Saudi Journal of Biological Sciences 29 (2022) 3408–3413

Contents lists available at ScienceDirect

Saudi Journal of Biological Sciences

journal homepage: www.sciencedirect.com

Original article

Chenopodium album extract ameliorates carbon tetrachloride induced hepatotoxicity in rat model

Saddam Hussain, Muhammad Asrar *, Azhar Rasul, Salma Sultana, Usama Saleem

Department of Zoology, Faculty of Life Sciences, Government College University Faisalabad, 38000 Faisalabad, Pakistan

ARTICLE INFO

Article history:
Received 30 December 2021
Revised 26 January 2022
Accepted 13 February 2022
Available online 17 February 2022

Keywords:
Hepatoprotective
Chenopodium album
Methanolic extract
In Vivo

ABSTRACT

Major objective of this study was to explore the protective effect of the methanolic extract of *Chenopodium album* against carbon tetrachloride induced hepatotoxicity in rats. *Chenopodium album* has locally been used for multiple medicinal proposes. Methanolic extract of *Chenopodium album* (whole plant) was prepared with Soxhlet extractor and rotatory evaporator. Antioxidant activity of *Chenopodium album* was determined by DPPH free radical scavenging assay. Thirty Wister (albino) rats (150–200 g) were divided into six groups for the evaluation of hepatoprotective potential of different concentrations of *Chenopodium album* against carbon tetrachloride (1:1 CCl_4: Olive oil) under the controlled laboratory conditions. Group-I rats were administrated with olive oil (Normal control), Group-II with CCl_4 only, Group-III with Silymarin (positive control), Group-IV with *Chenopodium album* (100 mg/kg), Group-V with *Chenopodium album* (200 mg/kg) and Group-VI rats with *Chenopodium album* (300 mg/kg) for the period of 28 days. Serum was taken to determine the levels of alanine transaminase, aspartate transaminase, alkaline phosphatase, cholesterol, triglyceride, creatinine and urea in the blood. Formalin stored tissues were examined for histopathological analysis. DPPH assay showed that *Chenopodium album* has the potential for reduction of oxidative stress. *Chenopodium album* minimized the levels of ALT (70 ± 8.68 U/L, 68.75 ± 8.38 U/L & 73.5 ± 10.28 U/L), AST (219.5 ± 19.16 U/L, 140.75 ± 13.35 U/L & 221. 25 ± 13.33 U/L) and ALP (289.5 ± 28.21 U/L, 258 ± 11.12 U/L & 248.25 ± 4.03 U/L) at different concentrations (100 mg/kg, 200 mg/kg, 300 mg/kg respectively). *Chenopodium album* enhanced triglyceride level (64.75 ± 12.66 mg/dl at 200 mg/kg) as compared to CCl_4 treated group (33.25 ± 1.26 mg/dl). Carbon tetrachloride elevated urea level (43.25 ± 6.6) was decreased by high dose of *Chenopodium album* (18 ± 8.17). Moreover, *Chenopodium album* also improved WBC level (9.69×10^3 /Cu.mr & 10.59×10^3 /Cu.mr at low and medium doses respectively), RBCs level (6.97×10^3 /Cu.mr) and hemoglobin level (13.95 G/dL, 13.467 G/dL & 14.05 G/dL at low, medium and high doses). *In vivo* study of *Chenopodium album* methanolic extract demonstrates the potential for protection of liver and after pre-clinical studies the plant can be used as a safe alternative of commercially available hepatoprotective medicines.

1. Introduction

The liver is a vital organ that deals with several biochemical reactions for different physiological processes. Liver plays important role in maintenance of immune system, regulation of blood volume by maintaining glucose and plasma proteins level, metabolism of macronutrients, production of bile, endocrine regulation of signaling pathways for growth and homeostasis of lipid & cholesterol. Catalysis of xenobiotic compounds including numerous drugs also takes place in the liver, as liver comes into contact with absorbed nutrients and also with xenobiotics via portal vein (Trefts et al., 2017; Michalopoulos & Bhushan, 2021). Liver disorders are one of the main reasons for mortality worldwide and also a direct burden to economy. In a recorded data, about 5% of total patients present in a general hospital are facing drug induced liver injuries (Zhao et al., 2018; Zhou et al., 2021). Toxins are present in our daily life, from pesticides to chemical production, alcohol drinks and detergents; we are in contact with different types of chemicals. Hepatotoxicity can also be induced with different xenobiotics

* Corresponding author.
E-mail address: asrar_agri@yahoo.com (M. Asrar).

Peer review under responsibility of King Saud University.

Production and hosting by Elsevier

https://doi.org/10.1016/j.sjbs.2022.02.014
1319-562X/

including chemicals like carbon tetrachloride for the experimental purposes (Weber et al., 2003).

The consumption of various fruits and vegetables, as well as the usage of some plants played important part in human health care. Traditional medicine, which is based primarily on plant materials, is used by around 80% of the world's population for health care (Deshwal et al., 2011). Around 160 phyto constituents taken from 101 plant species have been proved to possess hepatoprotective activity (Ali et al., 2019). Despite developments in modern medicine system, there are just a few effective natural medicines in the market that can be used to boost the liver function, protect the damage or help to regenerate hepatic cells (Bansal et al., 2014).

Chenopodium album locally known as lamb's quarters, is not only a natural weed and commonly used as a vegetable, salad & animal feed but also for medicinal uses. This plant belongs to the Chenopodium genus, which has the diversity of plants with medicinal importance. The plant has been used as an antiscorbutic, laxative, sedative, blood purifier, diuretic drug and anthelmintic against hookworms and other helminthic parasites (Poonia & Upadhayay, 2015). *Chenopodium album* has flavonoids like phenolic amide, which has hypotensive properties (Gohara and Elmazar, 1997). Cinnamic acid amide (Cutillo et al. 2003), alkaloid chenoalbicin (Cutillo et al. 2004) and saponins are also found in the plant (Lavaud et al. 2007). Other potential compounds reported from the *Chenopodium album* are phyto-hormones (DellaGreca et al. 2004), phenols, lignans and xylosides (Poonia & Upadhayay, 2015). The plant also contains potassium, magnesium, calcium, iron, phosphorous and manganese (Shahi, 1977). Tropolone derivated compounds, isolated from *Chenopodium album,* have been reported to lowers the ALT, AST and ALP levels and proved to be effective hepatoprotective agents against HepG2 cell line (Ma et al., 2020).

2. Materials and methods

2.1. Plant collection and extract preparation

Aerial parts of *Chenopodiun album* were collected from desert zone of Bhakkar (Punjab, Pakistan) in 2018. Locally identified plants were authenticated by Dr. Qasim Ali from the department of Botany. The plant was washed, shade dried for 2 weeks and grinded into course powder. Methanolic extract of *Chenopodium album* (MECA) was prepared by using Soxhlet apparatus. 250 ml of solvent (methanol 95%) was filled in distillation flask for 40 g of powder loaded in each thimble. Using a vacuum rotary evaporator, crude MECA was concentrated. After solidification, the extract was labeled with natural product extract number (NPE-27) and recorded in the catalogue of the natural product extract library.

2.2. Determination of antioxidant activity

Antioxidant activity of *Chenopodium album* methanolic extract was measured by DPPH assay. DPPH solution was initially prepared by dissolving DPPH solution (2 mg) into methanol (50 ml). Different concentrations of CAME were mixed with DPPH solution in 96 well plate. Methanol and Ascorbic acid were used as blank and control respectively. Absorbance was measured at 517 nm (De-torre et al., 2019). Following formula was applied for calculation of antioxidant percentage

$$\%\text{age of Antioxidant} = 1 - \frac{\text{Abs}_{\text{Sample}} - \text{Abs}_{\text{Blank}}}{\text{Abs}_{\text{Control}} - \text{Abs}_{\text{Blank}}} \times 100$$

Where: Abs, Absorbance

2.3. Experimental animals

Thirty healthy 8–10 week-old Wister rats (weight 150–200 g) were purchased from department of Physiology, Government College University Faisalabad. The animals were kept under the standard laboratory conditions, with controlled temperature (24 ± 2), relative humidity (55 ± 5%) & 12 h day/night cycle and had free access to standard diet and water. The rats were housed in controlled condition for 7 days with the attention of acclimatization. Government College University Faisalabad's Ethics Review Committee authorized the experimental protocol.

2.4. Experimental design

To test the hepatoprotective potential of *Chenopodium album* against CCl_4 induced hepatotoxicity, research experiment was conducted for the period of 28 days.

The rats were uniformly divided into 6 groups

Group I (Normal control)

Olive oil treatment (Orally gavage)

Group II

Carbon tetrachloride treatment (Orally gavage)

Group III (Positive control)

Silymarin treatment (100 mg/kg b.w) & Carbon tetrachloride treatment (Orally gavage)

Group IV

Chenopodium album methanolic extract (100 mg/kg b.w) treatment & Carbon tetrachloride treatment (Orally gavage)

Group V

Chenopodium album methanolic extract (200 mg/kg b.w) treatment & Carbon tetrachloride treatment (Orally gavage)

Group VI

Chenopodium album methanolic extract (300 mg/kg b.w) treatment & Carbon tetrachloride treatment (Orally gavage)

Olive oil was used as a vehicle (1:1 ratio of carbon tetrachloride: olive oil) for carbon tetrachloride treated (2 ml/kg b.w) rats of group II, III, IV, V & VI.

2.5. Sample collection

After 24 h of last dose of carbon tetrachloride, rats had been sacrificed by decapitation of the cervical region. Blood samples were collected by cardiac puncture using a sharp syringe. Blood collected in the purple top bottle (lavender) was mixed with EDTA by inverting the tube about 8–10 times. For the purpose of serum blood was collected into red top bottles, and the tubes were kept vertically for 30 min, and then centrifuged at 3000 rpm for 15 min. Supernatant (serum) was gently taken into eppendorf tubes. Liver was taken and stored in 10% formalin for the purpose of histopathology.

2.6. Assay of liver marker enzymes

Level of alanine transaminase (ALT), aspartate transaminase (AST) and alkaline phosphatase (ALP) in the serum was measured by using commercially available diagnostic kits. These biomarkers of liver functions were analyzed by using Dimension EXL 200 automatic biochemistry analyzer.

2.7. Assays for lipid profile and renal function tests

Serum stored at −40 °C, was utilized for the determination of cholesterol, triglycerides, urea and creatinine levels. Dimension 200 EXL automatic biochemistry analyzer was used for the analysis of cholesterol, triglycerides, urea and creatinine in the serum samples of rats.

2.8. Determination of hematological parameters

Hematological analyzer was used for the determination of red blood cells count, white blood cells count and hemoglobin level.

2.9. Histopathological examination

Formalin preserved liver was cut with the help of sharp blade, and a section of liver tissue was placed in labeled histology cassettes. Tissues were fixed in formalin, and dehydrated in gradually increasing concentrations of ethanol. Dehydrated tissues were embedded in wax. Tissues were taken out from wax and mounted on microtome (Histo-line MR 2258) and about 5 um thin sections were cut, transferred on albumenized glass slides. hematoxylin and eosin were used as stain (Kakadia et al., 2020). Microscopy of liver tissue damage was done under optical microscope (Nikon DS-Fi2) & photos were captured with camera attached with microscope.

2.10. Statistical analysis

All of the data was analyzed using IBM SPSS statistics. To analyze differences across groups, one-way analysis of variance (ANOVA) and Tukey's tests were applied. The processed data was expressed using the mean and standard deviation (mean SD). The results were considered significant unless the P value was less than 0.05.

3. Results

3.1. Antioxidant activity

Chemicals like CCl_4 initially damage the tissues by causing oxidative stress. With the entry of carbon tetrachloride in liver, CCl_4 is bio-transformed by Cyt-P_{450} enzymes and metabolized by CyP2E1 into $CCl_3^{\cdot}$ and $CCl_3OO^{\cdot}$. A chain of free radicals is started, generating oxidative stress. Different concentrations of CAME were used to determine the antioxidant activity, and plant showed maximum DPPH free radical scavenging activity at its highest concentration, as results are shown in Fig. 1.

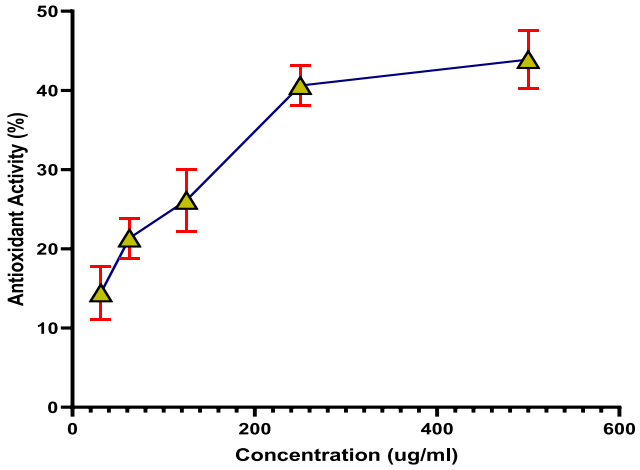

Fig. 1. Antioxidant activity of *Chenopodium album* methanolic extract Group I, Normal control; Group II, carbon tetrachloride intoxicated rats; Group III, Silymarin (100 mg/kg) + CCl_4 ; Group IV, CAME (100 mg/kg) + CCl_4; Group V, CAME (200 mg/kg) + CCl_4; Group VI, CAME (300 mg/kg) + CCl_4.

3.2. Effect of Chenopodium album extract on liver enzyme activities in CCl_4 intoxicated rats

The levels of ALT, AST, and ALP showed notable increase in the serum samples of carbon tetrachloride administrated rats compared with normal control group (80 ± 14.9 U/L, 247.75 ± 24.9 U/L & 308.25 ± 5.62 U/L Vs 73.25 ± 8.34 U/L, 213.5 ± 12.92 U/L & 261 ± 14.97U/L respectively). Pre-treatment of *Chenopodiun album* methanolic extracts (100 mg/kg, 200 kg/kg & 300 kg/mg) for 28 consecutive days showed considerable decrease in the activity of alanine transaminase (70 ± 8.68 U/L, 68.75 ± 8.38 U/L & 73.5 ± 10.28 U/L respectively), aspartate transaminase (219.5 ± 19.16 U/L, 140.75 ± 13.35 U/L & 221.25 ± 13.33 U/L respectively) and alkaline phosphatase (289.5 ± 28.21 U/L, 258 ± 11.12 U/L & 248.25 ± 4.03 U/L respectively) in the rats with CCl_4 induced hepatotoxicity, as showed in Table 1.

3.3. Effect of Chenopodium album extract on lipid profile of serum in CCl_4 intoxicated rats

The level of triglycerides in carbon tetrachloride administrated rats decreased significantly as compared to normal control rats (33.25 ± 1.26 mg/dl Vs 91.5 ± 9.75 mg/dl respectively). The rat administrated with Silymarin and CAME (*Chenopodium album* methanolic extract) chronically, showed significant increase in the levels of triglycerides (Table 2). Medium dose (200 mg/kg) of CAME showed maximum increase in triglyceride level (64.75 ± 12.66 mg/dl). Low dose (100 mg/ kg) showed significant decrease in total cholesterol level as compared to CCl_4 intoxicated rats (42 ± 3.56 mg/dl Vs 49.25 ± 12.5 mg/dl respectively).

3.4. Effect of Chenopodium album extract on serum RFTs in CCl_4 intoxicated rats

Carbon tetrachloride elevated the level of urea and Creatinine as compared to normal control group. Positive control (silymarin), CAME 100 mg/kg and CAME 300 mg/kg reduced the level of urea (39 ± 4.76 U/L, 27.5 ± 6.61U/L & 18 ± 8.17 U/L respectively). The decrease in Creatinine in Group III (silymarin treated), Group IV (CAME 100 mg/kg treated) & group V (CAME 200 mg/kg treated rats) was observed as 0.425 ± 0.13 mg/dl, 0.425 ± 0.26 mg/dl & 0.467 ± 0.24 mg/dl respectively (Table 3).

3.5. Effect of Chenopodium album extract on hematological parameters in CCl_4 intoxicated rats

Chenopodium album methanolic extract showed slight increase in white blood cell count, red blood cell count and hemoglobin level as compared to carbon tetrachloride intoxicated rat group, as results shown in Fig. 2. Treatment of 100 mg/kg & 200 mg/kg CAME showed significant increase in WBC count as compared to CCl_4 intoxicated group (9.69×10^3 /Cu.mr & 10.59×10^3 /Cu.mr VS 8.88×10^3 /Cu.mr). Along with carbon tetrachloride, silymarin also showed decrease in WBC level (8.88×10^3 /Cu.mr & 8.61×10^3 /Cu.mr respectively). *Chenopodium album* Treatment of 100 mg/kg & 200 mg/kg CAME showed slight increase in RBC count as compared to CCl_4 intoxicated group (6.97×10^3 /Cu.mr & 7.54×10^3 /Cu.mr VS 6.76×10^3 /Cu.mr). Low, medium and high doses of *Chenopodium album* showed significant increase in hemoglobin level as 13.95 G/dL, 13.467 G/dL & 14.05 G/dL respectively.

3.6. Histopathological examination

After the dissection of rats, morphological changes were observed with naked eye, and liver images were captured as shown in supplementary Fig. 2. Histopathological examination detected

Table 1
Effect of *Chenopodium album* methanolic extract on biochemical parameters of CCl_4 damaged livers in rats.

Group	Treatment	AST (U/L)	ALT (U/L)	ALP (U/L)
Group I	Negative Control	213.5 ± 12.92	73.25 ± 8.34	261 ± 14.97
Group II	CCl_4 Treated	247.75 ± 24.9	80 ± 14.99	308.25 ± 5.62
Group III	Silymarin & CCl_4 Treated	189.5 ± 13.53	79.75 ± 9.91	229.75 ± 13.87
Group IV	100 mg/kg CAME & CCl_4 Treated	219.5 ± 19.16	70 ± 8.68	289.5 ± 28.21
Group V	200 mg/kg CAME & CCl_4Treated	140.75 ± 13.35	68.75 ± 8.38	258 ± 11.12
Group VI	300 mg/kg CAME & CCl_4Treated	221.25 ± 13.33	73.5 ± 10.28	248.25 ± 4.03

CAME: *Chenopodium album* methanolic extract, CCl_4: Carbon tetrachloride, ALT: Alanine transaminase, AST: Aspartate transaminase, ALP: Alkaline Phosphatase.

Table 2
Effect of *Chenopodium album* methanolic extract on cholesterol and triglycerides of CCl_4 damaged livers in rats.

	Group I Negative Control	Group II CCl_4 Treated	Group III Silymarin & CCl_4 treated	Group IV 100 mg/kg CAME & CCl_4 Treated	Group V 200 mg/kg CAME & CCl_4 Treated	Group VI 300 mg/kg CAME & CCl_4 Treated
Cholesterol (mg/dl)	32.75 ± 2.5	49.25 ± 12.5	48.75 ± 11.03	42 ± 3.56	63.75 ± 8.96	50 ± 23.48
Triglycerides (mg/dl)	91.5 ± 9.75	33.25 ± 1.26	44.25 ± 15	61.75 ± 17.15	64.75 ± 12.66	37.75 ± 18.61

CAME: *Chenopodium* album methanolic extract CCl_4: Carbon tetrachloride.

Table 3
Effect of *Chenopodium album* methanolic extract on renal parameters of CCl_4 damaged livers in rats.

	Group I Negative Control	Group II CCl_4 Treated	Group III Silymarin & CCl_4 treated	Group IV 100 mg/kg CAME & CCl_4 treated	Group V 200 mg/kg CAME & CCl_4 Treated	Group VI 300 mg/kg CAME & CCl_4 Treated
Urea (U/L)	37.25 ± 3.4	43.25 ± 6.6	39 ± 4.76	27.5 ± 6.61	48.25 ± 4.5	18 ± 8.17
Creatinine (mg/dl)	0.468 ± 0.19	0.500 ± 0.14	0.425 ± 0.13	0.425 ± 0.26	0.467 ± 0.24	0.525 ± 0.15

CAME: *Chenopodium* album methanolic extract CCl_4: Carbon tetrachloride.

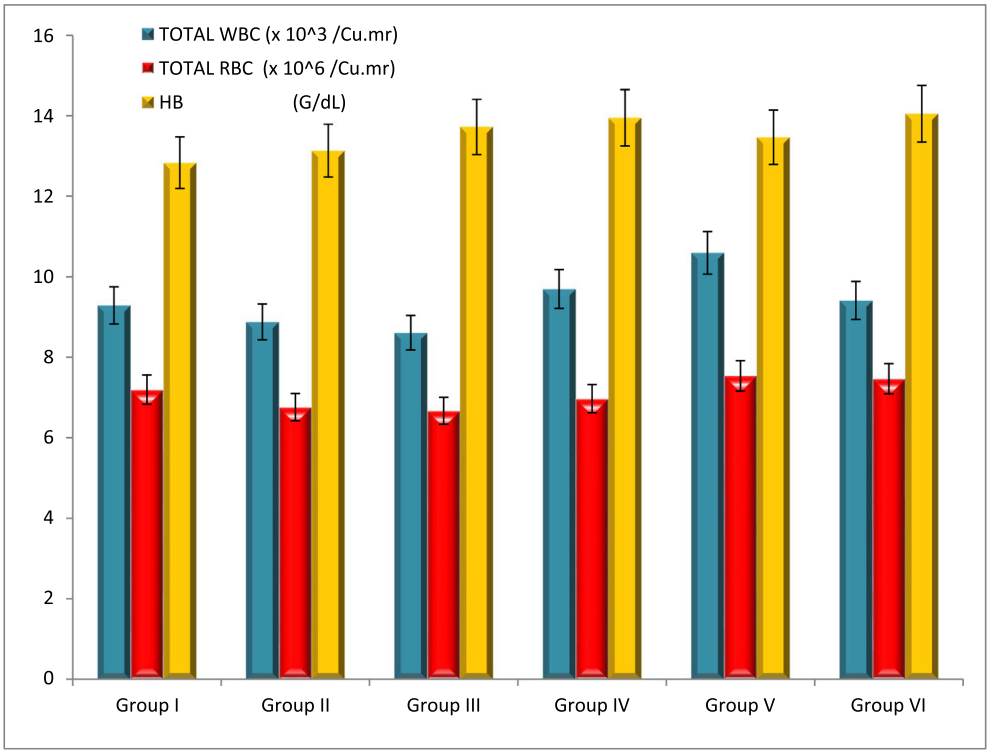

Fig. 2. Effect of *Chenopodium album* methanolic extract on hematological parameters Group I, Normal control; Group II, carbon tetrachloride intoxicated rats; Group III, CCl_4 + Silymarin (100 mg/kg); Group IV, CCl_4 + CAME (100 mg/kg); Group V, CCl_4 + CAME (200 mg/kg); Group VI, CCl_4 + CAME (300 mg/kg).

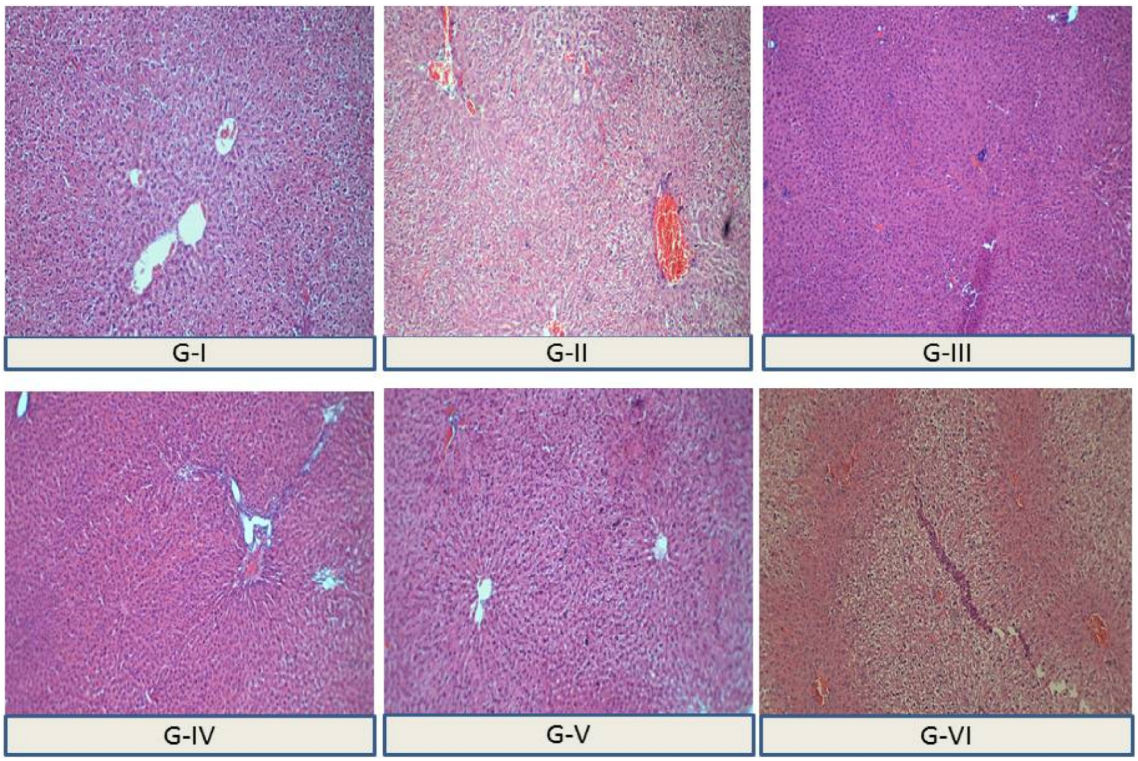

Fig. 3. Histopathological changes in all rat groups (10 X). G-I, Normal control; G-II, carbon tetrachloride intoxicated rats; G-III, CCl_4 + Silymarin (100 mg/kg); G-IV, CCl_4 + CAME (100 mg/kg); G-V, CCl_4 + CAME (200 mg/kg); G-VI, CCl_4 + CAME (300 mg/kg).CAME: *Chenopodium album* CCl_4: Carbon tetrachloride.

the evidences of liver damage in carbon tetrachloride intoxicated rats, particularly in hepatocytes, central vein and hepatic sinusoids. Low and medium doses of CAME improved the tissue, damaged by carbon tetrachloride as shown in Fig. 3.

4. Discussion

In this study, *Chenopodium album* methanolic extract is used for the protection of liver cells of selected rats against carbon tetrachloride induced toxicity. Different parameters were analyzed to assess the potential of *Chenopodium album* methanolic extract, and the extract accelerated the white blood cells & hemoglobin levels. The extract showed potential antioxidant capability and also lowered ALT, AST and ALP levels of serum, which indicated the hepatoprotective potential of the extract.

Hepatoprotective activity of *C. album* was primarily reported by Ma et al. (2020), the researchers isolated 23 tropolones derived compounds from *C. album*. Efficacy of tropolones was identified by using HepG2 cell line against H_2O_2 induced toxicity. In the results of the study, tropolones derived from EtOH extracted *Chenopodium album*, lowered the ALT (∼15.21 ± 1.18 to ∼20.29 ± 2.1 1 U/L) and AST (∼19.63 ± 2.34 to ∼29.87 ± 1.27U/L) levels against H_2O_2 induced hepatotoxicity. In the same manner our findings showed the protective potential of *Chenopodium album* in rat model. In the *In vivo* studies Alanine transaminase, Aspartate transaminase and alkaline phosphatase levels dropped by different concentrations of *Chenopodium album* methanolic extract against carbon tetrachloride.

Amodeo et al. (2019) examined the *In vitro* antioxidant activity of *Chenopodium album* methanolic extracts by β-carotene bleaching test and DPPH assay. *C. album* along with *Sisymbrium officinale* showed significant radical scavenging activity, and overall results verified our findings. In our studies, antioxidant activity was measured by DPPH assay at different concentrations; at 500 ul/g of concentration the maximum antioxidant activity was recorded at 517 nm absorbance.

In this study, hematological parameters were also focused, and CAME elevated the levels of white blood cells and hemoglobin. Although Positive control (Silymarin) shows hepatoprotective capabilities, but silymarin and its source (milk thistle) decline the level of white blood cells. Like many other authors, Jamalian et al. (2020) also reported the decrease in white blood cells due to silymarin. On the other hand, like other Chenopodium species CAME also showed distinct increase in white blood cells as well as hemoglobin because of its iron containing property.

Carbon tetrachloride has been used to expose liver and kidney damage in experimental animals. Carbon tetrachloride induced toxicity in kidney elevates the levels of urea and creatinine, while different doses of our extract decreased the levels of urea and creatinine. Jahan et al. (2019) worked on Sprague Dawley rats and reported that *Chenopodium album* decreased the levels of urea and creatinine in serum of rats, which also support our findings.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

Authors would like to acknowledge Department of Zoology, Government College University Faisalabad for providing research facilities and Department of Physiology for animals supply. Authors would like to extend their gratitude to the Chairperson

of Department of Zoology and team members of Muhammad Ali Laboratory for providing valuable suggestions.

References

Ali, S.A., Sharief, N.H., Mohamed, Y.S., 2019. Hepatoprotective Activity of Some Medicinal Plants in Sudan. Evidence-Based Complementary and Alternative Medicine 2019, 1–16.

Amodeo, V., Marrelli, M., Pontieri, V., Cassano, R., Trombino, S., Conforti, F., Statti, G., 2019. *Chenopodium album* L. and *Sisymbrium officinale* (L.) Scop.: Phytochemical Content and *In Vitro* Antioxidant and Anti-Inflammatory Potential. Plants 8 (11), 505.

Bansal, J., Kumar, N., Malviya, R., Sharma, P.K., 2014. Hepatoprotective Models and Various Natural Product Used in Hepatoprotective Agents: a Review. Pharmacogn. Commun. 4 (3).

Cutillo, F., Abrosca, B., Dellagreca, M., Marino, C.D., Golino, A., Previtera, L., Zarrellia, A., 2003. Cinnamic acid amides from *Chenopodium album*: effect on seed germination and plant growth. Phytochemistry 64, 1381–1387.

Cutillo, F., D'Abrosca, B., DellaGreca, M., Zarrelli, A., 2004. Chenoalbicin, a novel cinnamic acid amide alkaloid from *Chenopodium album*. Chem. Biodivers. 1 (10), 1579–1583.

De-torre, M.P., Cavero, R.Y., Calvo, M.I., Vizmanos, J.L., 2019. A Simple and a Reliable Method to Quantify Antioxidant Activity *In Vivo*. Antioxidants 8 (5), 142.

DellaGreca, M., Di Marino, C., Zarrelli, A., D'Abrosca, B., 2004. Isolation and phytotoxicity of apocarotenoids from *Chenopodium album*. J. Nat. Prod. 67 (9), 1492–1495.

Deshwal, N., Sharma, A.K., Sharma, P., 2011. Review on hepatoprotective plants. Int. J. Pharmacol. Res. 7, 15–26.

Gohara, A.A., Elmazar, M.M.A., 1997. Isolation of hypotensive flavonoids from Chenopodium species growing in Egypt. Phytother. Res. 11 (8), 564–567.

Jamalian, M., Mahmodiyeh, B., Saveiee, S., Solhi, H., 2020. Investigating the impact of silymarin on liver oxidative injury. Fam. Med. Prim. Care Rev. 9 (3), 1707–1711.

Lavaud, C., Voutquenne, L., Bal, P., Pouny, I., 2000. Saponins from *Chenopodium album*. Fitoterapia 71 (3), 338–340.

Kakadia, N.P., Amin, M.A., Deshpande, S.S., 2020. Hepatoprotective and antioxidant effect of *Adiantum lunulatum* Burm. F. leaf in alcohol-induced rat model. J. Complement. Integr. 17 (3).

Ma, Q.-G., Wei, R.-R., Zhang, X.-D., Sang, Z.-P., Dong, J.-H., Lu, Q.-X., Huang, H.-F., Guo, D.-M., Jiang, L., 2020. Tropolone derivatives with hepatoprotective and antiproliferative activities from the aerial parts of *Chenopodium album* Linn. Fitoterapia 146, 104733. https://doi.org/10.1016/j.fitote.2020.104733.

Michalopoulos, G.K., Bhushan, B., 2021. Liver regeneration: biological and pathological mechanisms and implications. Nat. Rev. Gastroenterol. Hepatol. Nat. Rev. 18 (1), 40–55.

Poonia, A., Upadhayay, A., 2015. *Chenopodium album* Linn: review of nutritive value and biological properties. J. Food Sci. Technol. 52 (7), 3977–3985.

Shahi, H.N., 1977. Studies on chemical composition of *Chenopodium album* L. Plant and Soil 46 (1), 271–273.

Trefts, E., Gannon, M., Wasserman, D.H., 2017. The liver. Curr. Biol. 27 (21), R1147–R1151.

Weber, L.W.D., Boll, M., Stampfl, A., 2003. Hepatotoxicity and mechanism of action of haloalkanes: carbon tetrachloride as a toxicological model. Crit. Rev. Toxicol. 33 (2), 105–136.

Zhao, Z.W., Chang, J.C., Lin, L.W., Tsai, F.H., Chang, H.C., Wu, C.R., 2018. Comparison of the Hepatoprotective Effects of Four Endemic Cirsium Species Extracts from Taiwan on CCl_4-Induced Acute Liver Damage in C57BL/6 Mice. International journal of molecular sciences, 19(5), 1329.Manco, R., & Itzkovitz, S. Liver zonation. J. Hepatol. 74(2), 466-468.

Zhou, M., Deng, Y., Liu, M., Liao, L., Dai, X., Guo, C., Zhao, X., He, L., Peng, C., Li, Y., 2021. The pharmacological activity of berberine, a review for liver protection. Eur. J. Pharmacol. 890, 173655.