This finding aligns with the established pathophysiology of cadmium toxicity, which is known to induce multi-organ damage, particularly in the liver and kidneys, organs central to nutrient metabolism and detoxification (Tchounwou *et al*., 2012). The observed growth suppression can be attributed to cadmium-induced anorexia, gastrointestinal distress, and a general disruption of metabolic processes (Tavakoli *et al*., 2023). Furthermore, cadmium exposure promotes oxidative stress, which can damage cellular structures and disrupt normal anabolic pathways, leading to reduced nutrient utilization and subsequent stunting of growth (Qu and Zheng, 2024). In contrast, the groups treated with the hydroethanolic extract of Citrullus lanatus rind posssessed a remarkable and dose-dependent amelioration of this cadmium-induced weight deficit. The group receiving the 500 mg/kg extract displayed the highest percentage weight increase (84.66%), closely followed by the 250 mg/kg group (83.66%). Thhe performance of these extract-treated groups was comparable to the group administered Vitamin C (85.53%), a recognized standard antioxidant. This can imply that the watermelon rind extract has protective properties against the toxicity of cadmium. The therapeutic effect is likely mediated by the rich profile of bioactive compounds present in the rind, including lycopene, β-carotene, vitamin C, and citrulline (Zamuz *et al*., 2021). These compounds are potent antioxidants that can scavenge the reactive oxygen species (ROS) generated by cadmium, thereby mitigating oxidative damage to the gastrointestinal tract, liver, and other metabolic

organs. By preserving the structural and functional integrity of these systems, the extract likely facilitated better nutrient absorption and utilization, which in turn supported normal growth and weight gain, effectively counteracting the catabolic state induced by cadmium.

The group treated with the high dose of the extract (500 mg/kg) showed a higher mean cadmium level (0.32 ± 0.08 µg/dL) than the negative control, though this was also not statistically significant as there was no significant difference among the groups

The absence of a significant reduction in blood cadmium levels in the treatment groups, especially at the 500 mg/kg dose, is an important observation. Cadmium's toxicokinetics are characterized by its rapid clearance from the bloodstream and subsequent strong, cumulative binding to metallothionein protein in soft tissues, primarily the liver and kidneys, where it can persist for decades with a biological half-life of 15-20 years (Wang *et al*., 2021; Peana *et al*., 2022). Blood cadmium is considered a marker of recent exposure, whereas urine cadmium reflects the total body burden. The primary mechanism of action for many therapeutic interventions is not necessarily to rapidly mobilize cadmium from deep tissue stores into the blood for excretion, which can sometimes be dangerous, but rather to prevent its initial absorption and/or mitigate its toxic effects at the cellular level. Increase in the 500 mg/kg group, while not significant, could be interpreted in two ways. One possibility is a limited mobilization of cadmium from tissue stores back into the bloodstream. However, a more plausible explanation, strongly supported by the positive findings on body weight and lipid profiles, is that the extract's primary role was one of cytoprotection rather than chelation. The bioactive compounds in *Citrullus lanatus*, such as polyphenols and flavonoids, are known for their potent antioxidant and metal-chelating properties. They may act by forming complexes with cadmium in the gut, reducing its bioavailability, or, more importantly, by upregulating endogenous protective

systems like glutathione and metallothioneins within cells. This intracellular sequestration renders the metal less toxic without significantly altering its overall distribution or concentration in the blood (Lin *et al*., 2021).

Lipid parameters gives understanding into the metabolic disturbances induced by cadmium and the corrective potential of the *Citrullus lanatus* rind extract. The results indicate that cadmium exposure exerted a pronounced dyslipidemic effect. The negative control group exhibited elevated levels of total cholesterol (CHOL: 150.28 ± 62.89 mg/dL) and triglycerides (TRI: 168.90 ± 21.36 mg/dL) compared to the normal control group. This aligns with existing research demonstrating that cadmium can disrupt hepatic cholesterol metabolism, leading to hyperlipidemia. A study on zebrafish showed that cadmium exposure significantly increased triglycerides and total cholesterol, impairing the beneficial functions of high-density lipoproteins (HDL) and promoting fatty liver changes (Kim *et al*., 2018). Similarly, research in rats has reported that cadmium increases serum levels of total cholesterol, triglycerides, and low-density lipoprotein (LDL) while reducing HDL levels (Samarghandian *et al*., 2015).

The administration of the *Citrullus lanatus* rind extract, particularly at the 500 mg/kg dose, demonstrated a normalizing effect on the lipid profile. This group showed a substantial reduction in total cholesterol (59.21 ± 7.73 mg/dL) and triglycerides (127.46 ± 14.51 mg/dL) compared to the negative control group. Furthermore, the calculated LDL cholesterol, a key atherogenic risk factor, was lower in the extract-treated groups (20.98 ± 4.51 mg/dL in the 500 mg/kg group) compared to the negative control (103.39 ± 68.44 mg/dL). This therapeutic action can be attributed to the rich antioxidant phytochemicals in watermelon rind. Compounds like lycopene and β-carotene are well-documented for their potent antioxidant activities (Rao and Rao, 2007;

Nadeem *et al*., 2021). By directly scavenging the ROS generated by cadmium, these compounds mitigate oxidative damage to liver cells. A healthier liver is more capable of maintaining proper lipid homeostasis, including the regulation of cholesterol synthesis and the catabolism of triglycerides (Alamri, 2018). The anti-inflammatory properties of flavonoids and other polyphenols in the extract may also have contributed to reducing the chronic inflammatory state often associated with dyslipidemia and cadmium toxicity.

5.1 CONCLUSION

Cadmium chloride exposure adversely affects body weight and lipid metabolism in Wistar rats. However, supplementation with hydroethanolic extract of watermelon rind effectively counteracts these toxic effects, demonstrating significant protective potential. This suggests that watermelon rind, an agricultural waste product, could be a valuable natural resource for developing interventions against heavy metal toxicity.

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