Investigational
Medicinal Chemistry & Pharmacology

Research Article Open Access

# Protective effect of hydroethanolic leaves extract of *Solanum macrocarpon* on Cisplatin-induced kidney injury in rats

Godwin Agbeka[1], Grace Aba Bart-Plange[2], Akosua Pokuah[2], Mercy Aning Ampofo[2], Janet Akorkor Kwetey[2], Mathew Bimpong[2], Ama Agyeiwaa Anyimadu[2], Gloria Asem[2], Naomi Mensah[2], Jeffery Kweku Dadson[2], Christopher Larbie[1], Paul Poku Sampene Osei[3], Shadrack Donkor[4] Benjamin O. Emikpe[5]

## Abstract

**Background:** Nephrotoxicity is a common kidney condition affecting many people worldwide, with conventional synthetic drugs not often yielding desirable results. This study, therefore, aimed to assess the protective effect of *Solanum macrocarpon* on Cisplatin-induced nephrotoxicity in Wistar rats.

**Methods:** Hydroethanolic extract of the leaves of *S. macrocarpon* was prepared and analyzed for basic phytochemical constituents. Cisplatin (5 mg/kg) was administered to induce nephrotoxicity. The extract was administered at 100, 250, and 500 mg/kg for 10 days, and Silymarin standard (120 mg). After 10 days, the rats were sacrificed, and their blood samples and kidneys were collected for biochemical, hematological, and histopathological analyses.

**Results:** The extract was rich in flavonoids, coumarins, terpenoids, and tannins. The serum levels of urea and creatinine were significantly higher in the Cisplatin group compared to the normal group. However, in the extract co-administered groups, there was a reduction in the urea and creatinine levels relative to the Cisplatin-only group. The kidney microarchitecture also improved with the administration of the extract.

**Conclusion:** *S. macrocarpon* extract was effective in treating acute nephrotoxicity caused by Cisplatin at the microarchitectural level of kidneys. This protective effect might be attributed to the phytochemical constituents. The extract's 250mg/kg dose showed the best nephroprotective ability.

**Keywords:** Nephrotoxicity, *Solanum macrocarpon,* Kidneys, Cisplatin, Creatinine, Urea.

*Correspondence: Tel.: +233242175669; E-mail address: shadrachdonkor2000@gmail.com; ORCID: https://orcid.org/0000-0002-8019-2393 (Shadrack Donkor)

[1]HepatoRenal Group, Department of Biochemistry and Biotechnology, College of Science, Kwame Nkrumah University of Science and Technology; [2]Department of Biochemistry and Biotechnology, College of Science, Kwame Nkrumah University of Science and Technology; [3]Department of Pathology, College of Health Sciences, Kwame Nkrumah University of Science and Technology; [4]Applied Radiation Biology Centre, Radiological and Medical Sciences Research Institute, Ghana Atomic Energy Commission, Legon, Accra, Ghana; [5]Department of Veterinary pathology, School of Veterinary Medicine, Kwame Nkrumah University of Science and Technology (KNUST), Kumasi, Ghana.

*Other authors:*
*E-mail: agbekagodwin24@gmail.com; ORCID: https://orcid.org/0009-0006-0971-6314 (Godwin Agbeka); E-mail: gracebartplange99@gmail.com; ORCID: https://orcid.0009-0006-7564-1656 (Grace Aba Bart-Plange); E-mail: ampofomercy3@gmail.com; ORCID: https://orcid.0009-0004-2227-9484 (Mercy Aning Ampofo); E-mail: kweteyjanet@gmail.com; ORCID: https://orcid.0009-0007-5323-4803 (Janet Akorkor Kwetey); E-mail: Mbimpong1@gmail.com; ORCID: https://orcid.0009-0003-6675-5342 (Mathew Bimpong); E-mail: anyimaduagyeiwaa@gmail.com; ORCID: https://orcid.0009-0004-7497-0613 (Ama Agyeiwaa Anyimadu); E-mail: asemg848@gmail.com (Gloria Asem); E-mail: mnaomi12345@gmail.com; ORCID: https://orcid.0009-0009-8385-1823 (Naomi Mensah); E-mail: jkdadaon@knust.edu.gh; ORCID: https://orcid.0000-0001-6783-2782 (Jeffery Kweku Dadson); E-mail: ekowlarbie@gmail.com; ORCID: https://orcid.org/0000-0003-4927-4419 (Christopher Larbie); E-mail: pOsei.chs@knust.edu.gh; ORCID: https://orcid.org/0000-0001-8810-2017 (Paul Poku Smapene Osei); E-mail: boemikpe.chs@knust.edu.gh; ORCID: https://orcid.0000-0003-2458-6504 (Benjamin O. Emikpe).*

*Citation on this article: Agbeka G, Bart-Plange GA, Pokuah A, Ampofo MA, Kwetey JA, Bimpong M, Anyimadu AA, Asem G, Mensah N, Dadson JK, Larbie C, Osei PPS, Donkor S, Emikpe BO. Protective effect of hydroethanolic leaves extract of Solanum macrocarpon on Cisplatin-induced kidney injury in rats. Investigational Medicinal Chemistry and Pharmacology (2024) 7(3):100; Doi: https://dx.doi.org/10.31183/imcp.2024.00100*

## Background

The Kidneys are one of the most important organs in the human body. They maintain the body in a steady state (homeostasis) by excreting metabolites (especially creatinine and urea) out of the body, regulating blood pressure, red blood cell production, and buffering blood pH [1]. However, when the kidneys become exposed to certain drugs and environmental toxicants, they get damaged. The condition, known as nephrotoxicity, occurs when drugs cause a rapid deterioration or worsening in kidney function as a result of their toxic effects [2]. Nephrotoxicity can lead to permanent kidney damage when kidney cells are exposed to stress for a prolonged period [3]. The prevalence of kidney disease is not something the world should take lightly. Studies suggest that approximately 756 million people suffer from kidney disorders, with 2.3 million Ghanaians being affected with kidney diseases from 1990 to 2017, resulting in 3,572 fatalities [4].

Currently, novel interventions like erythropoietin stimulating agents, endothelin antagonists, glycosaminoglycans, and anti-inflammatory agents are used to treat kidney ailments [5]. According to a study [6], the use of erythropoietin-stimulating agents may lead to various adverse effects, which include venous and arterial thromboembolism, thrombophlebitis, hypertension, ischemic heart disease, cardiac failure, arrhythmia, and cardiac arrest. Among these, venous thromboembolism is considered the most significant adverse effect. On the other hand, the use of endothelial antagonists may result in hepatic transaminitis, peripheral oedema, and anemia [7]. Non-steroidal anti-inflammatory drugs (NSAIDs) can lead to gastrointestinal complications and renal disturbances [8]. At the same time, glycosaminoglycans can trigger autoimmune disorders by binding to cells that cause inflammation and ultimately leading to rheumatoid arthritis [9].

As such, there is a need to look for new treatment options that are more efficacious with fewer adverse effects. *Solanum macrocarpon,* also known as 'Gboma,' is one of these promising treatment options, as it has traditionally been used to treat kidney ailments. Its name comes from the Ewe language and means "leaf-fruit," likely because the leaves and fruits are highly valued for their many uses – mainly in cooking food. This plant is predominantly found in the Volta region of Ghana and Togo [10]. *S. macrocarpon* is a tall nonwoody annual leafy and fruit vegetable which grows to an average height of 20 cm in Ghana. It has been reported to be the 3$^{rd}$ most crucial crop from the family Solanaceae [11-12]. The Gboma plant is widely distributed in West Africa. Both leaves and fruit are highly nutritious, containing protein, fiber, and minerals such as calcium, iron, and sodium [13-14]. A study by Oboh et al. [15] reported that *S. macrocarpon's* root has the potential to cure bronchitis, itching, body aches, asthma, and wounds. The seeds are commonly used to alleviate toothache, and the juice extracted from its leaves is used to treat gout, rheumatism, and angina. Additionally, it has been utilized as an anesthetic during childbirth, to treat inflammatory tumors and cancerous tissues, and to treat Parkinson's disease. This study was, therefore, designed to evaluate the nephroprotective ability of *S. macrocarpon* leaves in female Wistar rats.

## Methods

*Collection and preparation of plant materials*

*S. macrocarpon* leaves (Figure 1) were collected from Anwomaso in Kumasi (6.6666° N, 1.6163° W), Ghana. The leaves were carefully dried under shade for about three weeks to ensure thorough sample drying. They were then milled and then extracted.

*Animals*

The experiment was conducted using adult female rats weighing between 70 and 110 g. The animals were housed in the animal holding facility of the Department of Biochemistry and Biotechnology, KNUST, Kumasi. The animals had free access to standard feed (Mash, AGRICARE, Kumasi-Ghana) and tap water *ad libitum* except an overnight fast prior to commencement and at termination. Animals were handled as stated in the guidelines of the National Research Council's Guide for Care and Use of Laboratory Animals [16] and protocol was approved by a veterinarian on the research team. All animals were humanely handled during the experiment.

*Hydroethanolic extraction of plant material*

The plant material was treated and extracted as previously described [17]. Briefly, 200g of milled *S. macrocarpon* powder was soaked in 1 litre of 50% hydro-ethanol for 24 hours. The extract was carefully decanted. The filtrate was concentrated using rotary evaporator and freeze-dried to obtain hydroethanolic *S. macrocarpon leaf* extract (SME). The extract was placed in a sterile zip-lock bag to prevent contamination and phytochemical analysis performed to assess basic content using standard methods (Table 1). Doses were prepared based on each group's average body of the Wistar rats, with distilled water as the solvent.

*Experimental design*

In this experiment, 18 female Wistar rats were divided into six groups of three rats each. The SME was prepared at doses of 100, 250, and 500 mg/kg body weight and administered orally to the designated groups throughout the study period. Cisplatin was only administered intraperitoneally to specific groups on day 7 of the experiment. As a standard, 120 mg of Silymarin was used. All Wistar albino rats used in the experiment were within the same weight range. All animal research was carried out by the Committee for the Monitoring and Control of Animal Experimentation's guidelines. Protocols for all animal experiments were verified and approved by a veterinarian on the research team. The grouping and treatment of the experimental animals are outlined in Table 2.

*Sacrifice of rats and blood collection*

Extracts were administered for ten days. However, Cisplatin was injected on the seventh day. This allowed the extract to protect the kidney before the toxicant was injected. The rats were sacrificed on the 11$^{th}$ day by cervical dislocation after an overnight fast. Blood samples were collected into anticoagulant, dipotassium EDTA tubes via incision in the cervical region for hematological screening using the Sysmex Hematology System (USA). The other part was collected in gel and clot activator tubes and allowed to clot. The

clotted blood sample was centrifuged at 3500 rpm for 10 min to obtain the serum for biochemical indices. The kidneys were excised, weighed, rinsed in normal saline, and preserved in 10% formalin for histopathological analysis.

*Assessment of hematological and biochemical parameters*

Various hematological parameters, such as hemoglobin (HB), white blood cell levels (WBC), red blood cell levels (RBC), platelets (PLT), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC) and mean platelet volume (MPV), were analyzed. Blood samples containing anticoagulants were used for the profiling with an automated blood analyzer (Sysmex XS-1000i).

Additionally, biochemical indices, including alanine aminotransferase (ALT), urea, creatinine, potassium, and sodium, were determined using an automatic Chemistry analyzer (RX Monza) and manufacturer reagents.

*Histopathological assessment of kidney*

The kidneys were placed in 10% formalin for preservation, dehydrated using ascending grades of alcohol (50%, 70%, and 90%) and xylene, and then embedded in paraffin wax. From each block, 5µm sections were cut. Representative sections of the kidneys were rehydrated with xylene and descending grade of alcohol (90%, 70%, and 50%), and then stained with hematoxylin and eosin dyes for histopathological analysis. A pathologist examined sections from each group using a light microscope (Olympus et al. BX43) at X100 magnification to observe any changes in kidney microarchitecture and determine the effect of treatments on the kidney tissues.

*Statistical Analysis*

The hematological and biochemical data were analyzed using GraphPad Prism 8. The results were presented as the mean ± standard error of the mean (SEM). Each data's mean was compared using a one-way analysis of variance (ANOVA) and the Tukey multiple comparison test at the 95% significant level.

## Results

*Phytochemical analysis*

Table 3 shows the observed phytochemical components of SME: flavonoids, saponins, tannins, alkaloids, coumarins, and terpenoids are present.

*Effect of Treatments on Hematological Parameters*

The administration of Cisplatin reduced red blood cell, and platelet counts while white blood cell counts increased. However, treatment with the SME effectively maintained these levels close to normal, except for platelet count (Table 4).

*Effect of Treatments on Serum Biochemical Indicators*

The use of Cisplatin resulted in a significant increase in serum levels of kidney biomarkers (creatinine and urea). However, Silymarin and SME partially maintained the biomarker levels close to normal (Table 5).

*Effect of Treatment on Kidney Microarchitecture*

The kidney cells showed signs of toxicity when treated with Cisplatin. This included damage to the glomerular apparatus and bowman capsule, a reduction in the number of nephrons, and tubular degeneration. However, the administration of Silymarin appeared to have a protective effect on the kidneys. In Figure 2c, kidney tissues treated with Silymarin showed intact functional units. Additionally, oral administration of SME reduced the damage caused by Cisplatin. The extract helped preserve the infiltrating apparatus of the kidneys, including the glomerular, convoluted tubules, and nephrons

## Discussion

Kidney diseases are one of the leading causes of morbidity and mortality, with the actual incidence unknown in Ghana [18]. This study investigated the nephroprotective effects of *Solanum macrocarpon* against cisplatin-induced nephrotoxicity in female Wistar rats. Cisplatin is used as an antitumor drug. Although its use in cancer treatment has many advantages, it can cause damage to the nervous, auditory, gastrointestinal systems and kidneys [19].

This research/study observed that WBC levels increased after the administration of Cisplatin, possibly indicating an immune response to infection or inflammation [20]. Treatment with Silymarin and the extract successfully returned the levels to almost normal. This is inconsistent with previous findings [21, 22], which reported average to low levels of WBC when Cisplatin was injected for two to three weeks of the experiment. In their studies, the normal to low levels of WBC were attributed to the damage to bone marrow caused by prolonged tissue exposure to Cisplatin. However, a previous study reported that WBC levels significantly increased four days after receiving Cisplatin but returned to normal within a week of injection [23]. This is consistent with the current research. The sudden rise in WBCs may indicate an infection, as these cells protect the body against harmful pathogens.

The hematological results indicated a significant reduction in red blood cell (RBC) and hemoglobin (HB) levels. Usually, as the kidneys detect low levels of oxygen, they produce erythropoietin hormone through renal Epo-producing (REP) cells. This hormone stimulates the increased production of red blood cells [24]. However, in diseased kidneys, the REP cells cannot produce erythropoietin, resulting in a decrease in red blood cells known as renal anemia. Different mechanisms have been projected to explain various phenomena, such as the destruction of bone marrow cells, the increased vulnerability of red blood cells to osmotic pressure, and the altered permeability of red blood cell membranes caused by Cisplatin [25]. These factors may cause anemia by reducing the activity of blood-forming tissues, hindering the production of red blood cells, and speeding up the breakdown of red blood cells. Cisplatin can also reduce HB levels by inhibiting erythropoiesis and impairing iron supply to erythroblasts. The extract partially maintained the RBC levels, with the most activity attributed to the 250 mg/kg, which performed better than the standard drug (Silymarin) available for treating kidney diseases.

Furthermore, the platelet count was significantly lowered when Cisplatin was introduced. This decrease might be attributed to Cisplatin's inhibitory effects on bone marrow function, reduced platelet production, increased platelet consumption, or enhanced platelet aggregation following its administration. These findings affirm the intricate hematological alterations associated with

Cisplatin-induced nephrotoxicity and underscore the potential nephroprotective properties of *S. macrocarpon* leaf extract.

The biochemical results showed that there was an increase in both serum creatinine and urea levels after the administration of the toxicant. Urea is typically removed from the blood by the kidney's glomeruli and is then eliminated through urine. However, due to the harmful effects of Cisplatin on kidneys, the glomeruli's urea clearance rate was lowered, resulting in an increased serum level of urea [26]. The decrease in creatinine clearance by the glomeruli and tubules in the rats treated with Cisplatin caused an increase in creatinine levels in these rats. Nevertheless, treatment with Silymarin and the extract brought these biochemical indices to lower levels. The 250 mg/kg extract provided better kidney protection.

This protective function may be attributed to its ability to act as an antioxidant and anti-inflammatory agent against reactive oxygen species (ROS) and certain cytokines that may contribute to damage to the glomerular filtration rate. The effectiveness of *S. macrocarpon* extract may be attributed to the high antioxidant content generated from its phytochemical constituents -flavonoids, terpenoids, coumarins, and tannins [27]. These antioxidants are crucial in neutralizing free radicals generated when Cisplatin induces pores in the inner mitochondria membrane, releasing reactive oxygen species in the cells. These free radicals can cause oxidative stress, damaging vital tissues if not neutralized. This damage triggers the body's response involving two main mechanisms: programmed cell death (apoptosis) and accidental cell death (necrosis). Although apoptosis is generally safe, it can sometimes be pathological, while necrosis often leads to pathological conditions. The high antioxidant content of *S. macrocarpon* leaves containing flavonoids, terpenoids, coumarins, and tannins [28] likely contributed to its nephroprotective effect by preventing the destructive processes caused by free radicals. According to the results, the extract at a dosage of 250 mg/kg showed the best nephroprotection compared to 100 mg/kg and 500 mg/kg of the extracts.

**Figure 1.** *S. macrocarpon* leaves

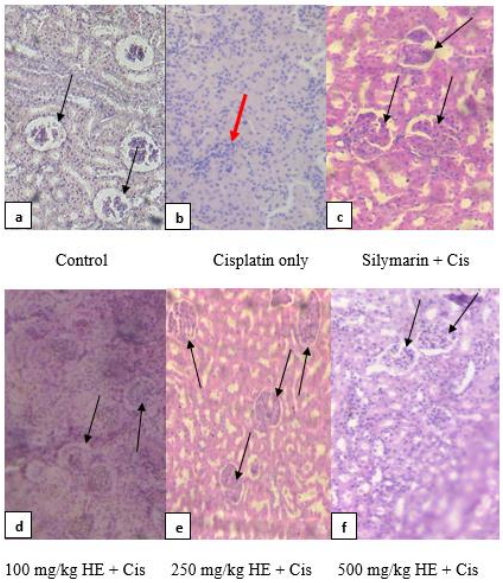


**Figure 2.** Micrograph of kidney tissues stained with Hematoxylin and Eosin dyes at X100 magnification.

*The arrows indicate the Bowman capsules. In Fig (a), the black arrow shows a regular Bowman capsule, while in Fig (b), the red arrow shows an effaced Bowman capsule. Silymarin and the extract were able to preserve the bowman capsule from damage, as indicated in Fig (c), (d), (e), and (f) with black arrows

**Table 1.** Phytochemical Screening

| Phytochemical | Method | Observation |
|---|---|---|
| Detection flavonoids | 1 mL extract + 5 drops of 20% NaOH + few 2ml dil. HCl | An intense yellow color becomes colorless on the addition of diluted acid |
| Detection of phenolic compound | 1 mL of extract few drops of oil. Iodine solution | No color change observed |
| Detection of coumarins | Plant extract + 10 of NaOH/chloroform | A yellow color |
| Detection of tannins | 0.4 mL of extract+ 4 mL of 10 NaOH | Formation of emulsion |
| Detection of terpenoids | 0.5 mL of chloroform +1 mL of extract few drops of conc. $H_2SO_4$. | A reddish-brown precipitate formed |
| Detection of cardiac glycosides | 1 mL of glacial acetic acid + 2.5 mL of extract drops of ferric chloride solution | No color change observed |
| Detection of saponins | 0.5 mL of extract + 2 mL of water (shaken vigorously) | Persistent foam for 10 min |
| Detection of alkaloids | 3 mL of extract + few drops of iodine solution | A blue color disappears on oiling |

**Table 2.** Experimental grouping and treatments given to rats

| No. | Groups | Treatment |
|---|---|---|
| I | Normal | Water and food without extract and toxicant throughout the 10 days of the experiment. |
| II | Cisplatin only | 5 mg/kg of Cisplatin on day 7 of the experiment. |
| III | Silymarin + Cisplatin | 120 mg of Silymarin for 10 days and 5 mg/kg of Cisplatin on day 7. |
| IV | 100 mg/kg SME + Cisplatin | 100 mg/kg of extract for 10 days and 5 mg/kg of Cisplatin on day 7. |
| V | 250 mg/kg SME + Cisplatin | 250 mg/kg of extract for 10 days and 5 mg/kg of Cisplatin on day 7. |
| VI | 500 mg/kg SME + Cisplatin | 500 mg/kg of extract for 10 days and 5 mg/kg of Cisplatin on day 7. |

*Cisplatin = Nephrotoxin, Silymarin = Standard drug used to treat kidney disease

**Table 3.** Phytochemical composition present in leaves of *S. macrocarpon* leaves

| **Phytochemicals** | ***Presence*** |
|---|---|
| Flavonoids | + |
| Saponins | + |
| Tannins | + |
| Phenols | - |
| Alkaloids | + |
| Cardiac glycosides | - |
| Coumarins | + |
| Terpenoids | + |

Key: + = present, - = absent

**Table 4.** Effect of treatments on hematological parameters

| **Parameters** | **Control** | **Cisplatin only** | **Cis + Sly** | **Cis+100 mg/kg** SME | **Cis+250 mg/kg** SME | **Cis+500 mg/kg** SME |
|---|---|---|---|---|---|---|
| WBC($X10^9$/L) | 11.27 ± 0.09$^a$ | 16.83 ± 0.55$^b$ | 14.10 ± 0.12$^c$ | 14.73 ± 0.33$^d$ | 14.07 ± 0.43$^c$ | 14.37 ± 0.64$^d$ |
| RBC ($x10^{12}$/L) | 7.89 ± 0.42$^a$ | 5.63 ± 0.19$^b$ | 7.82 ± 0.50$^c$ | 6.82 ± 0.65$^d$ | 8.23 ± 0.08$^c$ | 7.47 ± 0.25$^d$ |
| HGB(g/dL) | 13.40 ± 0.50$^a$ | 12.07 ± 0.44$^a$ | 14.33 ± 0.23$^{a,b}$ | 12.30 ± 0.58$^a$ | 14.40±0.31$^{a,b}$ | 13.30 ± 0.49$^a$ |
| HCT% | 53.93 ± 2.24$^a$ | 43.97 ± 1.03$^a$ | 47.40 ± 4.35$^a$ | 47.10 ± 3.88$^a$ | 52.57 ± 2.22$^a$ | 53.77 ± 0.91$^a$ |
| MCV (fL) | 74.13 ± 1.31$^a$ | 66.20 ± 2.06$^a$ | 75.00 ± 1.68$^a$ | 70.43 ± 4.79$^a$ | 77.33 ± 0.86$^a$ | 72.37 ± 12.07$^a$ |
| MCH (pg) | 18.23 ± 0.24$^a$ | 17.23 ± 0.87$^a$ | 17.57 ± 2.17$^a$ | 21.63 ± 2.60$^a$ | 25.97 ± 8.02$^a$ | 18.90 ± 1.08$^a$ |
| MCHC (g/dL) | 24.57 ± 0.22$^a$ | 24.00 ± 2.55$^a$ | 36.40 ± 5.29$^a$ | 30.57 ± 1.91$^a$ | 38.60 ± 11.80$^a$ | 27.07 ± 2.88$^a$ |
| MPV (fL) | 8.33 ± 0.03$^a$ | 7.47 ± 0.37$^a$ | 8.10 ± 0.46$^a$ | 7.27 ± 0.35$^a$ | 7.93 ± 0.35$^a$ | 7.20 ± 0.35$^a$ |
| PLT($x10^9$/L)) | 1022.57 ± 39.72$^a$ | 795.67 ± 7.84$^b$ | 868.67± 22.84$^c$ | 658.0 ± 43.51$^d$ | 972.00 ± 9.87$^e$ | 755.33±15.68$^d$ |

**Mean ± SEM (n = 3); different letters in superscripts indicate significant difference at p ≤ 0.05. white blood cells (WBC), red blood cells (RBC), hemoglobin (HGB), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentrations (MCHC), mean platelet volume (MPV), platelet (PLT).*

**Table 5.** Effect of treatments on serum biochemical parameters

| **Parameters** | **Control** | **Cisplatin only** | **Cis + Sly** | **Cis + 100 mg/kg SME** | **Cis + 250 mg/kg SME** | **Cis + 500 mg/kg SME** |
|---|---|---|---|---|---|---|
| ALT (U/L) | 79.93 ± 1.71 | 82.06 ± 0.50 | 75.13 ± 0.65 | 73.95 ± 1.65$^b$ | 73.15 ± 0.03$^b$ | 74.45 ± 1.93$^b$ |
| CREA. (mmol/L) | 40.90 ± 2.17 | 126.90 ± 16.28$^a$ | 81.10 ± 24.88$^b$ | 105.20 ± 14.20$^b$ | 57.10 ± 3.12$^b$ | 96.55 ± 15.79$^b$ |
| UREA (umol/L) | 8.96 ± 1.08 | 25.09 ± 0.19$^a$ | 18.07 ± 1.59$^a$ | 25.45 ± 0.47$^a$ | 9.90 ± 0.57$^b$ | 19.15 ± 0.66 |
| $K^+$ (mmol/L) | 6.73 ± 0.48 | 6.15 ± 0.09 | 6.45 ± 0.09 | 6.45 ± 0.03 | 7.35 ± 0.61 | 6.60 ± 0.12 |
| $Na^+$ (mmol/L) | 146.10±0.90 | 142.90 ± 0.98 | 144.90 ± 1.56 | 144.55 ± 1.41 | 142.80 ± 0.69 | 146.20 ± 1.33 |
| Cl- (mmol/L) | 104.70±0.32$^a$ | 101.15 ± 0.66$^b$ | 102.22 ± 0.39$^b$ | 102.30 ± 0.06$^b$ | 106.10 ± 0.64$^d$ | 103.50 ± 0.29$^d$ |

**Mean ± SEM (n = 3); different letters in superscript indicate significant difference at p ≤ 0.05. Alanine aminotransferase (ALT), creatinine (CREA.), sodium (Na), chloride (Cl-), potassium (K+).*

## Conclusion

The extract from *Solanum macrocarpon* leaves was found to effectively counter the harmful impact of Cisplatin on hematological and serum biochemical parameters. When used alongside Cisplatin, the extract safeguarded the proper functioning and protected the microarchitecture of the kidneys. The 250 mg/kg dosage provided the most effective nephroprotection among the tested doses.

### Abbreviations

RBC: Red blood cell count
WBC: White blood cell count
HGB: Hemoglobin concentration
MCV: Mean corpuscular volume
MCH: Mean corpuscular hemoglobin
MCHC: Mean corpuscular hemoglobin concentration
PLT: Platelet
HCT: Hematocrit
MPV: Mean platelet volume
ALT: Alanine aminotransferase
CREA: Creatinine

### Authors' Contribution

This work was carried out in collaboration among all authors. SD, GA, GABP and CL designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. AP AAA, GA, NM, and JKD ran hematological and biochemical analyses. CD and PPSO did histopathological tests. GA, GABP, AP, MAA, KAJ, MB, and JKD managed the literature searches. All authors cross-checked and approved the final manuscript.

### Conflict of interest

The authors declare no conflict of interest

**Article history:**

Received: 04 October 2024
Received in revised form: 31 October 2024
Accepted: 31 October 2024
Available online: 31 October 2024

## References


1. Mahadevan V. 2019. Anatomy of the kidney and ureter. *Surgery (United Kingdom)*, *37*(7):359–364.
2. Al-Naimi M, Rasheed H, Hussien N, Al-Kuraishy H, Al-Gareeb A. 2019. Nephrotoxicity: Role and significance of renal biomarkers in the early detection of acute renal injury. *J Adv Pharm Technol Res.* 10(3):95–99.
3. Nyarko RA, Larbie C, Anning AK, Baidoo PK, Emikpe BO, Oyagbemi AA, Jarikre TA. 2019. Griffonia simplicifolia (DC.) Baill. attenuates gentamicin and cisplatin-induced nephrotoxicty in rats. *Comp Clin Path. 28*(5):1293–1304.
4. Vos T, Bikbov B. 2017. *Global, regional , and national burden of chronic kidney disease , 1990 – 2017 : a systematic analysis for the Global Burden of Disease Study 2017*. https://doi.org/10.1016/S0140-6736(20)30045-3
5. Heerspink L, Jan H, de Zeeuw D. 2013. Novel drugs and intervention strategies for the treatment of chronic kidney disease. *Br J Clin Pharmacol.* 76(4):536–550.
6. Rao GG, Rao S, Bugazia S, Dhandapani TPM, Tara A, Garg I, Patel JN, Yeon J, Memon MS, Muralidharan A, Khan S. 2021. Efficacy and Cardiovascular Adverse Effects of Erythropoiesis Stimulating Agents in the Treatment of Cancer-Related Anemia: A Systematic Review of Randomized Controlled Trials. *Cureus*, *13*(9):1–12.
7. Wei A, Gu Z, Li J, Liu X, Wu X, Han Y, Pu J. 2016. Clinical adverse effects of endothelin receptor antagonists: Insights from the meta-analysis of 4894 patients from 24 randomized double-blind placebo-controlled clinical trials. *J Am Heart Assoc*. *5*(11): e003896.
8. Harirforoosh S, Asghar W, Jamali F. 2013. Adverse effects of nonsteroidal antiinflammatory drugs: An update of gastrointestinal, cardiovascular and renal complications. *J Pharm Pharm Sci. 16*(5):821–847.
9. Wang JY, Roehrl MH. 2002. Glycosaminoglycans are a potential cause of rheumatoid arthritis. *Proc Natl Acad Sci U S A. 99*(22):14362–14367.
10. Bonsu, KO, Fontem DA, Nkansah, GO, Iroume RN, Owusu EO, Schippers RR. 2002. Diversity within the Gboma eggplant (*Solanum macrocarpon*), an indigenous vegetable from West Africa. *Ghana Journal of Horticulture.* 1: 50-58.
11. Afolabi, S. G., Davidson, J. O., Ibrahim, H. M., Tijani, A. T., & Adeboye, M. K. A. 2020. *Response of Gboma Eggplant to Nitrogen Fertilization, In Minna*. 1(2): 95–98.
12. Nyadanu, D., Aboagye, L. M., Akromah, R., Osei, M. K., and Dordoe, M. B. 2014. *Agromorphological characterisation of gboma eggplant, an indigenous fruit and leafy vegetable in Ghana." Afr Crop Sci J.* 22 (4): *281-289.*
13. Nyadanu D, Lowor ST. 2015. Promoting the competitiveness of neglected and underutilized crop species: a comparative analysis of the nutritional composition of Ghana's indigenous and exotic leafy and fruit vegetables. *Genet Resour Crop Evol.* 62(1): 131–140.
14. Agoreyo B, Obansa E, Obanor E. 2012. Comparative nutritional and phytochemical analyses of two varieties of Solanum melongena. *Sci World J.* 7(1): 5–8.
15. Oboh G, Ekperigin MM, Kazeem MI. 2005. Nutritional and hemolytic properties of eggplant (*Solanum macrocarpon*) leaves. *J Food Compost Anal. 18*(2–3), 153–160.
16. NRC. 2011. Guide for the care and use of laboratory animals. Eight edition. National Academies Press.
17. Donkor S, Larbie C, KomLaga G, Emikpe BO. 2019. Phytochemical, antimicrobial, and antioxidant profiles of *Duranta erecta* L. parts. *Biochem Res Int.* 2019(1):8731595.
18. Tannor EK, Antwi S. 2023. Global Dialysis Perspective: Ghana. *Kidney 360.* 4(12):1776–1779.
19. Iqbal MO, Sial AS, Akhtar I, Naeem M, Hazafa A, Ansari RA, Rizvi SAA. 2021. The nephroprotective effects of *Daucus carota* and *Eclipta prostrata* against cisplatin-induced nephrotoxicity in rats. *Bioengineered*. 12(2):12702–12721.
20. Majesty D. 2013. Effect of Solanum Macrocarpon Fruit on Haematology, Hepatic and Renal Function. *Adv Biochem.* 1(2):28.
21. Ahmed A, Yousif M, Merghani MM, Babiker NE. 2021. The effect of Cisplatin on Complete blood count among chemotherapy Sudanese patients at Taiba Cancers Center in Khartoum state. *Journal of Drug Delivery and Therapeutics*. 11: 104–113.
22. Wood PA, Hrushesky WJM. 1995. Cisplatin-associated anemia: An erythropoietin deficiency syndrome. *J Clin Invest*. 95(4)1650–1659.
23. Qing L, Xiang T, Guofu Z, Weiwei F. 2014. *Leukemoid reaction in cervical cancer: a case report and review of the literature*. *BMC Cancer*. 14: 1-8.
24. Sato K, Hirano I, Sekine H, Miyauchi K, Nakai T, Kato KS, Yamamoto M, Suzuki N. 2019. An immortalized cell line derived from renal erythropoietin-producing (REP) cells demonstrates their potential to transform into myofibroblasts. *Sci Rep.* 9(1):1–15.
25. Bhalchandra W, Alqadhi YA, Ninawe AS. 2018. Ameliorative Role of Bee Honey and Royal Jelly Against Cisplatin Induced Alteration in Hematological Parameters in Male Wister Albino Rat. *Int J Pharm Sci.* 10(4):110.
26. Janakiraman M, Jeyaprakash K. 2015. Nephroprotective effect of Vitex negundo linn. on cisplatin induced nephrotoxicity in male albino rats. *World J Pharm Pharm Sci.* 3(4): 706-715.
27. Komlaga G, Sam GH, Dickson RA, Mensah MLK, Fleischer TC. 2014. Pharmacognostic studies and antioxidant properties of the leaves of *Solanum macrocarpon*. *Journal of Pharmaceutical Sciences and Research*, 6(1):1–4.
28. Chinedu SN, Olasumbo AC, Eboji OK, Emiloju OC, Olajumoke K, Dania DI. 2011. Proximate and Phytochemical analyses of *Solanum aethiopicum* L. and *Solanum macrocarpon* L. fruits. *Res J Chem Sci.* 1(3):63–71.