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(RESEARCH ARTICLE)

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Toxicity amelioration potentials of *Spondias mombin* aqueous leaf extract in cadmium and mercury co-exposed Wistar rats

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Abstract

This study investigated the corrective effects of aqueous leaf extract of *Spondias mombin* (SM) on liver and kidney function in Wistar rats co-exposed to mercury and cadmium toxicities. Thirty (30) male rats weighing 120–150g were randomly divided into ten (10) groups of three (3) rats each. Group I which served as negative control received normal rat feeds and distilled water *ad libitum*; Groups II and V received different doses of $CdCl_2$ and $HgCl_2$ respectively, with no plant extract administered. Groups III and VI received toxicants and 500 mg/kg b. w. of SM daily; Groups IV and VII received toxicants and 100 mg/kg b. w. of silymarin; Group VIII rats were co-exposed to $CdCl_2$ and $HgCl_2$ toxicants. Group IX rats were administered with $CdCl_2$, $HgCl_2$ and SM while Group X received $CdCl_2$, $HgCl_2$ and silymarin. The experimental animals were sacrificed at day 28; blood samples were collected for biochemical assays while the liver and kidney were harvested for histological investigations. Administration of $CdCl_2$ and $HgCl_2$ to rats resulted in significant ($P<0.05$) increase in serum liver enzymes activity. However, treatment of the exposed groups with SM resulted in reduced ALT activity. Administration of the toxicants also resulted significant ($P<0.05$) detrimental changes in kidney function; Creatinine levels increased from 159.67±0.88µmol/l in Group I to 213.67±34.21µmol/l in the $CdCl_2$ + $HgCl_2$ group. Histological assessment revealed that liver architecture was preserved by the administered leaf extract. Findings suggest that *S. mombin* leaves exhibit ameliorative effects against mercury and cadmium-triggered stress and organ damage in Wistar rats.

Keywords: Ameliorative Potentials; *Spondias Mombin*; Leaf Extract; Mercury; Cadmium; Co-Exposure

1. Introduction

Human activities have caused massive increases in human exposure to heavy metals [1, 2]. The unprecedented increase in metal exposure has been aided by modern industrialization and anthropogenic activities such as mining, smelting and domestic as well as agricultural use of metals and metal-containing compounds [3]. Metals, among other environmental pollutants, may also occur naturally and remain in the environment and as such, human exposure to metals is inevitable [4]. Mercury, lead, chromium, cadmium, and arsenic have been the most common heavy metals that induce human poisoning [1]. Heavy metals, unlike most organic pollutants, are not degraded rather accumulate in the environment and food chain [5]. Cadmium (Cd) and mercury (Hg) have proved to be extremely toxic to mankind [6]. There is a growing appreciation of the effects that exposure to heavy metals such as Hg may have on the body and, in particular, the brain and nervous system. This is because some of these metals can cross the blood-brain barrier and accumulate in the brain and cause damage [7]. Balali-Mood et al. [8] reported acute and chronic toxic effects of heavy metals to include gastrointestinal and kidney dysfunction, nervous system disorders, skin lesions, vascular damage, immune system dysfunction, birth defects and cancer. Simultaneous exposure to two or more metals may have cumulative effects [9 – 11]. Several metals have emerged as human carcinogens. The toxicity and carcinogenicity of heavy metals are dose-dependent. Carcinogenic metals such as arsenic, cadmium, and chromium can disrupt DNA

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synthesis and repair [12, 13]. The interaction between Cd and Hg has been previously reported. Cd and Hg have proved to be extremely toxic to mankind despite their usage in various industries [14].

Cd is classified by the International Agency for Research on Cancer (IARC) as carcinogenic to humans (Group 1) [15]. High levels of Cd in water, air, and soil can occur following industrial activities which could be a substantial human exposure to Cd. Moreover, the ingestion of contaminated food will cause major exposure to Cd. Cd exposure may also occur through smoking, which is capable of elevating blood and urine Cd concentrations. Presence of Cd in contaminated water could disturb the necessary mechanisms in the body, possibly resulting in short-term or long-term disorders [16, 17]. The outbreak of Itai-itai disease in Japan, where patients suffered from painful degenerative bone disease, kidney failure, gastrointestinal and lungs diseases, was due to the mass Cd contamination of food and water supplies [18]. Cd is more efficiently taken from the lungs via industrial dust and acute or chronic inhalation in industrial areas might lead to renal tubular dysfunction and lung injuries. Balali-Mood et al. [1] reported that Cd blood concentration in smokers is almost twice higher than that of non-smokers.

Hg represents the third most toxic element on the planet [19]. It is found in air, water, and soil and exists in three forms: elemental or metallic mercury (Hg^0), inorganic mercury (Hg^+, Hg^{2+}), and organic mercury (commonly methyl or ethyl mercury) [20]. The toxicity of mercury can result from vapor inhalation and ingestion or absorption through the skin. Nervous, digestive, and renal systems are most commonly affected by Hg exposure, while children and pregnant women are most vulnerable to Hg exposure [21]. Once absorbed, Hg distributes widely to all tissues. The principal target organs of the inorganic mercury are kidney and liver. Previous studies have revealed that $HgCl_2$ caused histopathological and ultrastructural lesions in the liver evidenced by periportal fatty degeneration and cell necrosis [22, 23]. Mercury chloride ($HgCl_2$) is one of the active ingredients of skin brightening creams which are used to remove freckles and spots of the skin due to excessive accumulation of melanin. $HgCl_2$ inhibits tyrosinase activity irreversibly, an enzyme which functions in melanin formation, by replacing the copper cofactor [24].

Over the past decade, interest in drugs derived from plants, especially the phytotherapeutic ones, has increased expressively [25]. *Spondias mombin* (SM) is a tree found in the rainforest and is known by various names across various languages in West Africa [26]. The leaves contain saponins, tannins, alkaloids, and flavonoids. Traditionally, various parts of SM are used for different medicinal purposes, including the treatment of diseases and as forage for domestic animals [27, 28]. Scientific investigations have shown that it has anthelmintic, antioxidant, antimicrobial and anti-inflammatory actions. *S. mombin* leaves have been reported to be responsible for various actions such as smooth muscle relaxant, antispasmodic, abortifacient, sedative and anticonvulsant and anxiolytic [29].

In real life, the human population is exposed to combination of heavy metals. Consequently, this study was performed to investigate toxicity triggered by cadmium and mercury on the liver and kidney, and the corrective effects of aqueous leaf extract of SM against cadmium and mercury co-exposure.

2. Materials and methods

2.1. Experimental Animals

Healthy adult male Wistar rats weighing 120-150g were obtained from the Animal House, Department of Biochemistry, University of Port Harcourt Nigeria. The rats were allowed to acclimatize under standard conditions (25 ± 2 °C, 12 h of light and 12 h of darkness) for 10 days and then assigned randomly into ten (10) groups of three (3) rats each. Experimental animals were fed standard chow diet and were given access to water *ad libitum*. All treatments were carried out via oral gavage and daily for a period of twenty-eight (28) days.

2.2. Chemicals/Reagents/Drug

All reagents used in this study were of analytical grade: Cadmium chloride ($CdCl_2$), Mercuric chloride ($HgCl_2$), Silymarin, Chloroform, Distilled water and Assay Kits. Diagnostic kits for serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin (TBIL) and total protein (TP) were purchased from Randox Laboratories Ltd., London, UK. All other chemicals and solvents were obtained either from Sigma Aldrich or Merck, UK. Silymarin drug was purchased from a Pharmacy in Alakahia Port Harcourt, Nigeria.

2.3. Plant collection and validation

Fresh leaves of *Spondias mombin* (SM) plant were obtained from a farm land in Omoku Community in Rivers State, Nigeria. The plant was identified and validated at the Department of Plant Science and Biotechnology, University of Port Harcourt, Nigeria and deposited in an Herbarium with voucher number UPH/N/324.

2.4. Preparation of aqueous Leaf Extract of Peperomia Pellucida

The harvested leaves of SM (320g) were thoroughly washed with both tap water and distilled water. The leaves were air-dried at 33°C ± 2°C, ground into a fine powder using mechanical grinder and kept in air-tight jars. Aqueous extract of the plant leaves was prepared according to a previously reported by Lemhadri et al. [30]. Thirty grams (30g) of dry powder was soaked in 300 ml distilled water for three days. The resultant suspension was filtered into sterile beakers, and filtrates collected were re-filtered using Whatman No.1 filter paper into sterile sample bottles and stored in the refrigerator before use in the study.

2.5. Experimental Grouping

Experimental rats received different doses of $CdCl_2$, $HgCl_2$, Silymarin drug and SM aqueous leaf extract as shown in Table 1.

Table 1 Experimental Groups in the study

Experimental Group	Group Description
Group-I Normal Control	Received Normal Rat Feed + Water Only (for 28 days).
Group-II ($CdCl_2$ only)	Received standard feed and water + 1.5 mg/kg b. w. of $CdCl_2$ (for 28 days).
Group-III ($CdCl_2$ + SME)	Received standard feed and water + 1.5 mg/kg b. w. of $CdCl_2$ + 500mg/kg b. w. of SM daily (for 28 days).
Group-IV ($CdCl_2$ + Silymarin)	Received standard feed and water + 1.5 mg/kg b. w. of $CdCl_2$ + 100 mg/kg b. w. of silymarin daily (for 28 days).
Group-V ($HgCl_2$ only)	Received standard feed and water + 1.2mg/kg b. w. of $HgCl_2$ (for 28 days).
Group-VI ($HgCl_2$ + SME)	Received standard feed and water + 1.2mg/kg b. w. of $HgCl_2$ + 500mg/kg b. w. of SM daily (for 28 days).
Group-VII ($HgCl_2$ + Silymarin)	Received standard feed and water + 1.2mg/kg b. w. of $HgCl_2$ + 100 mg/kg b. w. of silymarin daily (for 28 days).
Group-VIII ($CdCl_2$ + $HgCl_2$)	Received standard feed and water + 1.5 mg/kg b. w. of $CdCl_2$ + 1.2mg/kg b. w. of $HgCl_2$ (for 28 days).
Group-IX ($CdCl_2$ + $HgCl_2$ + SME)	Received standard feed and water + 1.5 mg/kg b. w. of $CdCl_2$ + 1.2mg/kg b. w. of $HgCl_2$ + 500mg/kg b. w. of SM daily (for 28 days).
Group-X ($CdCl_2$ + $HgCl_2$ + Silymarin)	Received standard feed and water + 1.5 mg/kg b. w. of $CdCl_2$ + 1.2mg/kg b. w. of $HgCl_2$ + 100 mg/kg b. w. of silymarin daily (for 28 days).

2.6. Acute toxicity study for *Spondias mombin* leaf extract

Acute toxicity level for *S. mombin* leaf extract was considered by leveraging a previous investigation by Nwidu et al. [31] that determined the approximate median lethal doses of *S. mombin* leaf extract.

2.7. Assay for Biochemical Parameters

Serum levels of ALT, AST, ALP, TBIL and total protein (TP) were assessed using Randox diagnostic kits. These analyses were performed at the Department of Chemical Pathology, University of Port Harcourt Teaching Hospital, Port Harcourt, Rivers State, Nigeria.

2.8. Sample preparation and metal analysis

Preparation and digestion of liver and kidney samples for heavy metals analysis were done according to method described by Bortey-Sam et al. [32]. Concentrations of metals were expressed in mg/kg dry weight (mg/kg d. w.).

2.9. Histological Investigation

Liver and kidney specimens were cut into pieces and fixed in 10% formalin, routinely processed for dehydration, and embedded in paraffin wax. Sections (5 mm-thick) were cut, fixed onto glass slides, and stained with hematoxylin and

eosin for light microscopic examination [33]. The slides were examined under a high-resolution microscope (Canada balsam) at a magnification of x400.

2.10. Statistical Analysis

All values were expressed as mean ± SD and then subjected to analysis of variance (ANOVA) using the Statistical Package for Social Sciences (SPSS) version 17.0 (SPSS Inc., Chicago Illinois). Statistical significance was considered at P=0.05.

3. Results and discussion

3.1. Effects of *S. mombin* Aqueous leaf extract on liver function parameters

Table 2 shows the activity of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) activities following administration of aqueous leaf extract of *S. mombin* in Wistar rats co-exposed to mercury and cadmium toxicities. Both heavy metals induced toxicity in the experimental animals as indicated by significant (P<0.05) increases in plasma AST, ALT & ALP activity in the $CdCl_2$ only, $HgCl_2$ only and $CdCl_2$ + $HgCl_2$-groups at day 28. However, administration of *S. mombin* aqueous leaf extract caused significant reduction in the activity of AST, ALT and ALP in the groups that were exposed to either individual or combined effects of mercury and cadmium. The drug, silymarin showed similar effect in decreasing activity of liver enzymes in the $CdCl_2$, $HgCl_2$ and $CdCl_2$ + $HgCl_2$-groups at day 28. This is an indication that *S. mombin* leaves have potentials to restore heavy metal-triggered reno-hepatic tissue dysfunction in Wistar rats.

While groups II, V and VIII showed decreases in the levels of total protein, significant ($p<0.05$) improvement in the plasma total protein was observed in groups III, IV, VI, VII, IX and X, following co-administration of *S. mombin* aqueous leaf extract and Silymarin.

For total bilirubin (TBIL), there was an attempt by *S. mombin* aqueous leaf extract and silymarin to reverse the significant ($p<0.05$) increases in TBIL levels observed in the $CdCl_2$ only, $HgCl_2$ only and $CdCl_2$ + $HgCl_2$-groups. Thus groups III, IV, VI, VII, IX and X showed reduction in TBIL levels at day 28.

3.2. Effects of *S. mombin* Aqueous leaf extract on kidney function parameters

Tables 3 shows the effects of *S. mombin* aqueous leaf extract on kidney function indices in Wistar rats co-exposed to mercury and cadmium toxicities. There was significant ($p<0.05$) increase in urea in the $CdCl_2$ only, $HgCl_2$ only and $CdCl_2$ + $HgCl_2$-groups, compared to the control group which recorded 2.17 ± 0.18 mg/dl at day 28. Similarly, creatinine levels in groups II, V and VIII increased significantly ($p<0.05$) when compared to groups the control group (group I) and groups III, IV, VI, VII, IX and X at the end of the 28-day treatment period.

3.3. Results for Histological Studies

3.3.1. Liver Photomicrographs

Plates L-G1 to L-G10 are light microscope photographs of liver paraffin sections obtained from groups 1 -10 at day 28, stained with hematoxylin and eosin.

3.3.2. Kidney Photomicrographs

Plates K-G1 to K-G10 are light microscope photographs of kidney paraffin sections obtained from groups 1 -10 at day 28, stained with hematoxylin and eosin.

Table 2 Effect of *S. mombin* Aqueous leaf Extract on some liver function markers in cadmium and mercury co-exposure

Experimental Group	AST (IU/l)	ALT (IU/l)	ALP (IU/l)	TP (g/l)	TB (µmol/l)
Group-I (Control)	6.67 ± 0.33	7.33 ± 0.67	63.00 ± 22.50	11.00 ± 1.16	3.00 ± 0.58
Group-II ($CdCl_2$ only)	9.00 ± 0.58^{a}	9.67 ± 0.33^{a}	85.67 ± 7.86^{a}	6.00 ± 0.58^{a}	8.00 ± 0.58^{a}
Group-III ($CdCl_2$ + SME)	7.33 ± 0.33^{b}	7.87 ± 1.33^{d}	79.00 ± 12.74^{b}	7.33 ± 0.67^{b}	5.00 ± 0.58^{b}
Group-IV ($CdCl_2$ + Silymarin)	6.77 ± 0.33^{e}	7.42 ± 1.00^{e}	69.33 ± 7.22^{c}	10.33 ± 1.33	5.00 ± 0.58^{c}
Group-V ($HgCl_2$ only)	11.33 ± 2.6^{a}	10.00 ± 0.58^{a}	79.67 ± 7.06^{a}	5.33 ± 0.67^{a}	11.00 ± 1.53^{a}
Group-VI ($HgCl_2$ + SME)	7.67 ± 0.67^{c}	8.67 ± 0.33	74.33 ± 7.80^{b}	7.33 ± 0.33^{b}	7.67 ± 0.33^{b}
Group-VII ($HgCl_2$ + Silymarin)	7.00 ± 0.58^{e}	7.59 ± 1.20^{e}	65.67 ± 4.26^{a}	10.00 ± 1.16	4.00 ± 0.58^{c}
Group-VIII ($CdCl_2$ + $HgCl_2$)	8.67 ± 0.33^{b}	9.33 ± 0.33^{a}	76.33 ± 8.45^{a}	8.00 ± 0.58^{a}	9.33 ± 0.33^{a}
Group-IX ($CdCl_2$ + $HgCl_2$ + SME)	7.67 ± 0.33^{c}	7.67 ± 0.33^{d}	68.00 ± 6.56^{b}	10.00 ± 0.58	7.00 ± 0.58^{b}
Group-X ($CdCl_2$ + $HgCl_2$ + Silymarin)	6.67 ± 0.33^{d}	7.64 ± 1.33^{e}	67.00 ± 2.52^{b}	9.33 ± 0.88^{c}	4.67 ± 0.33^{c}

Values are reported as Mean ± Standard Deviation, (n =3). Treatment with same or similar superscripts "a,b,c,d" are not statistical significantly difference (P≤ 0.05) from one another while treatments with different superscript are statistically significantly different from one another.

Table 3 Effect of *S. mombin* aqueous leaf extract on some renal function markers in cadmium and mercury co-exposure

Experimental Group	Creatinine (µmol/l)	Urea (mg/dl)
Group-I (Control)	159.67 ± 0.88	2.17 ± 0.18
Group-II ($CdCl_2$ only)	169.67 ± 4.26^{a}	4.9 ± 0.4^{a}
Group-III ($CdCl_2$ + SME)	155.67 ± 2.91^{d}	3.13 ± 0.15
Group-IV ($CdCl_2$ + Silymarin)	145.00 ± 11.53^{e}	2.77 ± 0.35^{e}
Group-V ($HgCl_2$ only)	182.33 ± 18.67^{a}	5.3 ± 0.23^{a}
Group-VI ($HgCl_2$ + SME)	172.67 ± 18.82^{bd}	3.63 ± 0.26
Group-VII ($HgCl_2$ + Silymarin)	173.67 ± 14.99^{c}	3.07 ± 0.09
Group-VIII ($CdCl_2$ + $HgCl_2$)	213.67 ± 34.21^{a}	5.90 ± 0.23^{a}
Group-IX ($CdCl_2$ + $HgCl_2$ + SME)	181.00 ± 12.29^{bd}	3.70 ± 0.29^{e}
Group-X ($CdCl_2$ + $HgCl_2$ + Silymarin)	182.33 ± 12.02^{ce}	3.43 ± 0.52^{e}

Values are reported as Mean ± Standard Deviation, (n =3). Treatment with same or similar superscripts "a,b,c,d,e" are not statistical significantly difference (P≤ 0.05) from one another while treatments with different superscript are statistically significantly different from one another.

Table 4 Estimation of cadmium and mercury in the liver of Wistar rats co-exposed to cadmium and mercury

Experimental Group	Cadmium (Cd) (mg/kg dw)	Mercury (Hg) (mg/kg dw)
Group-I (Control)	2.78E-02	2.51E-03
Group-II ($CdCl_2$ only)	1.35E-02[a]	1.25E-03[a]
Group-III ($CdCl_2$ + SME)	5.58E-03[bd]	BDL
Group-IV ($CdCl_2$ + Silymarin)	1.49E-02[c]	3.13E-03[ce]
Group-V ($HgCl_2$ only)	1.37E-02[a]	3.96E-03[a]
Group-VI ($HgCl_2$ + SME)	1.07E-02[b]	1.35E-03[bd]
Group-VII ($HgCl_2$ + Silymarin)	7.30E-02[ce]	3.72E-03[c]
Group-VIII ($CdCl_2$ + $HgCl_2$)	3.06E-02	5.45E-03[a]
Group-IX ($CdCl_2$ + $HgCl_2$ + SME)	5.94E-03[bd]	BDL
Group-X ($CdCl_2$ + $HgCl_2$ + Silymarin)	1.17E-02[ce]	2.93E-03[e]

Values are reported as Mean ± Standard Deviation, (n =3). Treatment with same or similar superscripts "a,b,c,d,e" are not statistical significantly difference (P≤ 0.05) from one another while treatments with different superscript are statistically significantly different from one another.

Table 5 Estimation of cadmium and mercury in the kidney of Wistar rats co-exposed to cadmium and mercury

Experimental Group	Cadmium (Cd) (mg/kg dw)	Mercury (Hg) (mg/kg dw)
Group-I (Control)	6.89E-02	1.01E-02
Group-II ($CdCl_2$ only)	8.22E-02[a]	1.06E-03
Group-III ($CdCl_2$ + SME)	1.57E-02[bd]	4.80E-03[bd]
Group-IV ($CdCl_2$ + Silymarin)	6.44E-03[e]	BDL
Group-V ($HgCl_2$ only)	6.27E-02	5.28E-03[a]
Group-VI ($HgCl_2$ + SME)	1.37E-02[bd]	3.95E-03[bd]
Group-VII ($HgCl_2$ + Silymarin)	2.66E-01[ce]	9.06E-03[ce]
Group-VIII ($CdCl_2$ + $HgCl_2$)	9.35E-02[a]	2.80E-03[a]
Group-IX ($CdCl_2$ + $HgCl_2$ + SME)	1.23E-02[bd]	1.54E-03[bd]
Group-X ($CdCl_2$ + $HgCl_2$ + Silymarin)	7.98E-02[ce]	3.26E-03[c]

Values are reported as Mean ± Standard Deviation, (n =3). Treatment with same or similar superscripts "a,b,c,d,e" are not statistical significantly difference (P≤ 0.05) from one another while treatments with different superscript are statistically significantly different from one another.

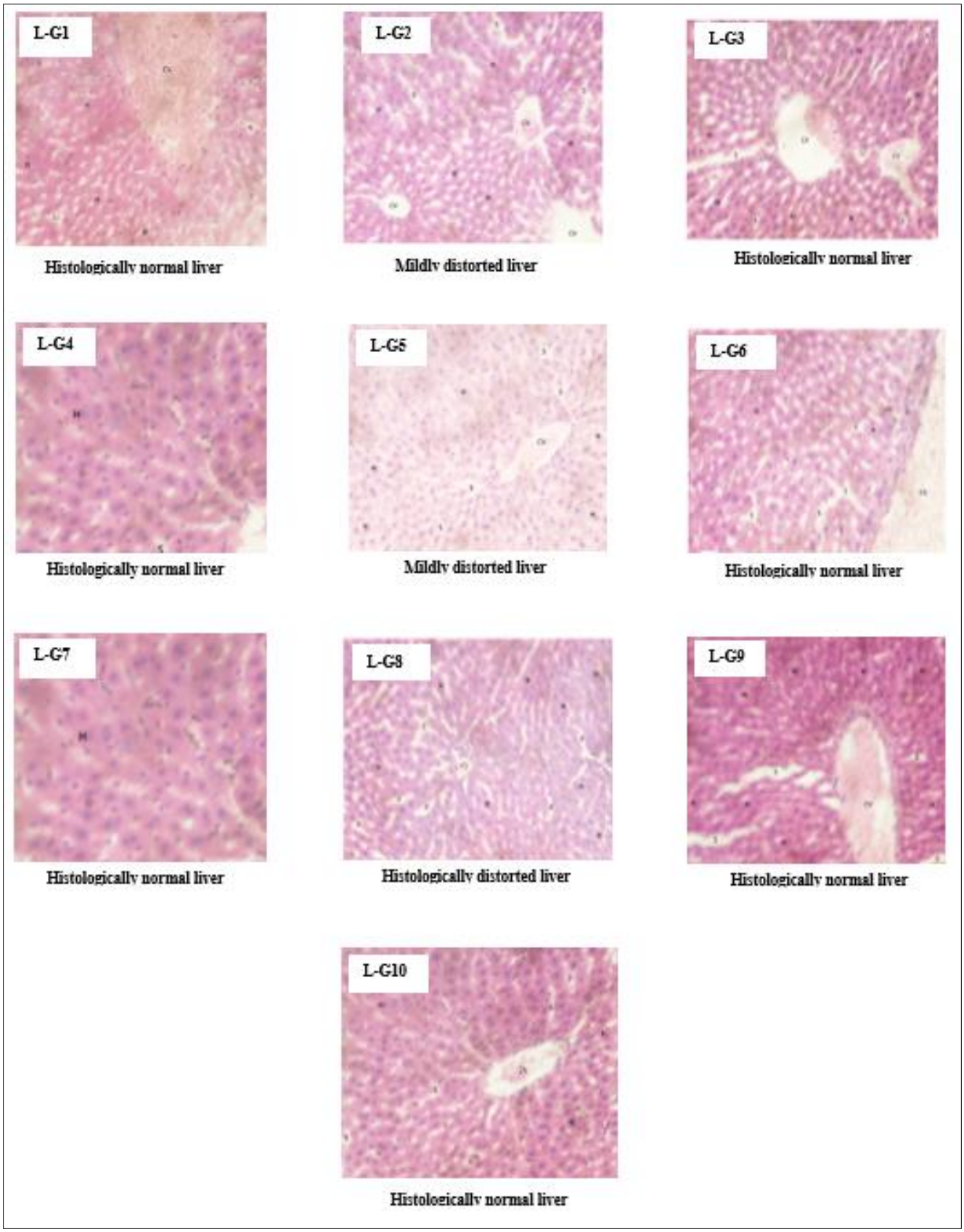

Figure 1 Plates L-G1 to L-G10. Light microscope photographs of liver paraffin sections (H & E stained), (Mag *400)

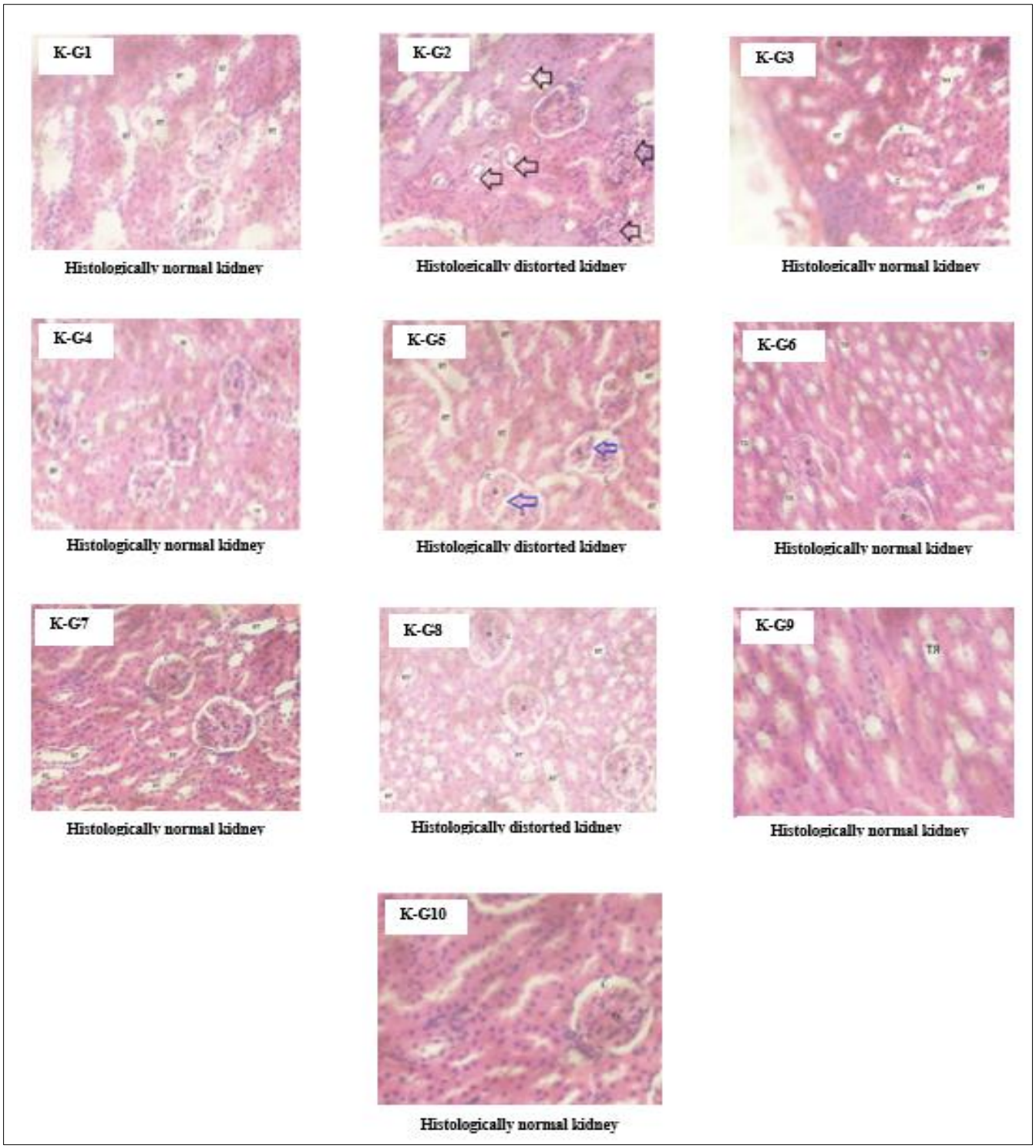

Figure 2 Plates K-G1 to K-G10. Light microscope photographs of liver paraffin sections (H & E stained), (Mag *400)

Results obtained in the present investigation showed that toxicity in Wistar rats triggered by exposure to mercury and cadmium resulted in elevated liver enzyme activity. Analysis of the activity of basic liver function enzymes in serum is used to indirectly access the integrity of tissues after exposure to pharmacological agents [34]. Mercury and cadmium triggered reno-hepatic tissue dysfunction in the experimental rats. Co-administration with *S. mombin* was effective in restoring reno-hepatic tissue dysfunction caused by the individual and synergistic effects of mercury and cadmium. Both toxicants are hepato- and nephrotoxic, but they affect these organs in different ways [35]. Liver injury following cadmium and mercury exposure is well established and evidenced by elevated levels of serum hepatic marker enzymes, indicating the cellular leakage and loss of functional integrity of hepatic membrane architecture [36, 37]. High activity

of aspartate transaminase (AST) and alanine transaminase (ALT) are the crucial parameters to detect liver damage [38]. This finding in the present study is similar to previous reports by Hwang et al. [39] and Hu et al. [40] who both observed liver damage in Cd-treated experimental animals which resulted in elevation of AST and ALT levels in the serum. Similarly, Youcef et al. [41] reported that mercury intoxication induces a significant elevation in serum AST and ALT activities which may be may be due to cellular necrosis of hepatocytes, which causes increases in the permeability of cell. Histological studies showed distorted liver in groups II, V and VIII.

Interestingly however, *S. mombin* aqueous leaf extract at the dosage administered (500 mg/kg) effectively and significantly lowered plasma activity of AST, ALT, ALP and TBIL levels, compared to groups II, V and VIII. In addition, treatment with *S. mombin* aqueous leaf extract significantly normalized TP levels compared to the mercury and cadmium-induced rats. These findings corroborate a previous report by Nwidu et al. [42] that *S. mombin* extracts were effective at significantly lowering conjugated bilirubin, total bilirubin, and ALP levels compared to the positive control group, in a study where hepatotoxicity was induced with carbon tetrachloride.

Studies have repeatedly shown that the kidney is one of the tissues most sensitive to the toxic effects of heavy metals. In cadmium administered rats, the heavy metal gets accumulated in the kidney, hence there is a defect in glomerular filtration. Increases in plasma levels of urea and creatinine is an indication of renal-tubular damage due to cadmium induced nephrotoxicity [43]. The present study showed that the level of plasma creatinine and urea increased in the mercury and cadmium-induced rats when compared to control rats. Also, histological studies showed distorted kidney tissues in groups II, V and VIII, similar to findings by Aughey et al. [44]. Mercuric chloride treatment has been shown to cause a significant increase in serum creatinine and serum urea indicating an impaired renal function. The increased blood urea and creatinine is in agreement with the results obtained by Dardouri et al. [45], Sheikh et al. [46] and Alam et al. [47] in rats treated with heavy metals.

The protective effect of plant extracts against heavy metal-triggered hepatotoxicity has been attributed to the presence of endogenous phytochemicals such as flavonoids, tannins, triterpenoids, and alkaloids [48, 49]. Flavonoids represent the most common and extensively distributed group of plant polyphenols, and serve as free radical scavengers and strong antioxidants that could protect against oxidative stress-induced cellular damage [50]. Igwe et al. [51] reported that flavonoids and saponins are present in *S. mombin* leaves. Antioxidant chemicals in *S. mombin*, particularly polyphenols, could contribute to its antioxidant and hepatoprotective activities [52]. The restoration of reno-hepatic tissue dysfunction indicates a protective and therapeutic effect of *S. mombin* leaves against hepatic and renal toxicity resulting from mercury and cadmium exposure.

4. Conclusion

From the present investigation, *S. mombin* aqueous leaf extract was found to exhibit hepatoprotective effects by stabilizing hepatocyte cell membranes, promoting repair of injured hepatic tissues, and has showed potentials to restore heavy metal-triggered reno-hepatic tissue dysfunction in Wistar rats. This finding is attributable to the wide array of phytochemicals reported to be present in the plant.

Compliance with ethical standards

Disclosure of conflict of interest

Authors have declared that no competing interests exist.

Statement of ethical approval

All authors hereby declare that "Principles of Laboratory Animal Care" (NIH Publication no. 85- 23, revised 1985) were followed. All experiments were examined and approved by the appropriate ethics committee.

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