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# Research Article
# *Moringa oleifera* Leaf Extracts Modulate Biochemical Alteration Associated with Cisplatin-induced Acute Hepatic Injury in Wistar Rats

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## Abstract

**Background and Objective:** Interest in *Moringa oleifera* continues to increases rapidly because of the widely acclaimed effectiveness of this plant against diverse disease conditions in folk medicine. The present study investigated the therapeutic potential of aqueous and methanol leaf extracts of *Moringa oleifera* (AEMO and MEMO) against hepatotoxicity induced by cisplatin in rats. **Materials and Methods:** Different groups of cisplatin (7.5 mg $kg^{-1}$, i.p.) intoxicated rats were treated separately with physiological saline (10 mL $kg^{-1}$), AEMO (50 mg $kg^{-1}$), AEMO (100 mg $kg^{-1}$), MEMO (50 mg $kg^{-1}$) or MEMO (100 mg $kg^{-1}$). Separate groups of normal rats also received physiological saline (10 mL $kg^{-1}$), AEMO (100 mg $kg^{-1}$) or MEMO (100 mg $kg^{-1}$). Treatments were administered orally for five consecutive days. Animals were sacrificed by cervical dislocation 24 h after last treatment (i.e. on the 6th day). Blood sample was collected by cardiac puncture and plasma separated for assessment of hepatic function. Liver was excised, homogenized and also used for other biochemical analysis. Data was analyzed by one-way analysis of variance (ANOVA) and least significant difference (LSD) for inter-group comparisons. **Results:** Cisplatin significantly elevated markers of liver function [aspartate aminotransferase (AST), alanine aminotransferase (ALT) activity, total cholesterol (TC) and triglyceride (TG)] and increased liver weight. This hepatic injury was associated with elevation in malondialdehyde together with diminished activity of antioxidant enzymes (catalase, glutathione-s-transferase and superoxide dismutase) and glutathione (GSH) concentration. TC, TG, catalase activity and liver weight improved significantly in the cisplatin intoxicated rats following treatment with AEMO. Although, MEMO (100 mg $kg^{-1}$) increased AST activity and TC of normal rats, the extract (50 and 100 mg $kg^{-1}$) significantly improved the lipid profile of cisplatin-treated rats. Similarly, glutathione-s-transferase, catalase, TC and liver weight of cisplatin intoxicated rats significantly improved after treatment with MEMO (50 and 100 mg $kg^{-1}$). **Conclusion:** Overall, data show that AEMO and MEMO ameliorated some aspects of cisplatin-mediated hepatotoxicity suggesting potential therapeutic benefit against liver injury when employed in appropriate doses.

Key words: Cisplatin, hepatotoxicity, oxidative stress, *Moringa oleifera*, leaf extract

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Data Availability: All relevant data are within the paper and its supporting information files.

## INTRODUCTION

Cisplatin (cis-diamminedichloroplatinum II) and other platinum-based antineoplastic agents continue to play important role in cancer chemotherapy. These agents are among the most effective and widely employed anticancer drugs in clinical practice. Cisplatin is one of the first generation platinum-based antitumor agents known to be very effective when used either alone or in combination with other chemotherapeutic agents for the treatment of a wide range of solid tumours including lung, ovarian, testicular, bladder, head and neck cancers[1-4]. Because cisplatin is preferentially taken up and accumulates in hepatic and renal cells, its use is often associated with serious damage to these organs. Despite the excellent anticancer activity of cisplatin, therefore, hepatotoxicity and nephrotoxicity in addition to other documented adverse effects tend to limit its full clinical benefits[1,5-6]. Although about 80% of patients treated with platinum-based agents respond to therapy, this initial response often decline significantly owing to the development of resistance and subsequent relapse within 18-24 months of treatment. Most often, an upward adjustment of the dose is necessary to overcome such relapse and this usually leads to severe cytotoxicity with hepatic toxicity also becoming very pronounced at such high doses[4,7-8].

While several studies have demonstrated the involvement of multiple mechanisms including hypoxia, generation of free radicals, inflammation and apoptosis with an increase in the pro-apoptotic protein Bax and a decrease in the anti-apoptotic protein BCl-2 in cisplatin-induced nephrotoxicity[9], the mechanisms by which it induces hepatic toxicity are still poorly understood[10]. Many experimental models, however, have linked free radical generation and oxidative stress and more recently mitochondrial stress to the development of this toxicity[11-14].

Dealing with the issues of cisplatin associated adverse effects and promoting its safe use in order to enhance and maximize its clinical utility for optimal therapeutic benefit in cancer patients continue to generate much attention. Several strategies have been suggested and a lot of efforts are being directed towards identifying safe compounds particularly from natural sources that could be administered concurrently with cisplatin to attenuate its toxic effects. Reports from different studies have demonstrated the ability of various agents to ameliorate nephrotoxicity induced by cisplatin via antioxidant mechanisms in experimental models[3,15-18]. Few recent experimental studies have also demonstrated the effectiveness of some antioxidants in attenuating cisplatin mediated hepatotoxicity[4,15,19-22]. While some progress has been recorded with regards to the search for novel compounds capable of counteracting renal, hepatic and other adverse effects of cisplatin, most of these studies have focused on the chemopreventive ability of the investigated agents or plants. There is still the need to broaden both search and strategy for counteracting the adverse effects of cisplatin.

*Moringa oleifera* Lam. (*Moringaceae*) is known to be a rich source of essential minerals and antioxidants and its widespread consumption or use in many parts of the world is not unconnected with the high nutritional and medicinal values placed on this plant[23-28]. Various biological activities, in addition to the well known antioxidant properties, have been attributed to this plant and its potential as an important source of drug has been reported in several experimental studies. The therapeutic potential of the leaf extract of *Moringa oleifera* in diabetes and dyslipidemia has been demonstrated in experimental models[24,29-30]. Anticancer activity of the leaf extracts of *Moringa oleifera* as well as its ability to enhance the cytotoxic effect of doxorubicin have also been demonstrated in recent studies[31-34]. A few recent studies have demonstrated the ability of the leaf extract of *Moringa oleifera* to ameliorate hepatic toxicity associated with acetaminophen administration[26,34]. In the present study, the potential therapeutic benefit of aqueous and methanolic leaf extracts of *Moringa oleifera* was investigated when administered separately in a rat model of acute liver injury induced by cisplatin.

## MATERIALS AND METHODS

**Drugs and chemicals:** Cisplatin was obtained from United Pharmaceutical Inc. (Sejong, South Korea), alanine aminotransferase (ALT), aspartate aminotransferase (AST), total cholesterol (TC), triglyceride (TG) assay kits were obtained from Randox Laboratory (Crumlin, UK). Thiobarbituric acid (TBA) and 5',5'-Dithiobis-2-nitrobenzoate (Ellman's reagent) were purchased from Sigma Chemical Company (St. Louis, MO, USA). Reduced glutathione (GSH), metaphosphoric acid and trichloroacetic acid (TCA) were purchased from J.T. Baker (Phillipsburg, New Jersey, USA). All other chemicals and reagents used were of analytical grade.

**Animals:** Male albino Wistar rats weighing between 170-200 g were obtained from the University of Ibadan, Oyo State, Nigeria. The animals were housed in the experimental animal facility of the College of Natural Sciences of the Redeemer's University, Nigeria at ambient temperature with a 12 h light/12 h dark schedule. They were nurtured and fed

with commercially available rat pelleted diet (Ladokun Feeds, Mokola, Ibadan, Nigeria) and water *ad libitum* for 3-4 weeks to attain desirable weight and acclimatize before commencement of study and also throughout the period of the drug administration.

**Plant material and extraction:** *Moringa oleifera* leaves were obtained in December 2011 from a private farmland on the Redeemer's University campus and verified in the Department of Biological Sciences of the same institution. Further authentication was done at the University of Lagos and the specimen (voucher number LUH/7515) was deposited in the institution's herbarium (University of Lagos Herbarium). The *Moringa* leaves were air-dried for a period of about three weeks and weighed. The aqueous extraction was done following the method used by Sreelatha and Padma[35]. The air-dried leaves (58 g) was soaked in seven parts (406 mL) of distilled water and heated for 2 h at 80°C. It was thereafter cooled at room temperature and filtered using a Buckner funnel and Whatman's No. 1 filter paper. Another portion of air-dried *Moringa* leaves was weighed (5 g), packed into the soxhlet apparatus and extracted in methanol at 70°C for 3 h. The aqueous extract filtrate and methanol extract from soxhlet extraction were concentrated in a rotary evaporator to obtain solid extracts. The solid extracts were reconstituted in normal saline and administered orally in doses expressed as mg $kg^{-1}$ rat body weight.

**Experimental design:** Forty two male albino Wistar rats (183.0±9.4 g) were assigned to eight experimental groups of five or six rats/group. Control rats (group I) received physiological saline (10 mL $kg^{-1}$/day p.o.) while rats in groups II and III were treated with methanolic leaf extract of *Moringa oleifera* (MEMO, 100 mg $kg^{-1}$/day p.o.) and aqueous leaf extract of *Moringa oleifera* (AEMO, 100 mg $kg^{-1}$/day p.o.), respectively for 5 days. Single i.p. injection of cisplatin (7.5 mg $kg^{-1}$) was administered to rats in groups IV-VIII on day 1 of experiment to induce hepatic toxicity and treated orally with physiological saline (10 mL $kg^{-1}$), MEMO (50 mg $kg^{-1}$), MEMO (100 mg $kg^{-1}$), AEMO (50 mg $kg^{-1}$) and AEMO (100 mg $kg^{-1}$), respectively 1 h after cisplatin administration. Subsequent treatments were given 24 h for 4 days to bring the duration of all treatments to 5 days. Study was carried out in compliance with standard guidelines for the Care and Use of Laboratory Animals[36]. These guidelines provide measures to ensure caring for and using animals in ways judged to be scientifically, technically and humanely appropriate. It also assists investigators in fulfilling their obligation to plan and conduct animal experiments in accord with the highest scientific, human and ethical principles.

**Necropsy:** Rats from both control and test groups were sacrificed by cervical dislocation 24 h after the last treatment (i.e. on day 6). Blood samples were obtained by cardiac puncture into lithium heparin bottles and centrifuged at 3000 rpm for 5 min to separate plasma. Liver from each animal was removed and immediately weighed and the relative weight was calculated based on kg body weight of the respective animal. A portion of this organ was weighed and homogenized in four volumes of ice-cold phosphate buffer (0.1M, pH 7.4). The liver homogenate was then centrifuged at 4500 rpm for 15 min at 4°C. Various biochemical parameters were subsequently estimated in plasma and supernatant of the tissue homogenate to assess hepatic function and oxidative stress.

**Biochemical assays:** Hepatic function was assessed by determining the activities of the aminotransferases, ALT and AST, following the principle described by Reitman and Frankel[37] as well as by measuring plasma levels of TC and TG as described by Trinder[38] using commercial kits obtained from Randox Laboratories Ltd. (Crumlin, UK). TP determination was carried out according to the principle based on biuret reaction[39]. Determination of catalase activity was based on the ability of this enzyme to induce disappearance of $H_2O_2$ as described by Sinha[40]. SOD activity was measured according to the method of Misra and Fridovich[41]. The assay was based on the ability of SOD to inhibit the auto-oxidation of epinephrine at pH 10.2. Glutathione-s-transferase activity was determined according to the method of Habig *et al.*[42], using 1-chloro-2, 4,-Dinitrobenzene (CDNB) as substrate. The method of Beutler *et al.*[43], was employed in estimating reduced glutathione (GSH) level. This method is based on the development of a relatively stable yellow colour when Ellman's reagent is added to sulfhydryl compounds. Lipid peroxidation was determined by measuring levels of thiobarbituric acid reactive substances according to the method of Varshney and Kale[44]. Myeloperoxidase (MPO) activity which is a good measure of polymorphonuclear leukocyte infiltration and accumulation was assessed according to the method described by Eiserich *et al.*[45].

**Statistical analysis:** Results were expressed as mean±standard error of mean (SEM) and analyzed by one-way analysis of variance (ANOVA) using Statistical Package for Social Sciences (SPSS) Software for Windows,

Version 16.0.(Chicago, SPSS Inc.). *Post hoc* test for inter-group comparisons was done using the least significant difference (LSD)[46] and p value<0.05 was considered significant.

## RESULTS

**Effect of *M. oleifera* extracts on marker enzymes of liver function in cisplatin-treated and normal rats:** The effects of *M. oleifera* extracts on liver function of normal and cisplatin intoxicated rats are presented in Fig. 1. Single i.p. injection of cisplatin (7.5 mg $kg^{-1}$) significantly ($p<0.05$) increased the activity of both ALT and AST (marker enzymes of liver function) when compared with saline control. Administration of either AEMO or MEMO to normal rats did not significantly ($p>0.05$) affect the activity of ALT when compared with control rats. While the activity of AST in the normal rats was not significantly affected by AEMO, MEMO on the other hand, significantly ($p<0.05$) increased the activity of this enzyme when compared with control. Both MEMO (50 and 100 mg $kg^{-1}$) and AEMO (100 mg $kg^{-1}$) decreased the activity of these marker enzymes of liver function in the cisplatin-treated rats, though not significantly different from cisplatin only-treated group.

**Total cholesterol and triglyceride levels of normal and cisplatin intoxicated rats treated with *M. oleifera* extracts:** Figure 2 shows the effect of cisplatin and *M. oleifera* extracts on total cholesterol and triglyceride concentrations. Rats injected with cisplatin exhibited significantly increased plasma concentrations of TC ($p<0.001$) and TG ($p<0.01$) when compared with saline control. MEMO at 50 and 100 mg $kg^{-1}$ significantly ($p<0.05$) reduced cisplatin-induced increase in plasma TC and TG concentrations, respectively. This extract (MEMO) when administered alone increased ($p<0.01$) TC level without significantly affecting TG level of normal rats. AEMO, on the other hand, did not significantly affect both plasma TC and TG concentrations of normal rats when administered alone, but significantly ($p<0.05$) reduced cisplatin-induced increases in the level of these lipids when compared with cisplatin only treated rats.

**Activity of anti-oxidant enzymes in normal and cisplatin intoxicated rats following treatment with *M. oleifera* extracts:** Cisplatin-induced hepatic toxicity was associated with significant decreases in CAT ($p<0.001$), GST ($p<0.01$) and SOD ($p<0.05$) (Fig. 3). MEMO significantly prevented cisplatin-induced decreases in CAT ($p<0.001$ and $p<0.01$) and GST ($p<0.01$ and $p<0.001$) activities at 50 and 100 mg $kg^{-1}$, respectively. AEMO, on the other hand, only significantly ($p<0.05$) increased CAT activity at 50 mg $kg^{-1}$ without producing any significant change in GST activity in the cisplatin treated rats when compared with cisplatin only group. Similarly, both extracts did not affect SOD activity in the cisplatin-treated rats. Both MEMO and AEMO when

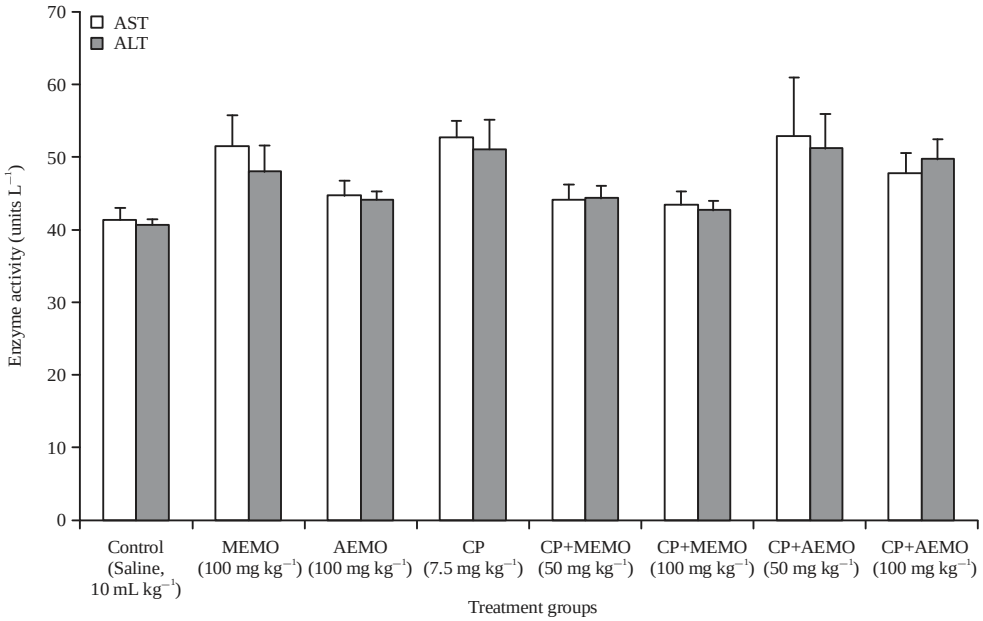


Fig. 1: Effect of aqueous and methanolic leaf extracts of *Moringa oleifera* on hepatic function of normal and cisplatin-treated rats

Data are expressed as mean±standard error of mean (n = 42). *$p<0.05$ when compared with control. CP: Cisplatin, MEMO: Methanolic extract of *Moringa oleifera*, AEMO: Aqueous extract of *Moringa oleifera*

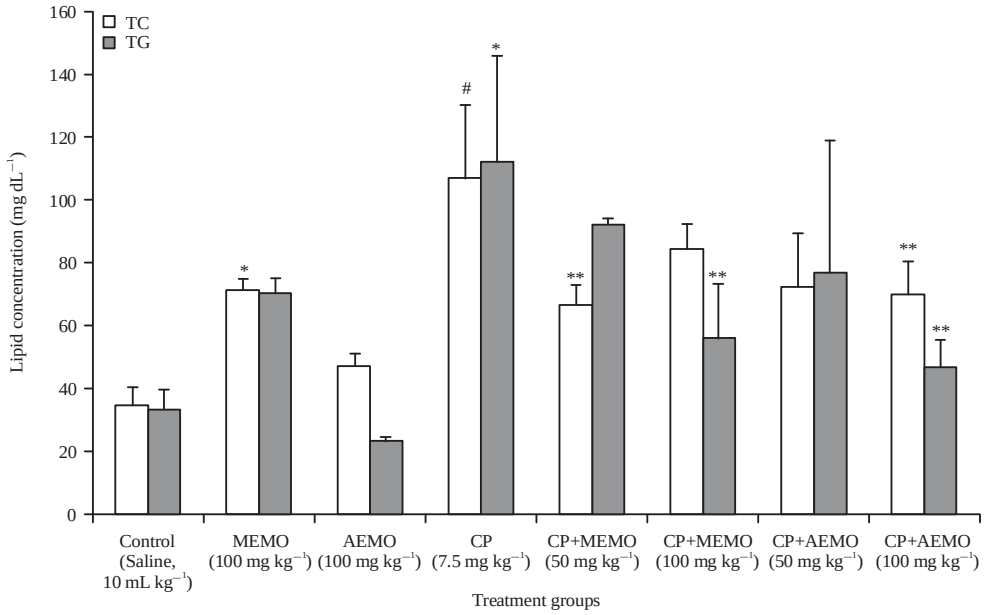


Fig. 2: Effect of aqueous and methanolic leaf extracts of *Moringa oleifera* on total cholesterol (TC) and triglyceride (TG) levels of normal and cisplatin-treated rats

Data are expressed as mean±standard error of mean (n = 42). *p<0.01 and #p<0.001 when compared with control. **p<0.05 and ***p<0.01 when compared with CP. CP: Cisplatin, MEMO: Methanolic extract of Moringa oleifera, AEMO: Aqueous extract of *Moringa oleifera*

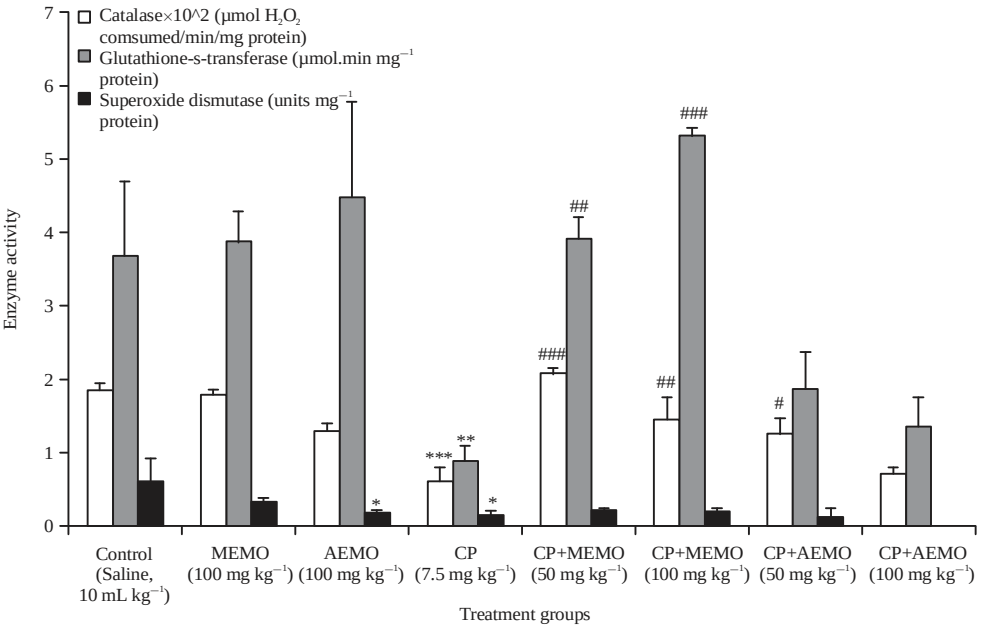


Fig. 3: Effect of aqueous and methanolic leaf extracts of *Moringa oleifera* on some hepatic enzymic antioxidants of normal and cisplatin-treated rats

Data are expressed as mean±standard error of mean (n = 42). *p<0.05, **p<0.01 and ***p<0.001 when compared with control. #p<0.05, ##p<0.01 and ###p<0.001 when compared with CP. CP: Cisplatin, MEMO: Methanolic extract of *Moringa oleifera*, AEMO: Aqueous extract of *Moringa oleifera*

administered alone at 100 mg kg$^{-1}$ did not significantly change the activities of CAT and GST of the normal rats. While MEMO (100 mg kg$^{-1}$) did not significantly affect SOD activity, AEMO (100 mg kg$^{-1}$) on the other hand, significantly decreased the activity of this enzyme in the normal rats when compared with saline control.

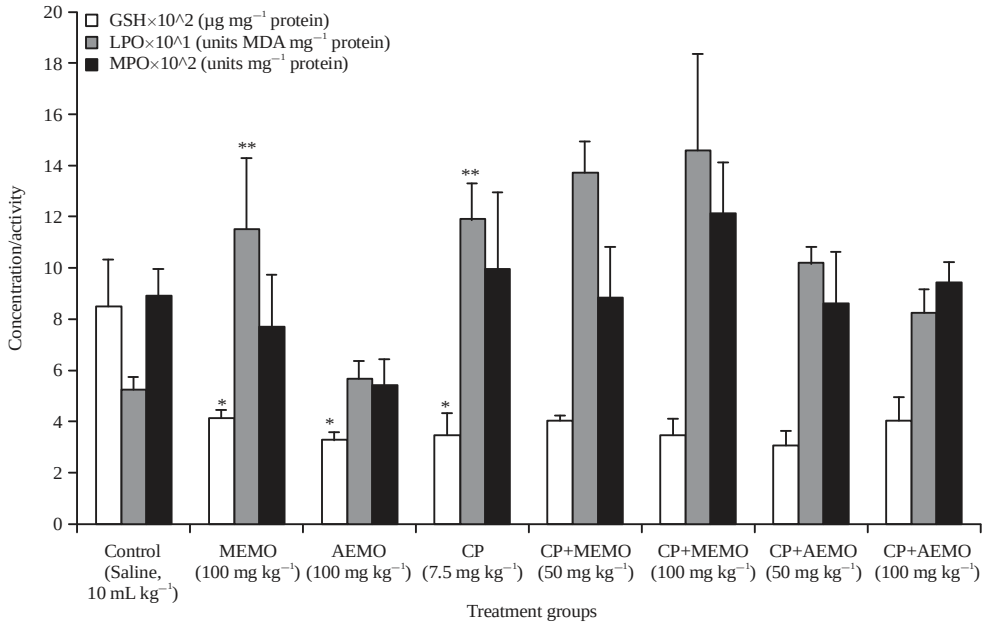


Fig. 4: Effect of aqueous and methanolic leaf extracts of *Moringa oleifera* on hepatic reduced glutathione (GSH), lipid peroxidation (LPO) and myeloperoxidase (MPO) activity in normal and cisplatin-treated rats

Data are expressed as mean±standard error of mean (n = 42). *p<0.01 and **p<0.05 when compared with control. CP: Cisplatin, MEMO: Methanolic extract of *Moringa oleifera*, AEMO: Aqueous extract of *Moringa oleifera*

**Effect of *M. oleifera* extracts on reduced glutathione, lipid peroxidation and myeloperoxidase activity in normal and cisplatin intoxicated rats:** The effect of *M. oleifera* extracts on hepatic GSH, LPO and MPO in normal and cisplatin-treated rats is presented in Fig. 4. Cisplatin-induced hepatic toxicity was associated with a significant decrease in hepatic glutathione ($p<0.01$) and a corresponding increase in LPO ($p<0.05$). Cisplatin also increased the activity of hepatic MPO, though not significantly ($p>0.05$) different from control. Similarly, hepatic GSH was significantly reduced ($p<0.01$) and LPO increased ($p<0.05$) by MEMO (100 mg kg$^{-1}$) following daily administration for 5 days to normal rats. AEMO (100 mg kg$^{-1}$) administration, on the other hand, significantly ($p<0.01$) decreased hepatic GSH in normal rats without producing any significant change in the extent of LPO. Both MEMO (50 and 100 mg kg$^{-1}$) and AEMO (50 and 100 mg kg$^{-1}$) did not produce any significant change in hepatic GSH concentration and LPO in the cisplatin-treated rats when compared with the group treated with cisplatin only. The extracts also did not exert any significant change in the activity of MPO across all treatment groups.

**Liver and total body weights of rats in all treatment groups:** Figure 5 and 6 present the effects of various treatments on rats' relative liver weight and total body weight before the start of treatment and after 5 days of treatment, respectively. Cisplatin-induced increase in rats' relative liver weight was significantly reduced by MEMO (50 mg kg$^{-1}$) and AEMO (50 and 100 mg kg$^{-1}$). The liver weight of normal rats treated with AEMO (100 mg kg$^{-1}$) was also significantly higher than those of the controls (Fig. 5). Single injection of cisplatin (7.5 mg kg$^{-1}$, i.p.) significantly decreased rats' body weight by 21.9% and treatment with both MEMO and AEMO did not significantly prevent this weight loss after 5 days of daily administration (Fig. 6).

## DISCUSSION

Single intraperitoneal injection of cisplatin (7.5 mg kg$^{-1}$) significantly produced hepatotoxicity in this study as revealed by the significant increase in the activity of the plasma aminotransferases (AST and ALT). The marked elevation of plasma TC and TG levels produced by cisplatin also reveals severe impairment of hepatic function. Data from this study support observations from previous studies which reveal that cisplatin mediated hepatotoxicity is partly due to the liver's inability to mount an effective antioxidant defense against oxidative stress induced by this chemotherapeutic agent within the hepatic tissue[12,21-22]. It therefore appears that the impairment of function and damage to the liver as suggested

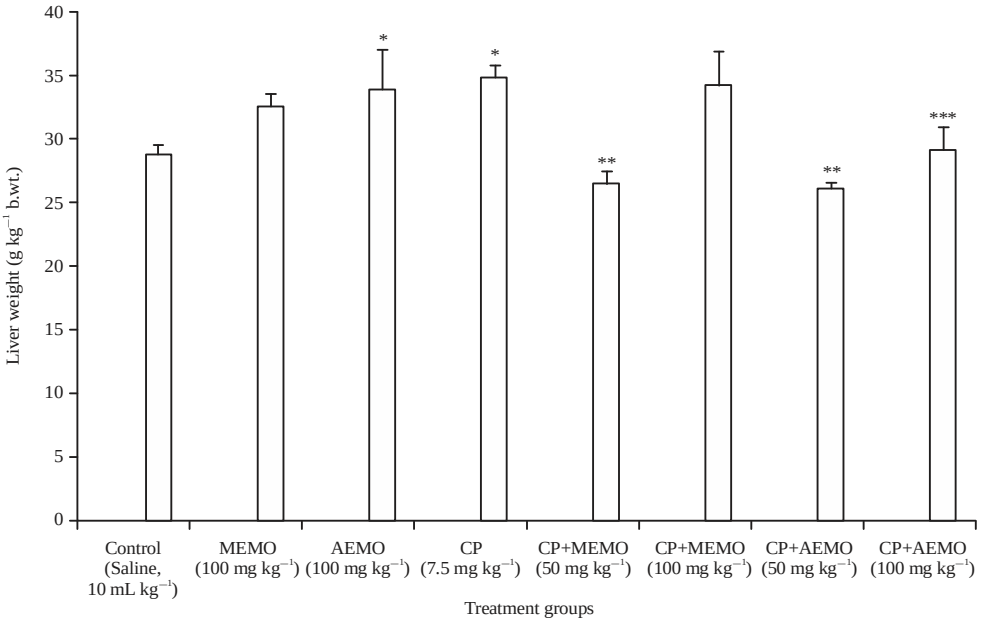


Fig. 5: Effect of aqueous and methanolic leaf extracts of *Moringa oleifera* on liver weight of normal and cisplatin-treated rats relative to body weight

Data are expressed as mean±standard error of mean (n = 42). *p<0.05 when compared with control. **p<0.001 and ***p<0.05 when compared with CP. CP: Cisplatin, MEMO: Methanolic extract of *Moringa oleifera*, AEMO: Aqueous extract of *Moringa oleifera*

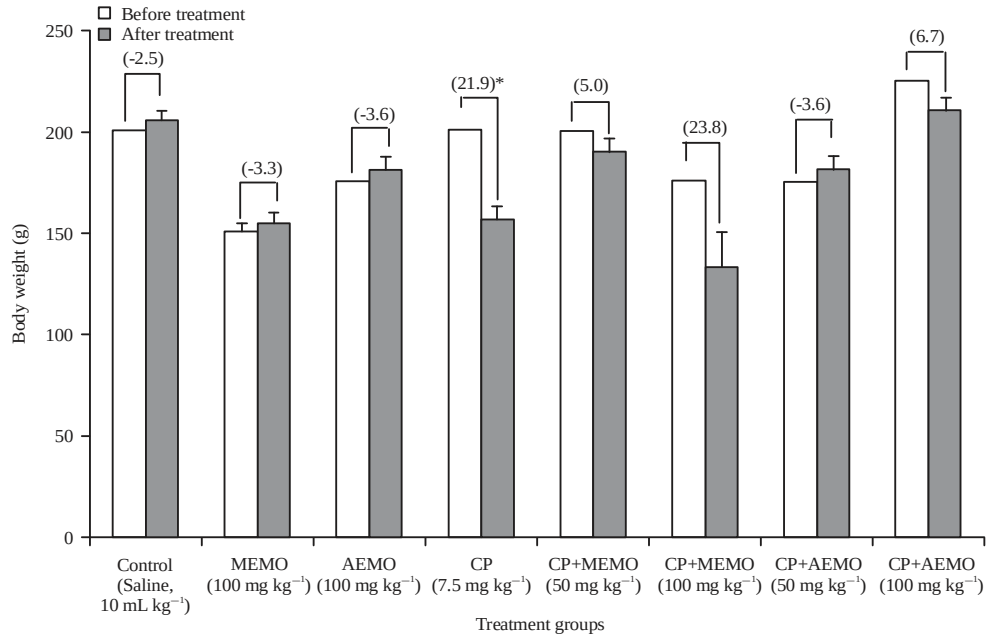


Fig. 6: Effect of aqueous and methanolic leaf extracts of *Moringa oleifera* on body weight of normal and cisplatin-treated rats

Data are expressed as mean±standard error of mean (n = 42). *p<0.01 when compared with body weight before treatment. Values in parenthesis represent % increase (-ve) or decrease (+ve) relative to rat body weight before treatment. CP: Cisplatin, MEMO: Methanolic extract of *Moringa oleifera*, AEMO: Aqueous extract of *Moringa oleifera*

by the marked rise in plasma lipid levels and activities of the aminotransferases in this study is related to loss of the liver's protective antioxidant defense machinery owing to an overwhelming pro-oxidant action of cisplatin. Similar to our previous observation on the involvement of oxidative stress in cisplatin-mediated renal damage[3], significant decreases were

also observed in hepatic CAT, SOD and GST activities of cisplatin-treated rats in this study. The decrease in the activity of these enzymatic antioxidants was also associated with marked depletion of GSH and significant increase in LPO within the liver. Studies have demonstrated the ability of cisplatin to cause hepatic mitochondrial oxidative stress via the depletion of endogenous antioxidants[8-47]. Reduced glutathione plays an important role in detoxifying cisplatin. The detoxification occurs when the platinum in cisplatin complexes with GSH by binding to the thiol group of this endogenous antioxidant[48]. This process, which may result in depletion of GSH store when its rate of utilization exceeds replenishment, is responsible for preventing or ameliorating the effects of free radicals generated by cisplatin in the system[49]. Since GSH is necessary for the recycling of some other antioxidants such as glutathione peroxidase and GST, the bioavailability of these GSH-dependent antioxidants becomes significantly reduced following GSH depletion[50-51]. Furthermore, cellular events in cisplatin-induced oxidative stress have also been associated with increased generation of reactive oxygen species (ROS) like superoxide anion and hydroxyl radical[15,49,52-53]. The decrease in activity of antioxidant enzymes like SOD, CAT and decrease in GSH concentration observed in this study may facilitate or promote the build-up of ROS like $O^{-}_{2}$ and $H_2O_2$. The rise in levels of $O^{-}_{2}$ and $H_2O_2$ may in turn lead to increase generation of the more reactive hydroxyl (·OH) radicals via Fenton and Haber-Weiss reactions[54]. Therefore, the significant increase in lipid peroxidation as suggested by the increase in malondialdehyde level observed in the cisplatin-treated rats may be as a result of increase production of OH radicals which react at nearly diffusion limited rates with any component of the cell including lipids, DNA and proteins. The net result of this non-specific free radical attack is a loss of cell integrity, enzyme function and genomic stability[55]. All these observations are in line with existing information regarding involvement of oxidative stress as one of the key mechanisms in hepatic toxicity induced by cisplatin[4,11-13,21-22].

Previous studies from different authors have demonstrated the antioxidant and free radical scavenging properties of *Moringa oleifera* leaves[24-27]. Results from this study show that both aqueous and methanolic leaf extracts of *Moringa oleifera* (MEMO and AEMO) ameliorated some aspects of cisplatin-mediated acute hepatic toxicity. This seems to suggest that this plant may provide some therapeutic benefit in the management of hepatic impairment or injury associated with cisplatin treatment. It was observed that MEMO (100 mg $kg^{-1}$) when administered alone to normal rats did not produce any significant alteration in CAT activity when compared with saline control. This extract (MEMO), however, significantly reversed the decrease in CAT activity associated with cisplatin intoxication at the two dose levels (50 and 100 mg $kg^{-1}$) administered in this study. Similar effect was also observed with GST activity, as MEMO (50 and 100 mg $kg^{-1}$) significantly reversed the cisplatin-induced decrease in the activity of this enzyme. Although, MEMO produced a mild increase in the activity of SOD in the cisplatin-treated rats, this effect was not significant when compared with the cisplatin-only group. The inability of MEMO to exert significant effectiveness in enhancing SOD activity in this study may promote $O^{-}_{2}$ accumulation which in turn may lead to production of the toxic reaction product, peroxynitrite, when it reacts with NO· which is also known to be elevated during cisplatin toxicity[3] or ·OH radicals via Haber-Weiss reactions[54]. This may probably account for the inability of MEMO to exert any significant change or reversal of cisplatin-induced GSH depletion and lipid peroxidation as well as the insignificant reduction in the plasma activity of AST and ALT, marker enzymes for liver function. MEMO, however, significantly lowered the elevated plasma TC and TG levels associated with cisplatin acute hepatic toxicity at 50 and 100 mg $kg^{-1}$, respectively.

The aqueous extract of *Moringa oleifera* (AEMO), on the other hand, significantly increased CAT activity at 50 mg $kg^{-1}$ in the cisplatin-treated rats without significantly affecting activity of GST and SOD. Similarly, AEMO was not effective in reversing cisplatin-associated GSH depletion and lipid peroxidation in this study. It is, therefore, not surprising that AEMO did not significantly reverse cisplatin-mediated acute hepatic oxidative injury in this study since the marker enzymes for liver function, AST and ALT, did not change considerably when compared with the cisplatin-only group. Like MEMO, AEMO at 100 mg $kg^{-1}$ was effective in lowering the elevated plasma TC and TG levels induced by cisplatin in the rats. In addition, the marked decrease in animals' body weight and the significant increase in liver weight relative to body weight that characterized cisplatin acute hepatic oxidative injury in this study were significantly reversed by both extracts. While MEMO significantly decreased liver weight and prevented significant loss in body weight of cisplatin-treated rats at 50 mg $kg^{-1}$, AEMO exerted same effects at the two dose levels (50 and 100 mg $kg^{-1}$).

## CONCLUSION

In conclusion, while reversing toxicity after induction still pose major challenge in many instances, the methanolic and aqueous leaf extracts of *Moringa oleifera* at the dose levels

used modulated some aspects of biochemical alteration associated with cisplatin-induced hepatic toxicity in this study. Our data, suggested possible therapeutic benefit of this plant in hepatic oxidative injury associated with cisplatin administration. It is important, therefore, to ascertain the appropriate dose levels in which these extracts should be administered to achieve maximum effectiveness.

## SIGNIFICANCE STATEMENTS

This study reveals that leaf extracts (methanol and aqueous) of *Moringa oleifera* may be of therapeutic benefit in acute liver conditions especially those related to injuries arising from exposure to xenobiotics. The study also shows that this potential therapeutic benefit of *Moringa oleifera* is dose-dependent and provides a basis to further explore the effective and safe dose ranges in this model of acute liver injury.

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