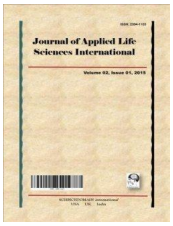

Journal of Applied Life Sciences International

19(4): 1-11, 2018; Article no.JALSI.47000
ISSN: 2394-1103

Investigation of Hepatoprotective and Antioxidant Activity of *Celosia argentea* against Tissue Injury Caused by Rifampicin Administration

Abiodun Olusoji Owoade[1*], Adewale Adetutu[1], Olubukola Sinbad Olorunnisola[1] and Olufemi Ogundeji Ogundipe[2]

[1]Department of Biochemistry, Ladoke Akintola University of Technology, Ogbomosho, Nigeria.
[2]Department of Physiology, Ladoke Akintola University of Technology, Ogbomosho, Nigeria.

Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JALSI/2018/v19i430068
Editor(s):
(1) Dr. Palanisamy Arulselvan, Institute of Bioscience, Universiti Putra Malaysia, Malaysia.
Reviewers:
(1) Muhammad Shahzad Aslam, Pakistan.
(2) Veeravan Lekskulchai, Srinakharinwirot University, Thailand.
(3) G. Bupesh, Sree Balaji Medical College & Hospital, Tamil Nadu.
Complete Peer review History: http://www.sdiarticle3.com/review-history/47000

Original Research Article

Received 16 November 2018
Accepted 28 January 2019
Published 21 February 2019

ABSTRACT

This study evaluated the antioxidant and possible protective effects of *Celosia argentea* against tissue injury caused by rifampicin administration. The antioxidant property of the aqueous extract of *C. argentea* was assessed in-vitro using 2,2-Diphenyl-1- picrylhydrazyl (DPPH), and 2,2-azino-bis (3-ethylbenzthiazoline-6-sufonic acid) (ABTS) assays. The results obtained revealed the free radical scavenging ability of the extract against the radicals in a concentration-dependent manner. Administration of rifampicin to rats for 28 days induced a significant increase in the activities of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and increase cholesterol levels in the plasma, liver and kidney while HDL cholesterol was decreased. It also elevated the levels of malondialdehyde (MDA) and decreased superoxide dismutase (SOD) activities in the liver and kidney. However, co-administration of *C. argentea* extract to rifampicin treated rats significantly reversed all these rifampicin induced changes. The levels of AST, ALT, ALP and cholesterol in the plasma, liver and kidney were decreased while HDL cholesterol level was increased. In addition, SOD activity was elevated while MDA was depressed

**Corresponding author: E-mail: aoowoade@lautech.edu.ng;*

when compared to the rifampicin treated rats. The extract of *C. argentea* was found to be rich in phenolic content and was proved to have no toxic effects on rats when administered alone to normal rats at a dose level of 400mg/kg/day. This study demonstrated that *C. argentea* leaf extract ameliorates rifampicin-induced hepatotoxicity and could be exploited in the management of hepatotoxic effect associated with rifampicin treatment.

Keywords: Tissue injury; rifampicin; Celosia argentea; malondialdehyde; hepatoprotective.

1. INTRODUCTION

Tuberculosis (TB) is one of the most common problems in undeveloped and developing countries [1]. It is the ninth principal cause of death worldwide and responsible for the death of 1.7 million people in 2016 alone [2]. Although the rate of new TB infection and mortality are decreasing by about 2% and 3% per year respectively not less than 16% of TB cases resulted in death [3]. Rifampicin which is an important drug used in the treatment of tuberculosis has been reported to induced hepatotoxicity has its main side effect [4]. It is on record that about 5–10% of TB patients that received treatment suffer from hepatotoxicity complication [5].

The mechanism of hepatotoxicity effect of TB drugs has been linked to their generation of reactive oxygen species (ROS) [6]. Therefore, hepatic toxicity and hepatitis are common features of rifampicin medication and this has been reported to caused steatosis and increased apoptosis of the hepatocytes and hepatic oxidative stress [7]. Though there is no suitable drug to weaken the hepatotoxicity effect of TB drugs presently [8], herbs are believed to possess potential hepatoprotective agents [9]. Some plant extracts have been shown to contain constituents that improved antioxidant status which is usually depleted during treatment with TB drugs [10,11]. Many synthetic antioxidants have been shown to produce toxic or mutagenic effects [12], therefore antioxidants from natural sources will be more appropriate for the prevention of TB drugs toxicity [13]. *Celosia argentea* L. is an annual herb that belongs to the amaranthaceae family. It has fascinating red flowers and dark green leaves. It is used in traditional medicine for its diuretic, antimitotic, antidiabetic, antihypertensive, anti-inflammatory and antitumor potentials [14,15]. Phytochemical screenings of the plant detected the presence of phenols, flavonoids, alkaloids, saponins, tannins, terpenes, glycosides, fatty acids, amino acids, carbohydrates and steroids in previous studies [16,17,18]. The plant has been demonstrated to possesses hepatoprotective, anti-tumour, anti-diarrhoea, anti-diabetes and anti-oxidant properties in several pharmacological studies [19,20,21].

Therefore, base on reported scientific and traditional evidence for the hepatoprotective potential of *C. argentea,* this present study was designed to investigate the protective potential of aqueous extract of *C. argentea* against rifampicin-induced hepatotoxicity.

2. MATERIALS AND METHODS

2.1 Reagents

Trichloroacetic acid (TCA), Folin-Ciocalteau reagent, 6-Hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid (Trolox), 2,2-Diphenyl-1-picrylhydrazyl (DPPH), 2,2-azino-bis (3-ethylbenzthiazoline-6-sufonic acid) ABTS, gallic acid, thiobarbituric acid (TBA), nicotinamide adenine dinucleotide reduced (NADH) were obtained from Sigma–Aldrich Chemical Co. Ltd. (England). Rifampicin was obtained from (Ziel Medicare Ltd, India), while Nitrobluetetrazolium (NBT) was the product of Fluka (Buchs, Switzerland). All other chemicals used were of analytical grade.

2.2 Plant Materials

The fresh leaves of *C. argentea* were collected from the research farm of Faculty of Agricultural science, Ladoke Akintola University of Technology, Ogbomosho. The identification and authentication of the plant were done by Prof A.J. Ogunkunle at Department of Pure and Applied Biology, Ladoke Akintola University of Technology, Ogbomoso, where a specimen was deposited in the herbarium with voucher number UIH 802. The leaves were dried at room temperature and blended to a coarse powder.

2.3 Preparation of Aqueous Extract

The powdered leaves of *C. argentea* (200g) were extracted with distilled water (1.2litres) overnight

in a Soxhlet extractor. The aqueous extract was concentrated and evaporated to dryness at 50°C with a Vacuum air dryer to obtain a flake-type extract and the yield of the preparation was 36.74g (18.37% w/w). The extractive yield was calculated using the relation:

Yield (%) = (Weight of extract $_{(g)}$ / Weight of plant material $_{(g)}$) X 100.

2.4 Animals

A total of twenty-five (25) male wistar strain albino rats with body weights between 200 and 220g were used in this experiment. They were housed in the Ladoke Akintola University of Technology, (LAUTECH) animal house. They were allowed fourteen (14) days to acclimatize before the commencement of the experiment. The animals were maintained on a standard pellet diet throughout the acclimatization and administration period. The animal experimental procedures were conducted in accordance with the National Institutes of Health guide for the care and use of laboratory animals (NIH Publications No. 8023) revised in 2002 and approved by LAUTECH research committee with the reference number: EC/LAU/2018/26.

2.5 Experimental Design

Twenty-five (25) male wistar strain albino rats were divided into five groups with each group comprising of five rats. Group 1 rats were given distilled water for 28 days and taken as control, group 2 rats received 400 mg/kg body weight of *C. argentea* extract only, group 3 rats received 100 mg/kg body weight of rifampicin only, group 4 rats received 100 mg/kg body weight of rifampicin plus 200 mg/kg body weight of *C. argentea* extract and group 5 rats received 100 mg/kg body weight of rifampicin plus 400 mg/kg body weight of *C. argentea* extract. Different concentrations of *C. argentea* extract and rifampicin was administered for a period of 28 days and were given through the oral route with the use of the oral cannula. At the end of the *C. argentea* treatment, blood was collected from the animals into heparinised tubes by cardiac puncture under light ether anaesthesia and after an overnight fast. Liver and kidney were removed from the animals for biochemical analyses. Blood samples were centrifuged to separate plasma and red blood cells. All samples were stored at -20°C until analysed.

2.6 Trolox Equivalent Antioxidant Capacity (TEAC) Assay

The assay was performed essentially as described by Re et al. [22]. ABTS radical cation was produced by reacting 7 mM ABTS stock solution with 2.45 mM potassium persulphate and allowing the mixture to stand in the dark at room temperature for 12–24 h before use. The $ABTS^{\bullet+}$ solution was diluted with water and adjusted to an absorbance of 0.700 ± 0.020 at 734 nm. For the photometric assay, 1 ml of the $ABTS^{\bullet+}$ solution and various concentrations of the extracts were mixed for 45 seconds and measured immediately after 1 minute at 734 nm. The antioxidant activity of the extracts was calculated by determining the decrease in absorbance at different concentrations by using the following equation.

% antioxidant activity = ((A($ABTS^{\bullet+}$) - A(Extracts))/ (A($ABTS^{\bullet+}$)) X 100.

2.7 DPPH (2, 2-Diphenyl-1-picrylhydrazyl) Radical Scavenging Activity

The assay was performed as previously described by Schelesier et al. [23]. The radical solution is prepared by dissolving 2.4 mg DPPH• in 100 ml methanol. For the photometric assay 1.95 ml DPPH• solution and 50 µl antioxidant solution were mixed. At first, the absorbance of the disposable cuvette with 1.95 ml DPPH• was measured as blank, then the antioxidant solution was added and mixed. The reaction was measured at 5 min interval at 515 nm until ΔA=0.003 min-1. The anti-oxidative activity was calculated by determining the decrease in absorbance at different concentrations by using the following equation:

%Inhibition activity = ((A ($DPPH^{\bullet}$) –A (Extracts)) / (A ($DPPH^{\bullet}$)) X 100

2.8 Determination of Total Phenolic Compounds

The content of total phenolic compounds in *C. argentea* was determined by the Folin–Ciocalteu method as described by Miliauskas et al. [24]. Briefly, l ml aliquots of 0.024, 0.075, 0.0105 and 0.3 mg/ml ethanolic garlic acid solutions were mixed with 5 ml Folin-ciocalteu reagent (diluted ten-fold) and 4 ml (75 g/L) sodium carbonate. The absorption was read after 30 min at 20°C at 765 nm and the calibration curve was drawn.

One ml of *C. argentea* (1 mg/ml) was mixed with the same reagents as described above, and after l h the absorption was measured for the determination of plant phenolics. All determinations were performed in triplicate. The total content of phenolic compounds in plant methanol extracts in gallic acid equivalents (GAE) was calculated by the following formula:

$$C = c \bullet V/m'$$

Where: C-total content of phenolic compounds, mg/g plant extract, in GAE; c-the concentration of gallic acid established from the calibration curve, mg/ml; V- the volume of extract, ml; m´- the weight of pure plant methanolic extract, g.

2.9 Preparation of Liver and Kidney Homogenates

Prior to biochemical analyses, the liver and kidney samples were cut into small pieces and homogenized in Phosphate buffer saline (PBS) with a homogenizer to give a 10 % (w/v) liver and kidney homogenate. The homogenates were then centrifuged at 12,000 rpm for 15 min. The supernatant obtained was used for the assay of superoxide dismutase, thiobarbituric acid reactive substances (TBARS) content, and protein estimation.

2.10 Determination of Blood Lipid Profiles and ALP, AST, ALT Activities in Plasma

Plasma concentrations of total cholesterol, triglycerides, alkaline phosphatase (ALP), aspartate aminotransferase (AST), and alanine aminotransferase (ALT) were determined with commercial kits (CYPRESS® Diagnostics, Langdorp, Belgium). HDL cholesterol and triglycerides were determined in plasma with the same commercial kits for total cholesterol and triglycerides after very low-density lipoproteins (VLDL) and LDL were precipitated with a heparin-$MnCl_2$ solution [25].

2.11 Liver and Kidney Lipid Profiles

Lipids were extracted from the liver and kidney as described by Folch et al. [26]. After washing with 0.05 M KCl solution, aliquots of the lipid extracts were then used for the determination of lipid profiles. Details of these are given as reported earlier [27].

2.12 Determination of Hepatic and Renal SOD Activities and MDA Levels

Hepatic and renal superoxide dismutase (SOD) activities were assayed in the tissue homogenates by the method of Kakkar et al. [28] at 560 nm. One unit of enzyme activity was defined as that amount of enzyme which caused 50% inhibition of nitrobluetetrazolium reduction/mg protein. The SOD activity was expressed as per mg of protein and the tissue protein was estimated according to the method of Lowry et al. [29], using bovine serum albumin (BSA) as a standard. The extent of lipid peroxidation was estimated as the concentration of thiobarbituric acid-reactive product malondialdehyde (MDA), using the method of Draper and Hadley [30].

2.13 Statistical Analysis

Results are expressed as mean ± S.E.M. The levels of homogeneity among the groups were assessed using One-way Analysis of Variance (ANOVA) followed by Tukey's test. All analyses were done using Graph Pad Prism software Version 5.00 and p values < 0.05 were considered statistically significant.

3. RESULTS

3.1 The Total Phenolic Compounds and In-vitro Antioxidant Potential

The *C. argentea* demonstrated a concentration and time-dependent scavenging activity by quenching DPPH radicals (Fig. 1) and was compared with gallic acid, as a positive control. The IC50 values (defined as the concentration of test compound required to produce 50% inhibition) for DPPH scavenging by *C. argentea* and gallic acid were 582.75 ± 8.58 µg/dL and 16.32 ± 1.50 µg/dL respectively (Table 1). In the TEAC assay, the TEAC value of Trolox is 1.00. Gallic acid responded as the strongest with TEAC value of 4.25 ± 0.12 while *C. argentea* responded lowest with TEAC value of 0.45 ± 0.09 (Table 1 & Fig. 1). The phenolic content of *C. argentea* was determined using Folin-Ciocalteu assay and was found to be 29.57 ± 1.23 mg/g in Gallic acid equivalent (Table 1).

3.2 Effects of the Extract on Blood and Tissue Lipids of Rats

Results of plasma and tissue lipids analyses are presented in Table 2. Administration of 400

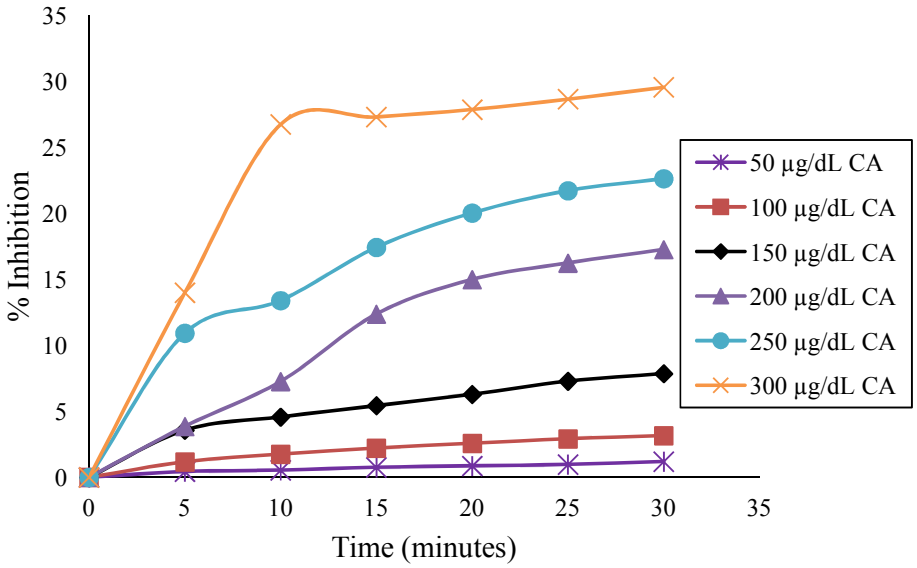

Fig. 1. The effects of time on different concentration of aqueous extract of *C. argentea* on inhibition of DPPH radical

Table 1. Total phenolic content, DPPH radical scavenging value and Trolox equivalent antioxidant capacity (TEAC) of *Celosia argentea*

Sample	Total phenol [a]	DPPH scavenging activity (IC 50) [b]	Trolox equivalent antioxidant capacities (TEAC) [c]
Trolox	ND	ND	1
Gallic	ND	16.32 ± 1.50	4.25 ± 0.12
C. argentea	29.57 ± 1.23	582.75 ± 8.58	0.45 ± 0.09

Each value represents the mean ± SEM (n=3); a Total phenolic content was expressed as mg gallic acid equivalents/g dried extract; b Expressed as µg/mL; c Expressed as mmol/L

mg/kg body weight of *C. argentea* alone did not produce any significant changes in lipid parameters in all the compartment studied when compared with control animals. However, administration of rifampicin alone significantly increased plasma, hepatic and renal cholesterol concentrations by 70.27 %, 100.52 % and 67.28% respectively while it reduced HDL cholesterol by 64.41 % when compared with the control animals. Administration of rifampicin also resulted in non-significant changes in plasma, HDL, hepatic and renal triglycerides and phospholipids concentrations when compared with the control animals. However, co-administration of 200 mg/kg and 400 mg/kg body weight of *C. argentea* extract to rifampicin treated rats resulted in reduction of plasma cholesterol concentrations by 27.15 % and 31.64 % respectively, reduction in hepatic cholesterol concentrations by 33.25 % and 36.36 % respectively and reduction in renal cholesterol concentrations by 33.06 % and 37.74 % respectively while HDL cholesterol concentrations were increased by 88.49 % and 116.10 % respectively when compared with the rats treated with rifampicin only.

3.3 Effect of Extract on Activities of ALT, ALP and AST

Administration of rifampicin only significantly increased enzymatic activity of ALT, ALP and AST by 209.03 %, 45.69 % and 66.34 % respectively when compared with the normal rats while administration of 400 mg/kg body weight of *C. argentea* alone did not produce any significant changes in the enzyme's activities. However, co-administration of 200 mg/kg and 400 mg/kg body weight of *C. argentea* extract to rifampicin treated rats caused reduction in plasma ALT activity by 42.88 % and 43.68 % respectively, reduction in plasma ALP activity by 24.60 % and 29.23 %

Table 2. Effects of aqueous leaf extract of *C. argentea* on blood, hepatic and renal lipids in rats

Parameters (mg/dL)	Control	400 mg/kg CA	Rifampicin	Rifampicin + 200 mg/kg CA	Rifampicin + 400 mg/kg CA
Plasma cholesterol	54.39 ± 2.75	57.92 ± 1.78	92.61 ± 3.63*	67.47 ± 2.10**	63.31 ± 2.52**
Plasma triglyceride	99.47 ± 3.29	104.62 ± 3.95	123.83 ± 4.53	96.21 ± 3.01	108.94 ± 3.72
HDL cholesterol	37.35 ± 1.93	36.15 ± 2.1	13.29 ± 0.75*	25.05 ± 2.11**	28.72 ± 1.73**
HDL triglyceride	57.66 ± 2.82	55.38 ± 3.51	58.95 ± 3.71	52.42 ± 2.23	74.48 ± 4.32
Hepatic cholesterol	1.92 ± 0.25	2.02 ± 0.31	3.85 ± 0.42*	2.57 ± 0.21**	2.45 ± 0.17**
Hepatic triglyceride	2.75 ± 0.31	2.91 ± 0.27	3.34 ± 0.28	3.12 ± 0.44	2.83 ± 0.22
Hepatic phospholipid	18.38 ± 1.54	20.47 ± 1.27	23.78 ± 0.97	19.33 ± 1.01	17.06 ± 0.82
Renal cholesterol	2.17 ± 0.28	2.14 ± 0.12	3.63 ± 0.33*	2.43 ± 0.14**	2.26 ± 0.25**
Renal triglyceride	2.15 ± 0.24	2.32 ± 0.18	2.54 ± 0.22	1.88 ± 0.17	2.52 ± 0.27
Renal phospholipid	47.45 ± 3.63	45.24 ± 2.12	35.96 ± 1.75	40.25 ± 2.15	41.08 ± 2.48

*Each value represents the Mean of 5 rats. *($p < 0.05$) Groups 2 and 3 (C. argentea and rifampicin treated rat respectively) compared with group 1 (control rats). **($p < 0.05$) Groups 4 and 5 (C. argentea treated rats) compared with group 3 (rifampicin treated rats)*

respectively and reduction in plasma AST activity by 21.50 % and 34.98 % respectively, when compared with the rats treated with rifampicin only (Fig. 2).

3.4 Effect of *Celosia argentea* Extract on Hepatic and Renal Malonaldehyde Levels

Hepatic and renal MDA levels of rats treated with rifampicin only were significantly increased by 151.36 % and 246.41 % respectively when compared with the normal rats while administration of 400 mg/kg body weight of *C. argentea* alone did not produce any significant change in MDA levels. However, co-administration of 200 mg/kg and 400 mg/kg body weight of *C. argentea* extract to rifampicin treated rats caused a reduction in hepatic MDA level by 25.30 % and 34.94 % respectively, and reduction in renal MDA level by 43.30 % and 51.53 % respectively when compared with the rats treated with rifampicin only (Fig. 3).

3.5 Effect of *Celosia argentea* Extract on Hepatic and Renal SOD Activity

Hepatic and renal SOD levels of rats treated with rifampicin only were significantly reduced by 68.15 % and 67.00 % respectively when compared with the normal rats while administration of 400 mg/kg of *C. argentea* alone did not produce any significant change in SOD levels. However, co-administration of 200 mg/kg and 400 mg/kg body weight of *C. argentea* extract to rifampicin treated rats caused increased in hepatic SOD level was by 56.16 % and 143.84 % respectively and increased in renal SOD level 26.48 % and 114.74 % respectively when compared with the rats treated with rifampicin only (Fig. 4).

4. DISCUSSION

Rifampicin a synthetic drug used for TB treatment is known for causing hepatic injury [7]. Rifampicin is a known inducer of many metabolizing enzymes; some metabolites produce through these reactions are toxic and their accumulation would result in the induction of liver injury or immune responses [31]. Rifampicin could also cause the accumulation of reactive oxygen species (ROS) as a result of mitochondrial toxicity [32]. The liver injury caused by chemicals or infectious agents if not treated may progress to liver fibrosis, cirrhosis and liver failure [7]. It has been suggested in previous studies that traditional herbs and micronutrients

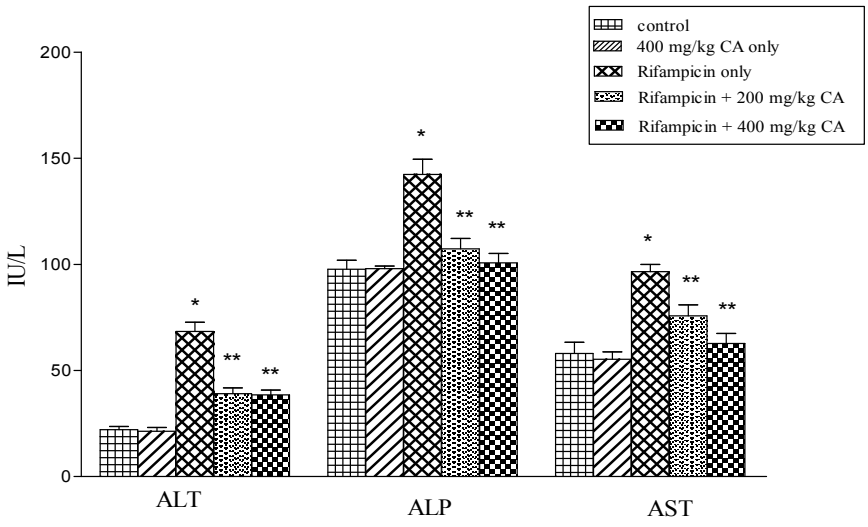

Fig. 2. Effect of aqueous extract of *Celosia argentea* on activities of ALT, ALP and AST in rifampicin-treated rats.

*Values are mean ± SEM (n=5). *(p < 0.05) Groups 2 and 3 (C. argentea and rifampicin treated rat respectively) compared with group 1 (control rats). **(p < 0.05) Groups 4 and 5 (C. argentea treated rats) compared with group 3 (rifampicin treated rats)*

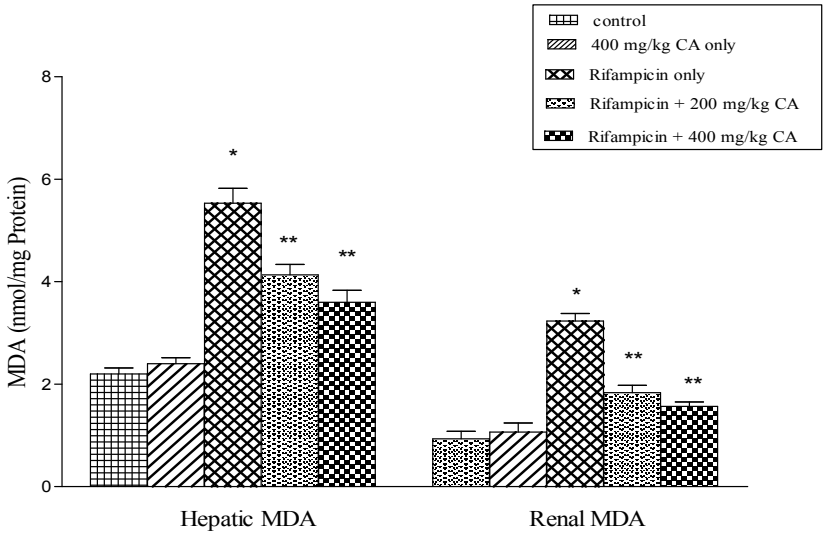

Fig. 3. Effect of aqueous extract of *Celosia argentea* on MDA level of rifampicin treated rats.

*Values are mean ± SEM (n=5). *(p < 0.05) Groups 2 and 3 (C. argentea and rifampicin treated rat respectively) compared with group 1 (control rats). **(p < 0.05) Groups 4 and 5 (C. argentea treated rats) compared with group 3 (rifampicin treated rats)*

may help in the prevention of liver injury [33,34]. In recent time, one plant that has been subjected to several studies for its medicinal values is *C. argentea*. The current investigation was undertaken to evaluate the possible protective effect of *C. argentea* against rifampicin-induced hepatotoxicity and oxidative stress in rats.

The ABTS•+ and DPPH radical scavenging assay are among the common methods used to evaluate the total antioxidant activity of vegetables or other plants [33,34]. In the present study, *C. argentea* showed DPPH radical scavenging activity which is attributed to its hydrogen donating ability. The extract also

showed a strong ABTS radical scavenging ability in a concentration-dependent manner suggesting that *C. argentea* extract has strong antioxidant potential.

Rats treated with rifampicin in this study developed hepatic damage as revealed by an increase in the activities of ALT, ALP and AST which is in support of previous study [1]. The increased activities of these liver enzymes in the blood are evidence of liver cell damage and loss of functional integrity [35]. There was a reduction in the elevated levels of these enzymes in rats co-administered with *C. argentea* extract and rifampicin when compared to the rifampicin group only which is an indication of the stabilization of plasma membrane as well as repair of liver damage caused by rifampicin. This observation agrees with the commonly accepted view that serum levels of transaminases return to normal with the healing of hepatic parenchyma and the regeneration of hepatocytes [36].

Rifampicin administration significantly increases plasma cholesterol level and decrease HDL cholesterol level when compared with the control group a strong indication of disturbances in cholesterol metabolism, a result that agrees with similar studies [8,37]. Administration of rifampicin also leads to the significant accumulation of cholesterol in the hepatic and renal tissues which is in support of a previous study [38]. In all the compartment, there was a reduction in cholesterol levels of rats co-administered with rifampicin and *C. argentea* extract when compared with rifampicin group only. Although it is not clear how *C. argentea* leaf extract reduced the levels of cholesterol, it may be due to its ability to modulate cholesterol metabolism by the liver or lipoprotein lipase activity [39]. The chemical constituents in *C. argentea* leaf extracts probably downregulate cholesterol biosynthesis or inactivate the enzymatic pathways or both.

Enhanced lipid peroxidation expressed in terms of MDA contents was observed in rifampicin-treated rats in our study which indicates the damage to the hepatic and renal cells this agrees with a previous study [3]. Rifampicin is a strong inducer of several metabolizing enzymes thereby resulting in increased accumulation of metabolites, the metabolites can initiate peroxidative damage to lipid membranes and other poly-unsaturated fatty acid-rich structures like endoplasmic reticulum through free radical-mediated reactions [8]. The induced lipid peroxides activated significant upsurge in MDA-like products with a resulting loss in cellular integrity and destruction of liver and kidney tissues. There was a significant reduction in MDA levels of rats simultaneously treated with *C. argentea* extract and rifampicin when compared to the rifampicin group only, suggesting that the extract inhibit lipid peroxidation and its propagation in the liver and kidney.

The activity of antioxidant enzyme SOD was significantly decreased in hepatic and renal

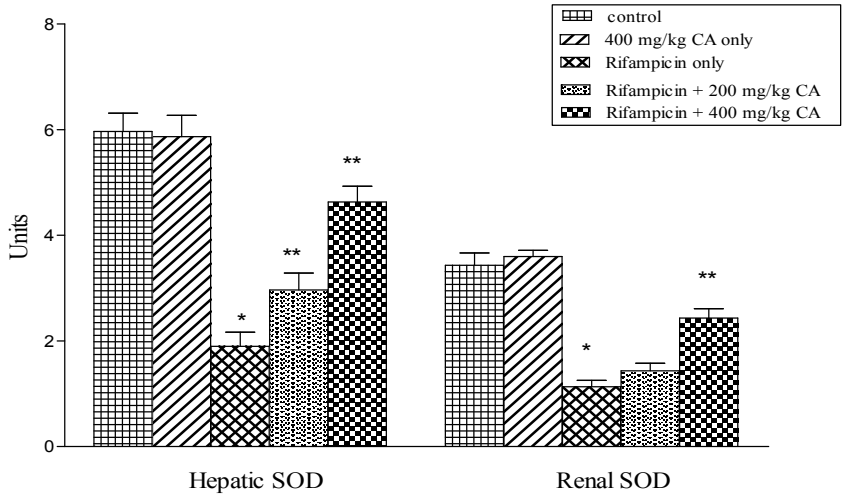

Fig. 4. Effect of aqueous extract of *C. argentea* on SOD activity of rifampicin treated rats

*Values are mean ± SEM (n=5). *(p < 0.05) Groups 2 and 3 (C. argentea and rifampicin treated rat respectively) compared with group 1 (control rats). **(p < 0.05) Groups 4 and 5 (C. argentea treated rats) compared with group 3 (rifampicin treated rats)*

tissues of rifampicin treated rats in this study. The decreased activity of SOD in the liver and kidney tissues of rifampicin treated rats may be due to increased utilisation of the enzyme against reactive oxygen species [40]. However, co-administration of rats with *C. argentea* extract and rifampicin reversed the reduction in SOD levels when compared to the rifampicin group only, which demonstrates that *C. argentea* leaf extract protects the liver and kidney from oxidative damage.

Our present study revealed that *C. argentea* contains a considerable amount of phenolic compounds and exhibited strong free radical scavenging property. A number of researchers have reported that phenolic compounds in plants extract have antioxidant properties in various experimental models [41,42]. Therefore, the ability of *C. argentea* to protect the rats against rifampicin induced liver and kidney damaged may be attributed to the presence of phenolic compounds in the extract. The phenolic substances are known to possess the ability to reduce oxidative damage and acts as an antioxidant. They can trap the free radicals directly or scavenge them through a series of coupled reactions with antioxidant enzymes [43]. The hepatoprotective effects of *C. argentea* demonstrated in this study could be exploited in alleviating xenobiotic-induced hepatotoxicity and nephrotoxicity. This finding justifies the use of *C. argentea* in traditional medicine, in the prevention of free radical-mediated diseases.

5. CONCLUSION

The results obtained in this study gave credence to hepatoprotective effects of *C. argentea* and its use in ethnomedicine. The regular consumption of *C. argentea* by patients undergoing TB treatment might ameliorate the hepatotoxic effect associated with rifampicin treatment. The hepatoprotective effect of *C. argentea* demonstrated in this work is due to its antioxidant effects.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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