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Original Article

Modification of Hexavalent Chromate Hepatotoxicity by Ethanol Extract of *Moringa oleifera* in Wistar Rats

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ABSTRACT

Background: The association of hexavalent chromate toxicity with oxidative stress necessitated the search for antidote from medicinal plants with antioxidant properties. One of such plants is *Moringa oleifera*. **Objective**: To investigate the hepatoprotective and antioxidative properties of ethanol extract of *Moringa oleifera* (EEMO) against potassium dichromate ($K_2Cr_2O_7$) induced hepatocellular damage and oxidative stress in male Wistar rats. **Materials and Methods**: Thirty rats were assigned into six groups of five animals each: distilled water, 12 mg/kg bd.wt $K_2Cr_2O_7$ 3.5 mg/kg bd.wt EEMO, 7.0 mg/Kg bd.wt EEMO, 3.5 mg/Kg bd.wt EEMO+$K_2Cr_2O_7$, 7.0 mg/kg bd.wt EEMO+$K_2Cr_2O_7$ The EEMO was administered consecutively for thirty-five days, while $K_2Cr_2O_7$ was injected intraperitoneally once weekly before the animals were sacrificed. Liver function and oxidative stress markers including alanine aminotransferase (ALT), aspartate aminotransferase (AST), superoxide dismutase (SOD), glutathione -S-transferase (GST) and malondialdehyde (MDA) levels were monitored in the serum and liver. Histopathology of the liver was also carried out. In addition, proximate analysis of the powdered leaves and phytochemical composition of EEMO were also evaluated. **Results**: The $K_2Cr_2O_7$ significantly ($p < 0.05$) increased AST, ALT and MDA levels coupled with decreased SOD and GST activities as well as hepatic lesions when compared with control. However, the two doses of EEMO modified the hepatotoxicity and oxidative stress towards that of control. The EEMO is rich in phenolics and other phytochemicals including hexamethylquercetagetin and hexa-O-methylmyricitin that may account for the observed antioxidative and ameliorative effect. **Conclusion**: Our results suggest that ethanol extract of *Moringa oleifera* modify hexavalent chromate hepatotoxicity by reducing oxidative stress.

Key words: Antioxidant, Hepatotoxicity, *Moringa oleifera*, Oxidative stress and potassium dichromate.

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INTRODUCTION

Hexavalent chromium [Cr (VI)] is a global non-negligible pollutant in our ecosystem. Occupational exposure from the use of Cr (VI) in chrome pigment production, chrome plating, stainless steel manufacturing and leather tanning is a primary route of contact. Additionally, millions of people worldwide are exposed to the metal via consumption of contaminated water and foods especially in developing countries. Epidemiological and animal studies indicate that Cr (VI) increases the risk of leukemia, lung and bone cancers. Other health hazards including dermatitis, hepatic damage, nephrotoxicity, male and female infertility, developmental toxicity, ischemic heart diseases and diabetes have also been observed.[1,2] The exact mechanism of carcinogenicity from Cr (VI) exposure is not fully elucidated, but Cr (VI) upon entry into the cell, can be reduced to active intermediates including Cr (V), Cr (IV) and Cr (III). These active intermediates may bind directly to DNA forming stable DNA-chromium complexes, DNA strand breaks, DNA-DNA cross links resulting in cellular transformation.[3,4] Similarly, the intracellular reduction of Cr (VI) is accompanied by the generation of free radicals that provoke oxidative DNA damage, lipid peroxidation, alteration of cellular antioxidants and cell death.[4-7] Association of the pathogenesis of Cr (VI) with free radicals and oxidative stress has raised considerable interest, because it may represent an attractive target for the development of novel compounds with chemo-protection against Cr (VI) toxicity. Current therapies for treatment of Cr (VI) exposure have side effects including vomiting, nephrotoxicity, anemia, hypertension, anxiety and decreased plasma concentration of essential metals.[8] Consequently, there is continued research into medical interventions that include the use of medicinal plants and natural products with antioxidant properties in the management of Cr (VI) toxicity.

Moringa oleifera Lam. (Moringaceae) has caught the attention of the scientific, therapeutic and ethno-medicinal world because of its nutritional and medicinal potential. The plant is indigenous to Northwest India, but it is widely distributed in several parts of Africa.[9] It is a member of the Moringacae family and commonly known as Drumstick or Horse Radish tree. The leave is highly nutritious and therefore incorporated into the diet of both humans and livestock.[10] The leaf extract is used in the management of diabetics, hyperglycemia, dyslipidemia, rheumatism, hepatotoxicity, venomous bites and cardiac stimulation.[11,12] Antiulcer,

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diuretic, anti-inflammatory, anti-fungal anti-infertility and wound healing effects have all been documented.[9-13] The antiproliferative and apoptosis inducing activities of *Moringa oleifera* on tumor (KB) cell line and pancreatic cancer cells have also been reported.[14,15] Most of the therapeutic benefits of *Moringa oleifera* have been linked to its antioxidant properties.[15] Powerful antioxidants including carotenoids, ascorbic acid, α- tocopherol, kaemferol, myricetin, quercetin, ellagic acid, chlorogenic acid, glucosinolates and isothiocyanates have all been detected in *Moringa oleifera* leaves.[15,16] In the present study therefore, we examined the effect of ethanol extract of *Moringa oleifera* (EEMO) on potassium dichromate induced toxicity and oxidative stress in the liver of male Wistar albino rats.

MATERIALS AND METHODS

Chemical reagents

Potassium dichromate ($K_2Cr_2O_7$) [Mol wt., 294.18, CAS No. 7778-50-9] was obtained from Sigma Chemical Co., St. Louis, MO. The transaminase kits were obtained from Randox Laboratories Ltd, United Kingdom. All other chemicals used were of analytical grade.

Plant extract

Fresh leaves of *Moringa oleifera* were collected and identified at the herbarium in the Forestry Research Institute of Nigeria (FRIN), Ibadan. A and voucher specimen was deposited at the same herbarium (Voucher No: FHI109840). The fresh leaves were air dried for 2 weeks at room temperature, after which they were completely dried in a solar drier at 40ºC. They were then milled in a hammer-mill with mesh size 0.27 µm. One hundred grams (100 g) of the powdered leaves was soaked in 500 ml of 7% ethanol at room temperature for 48 h. The suspension obtained was filtered and concentrated in a rotary evaporator under reduced pressure at 40ºC to obtain a dark brown semi-solid extract that was evaporated to constant weight in an oven at 40ºC. The yield of the extract was 11.1%.

Experimental animals and treatment

Thirty male Swiss albino rats between 7-8 weeks old with average weight of 70 g were obtained from the institutional animal house. The animals were housed in polypropylene cages under standard environmental conditions at the institutional animal house. They were fed standard diet and water *adlibitum*. Generally, the animals were maintained and handled in conformity with guide for care and use of laboratory animals.[17] A period of two weeks was allowed for the animals to acclimate before the commencement of the experiment.

Experimental design

The rats were assigned to six groups of five animals each based on their body weights in order to ensure even distribution and eliminating variation in mean body weight among the groups. Test rats were exposed daily to 3.5 and 7.0 mg/kg bd. wt. EEMO alone for six weeks or with 12 mg/kg bd. wt. $K_2Cr_2O_7$ once every Friday throughout the duration of the study. Both $K_2Cr_2O_7$ and EEMO were dissolved in deionized water and doses were selected based on our previous study and dose cited in literature.[18-20] The negative control rats were fed distilled water throughout the experiment, while the positive control rats were intraperitoneally injected with 12 mg/kg body weight $K_2Cr_2O_7$ once per week. Twenty-four hours after the last treatment, the final body weights of the animals were obtained and blood samples were collected from the retro-orbital plexus of each rat directly into heparinized tubes. The animals were thereafter sacrificed by cervical dislocation. The sacrificed animals were quickly dissected and the liver collected from each animal was weighed, before they were used for the determination of oxidative stress parameters and histopathological analysis. The blood samples were used for the assessment of liver function markers in test and control animals.

Assays for liver function markers

The collected blood samples in anticoagulant tubes were centrifuged at 2000 g for 20 min. The supernatants obtained were immediately used for the determination of plasma ALT and AST using commercial diagnostic kits purchased from Randox Laboratories Ltd., UK and following the manufacturer's directions.

Assays for oxidative stress markers

The liver samples were washed in ice cold 1.15% potassium chloride (KCl) weighed and homogenized in four volumes of the homogenate buffer containing 50 mM Tris-HCl at pH 7.4 using a Potter-Elvejhem homogenizer equipped with a teflon pestle. The homogenate was then centrifuged at 10,000 g for 20 min using a HimacCR21G cold centrifuge at 4°C. The supernatant obtained was used for the determination of oxidative stress parameters. Lipid peroxidation was measured by assessing the level of malondialdehyde (MDA) following the methods described by Esterbauer and Cheeseman.[21] Superoxide dismutase activity was assayed by monitoring the autooxidation of adrenaline to adenochrome at 480 nm as described by Sun and Zigma.[22] Glutathione-.S-transferase (GST) activity was assayed spectrophotometrically using 1-chloro-2-4 dinitrobenzene (CDNB) as described by Habig *et al.*[23]

Proximate and phytochemical analysis

The crude protein, fats, moisture, crude fiber, ash and carbohydrate composition of the dried *Moringa oleifera* leaf powder were determined following standard methods as described by AOAC.[24] Phytochemical analysis of the extract was determined following standard methods previously described by Sofowara,[25] Trease and Evans[26] and Harborne.[27]

Gas chromatography-mass spectrometry (GC-MS) analysis

The GC-MS analysis of the extract was performed using a Shimadzu gas chromatograph model QP2010 (Shimadzu Co., Kyoto, Japan) equipped with a mass selective detector in electron impact mode at a 70 eV ionization voltage and capillary column (30 m x 0.25 mm, film thickness 0.25 µm). Column oven temperature was programmed from 80-220°C at the rate of 4°C/min. Initial and final temperatures were maintained for 3 and 10 min, respectively. Mass scanning range was 40-700 *m/z,* while injector and MS transfer line temperatures were set at 220 and 290ºC, respectively. Helium was used as a carrier gas at a flow rate of 1.5 ml min^{-1} and an injector volume of 1.0 µL, using a 1:10 split ratio. The compounds in EEMO were detected by dissolving 1.0 mg of the sample in 1.0 ml of methanol, filtered with a micro-syringe and aliquots were injected in the GC-MS. Components were identified by matching their mass spectra with those of the spectrometer data base using the NIST computer data bank, as well as by comparison of the fragmentation pattern with those reported in the literature.

Histopathology

The liver samples harvested during postmortem were immediately fixed in 10% buffered formalin and processed for histology. Basic procedures involving sample fixation, dehydration, clearing, embedding, blocking, sectioning, dewaxing, staining and counter staining with hematoxylin and eosin was carried out to prepare slides for each of the liver tissue. The sections were examined under light microscope (Olympus BX 41) for the histopathology in the organ.

Statistical analysis

The data obtained were expressed as means ± SEM and analyzed by One-way analysis of variance (ANOVA) using 17th version of SPSS

(Chicago, IL, USA). The Duncan Multiple Range test was used to detect the significant differences between the means of different group. Significance was set at $p < 0.05$.

RESULTS

The initial weight, final body weight, liver weight, percentage body weight change and relative liver weight of test and control animals are presented in Table 1. At the end of the treatment, there was decrease in body weight in the animals exposed to $K_2Cr_2O_7$ when compared to those exposed to water. In contrast, administration of EEMO alone or with $K_2Cr_2O_7$ resulted in a dose dependent increase in body weight as compared with the control. Similarly, the percentage weight gained was in the order: $K_2Cr_2O_7$ < deionized water < 3.5 mg/ kg bd. wt. EEMO + $K_2Cr_2O_7$ < 7.0 mg/ kg bd. wt. EEMO + $K_2Cr_2O_7$ < 3.5 mg/ kg bd. wt. EEMO < 7.0 mg/ kg bd. wt. The relative liver weight was significantly ($p < 0.05$) increased in the animals administered $K_2Cr_2O_7$ as compared to the control. However, simultaneous administration of EEMO reversed the relative liver weight towards the level of the control. The relative liver weight was not significantly different in the groups exposed to the two doses of EEMO alone and the control.

The result of the liver enzymes (ALT and AST) in the treated and control rats are presented in Figure 1. There was significant ($p < 0.05$) increase in serum ALT and AST activities and a corresponding decrease in liver ALT and AST activities in the animals exposed to $K_2Cr_2O_7$ when compared with control. While the decrease in liver AST activity was significant ($p < 0.05$), the decreased liver ALT activity observed in the animals exposed to $K_2Cr_2O_7$ was however marginal. In contrast, EEMO significantly ($p < 0.05$) reduced the elevated serum ALT and AST activities induced by $K_2Cr_2O_7$. Liver AST activity in the groups given the two doses of EEMO and K_2Cr_2O7 was also increased towards the level of the control.

The effect of EEMO on malondialdehydes (MDA) levels, super oxide dismutase (SOD) and glutathione –S-transferase (GST) activities in treated and control rats is shown in Figure 2. There was significant ($p < 0.05$) increase in MDA level in the liver of animals treated with $K_2Cr_2O_7$ when compared to the control. However, pretreatment with 3.5 and 7.0 mg/kg body weight of EEMO resulted in a dose dependent reduction in the elevated MDA levels induced by $K_2Cr_2O_7$. Administration of $K_2Cr_2O_7$ alone to the rats resulted a significant ($p < 0.05$) decreased liver SOD and GST activities when compared to the value obtained for the control rats treated with water. Conversely, simultaneous treatment of the rats with EEMO and $K_2Cr_2O_7$ resulted in a dose dependent elevation of both SOD and GST activities in the liver towards that of the controls. The SOD and GST activities in animals treated with the two doses of EEMO alone were comparable to that of the control animals.

The results of the liver histopathological analysis in treated and control rats are presented in Figure 3. The liver of the control rats and those fed 3.5 or 7.0 mg/kg bd. wt. EEMO showed normal hepatocyte structure (Figure 3A), while hepatocellular degeneration and severe necrosis was observed in the rats exposed to $K_2Cr_2O_7$ (Figures 3B and C). In contrast, simultaneous exposure of the rats to $K_2Cr_2O_7$ and the two doses of EEMO ameliorated these lesions (Figure 3.3D)

The result of the proximate analysis of *Moringa oleifera* leaves as well as the phytochemical and GC-MS analysis of EEMO is presented in Tables 2, 3 and 4 respectively. Our result showed that *Moringa oleifera* leaves contained appreciable amount of carbohydrate, proteins, minerals and

Table 1: Body and organ weight of test and control animal.

S/N	Treatment	Initial weight (g)	Final weight (g)	Percentage change in weight (g)	Liver weight (g)	Relative liver weight (%)
1	Deionized water	80.87 ± 9.62	132.34 ± 8.82	63.65	4.94 ± 0.45	3.47 ± 0.25
2	$K_2Cr_2O_7$	83.28 ± 8.50	122.88 ± 8.21	47.55	6.40 ± 0.99	5.13 ± 0.45*
3.	3.5 mg/kg EEMO	82.04 ± 8.56	152.94 ± 17.74	86.30	6.19 ± 0.26	4.22 ± 0.55
4.	7.0 mg/kg EEMO	81.28 ± 8.19	157.73 ± 10.21	94.06	5.80 ± 0.24	3.74 ± 0.33
5.	3.5 mg/kg EEMO + $K_2Cr_2O_7$	79.26 ± 5.81	126.60 ± 24.50	62.25	5.82 ± 0.89	4.75 ± 0.37
6.	7.0 mg/kg EEMO + $K_2Cr_2O_7$	79.82 ± 8.31	142.52 ± 14.34	78.55	5.84 ± 0.21	4.19 ± 0.31

*Significantly different from the control.

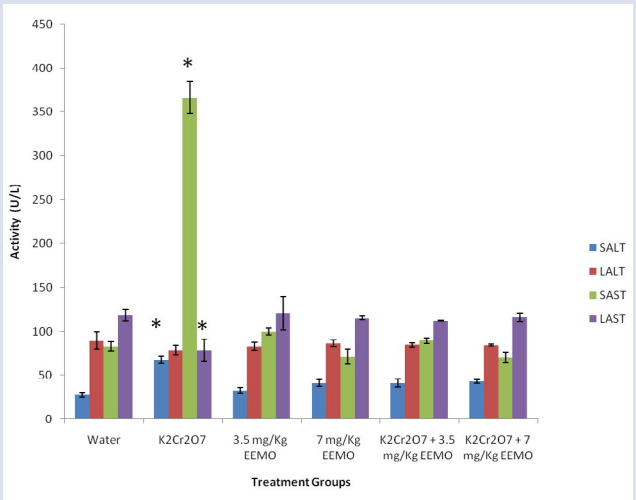

Figure 1: Serum and liver activities of alanine aminoamino transferase (ALT) and aspartate amino transferase (AST) in rats exposed to ethanol extract of *Moringa oleifera* $K_2Cr_2O_7$. Data are expressed as Mean ± S.EM.*Significantly different at $p < 0.05$.

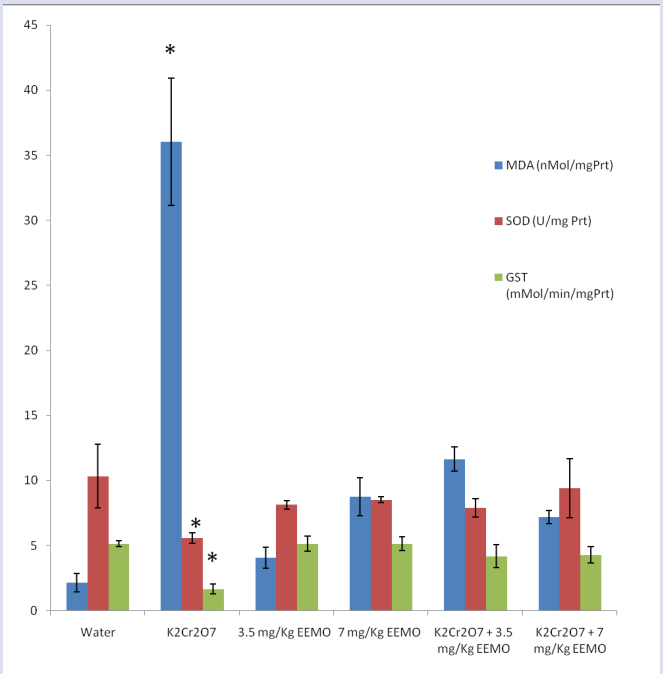

Figure 2: Oxidative stress markers in test and control animals. Data are expressed as Mean ± S.EM. *Significantly different at $p < 0.05$.

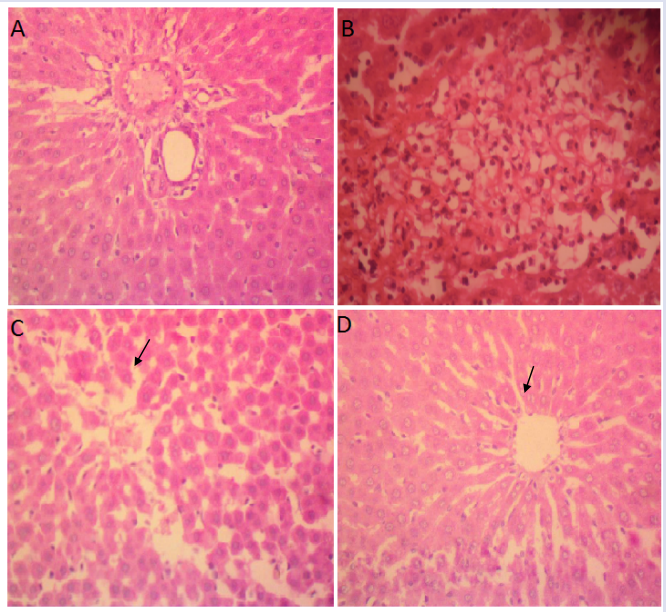

Figure 3: Representative pictomicrograph showing the effect of ethanol extract of *Moringa oleifera* (EEMO) *on* $K_2Cr_2O_7$-induced hepatic lesion in rats (HEX400). (A) normal liver hepatocyte structures observed in the control and animals exposed alone to either 3.5 or 7.0 mg/ Kg body weight of EEMO (B) hepatocellular necrosis observed in animals treated alone with $K_2Cr_2O_7$ (C) diffuse tubular epithelial coagulation necrosis (arrow) seen in rats exposed to $K_2Cr_2O_7$ only (D) mild vacuolar changes and centrilobular atrophy of hepatocytes (arrow) observed in rats exposed to a combination of $K_2Cr_2O_7$ and either 3.5 or 7.0 mg/ Kg body weight of EEMO.

Table 2: Proximate analysis of *Moringa oleifera* leaves.

S/N	Proximate parameter	Percentage (Mean ± SEM)
1	Moisture content	8.33 ± 0.04
2.	Fat	8.75 ± 0.14
3.	Ash content	9.90 ± 0.35
4.	Protein	17.52 ± 0.06
5	Carbohydrate	55.50 ± 0.28
6.	Crude fiber	5.42 ± 0.08

Table 3: The phytochemical screening of ethanol leaf extract of *Moringa oleifera*.

Phytoconstituents	Ethanol extract	Quantity (mg/100g powdered leaves)
Alkaloids	+	39.09 ± 0.34
Flavonoids	+	39.42 ± 0.64
Terpenoids	+	-
Tannis	+	59.80 ± 0.62
Saponins	+	-
Reducing sugar	+	21.57 ± 3.68
Phenolics	+	95.10 ± 0.54
Anthraquinones	ND	-
Cardiac glycoside	+	48.58 ± 0.25

Key: + = present, ND = not detected, - = not quantified

Table 4: Results of the gas chromatography mass spectroscopy of ethanol extract of *Moringaoleifera*.

S/N	Compounds	Retention Index	Composition (%)
1	Cis-1,9-hexadecadiene	1610	12
2	Cis-10-pentadecen-1-ol	1763	12
3	Palmitic acid	1968	5.3
4	Cyclohexaneacetic acid, alpha.-ethyl-2,2,3,3,4,4,5,5,6,6,7,7-dodecafluoroheptyl ester	1066	5.3
5	9-octadecenal	2007	12.1
6	Trans-2-octadecadecen-1-ol	2061	12
7	n-nonadecanoic acid	2266	3.6
8	Oleic acid	2175	12
9	Hexa-O-methylmyricitin	3083	6
10	2-(1,3-benzodioxol-5-yl)-5-hydroxy-3,6,7,8-tetramethoxy- 4H-1-benzopyran-4-one	3269	6
11	5,5'-dimethoxy-3,3'-dimethyl-2,2'-binaphthalene-1,1',4,4'-tetrone	3499	12.2
12	Hexa methyl quercetagetin	3084	0.8
	Percentage total		**99.3**

fibers. In addition, the qualitative analysis of EEMO revealed the presence of different phytochemicals including alkaloids, flavonoids, tannins, saponins, terpenoids, reducing sugar, phenolics, steroid and cardiac glycoside. Quantitative estimation of EEMO confirmed that the extract is rich in phenolic compounds and other secondary metabolites including saponins, flavonoids, alkaloids and cardiac glycosides. Under our experimental condition, the GCMS was able to separate 12 compounds from EEMO. These include 9-octadecenal, *cis*-10-pentadecen-1-ol, *trans*-2-octadecadecen-1-ol, oleic acid, hexa-O-methylmyricitin, 2-(1,3-benzodioxol-5-yl)-5-hydroxy-3,6,7,8-tetramethoxy-4H-1-benzopyran-4-one, palmitic acid, cyclohexaneacetic acid-alpha-ethyl-2,2,3,3,4,4,5,5,6,6,7,7-dodecafluoroheptyl ester, n-nonadecanoic acid and hexamethylquercetagetin.

DISCUSSION

Body and liver weight assessment are often employed as biomarkers of adverse effect of toxicants in toxicological studies.[28-30] Decreased weight gained is usually linked to growth impairment, while changes in liver weight often precede morphological changes associated with liver toxicity.[28] The decrease in body weight in the animals exposed to $K_2Cr_2O_7$ alone in the current study may be due to growth impairment resulting from decreased food intake as earlier observed by Petrovici, *et al.* [31] and Garcia-Nino, *et al.*[32] The increase in relative liver weight observed in $K_2Cr_2O_7$ treated animal may be due to the induction of drug metabolizing enzymes and toxicity to hepatic cells. In contrast, the positive growth promoting effect of EEMO was demonstrated by increased percentage weight gained in the rats fed with the two doses of EEMO alone and in combination with $K_2Cr_2O_7$. The growth enhancing effect of *Moringa oleifera* was recently reported in different animal models and has been attributed to phytochemicals and high levels of crude proteins, carbohydrate and crude fibers in *Moringa oleifera*.[33-35] Similarly, the reversal of the increased relative liver weight induced by $K_2Cr_2O_7$ in the present study is suggestive of the hepato-protection offered by EEMO against $K_2Cr_2O_7$.

The toxicity of $K_2Cr_2O_7$ and hepatoprotection offered by EEMO against $K_2Cr_2O_7$ induced hepatotoxicity was corroborated in the experiment designed to assess liver function in test and control animals. The increase in serum ALT and AST activities coupled with a corresponding decrease in both enzymes in the liver homogenate is suggestive of hepatocellular damage in the animals exposed to $K_2Cr_2O_7$. This result is in agreement with earlier findings in our laboratory and those of others researchers.[18,36] However, EEMO treatment improved the liver function by decreasing the elevated serum ALT and AST caused by $K_2Cr_2O_7$ administration. Aqueous extract of *Moringa oleifera* has been reported to protect the liver against rifampicin and isoniazid induced hepatic damage.[37] The improvement in the biochemical profiles of

animals simultaneously exposed to Cr (VI) and EEMO was further supported by the amelioration of the histological changes in the liver of the exposed animals. The vacuolar degeneration and necrosis observed in the hepatocytes of the rats treated with $K_2Cr_2O_7$ was reduced to moderate dissociation in the hepatocytes of the animals simultaneously exposed to two doses of EEMO and $K_2Cr_2O_7$.

The exact mechanism of Cr (VI) hepatoxicity is not fully understood. However, recent studies have suggested that the generation of oxygen species from chromate (VI) metabolism results in oxidative liver damage.[38,39] Therefore, the depletion of SOD and GST levels observed in the $K_2Cr_2O_7$ treated group in the current study is suggestive of oxidative stress. The fall in SOD activity may lead to the surplus superoxide anions that may inhibit the enzyme in the liver. Excess superoxide anion could also participate in Haber–Weiss reaction, resulting in the generation of highly destructive hydroxyl radicals.[40] Similarly, intermediates generated in the course of Cr (VI) metabolism, Cr (IV) and Cr (V) can participate in Fenton reaction, which may also result in hydroxyl generation. In addition, inhibition of the GST observed in the $K_2Cr_2O_7$ treated group may further compromise the ability of the liver to counter hydroxyl radical and other ROS generated by $K_2Cr_2O_7$. The free radicals may then cause hepatic injury by attacking the cellular macromolecules including lipids. Therefore, the increase in MDA levels in rats exposed to $K_2Cr_2O_7$ in this study may be an indication of lipid peroxidation and oxidative stress. Previous studies have found similar elevation in MDA concentration in different animal models exposed to $K_2Cr_2O_7$.[41,42] Intriguingly, administration of EEMO boosted the SOD and GST activities as well as inhibited the elevation of MDA levels in the liver suggesting amelioration of $K_2Cr_2O_7$ -induced injury observed in the liver of the animals exposed to the two doses of EEMO and $K_2Cr_2O_7$ may be due to the antioxidant property of EEMO. Recent studies have also shown that *Moringa oleifera* elicited protection against oxidative injury caused by drugs, radiation and other environmental toxicants.[15,43,44]

Phytochemical analysis of the EEMO revealed that it is rich in antioxidants such as flavonoids, phenolic compounds and tannins. In addition, the GCMS analysis of EEMO confirmed that the extract is rich in antioxidant compounds including, oleic acids, *cis*-1, 9-hexadecadiene, hexa-*O*-methyl-myricitrin and hexa-methyl-quercetagetin. These compounds in addition to other antioxidants[16] that have been detected in the extract of *Moringa oleifera* may be responsible for the observed amelioration of $K_2Cr_2O_7$ induced oxidative stress and toxicity. Myricitrin, an antioxidant used as flavor modifier in food and the parent compound of hexa-O-methyl myricitrin detected in EEMO in the present study was recently shown to ameliorate CCl_4-induced increase in serum ALT and AST levels as well as histopathological changes in the liver of BALB/cN mice by reducing lipid peroxidation and hepatic oxidative stress in addition to regeneration of hepatic tissue.[45] Similarly the parent compound of hexamethyl-quercetagetin, quercetagetin was also reported to have a strong protective effect on DNA damage induced by H_2O_2 and inhibit UV- induced phosphorylation of c-Jun and AKT by binding to the JNK1 and PI3-K.[46,47]

CONCLUSION

In summary, our findings suggest that ethanol extract of *Moringa olifera* leaves modified $K_2Cr_2O_7$-induced hepatotoxicity by reducing lipid peroxidation and oxidative stress as well as augmenting antioxidant enzyme defense system in the liver of exposed rats. Therefore, *Moringa oleifera* may be beneficial in the management of chromate (VI) induced oxidative stress and liver damage. However, further fractionation and purification may reveal the actual compound(s) responsible for the observed attenuation of $K_2Cr_2O_7$ induced hepatotoxicity. This will be addressed in future studies.

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CONFLICTS OF INTEREST

Authors declared that there are no conflicts of interest.

ABBREVIATIONS

EEMO: Ethanol Extract of *Moringa oleifera;* ALT: Alanine Amino Transferase; AST: Aspartate Amino Transferase; GST: Glutathione –S-Transferase; SOD: Superoxide Dismutase; MDA: Malondialdehyde; GCMS: Gas Chromatography Mass Spectroscopy; bd.wt: Body Weight.

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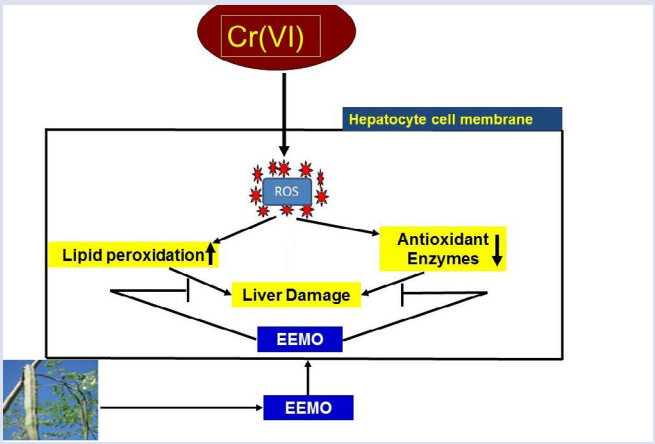
GRAPHICAL ABSTRACT



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