ASSESSMENT OF THE EFFECTS OF WATERMELON (*Citrullus lanatus*) PHYTOWASTE EXTRACT ON LIVER MARKERS IN CADMIUM EXPOSED RAT

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CERTIFICATION

This is to certify that this project titled "**ASSESSMENT OF THE EFFECTS OF HYDROETHANOLIC EFFECT OF *Citrullus lanatus* PHYTOWASTES EXTRACT ON LIVER MARKERS IN CADMIUM EXPOSED RAT"** was carried out by **Miracle Osaro IGIOZEE,** with matriculation number **LSC2003157**, of the Department of Science Laboratory Technology (Physiology/Pharmacology), Faculty of Life Sciences, University, Benin City, Edo state, Under the supervision of DR. O. C. EKHATOR.

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EXTERNAL EXAMINER	Date

DEDICATION

This work is dedicated to God Almighty and my late dad Mr Gauis Uyikpen Igiozee

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I sincerely express my profound gratitude to Almighty God for His grace, guidance, and wisdom throughout the course of this project and my academic journey.

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ABSTRACT

Cadmium (Cd) is a pervasive environmental toxicant known to induce hepatotoxicity through oxidative stress. This study investigated the protective effect of a hydroethanolic extract of *Citrullus lanatus* (watermelon) rind against cadmium-induced liver damage in Wistar rats. Twenty five rats were divided into five groups: control, negative control ($CdCl_2$ only), Vitamin C, and two groups receiving *C. lanatus* extract (250 mg/kg and 500 mg/kg). After 60 days, biochemical liver markers were analyzed. The negative control group showed elevated levels of AST, ALT, and total bilirubin, indicating hepatocellular injury. In contrast, treatment with the *C. lanatus* extract, particularly at 500 mg/kg, significantly ameliorated these alterations, bringing the enzyme and bilirubin levels closer to those of the control and Vitamin C groups. The extract also counteracted the growth-suppressive effect of cadmium, with treated groups showing significantly higher body weight gain. There were no significant changes in liver cadmium concentration or liver to body weight ratio across groups. This can imply that the hydroethanolic extract of *C. lanatus* rind possesses potent hepatoprotective properties against cadmium toxicity, likely mediated by its antioxidant phytoconstituents, which stabilize hepatocyte membranes and improve metabolic function without altering cadmium accumulation.

CHAPTER ONE

INTRODUCTION

1.1 BACKGROUND OF STUDY

The problem of heavy metal pollution is growing increasingly severe in developing nations, driven by a rise in both natural geological processes and human activities. These activities have elevated concentrations of these elements to levels that are damaging to the ecosystem (Chibuike and Obiora, 2014). Rapid industrial and urban expansion, along with increasing traffic, significantly adds to the buildup of heavy metals released by vehicles into the environment. In agricultural zones, contamination from traffic emissions can lead to the uptake of heavy metals by crops (Chen *et al*., 2010). This results in stunted growth, lower performance, and reduced yields for plants in these areas. Documented evidence shows that growth inhibition occurs due to alterations in the plants' physiological and biochemical processes when they are cultivated in heavy metal-contaminated soil (Taofeek and Tolulope, 2012). This decline in plant growth diminishes agricultural output, which can ultimately threaten food security. For humans, the primary pathway for exposure to these metals in agricultural regions is through their absorption from soil into crops.

People living near contamination sources can be easily affected by heavy metals through inhaled dust or direct contact. If farmlands are within the reach of the pollutants, these metals can be absorbed by food crops and enter the food chain (Taofeek and Tolulope, 2012), creating significant health hazards. Given their toxicity (notably cadmium and lead), persistence, and inability to break down, monitoring environmental levels of heavy metals is critically important. Regardless of their atomic mass or density, any poisonous metal can be referred to as a heavy

metal (Zhang *et al*., 2012). A vaguely defined collection of elements with metallic characteristics includes heavy metals. These consist of actinides, lanthanides, some metalloids, and transition metals. Nies (2018) claims that heavy metals, such copper, lead, and zinc, are among the common transition metals.

Of the world's vascular plants, 10% serve as medicinal plants, with total species estimates ranging from 350,000 (Joppa *et al*., 2011) to nearly half a million (Pimm *et al*., 2014). The application of plants for healing dates back to ancient times and continues in the present day. Initially, their use for treating ailments or improving well-being was discovered through a process of trial and error, which helped identify beneficial species with positive properties (Kunle *et al*., 2012). This knowledge was refined over generations, evolving into what is widely recognized as traditional medicine. According to an official definition, traditional medicine is "the sum total of the knowledge, skills and practices based on the theories, beliefs and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health, as well as in the prevention, diagnosis, improvement or treatment of physical and mental illnesses" (Kunle *et al*., 2012).

Every civilization has historically developed its own form of this medicine, utilizing the plant life available in its local environment. Some scholars argue that this accumulated, shared knowledge represents the very foundation of medicine and pharmacy. Presently, a vast number of plant species are cultivated globally to extract compounds for use in medical and pharmaceutical products. The healing potential of plants led directly to the development of medicinal preparations derived from species possessing these therapeutic qualities (Atanasov *et al*., 2015). *Citrullus lanatus* belongs to the family Cucurbitaceae. In the temperate regions of the world, this plant is one of the most widely grown horticulture crops. It is a prostrate, wandering,

annual vine with hairy, pinnately-lobed leaves and curly tendrils. Watermelon is another name for its fruit (Wehner *et al*., 2001). According to Johnson and Walcott *et al*. (2013), free radicals aid in the quenching of diseases like diabetes, colon cancer, atherosclerosis, arthritis, and asthma. Although it lacks oxalate and flavonoids, watermelon is also made up of phenolic components, and its seeds contain glycosides, alkaloids, saponins, tripterpenoid, phytates, and tannins (Oseni and Okoye *et al*., 2013).

1.2 STATEMENT OF PROBLEM

The increasing severity of heavy metal pollution, particularly from elements like cadmium, poses a significant threat to ecosystems and public health. These persistent and toxic metals accumulate in the environment through industrial, urban, and agricultural activities, leading to their uptake by plants and subsequent entry into the food chain. Chronic exposure to cadmium is known to induce severe toxicological effects in mammals, including organ damage and oxidative stress. While the adverse effects of cadmium are well documented, there is a continuous need for effective and accessible therapeutic or prophylactic agents to mitigate its toxicity. Conventional treatments often have limitations, including cost and side effects, which requires the search for natural alternatives like medicinal plants.

1.3 JUSTIFICATION OF THE STUDY

This research aims to discover compounds from medicinal plants with healing potential. The knowledge of using plants for treating ailments, studied over generations, is the foundation of traditional medicine. Watermelon (*Citrullus lanatus*) is a plant cultivated globally, and its rinds may possess therapeutic qualities. Given that heavy metals like cadmium are toxic, persistent, and create significant health hazards by entering the food chain, it is critically important to find

ways to counteract their effects. This research aims to contribute to this need by investigating the therapeutic effect of a plant-derived extract against heavy metal toxicity.

1.4 AIM

To evaluate the effect of Watermelon (*Citrullus lanatus*) on Liver markers in Cadmium exposed rats.

1.5 THE SPECIFIC OBJECTIVES ARE TO;

- evaluate the Liver markers of Wistar rats
- evaluate the level of heavy metals in blood and liver

CHAPTER TWO

LITERATURE REVIEW

2.1 CADMIUM

Cadmium (Cd) is a malleable, blueish or silvery-white metallic powder known for its reactivity with various compounds. This property makes it valuable for applications in cells and batteries (e.g., nickel-cadmium), as well as in the production of alloys, pigments, stabilizers for plastics, dyes, paints, glass, and galvanic processes (Qing *et al*., 2021; Balali-Mood *et al*., 2021). The element was first discovered by F. Stromeyer in 1817 in Göttingen, Germany (Qing *et al*., 2021). In nuclear technology, cadmium regulates uranium fission by capturing neutrons (Qing *et al*., 2021). It occurs naturally in the environment within soil, water, and mineral ores such as sulfides and carbonates (Qing *et al*., 2021). Since it shares properties with zinc, lead, and copper, cadmium is obtained as a by-product of zinc smelting (from ZnS) (Tchounwou *et al*., 2012). The most significant human exposure to cadmium occurs in metallurgical settings, including zinc smelters and plants that purify pig iron (Charkiewicz *et al*., 2019). Every year, a contaminated environment affects about 600 million individuals. Food contamination by heavy metals is a major issue globally and is particularly prevalent in agricultural areas that are contaminated (Kayiranga *et al*., 2023). Additionally, it is estimated that approximately 40% of lakes and rivers and over 13% (or 0.24 billion hectares) of the world's total arable land are contaminated by heavy metals (Kayiranga *et al*., 2023). The environment is severely impacted by the ongoing industrial usage of Cd, which exposes people to high levels of the element.

The human body eliminates cadmium very slowly, with a biological half-life ranging from 16 to 30 years (Genchi *et al*., 2020). Scientific evidence suggests that slow poisoning from small doses of cadmium is connected to the development of chronic lung ailments (emphysema, asthma, bronchitis) and hypertension (Omeljaniuk *et al*., 2018). Furthermore, long-term exposure is associated with severe diseases, including cancer, leukemia, and genetic toxicity (Tchounwou *et al*., 2012). Studies confirm that heavy metals like cadmium are damaging to human organs even at low concentrations. A high, acute dose can induce rapid symptoms, such as abdominal pain, nausea, vomiting, salivation, muscle cramps, shock, and convulsions within 15 to 30 minutes (Nejabat *et al*., 2017). Recent data link cadmium exposure to specific cancers (e.g., prostate, kidney, breast), neurodegenerative disorders (Alzheimer's, Parkinson's, ALS), and skeletal diseases like osteoporosis (Nawrot *et al*., 2015; Julin *et al*., 2012). Its ability to cross the placenta can cause fetal malformations, and it is also implicated in Itai-Itai disease, cardiovascular illness, and lung function abnormalities. The kidneys are the principal organ affected by cadmium toxicity, showing high sensitivity and often experiencing impaired reabsorption function (Qing *et al*., 2021).

2.1.1 SOURCES OF CADMIUM

The primary source of cadmium is stack dust, which is produced during the distillation process of purifying zinc and is deposited in all fractions because of its high volatility. The primary applications of cadmium are as an anticorrosion coating for steel sheets or for coating other metals, primarily steel. It is frequently used to create low-melting alloys, like Wood's metal, which are utilized in fire safety systems, and it also functions as an excellent protective coating in alkaline environments (Tchounwou *et al*., 2012). Since heavy industries are all but extinct in

Poland right now, smoking cigarettes and eating tainted food are the primary ways that people there are exposed to cadmium. The same routes of Cd exposure were also documented in the United States by Tchounwou *et al*. (2012). Apart from smoking and eating tainted food, other ways that people might be exposed to cadmium include working in the metal industry or in locations that are contaminated with cadmium (Paschal *et al*., 2000).

2.1.2 EXPOSURE TO CADMIUM

The clinical presentation of cadmium poisoning varies based on the length of exposure, dietary habits, and the age and general health of the affected person. The element's physiological impact is also modulated by its interplay with other metals, including zinc, selenium, copper, iron, and manganese. Tobacco smoke acts synergistically with cadmium, accelerating its toxic effects (Genchi *et al*., 2020). The principal routes of cadmium absorption are inhalation and, partially, the digestive tract following the ingestion of dust-containing saliva (Tchounwou *et al*., 2012). This element bioaccumulates preferentially in the lungs, liver, kidneys, pancreas, testicles, muscles, adipose tissue, and skin, and it functions by inhibiting enzymes that contain sulfur (Tchounwou *et al*., 2012). An estimated 13–19% of inhaled cadmium is absorbed from the air, while 10 - 44% is absorbed through the gastrointestinal system, mainly in the small intestine. In the bloodstream, cadmium forms complexes with red blood cells; albumin-bound complexes deposit in the liver, while those bound to the small protein metallothionein (MT) are reabsorbed in the renal tubules (Lech and Sadlik, 2017). The accumulated levels of cadmium are measured at 0.14–3.2 ppm in muscle tissue, 1.8 ppm in bones, and 0.0052 ppm in blood.

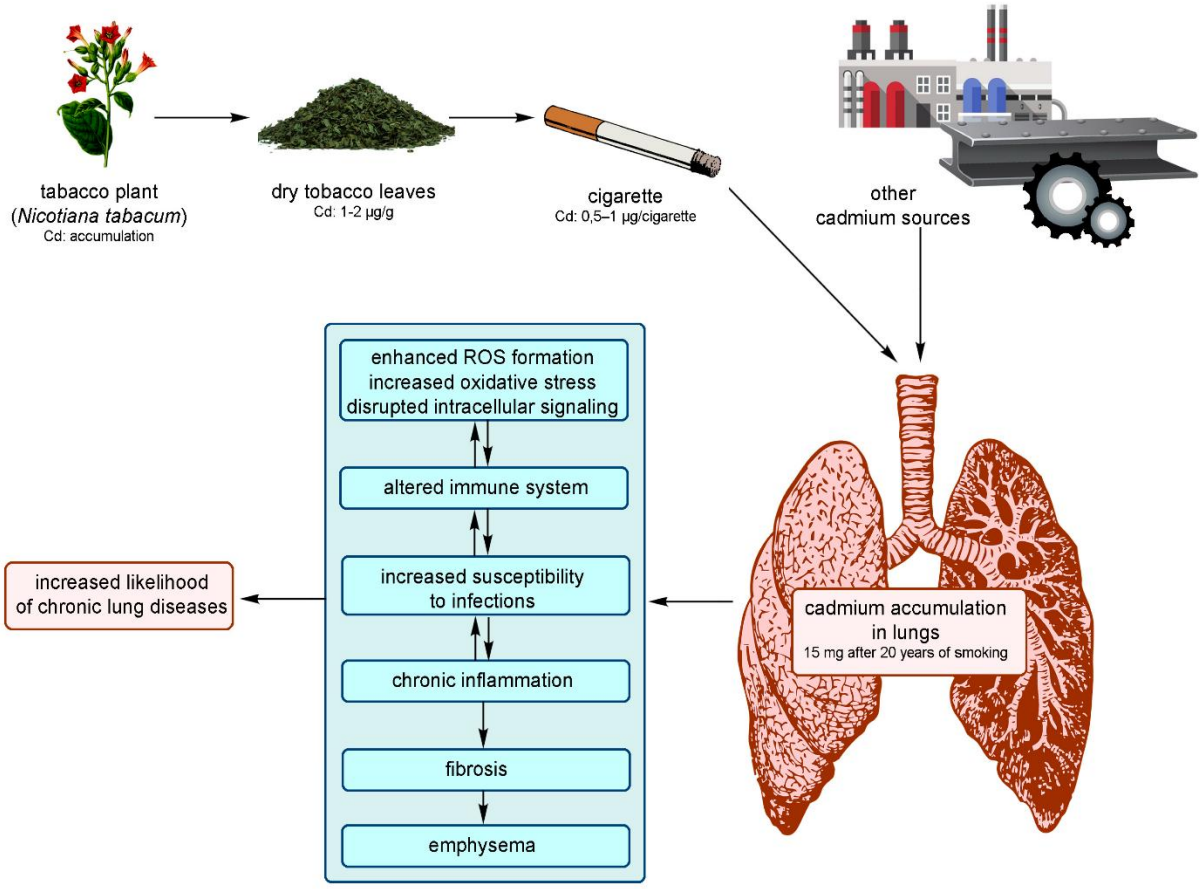

Plate 2.1: Exposure to cadmium (Qing *et al*., 2021)

2.1.3 PATHOLOGICAL EFFECTS OF CADMIUM

2.1.3.1 IN THE RESPIRATORY SYSTEM

Cadmium exposure exerts an irritant effect on the respiratory system, impacting the mucous membranes of the nose and the upper airways. Poisoning related to occupational exposure, predominantly in the metallurgical industry, arises from the inhalation of fumes generated during processes such as welding, melting, or soldering of cadmium-based materials (Charkiewicz *et al*., 2019). Diagnostic detection of these changes can be achieved via laryngological examination, spirometry, and chest radiography. The presenting symptoms, which may manifest within a 24-hour period, are analogous to those of metal fume fever and pulmonary edema. Acute intoxication is caused by exposure to fumes at a concentration of 0.5 mg/m^3 or to the respirable fraction of dust at 3 mg/m^3, typically resulting in chronic bronchitis. Workers frequently report anosmia (complete loss of smell) or hyposmia (reduced smell), xerosis (drying) or ulceration of the nasal mucosa, and a dry cough that progresses to a productive one. Probable cadmium-induced emphysema presents with symptoms of exertional dyspnea, decreased tolerance for physical activity, and diminished lung ventilation efficiency (Lech and Sadlik, 2017). Furthermore, long-term inhalation of Cd particles is correlated with both functional lung abnormalities and radiographic evidence of emphysema, and occupational exposure to Cd-laden air is linked to impaired olfactory capability (Tchounwou *et al*., 2012).

2.1.3.2 IN THE NEPHROLOGICAL SYSTEM

Renal damage from cadmium, is proportional to the organ's accumulation of cadmium-bound metallothionein (MT), with pathological changes chiefly observed in the proximal tubules alongside initial signs of proteinuria. Notably, acute oral poisoning is no longer encountered in occupational environments. Conversely, chronic intoxication develops following several years of exposure and may present even after exposure has terminated. Past prolonged exposure to Cd is associated with detectable urinary cadmium (Cd-U) concentrations, which, when calculated relative to creatinine, signify the cumulative renal cadmium burden. The kidneys are the most critically affected organ. Among exposed individuals, the cadmium concentration in the renal cortex can reach a critical level of 200 mg/kg, while urinary concentrations range from 0.889 µmol/l (10 µg/g creatinine) to 1.333 µmol/l (15 µg/g creatinine). The permissible biological concentration for cadmium in urine is 0.0445 µmol/l (5 µg/g creatinine) (Jarup and Akesson, 2009). It is estimated that approximately 2.3% of the U.S. population exhibits elevated urinary cadmium levels (>2 µg/g creatinine) (Tchounwou *et al*., 2012). The clinical presentation may include proteinuria as a longer-term symptom, subsequently followed by glycosuria, aminoaciduria, hypercalciuria, hyperphosphaturia, and elevated creatinine. Toxic nephropathy is often the exclusive consequence of cadmium exposure (Li *et al*., 2019).

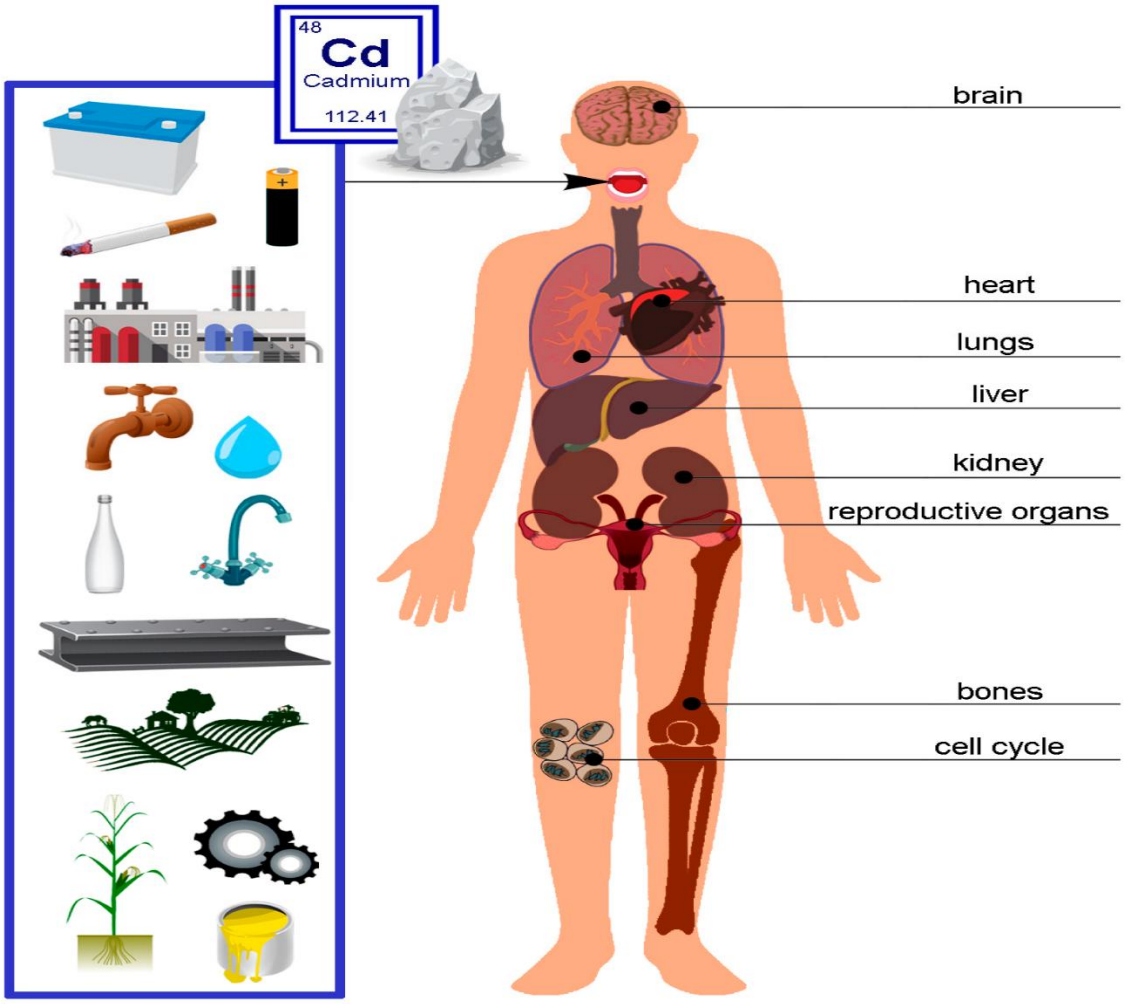

Plate 2.2: Effects of Cadmium in the human body (Li *et al*., 2019)

2.1.3.3 IN THE CARDIOVASCULAR SYSTEM

Cadmium plays a significant role in the pathogenesis of specific cardiovascular conditions linked to smoking, such as peripheral arterial disease and ischemic heart disease. Prolonged exposure to this metal can lead to the development of arterial hypertension, atherosclerosis, and cardiac dysfunction (Lin *et al*., 2021). The concentration of cadmium in the blood serves as a biomarker for recent exposure, for instance from smoking or occupational environments (Tchounwou *et al*., 2012). However, the element's effect on the cardiovascular system remains contentious, as some studies report detrimental impacts at extremely low doses. Research by Li *et al*. (2019) identified an association between cadmium exposure and cardiovascular disease pathways, positing that cadmium mediates the development of some smoking-related cardiovascular ailments (Li *et al*., 2019). Established biological exposure limits for blood cadmium are 5 µg/L (American Conference of Governmental Industrial Hygienists) and 2.7 µg/L (Neumeister *et al*.) (2015). A positive correlation between lead (Pb) and cadmium levels points to mixed exposure to both metals (Charkiewicz *et al*., 2019). Swedish research has substantiated the relationship between cadmium exposure and the progression of atherosclerosis and ischemic stroke (Borne *et al*., 2017), while subsequent investigations have documented additional circulatory system alterations from chronic heavy metal exposure (Charkiewicz *et al*., 2022).

2.1.3.4 IN THE REPRODUCTIVE SYSTEM

Cadmium possesses the ability to traverse the placental barrier, albeit at a slow rate, and can exert teratogenic impacts on the developing fetus (Genchi *et al*., 2020). The majority of the element is sequestered within the placental tissue; however, comprehensive data regarding its contribution to early pregnancy loss (Omeljaniuk *et al*., 2018) and its direct consequences for

human fetal development remain limited (Czeczot and Majewska, 2010). An analysis by Omeljaniuk *et al*. (2018) substantiated that concentrations of both cadmium and lead were markedly elevated in the blood and substantially higher in the placental tissue of women with spontaneous abortion relative to the control cohort. It is important to highlight that females typically demonstrate greater cadmium concentrations in blood, urine, and renal tissue than males, a phenomenon potentially attributable to iron depletion and deficiency, which are common among women of childbearing age. Additionally, the breast milk of smoking mothers may contain double the cadmium concentration of that from non-smokers. With regard to male reproduction, the research of Kasperczyk *et al*. indicated an inverse relationship between blood cadmium concentration and the proportion of morphologically normal spermatozoa (Kasperczyk *et al*., 2008). The toxic action of cadmium primarily disrupts testicular physiology by inducing damage to the vascular endothelium, Leydig and Sertoli cells, and the seminiferous tubules, thereby suppressing testosterone synthesis and impairing sperm production. The metal also adversely affects prostate gland function, leading to hormonal and secretory dysregulation that compromises male fertility (Czeczot and Majewska, 2010).

2.1.3.5 IN THE NERVOUS SYSTEM

The neurotoxic impact of cadmium remains incompletely reported. The metal can exert adverse effects on the nervous system once its concentration surpasses 0.8 μg/L in urine and 0.6 μg/L in blood. Given that such concentrations are presently documented in industrialized regions, it can be inferred that environmental exposure poses a risk to neurological integrity. Cadmium may also be implicated in the etiopathogenesis of neurodegenerative diseases, with evidence suggesting a role in central nervous system (CNS) disorders including Alzheimer's disease (AD),

Parkinsonism and Parkinson's disease (PD), Huntington's disease (HD), amyotrophic lateral sclerosis (ALS), and multiple sclerosis (MS), alongside deteriorations in cognitive and behavioral performance (Syeda and Cannon, 2021). Earlier investigations revealed elevated cadmium concentrations in the hair of children affected by neurological disorders, learning and behavioral difficulties, neuropathy, and impairments in memory, attention, and psychomotor function. As cadmium can interfere with neurological function in children at significantly lower levels (>0.38 μg/L in blood and >0.1802 μg/L in urine), it is regarded as a potential contributor to these pathologies within this demographic (Wang and Du, 2013).

2.2 HEPATOTOXICITY AND BIOMARKERS

Hepatotoxicity, presents a significant clinical challenge due to the liver's central role in metabolism and detoxification, and the often nonspecific nature of early symptoms. The diagnosis and monitoring of this condition therefore rely heavily on biomarkers, which are measurable indicators of biological processes. Traditional biomarkers form the cornerstone of clinical assessment for liver injury. Among the most prominent are the aminotransferases, alanine aminotransferase (ALT) and aspartate aminotransferase (AST), which are enzymes released into the bloodstream upon hepatocyte necrosis or inflammation. While ALT is considered more liver-specific, AST is also found in other tissues like the heart and skeletal muscle, which can sometimes complicate interpretation (Kwo *et al*., 2017). The clinical structure of ALT, for instance, varies with the cause; in Hepatitis B virus (HBV) infection, its levels are closely tied to the cytolytic immune response, whereas in Hepatitis C virus (HCV), significant liver damage can persist even with normal or only slightly elevated ALT levels (Liu *et al*., 2014). Beyond cellular integrity, biomarkers of the liver's functional capacity are crucial. Bilirubin, a

byproduct of heme breakdown, accumulates in the blood a condition known as hyperbilirubinemia, when the liver cannot properly conjugate or excrete it, signaling hepatocellular dysfunction or biliary obstruction, and severe elevation is a poor prognostic sign (Zhang *et al*., 2017; Dosch *et al*., 2019). Similarly, Alkaline Phosphatase (ALP) and Gamma-Glutamyl Transferase (GGT) are key indicators of cholestatic liver disease, rising with bile duct obstruction, with GGT being particularly sensitive to alcohol-induced liver injury and also associated with metabolic risks like fatty liver disease (Green and Sambrook, 2020; Fujii *et al*., 2020). The liver's synthetic function is assessed through proteins it produces, such as albumin, and coagulation factors measured via Prothrombin Time (PT). A decline in albumin levels or a prolonged PT indicates significant impairment of the liver's biosynthetic capacity, a hallmark of advanced conditions like cirrhosis (Ge *et al*., 2016; Zermatten *et al*., 2020). Other enzymes like Arginase and Alpha-Glutathione S-Transferase (α-GST) have been investigated for their potential to offer greater specificity or earlier detection than ALT, with α-GST showing promise for identifying subclinical injury in patients with otherwise normal aminotransferase levels (Czuczejko *et al*., 2019; Abdel-Moneim and Sliem, 2011). Collectively, these traditional biomarkers are indispensable for the early detection of drug-induced liver injury (DILI), differential diagnosis of conditions like hepatitis and cholestasis, assessment of disease severity, and guiding treatment decisions (Neuman, 2019). However, their limitations are well-recognized, including a lack of specificity for the liver, as seen with AST, and the fact that some markers, like bilirubin, only elevate after substantial damage has already occurred, which can delay diagnosis and intervention (Kalas *et al*., 2021). Despite these constraints, traditional biomarkers remain the fundamental toolkit for evaluating hepatotoxicity in clinical practice.

2.2.1 CADMIUM INDUCED HEPATOTOXICITY

Cadmium (Cd) is a heavy metal of significant toxicological concern. It is virtually absent at birth in mammals but accumulates progressively in the liver and kidneys over time. In fact, up to 85% of the body's total cadmium burden can be found in these two organs (Renugadevi and Prabu, 2010; Yan *et al*., 2020). This bioaccumulation occurs due to both short-term and long-term environmental or occupational exposure (Karmakar *et al*., 2000).

The primary mechanism through which cadmium inflicts liver damage is the induction of oxidative stress. Cadmium exposure leads to the generation of reactive oxygen species (ROS), such as superoxide, nitric oxide, and hydroxyl radicals. Rather than directly generating free radicals, Cd disrupts cellular processes, leading to oxidative stress-mediated damage (Renugadevi and Prabu, 2010). This oxidative assault results in the peroxidation of membrane lipids in the liver, which attacks the cell membrane, leading to its instability and eventual disintegration (Renugadevi and Prabu, 2010). Bagchi *et al*. (1996), as cited by Karmakar *et al*. (2000), demonstrated that following Cd exposure, there is a significant increase in hepatic, mitochondrial, and microsomal lipid peroxidation, coupled with a depletion of the critical antioxidant glutathione (GSH).

The antioxidant defence system is severely compromised by cadmium. Cd depletes selenium in the body, which in turn reduces the activity of GSH peroxidase. This leads to an accumulation of hydrogen peroxide and other ROS, as well as a depletion of reduced GSH. This oxidative stress subsequently activates key signalling pathways like NF-κB and AP-1 (Sarkar *et al*., 2013). Furthermore, a recent study showed that Cd exposure inhibits the protective Nrf2 pathway and its downstream target heme oxygenase 1 (HO-1), while increasing the level of its repressor,

Keap1 protein. Cd intoxication also results in the activation of MAPKs, NLRP3, and NF-κB pathways, all contributing to liver injury (Liu *et al*., 2020).

Cadmium also causes significant ultrastructural and sub-cellular damage in hepatocytes. One of the earliest morphological changes is the dilation of the endoplasmic reticulum (ER) and loss of ribosomes (Rikans and Yamano, 2000). Cd toxicity can lead to the destruction of the ER and the formation of intracellular vesicles, affecting hepatic endothelial cells and causing ischemia, which impairs hepatic microcirculation and results in hypoxia and further injury (Kuester *et al*., 2002). In the nucleus, condensation of the nucleolar region is an early sign of Cd-induced hepatotoxicity (Rikans and Yamano, 2000). Transmission Electron Microscopy (TEM) analyses have confirmed morphological changes in the mitochondria and nuclei of hepatocytes (Venter *et al*., 2015). The primary injury is often due to Cd binding to sulfhydryl groups on critical mitochondrial molecules, leading to mitochondrial dysfunction and increased permeability (Rani *et al*., 2014). Sub-chronic Cd administration can inhibit the activity of enzymes like UDGPT and cytochrome P450, further disrupting liver function (Karmakar *et al*., 2000).

The inflammatory response is a key feature of cadmium hepatotoxicity. Activation of Kupffer cells (liver-resident macrophages) by Cd exposure initiates a cascade involving various liver cells, cytotoxic mediators, and inflammatory cytokines, leading to secondary liver injury (Rikans and Yamano, 2000). This is often mediated by the release of Tumour Necrosis Factor-alpha (TNF-α) from non-parenchymal cells, which is responsible for many manifestations of Cd-induced hepatotoxicity (Koyu *et al*., 2006). Studies on rats have shown that administration of $CdCl_2$ leads to Kupffer cell hyperplasia and swollen hepatocytes (Mantur *et al*., 2014).

Cadmium exposure can also alter epigenetic mechanisms. Studies have shown that Cd can act via epigenetic pathways, with initial exposure reducing DNA methyltransferase activity and

causing slight genomic hypomethylation. In contrast, prolonged exposure increases DNA methyltransferase activity and leads to DNA hypermethylation, which is associated with increased cellular invasiveness and hyperproliferation (Takiguchi *et al*., 2003). Research on European eels demonstrated that low-level Cd exposure causes DNA hypermethylation and a decrease in RNA synthesis (Pierron *et al*., 2014).

The metal also disrupts hepatic cholesterol metabolism. In zebrafish, exposure to $CdCl_2$ for four weeks resulted in a significant increase in triglycerides (TG), total cholesterol (TC), and cholesteryl ester transfer (CE) activity. It also caused structural modifications to HDL3, impairing its beneficial functions and leading to hyperlipidemia and fatty liver changes via enhancement of cholesteryl ester transfer protein (CETP) activity (Kim *et al*., 2018). Similarly, a study on rats showed that Cd increased serum levels of TC, TG, MDA, and LDL-C, while reducing HDL-C levels (Samarghandian *et al*., 2015).

Finally, cadmium induces cell death through both apoptosis and necrosis. Cadmium can activate caspase-8 and upregulate the expression of IP3R1, leading to calcium release from the ER, which activates calpain and induces apoptosis. It can also trigger the mitochondrial pathway by activating caspase-9 via cytochrome c release (Rani *et al*., 2014). Furthermore, Cd may induce apoptosis by disturbing transcription factors like NF-κB, which regulate apoptotic gene expression (Xie and Shaikh, 2006). A shift in redox balance towards oxidative stress can promote mitochondrial permeability transition, a key event in apoptosis (Rikans and Yamano, 2000). If the oxidative stress is not balanced by repair mechanisms, the affected cells undergo necrosis (Renugadevi and Prabu, 2010). Histopathological examinations in chickens and mice have confirmed that Cd exposure leads to necrosis and sinusoidal dilation in the liver (Venter *et al*., 2015; Liu *et al*., 2020).

2.3 WATERMELON (*Citrullus lanatus*)

Human life on Earth is sustained by a complex interplay of living and non-living elements. Since the dawn of civilization, nature has been the fundamental source of sustenance, enabling humanity to thrive and adjust to changing environments. Historically, people depended profoundly on various plants, including herbs, shrubs, and trees, to meet their essential requirements, primarily for nourishment and healing. The animal kingdom's continued survival is deeply interconnected with the plant world, which provides indispensable resources such as food, materials for clothing and shelter, and remedies for illness. Since ancient times, numerous plants and their derivatives have been documented for addressing a wide spectrum of health problems, from minor to severe. In this context, the forests of India are renowned for their immense diversity of medicinal flora. The Botanical Survey of India has officially catalogued approximately 8,000 plant species used within Indian Ayurveda for treating various ailments (Pandey *et al*., 2013). In the face of contemporary lifestyles and the surge of numerous diseases, the role and value of medicinal plants have become critically important for those seeking a long and healthy life. Their accessibility, low cost, and favorable safety profile have elevated their status to global significance. Consequently, a growing segment of the world's population is shifting its focus towards natural and plant-based solutions over synthetic alternatives (Gupta and Raina, 1998; Sofowora *et al*., 2013; Ekor, 2013).

The vast and varied plant kingdom represents an invaluable asset for the animal kingdom's well-being. This botanical diversity is not confined to one area but spans the globe, from tropical to

temperate zones. This geographical spread is key to the unique characteristics and variety of plant species. A plant's environment dictates its ecological importance and adaptive features. The specific conditions in which a plant grows are instrumental in shaping the types of bioactive compounds it produces, which ultimately defines its therapeutic potential. It is for this reason that many common fruits and vegetables are recognized as rich sources of beneficial phyto-constituents. These include compounds like flavonoids, phenols, tannins, vitamins, minerals, and amino acids, which have been scientifically reported to both treat and prevent a multitude of diseases (Pennington and Fisher, 2010; Johnson *et al*., 2012).

Citrullus lanatus, also a species within the Cucurbitaceae family, holds significant value due to its therapeutic potential. Historical texts suggest that this plant possesses a wider range of applications in treating specific health conditions compared to many other commonly consumed plants (Sorokina *et al*., 2021).

2.3.1 TAXONOMY OF WATERMELON

Domain : Eukaryota

Kingdom : Plantae

Division : Mangoliophyta

Phylum : Spermatophyta

Subphylum : Angiospermae

Class : Dictyledonae

Order : Violales

Family : Cucurbitaceae

Genus : Citrullus

Species : lanatus

Botanical Name : *Citrullus lanatus*

Common Name : Watermelon (Sorokina *et al*., 2021).

Plate 2.3: watermelon (Sorokina *et al*., 2021)

2.3.2 PHYTOCHEMICAL PROPERTIES OF *Citrullus lanatus*

Citrullus lanatus possesses a diverse and significant phytochemical profile, with different bioactive compounds concentrated in its various parts. The seeds are a particularly rich source, containing compounds such as lycopene, beta-carotene, phenols, vitamin C, and flavonoids. They are also a notable reservoir of proteins, including globulin and albumin, and contain minerals like sodium, calcium, and magnesium. The leaves of the plant have been found to contain alkaloids, flavonoids, saponins, and tannins, alongside vitamin C. The fruit's pulp contains triterpenoids and alkaloids, while the peel or rind is rich in tannins, flavonoids, and antioxidants. This comprehensive array of phytoconstituents, including glycosides, terpenoids, and amino acids, underpins the plant's extensive pharmacological properties, contributing to its therapeutic potential for a wide range of health applications (Pennington and Fisher, 2010; Johnson *et al*., 2012).

2.3.3 PHARMACOLOGICAL PROPERTIES

2.3.3.1 Antioxidant Activity

Citrullus lanatus contains compounds that can neutralize harmful free radicals in the body. According to Rahman *et al.* (2013), the n-hexane extract from the plant is particularly rich in antioxidants, with lycopene being the most prominent. Rao and Rao (2007) explained that lycopene, a carotenoid, contributes to skin health by offering a defence mechanism against the damaging effects of ultraviolet radiation, thereby potentially lowering the risk of skin cancer.

2.3.3.2 Antimicrobial Activity

Extracts derived from the fruit and seeds of *Citrullus lanatus* contain bioactive compounds such as tannins, flavonoids, and alkaloids. These substances have demonstrated effectiveness in inhibiting the growth of various bacteria and fungi. Research indicates that these extracts are active against gram-negative and gram-positive bacteria, including *E. coli* and *Bacillus subtilis*, as well as fungal strains like *Candida albicans* and *Aspergillus niger* (Thirunavukkarasu *et al.*, 2010). Furthermore, methanolic seed extracts have shown significant antimicrobial potency against pathogens such as *Vibrio cholerae* and *Shigella dysenteriae* (Sathya and Shoba, 2014).

2.3.3.3 Anti-depressant Activity

Different extracts of *Citrullus lanatus* have shown promise in alleviating symptoms of depression and anxiety. An aqueous extract of the fruit pulp was found to reduce immobility in behavioural tests on rats, indicating an antidepressant-like effect comparable to the synthetic drug fluoxetine (Sandhya *et al.*, 2020). Similarly, a hexane extract from the seeds exhibited both antidepressant and anxiolytic activities without adversely affecting skeletal muscle function (Rahman *et al.*, 2013). The high concentration of lycopene in the fruit pulp is thought to contribute to this effect by helping to restore the balance of antioxidant enzymes and reducing oxidative stress (Bose and Agrawal, 2007; Naz *et al.*, 2014).

2.3.3.4 Fertility Enhancer

Phytochemicals in *Citrullus lanatus*, including saponins, citrulline, and arginine, are known to support and enhance fertility. Saponins from the seeds have been linked to improved sexual performance and fertility (Rimando and Perkins-Veazie, 2005). The amino acids citrulline and arginine play a role in the production of nitric oxide, which is crucial for penile erection and is regulated through the guanosine monophosphate pathway (Davies, 2015; Drewes *et al.*, 2003).

Administration of ethanolic seed extract in rats led to improved testicular structure, enhanced male sexual behaviour, and increased levels of testosterone and luteinizing hormone (Onyinye and Emeka, 2019). The plant also appears to support female fertility by influencing follicular stimulating hormone levels (Chike *et al.*, 2011).

2.3.3.5 Hepatoprotective Activity

The oil extracted from *Citrullus lanatus* seeds offers protection to the liver. In studies where liver toxicity was induced in rats using carbon tetrachloride (CCl_4), treatment with the seed extract resulted in a significant normalisation of liver enzyme levels specifically alanine transaminase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP). This biochemical improvement was accompanied by a recovery in the liver's histological structure, demonstrating its hepatoprotective efficacy (Madhavi *et al.*, 2012).

2.4 PHYTOWASTE AND THEIR ROLE AS NUTRACEUTICALS

It is commonly known that parallel evolutionary processes are the cause of the interdependence and relatedness of living things (Shil *et al*., 2014). Due to their traditional use as food and medicine, plants are used in ethnomedicine to treat and cure a variety of illnesses, diseases, and poisonings by reducing or reversing their toxicity. When using these plant products, the outer skins are frequently peeled off and thrown away because they are typically deemed useless and inedible. Hard seeds and peels that were formerly considered inedible are frequently treated as phytowastes and thrown away as such. Street and market fruit vendors as well as the fruit processing industries produce a lot of trash, which, if not managed and used appropriately, could be harmful to the environment and cause illness. Reusing them as a different source of

antioxidants could therefore help reduce pollution and provide the pharmaceutical and nutraceutical industries with quantifiable economic profits as well as affordable new generational therapies (Duda-Chodal and Tarko, 2007). The same beneficial ingredients that are often present in fruit may also be present in fruit peel trash. These essential ingredients can be combined to create formulations with nutritional, energetic, and pharmacologic/medical benefits. Fruit peel trash recycling has not only reduced solid waste issues but also aided in the discovery of significant compounds with demonstrated critical applications. Through appropriate distillation, industrial extraction, scientific incorporation, and management of these fruit peels, phytochemicals of interest can also be isolated. Extracts from fruit peels are currently one of the main resources used to isolate and extract secondary metabolites (Altemimi *et al*., 2017; Rafiq *et al*., 2018). In addition to their therapeutic and advantageous effects, which have been scientifically demonstrated and recorded through numerous in vitro, in vivo, and clinical phase trials conducted across various cultures and civilizations, they have been shown to have positive effects on a wide range of illnesses, such as cancer, diabetes, cardiovascular diseases, and osteoarthritis. This is due to the abundance of bioactive substances, including gallic acid derivatives, phenolic acids, gallic acid flavonoids, catechin, and mangiferin.

A healthy balance between oxidants and antioxidants is maintained in modern medicine since oxidative stress is frequently linked to a number of illnesses and tissue damage (Sharma and Akansha, 2018). However, the use of plants or herbal preparations raises questions due to the absence of a recommended dosage, the effectiveness of counteractives when many plants are used, the safety of the preparation process, and the antagonistic effects when used with other pharmaceuticals.

CHAPTER THREE

MATERIALS AND METHODOLOGY

3.1 MATERIALS

3.2 APPARATUS, MATERIALS AND EQUIPMENTS

Plain bottles, cotton wool, analytical weighing balance, Handgloves, Soxhlet extractor apparatus, Whatmann paper, filter cloth, oral gastric tube, Syringes, Spatula, Beakers, Measuring cylinders, foil paper, Dissecting kits, Surgical blades, Bulk scientific atomic absorption spectrophotometer with (VGP 210), UV spectrophptometer (T80 + UV), Absolute ethanol, normal saline, Chloroform, distilled water, Cadmium chloride, Em Vit vitamin C, 10 percent formaline.

3.3 COLLECTION OF THE PHYTOWASTE AND PREPARATION OF EXTRACT

The rinds of *Citrullus lanatus* (watermelon) were procured from Uselu market, located in the Egor local government area of Benin City. Following peeling, the rinds were dehydrated at a controlled temperature of 37°C. The dried material was subsequently pulverized, and the powder was weighed and loaded into a thimble for Soxhlet extraction. The extracted liquid was purified through filtration with Whatman paper and then concentrated to a semi-solid consistency via a crude method. The final extract was dispensed into a container, appropriately labeled, and stored under refrigeration.

3.4 EXPERIMENTAL ANIMALS

Twenty five Wistar rats weighing 80g to 150g were purchased from Ibadan and were housed in the Faculty of Science Laboratory technology, University of Benin. Appropriate ventilation, feed and lighting were provided for them. They were acclimatized for 7 days before experiment.

3.5 EXPERIMENTAL DESIGN

Table 3.1: Experimental design

GROUPS	TREATMENT
1	Distilled water
2	Cadmium chloride (15mg/kg)
3	Vitamin C (50mg/kg)
4	250mg/kg *Citrullus lanatus*
5	500mg/kg *Citrullus lanatus*

The rats used for the study were maintained based on the guild lines of the national institute of health guide for the care and use of laboratory (animals and approval was obtained from the department of science laboratory technology, university of Benin, with approval number UNIBEN/FSLT/00031

3.6 COLLECTION OF SAMPLES

60 days after administration, the animals were sacrificed. They were euthanized using an analytical chloroform and their blood was collected through the abdominal aorta using a 5ml syringe, and put in a plain bottle and EDTA bottle and prepped for hematology analysis.

3.7 ORGAN TO BODY WEIGHT RATIO

The organ to body weight ratio was calculated using the formula:

Organ weight/ final body weight on day 28 (g)

3.8 BIOCHEMICAL ANALYSIS

Blood plasma for biochemical assays was obtained from the blood samples collected in Plain bottles following centrifugation at 3000 rpm for 5 minutes. The plasma samples were stored in a deep freezer at -20°C until analyzed. Aspartate transaminase (AST) and Alanine transaminase (ALT) were analyzed as described by (Schumann *et al*., 2002), alkaline phosphatase (ALP) as described by (Raymond-Habecke and Lott, 1995), bilirubin analyzed as described by (Doumas and Wu, 1991), albumin as described by (Ozolua *et al*., 2010), total protein was assayed by the biuret method

3.9 HEAVY METAL ASSAY

The blood samples were first homogenized to ensure a consistent mixture. A 0.5 ml aliquot of the homogenized blood was then pipetted into a digestion tube that had been cleaned beforehand. Next, 10 ml of a mixed acid solution, with a nitric-perchloric-sulphuric acid ratio of 5:2:1, was added to the tube. The tube was placed on a heater and warmed until the contents turned into a

clear solution, continuing the heating process even after white fumes appeared. After cooling, a small quantity of deionized water was introduced. This solution was then filtered into a 100 ml volumetric flask, and deionized water was added to bring the total volume to the 100 ml mark. A reagent blank was also prepared, and the concentrations of the target metals were analyzed using an Atomic Absorption Spectrophotometer (AAS).

3.10 STATISTICAL ANALYSIS

Data was subjected to one way analysis of variance (ANOVA) and Tukey's multiple comparison test of significant difference ($p< 0.05$) and represented with mean and standard error of mean. The statistical package of social sciences (SPSS) version 19 was used for analysis

CHAPTER FOUR

RESULTS

Table 4.1: Effect of the hydroethanolic extract of watermelon rind on the body weight of the rats

GROUPS	INITIAL WEIGHT	FINAL WEIGHT	% WEIGHT CHANGE
Control	155.50 ± 6.20	228.50 ± 9.75	47.31 %
Negative control(15mg/kg)	177.75 ± 17.24	238.00 ± 26.11	37.41 %
Vitamin C (50mg/kg)	140.25 ± 8.96	253.75 ± 19.03	85.53%
250mg/kg *Citrullus lanatus*	131.25 ± 3.50	241.25 ± 19.72	83.66 %
500mg/kg *Citrullus lanatus*	112.67 ± 4.48	201.67 ± 15.90	84.66 %

Table 4.1: Effect of the hydroethanolic extract of watermelon on the percentage weight change of the rats after 60 days. 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

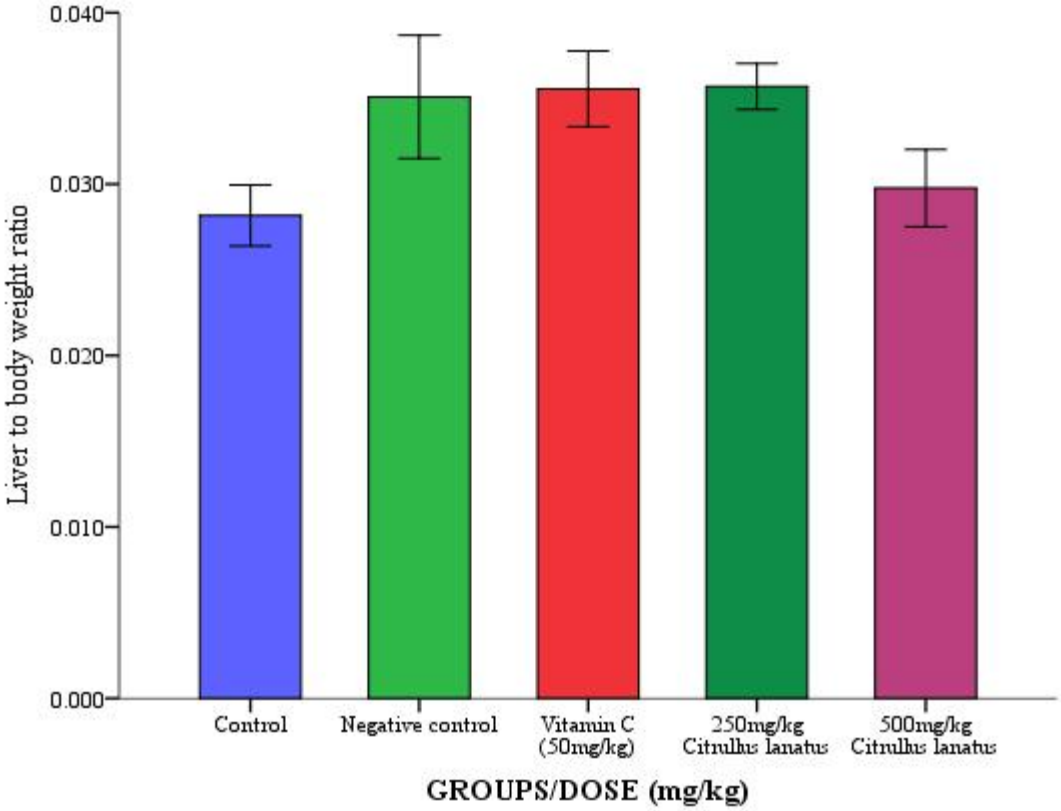
0.040
0.030
0.020
0.010
0.000
Liver to body weight ratio
Control
Negative control
Vitamin C (50mg/kg)
250mg/kg Citrullus lanatus
500mg/kg Citrullus lanatus
GROUPS/DOSE (mg/kg)

Figure 4.1: Liver to body weight ratio. mean ± SEM was used. There was no significant difference among the Liver to body weight ratio of the groups. n =4. The extract group and the vitamin c group had the highest liver to body weight ratio but it was similar to the other groups. This suggest there was no sign of inflammation or hepatomegaly.

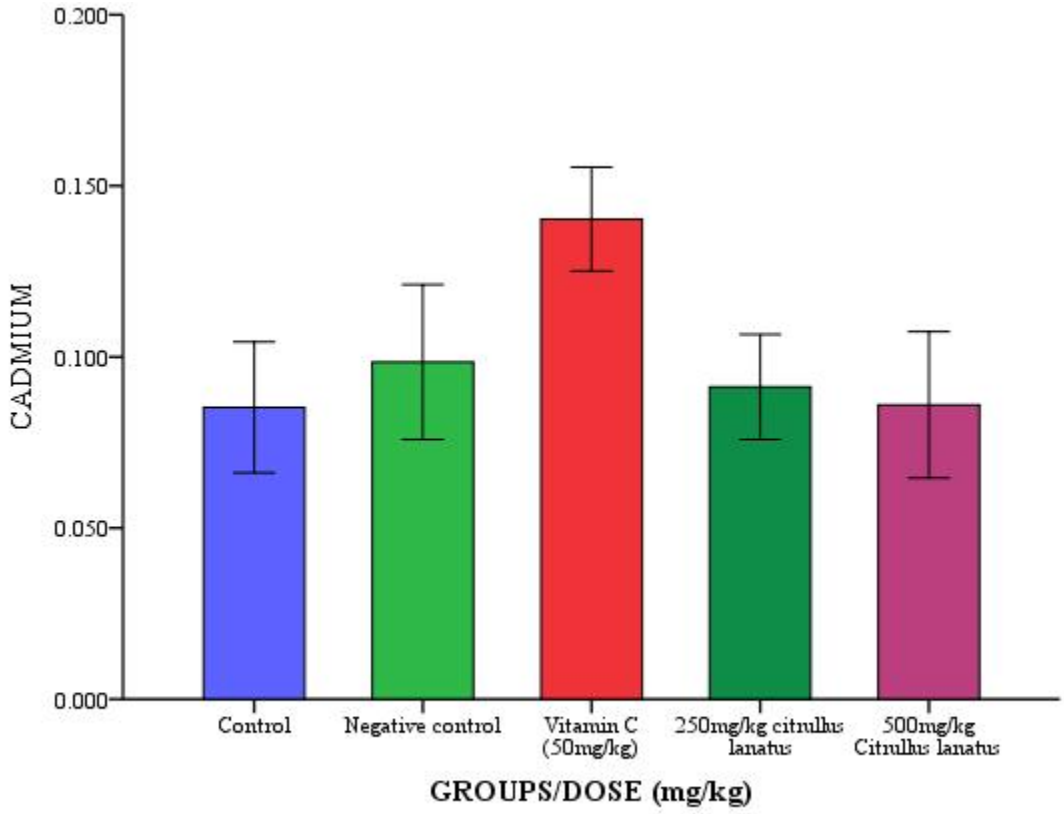
0.200
0.150
0.100
0.050
0.000
CADMIUM
Control
Negative control
Vitamin C (50mg/kg)
250mg/kg citrullus lanatus
500mg/kg Citrullus lanatus
GROUPS/DOSE (mg/kg)

Figure 4.2: Effect of the extract on the Level of Cadmium in the Liver. Mean ± SEM was used. There was no significant difference between the cadmium level among the groups. The 500mg/kg group had the highest cadmium level in the kidney even though there was no significant difference. The control group had the lowest as evidenced by the lack of exposure to cadmium level. The extract didn't reduce cadmium exposure because the cadmium level was higher in the 500mg/kg group

Table 4.2: Liver markers

GROUPS	ALT	ALP	AST	TP	ALB	T.BIL	D.BIL
Control	9.09 ± 4.56	124.99 ± 1.27	33.42 ± 10.62	6.27 ± 1.51	1.72 ± 0.11	3.70 ± 1.34	3.37 ± 1.30
Negative control (15mg/kg)	13.46 ± 6.03	123.34 ± 0.57	64.41 ± 20.65	11.65 ± 2.80c	1.75 ± 0.13	5.16 ± 2.72	5.06 ± 2.42
Vitamin C (50mg/kg)	16.50 ± 5.51	119.90 ± 1.33	17.36 ± 5.91	4.12 ± 0.35b	1.70 ± 0.18	1.05 ± 0.31	1.50 ± 0.40
250mg/kg *Citrullus lanatus*	23.41 ± 3.61	126.91 ± 7.59	21.84 ± 6.42	5.90 ± 0.50	1.82 ± 0.05	1.26 ± 0.61	1.81 ± 0.63
500mg/kg *Citrullus lanatus*	17.89 ± 3.15	118.43 ± 1.28	19.48 ± 2.65	5.87 ± 0.88	1.73 ± 0.10	1.68 ± 0.95	2.03 ± 0.93

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.

ALT: Alanine Transaminase, AST: Aspartate Transaminase, ALP: Alkaline Phosphatase, TP: Total protein, ALB: Albumin, T.BIL: Total Bilirubin, B.BIL: Direct Bilirubin

CHAPTER FIVE

DISCUSSION

The present study was to evaluate the potential protective effect of a hydroethanolic extract of *Citrullus lanatus* (watermelon) rind against cadmium-induced hepatotoxicity in Wistar rats. The significant differences in percentage body weight change among the experimental groups is a primary indicator of cadmium's systemic toxicity and the potential ameliorative effect of the *C. lanatus* extract. The group exposed to cadmium alone (Negative control) exhibited the lowest weight gain (37.41%). Chronic exposure to cadmium is known to induce anorexia, disrupt metabolic processes, and cause general wasting, leading to reduced growth and weight loss (Tchounwou *et al*., 2012; Genchi *et al*., 2020). The groups treated with the *C. lanatus* extract at both 250 mg/kg and 500 mg/kg showed higher percentage weight gains (83.66% and 84.66%, respectively), which were comparable to the group receiving the standard antioxidant, Vitamin C (83.53%). This suggests that the phytoconstituents in the watermelon rind extract, potentially including its documented antioxidants like phenols and flavonoids (Pennington and Fisher, 2010), effectively counteracted the metabolic and anorexigenic effects of cadmium.
The liver-to-body weight ratio showed no statistically significant differences across all groups ($p > 0.05$). This indicates that despite the biochemical evidence of toxicity, the chronic cadmium exposure in this model did not cause gross morphological changes, such as pronounced hepatomegaly or atrophy, that would significantly alter the relative liver weight (Linguraru *et al*., 2012). While cadmium is a known hepatotoxin that can induce inflammation, necrosis, and

fibrosis, the dose and duration of exposure in this study may have been sufficient to cause cellular and biochemical damage without leading to overt organ enlargement or reduction.

Cadmium levels in the liver tissue revealed no significant difference between the cadmium-exposed group (negative control), and the groups that received cadmium along with the extract or Vitamin C ($p > 0.05$). Cadmium is a toxin with an extremely long biological half-life, estimated between 16 to 30 years in humans, and it predominantly accumulates in the liver and kidneys (Genchi *et al*., 2020; Renugadevi and Prabu, 2010). The primary mechanism of action for many chelating agents is to bind the metal and enhance its excretion. The results suggest that the protective mechanism of the *C. lanatus* extract might not be through the chelation or enhanced elimination of cadmium from its primary storage site. Instead, the hepatoprotection is likely conferred downstream of accumulation, possibly by ehnancing the endogenous antioxidant defense systems. The extract's rich phytochemical profile, including compounds with known antioxidant activity, may neutralize the reactive oxygen species (ROS) generated by cadmium, thus protecting hepatocytes from oxidative damage without affecting the total body burden of the metal (Madhavi *et al*., 2012; Rahman *et al*., 2013).

Cadmium inflicts liver damage primarily through the induction of oxidative stress, leading to lipid peroxidation, membrane instability, and the leakage of intracellular enzymes into the bloodstream (Renugadevi and Prabu, 2010; Rikans and Yamano, 2000). The negative control group showed elevated levels of AST and ALT compared to the normal control, indicating hepatocellular necrosis. The rise in AST was more pronounced, which can occur in severe hepatic injury. Treatment with the *C. lanatus* extract, particularly at the 500 mg/kg dose, resulted in a reduction in these enzyme levels, bringing them closer to those of the normal control and

Vitamin C groups. This normalization signifies the stabilization of hepatocyte membranes and a reduction in the leakage of these enzymes, a classic sign of hepatoprotection. This effect can be attributed to the antioxidant properties of the extract, which likely mitigated the cadmium-induced lipid peroxidation and preserved the integrity of the hepatic cell membranes. The presence of lycopene, flavonoids, and other antioxidants in watermelon is well-documented to scavenge free radicals and support cellular defense mechanisms (Rao and Rao, 2007; Naz *et al*., 2014).

The levels of ALP, a marker often associated with cholestatic injury, remained relatively stable across all groups, suggesting that cadmium toxicity in this model was predominantly hepatocytic rather than primarily affecting the biliary system. The negative control group exhibited a significant increase in Total Protein (TP) ($p < 0.05$), and a trend towards elevated bilirubin levels. While liver damage often impairs protein synthesis, an increase in total protein can sometimes be associated with an inflammatory response or dehydration. The elevation in the cadmium-only group, which was significantly higher than in the Vitamin C and extract-treated groups, suggests a dysregulated systemic or hepatic response to toxicity that was ameliorated by the treatments. The extract at both doses effectively prevented this abnormal rise, maintaining TP levels comparable to the normal control. Similarly, the elevated total and direct bilirubin in the negative control group indicate impaired conjugation and excretory function of the liver, a consequence of hepatocellular dysfunction. The *C. lanatus* extract and Vitamin C treatments successfully prevented this hyperbilirubinemia, underscoring their role in maintaining functional hepatic integrity against cadmium insult. Albumin levels remained stable across all groups, indicating that the synthetic capacity for this specific protein was not severely compromised in this model, likely due to the liver's significant functional reserve.

CONCLUSION

The findings of this study demonstrate that the hydroethanolic extract of *Citrullus lanatus* rind offers significant protection against cadmium-induced hepatotoxicity in Wistar rats. The extract effectively mitigated the biochemical dysregulation caused by cadmium, as evidenced by the normalization of key liver enzymes (AST, ALT) and bilirubin levels. Furthermore, it reversed the growth retardation associated with cadmium exposure. The mechanism of protection appears not to involve the reduction of cadmium burden in the liver, but rather the enhancement of the body's antioxidant defense system to counteract oxidative stress, a primary pathway of cadmium toxicity.

LIMITATIONS

1. Electricity issues to properly preserve specimens and extracts.
2. Lack of funds restricted the access to essential reagents and equipment, it reduced the number of samples and tests that would have been conducted
3. No proper time management to properly standardize the plant compounds

RECOMMENDATIONS

1. Plant should be well standardized to understand the secondary metabolite present
2. Universities should attract more grants to properly fund research and provide proper electricity

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APPENDIX

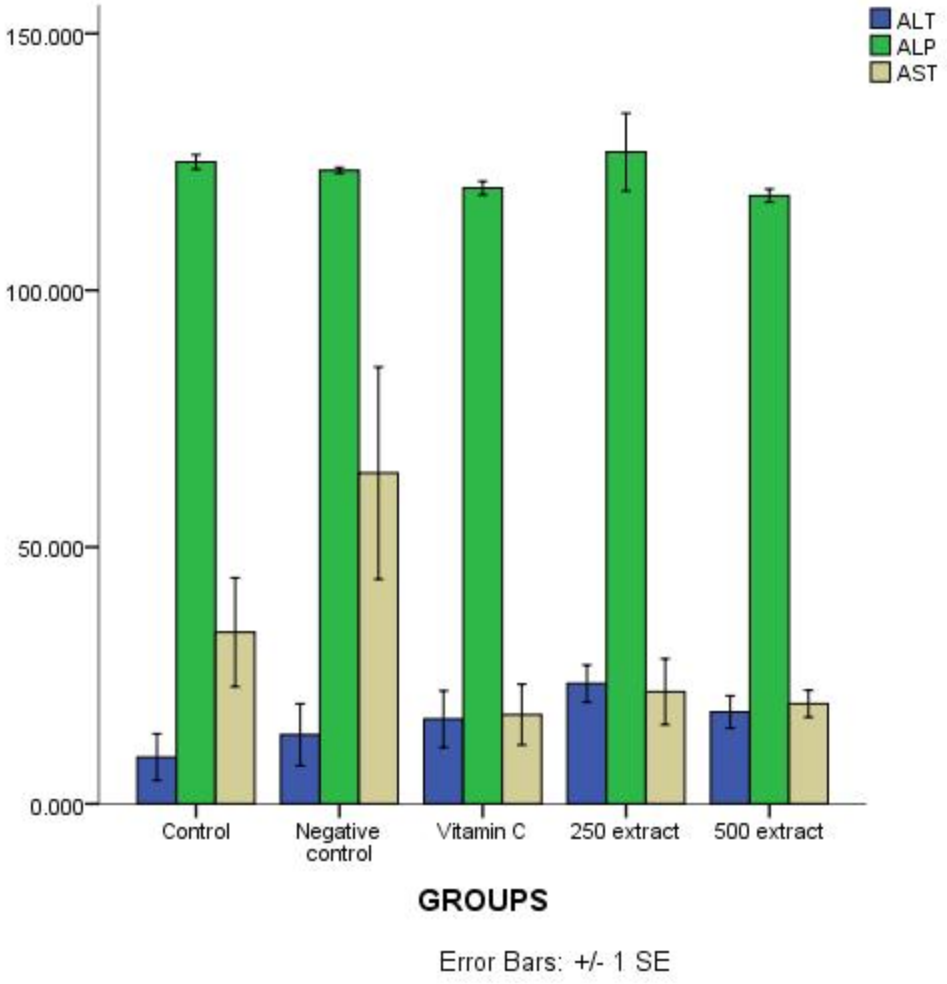

Figure 1: Effects of the extract on the liver markers

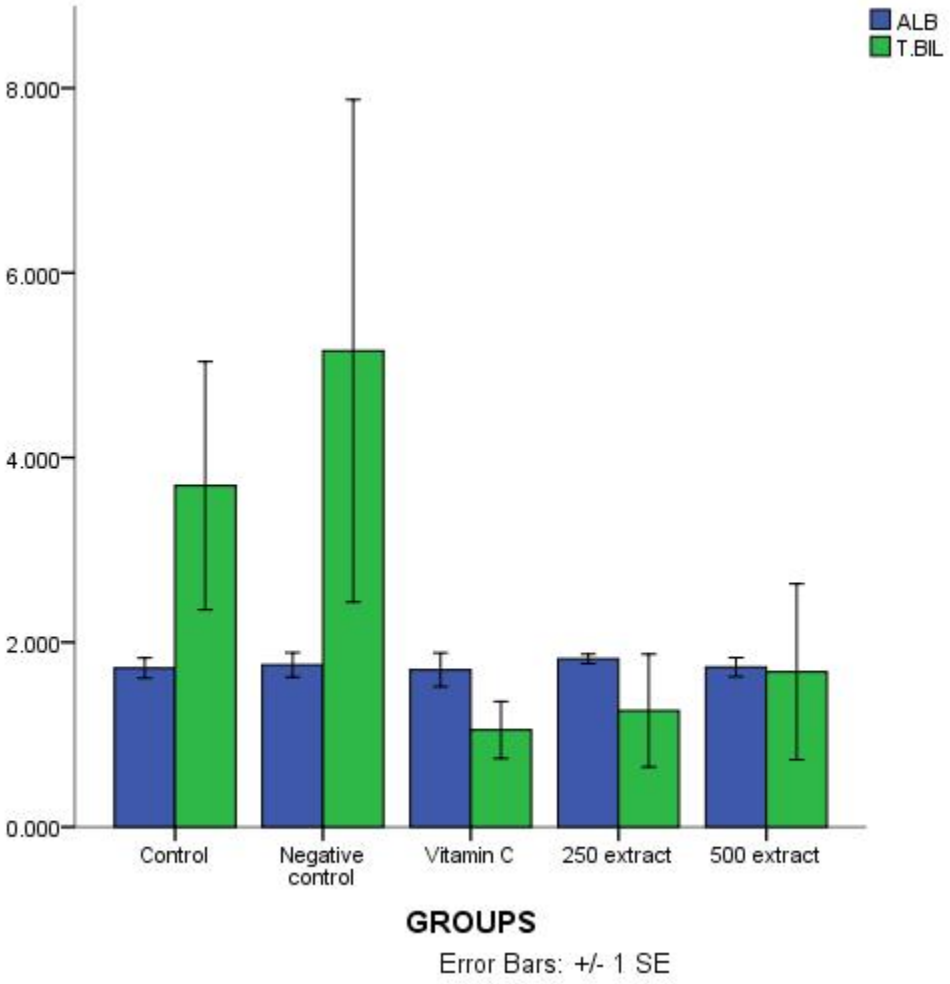

Figure 2: Effect of the extract on liver markers