Assessment of Eruca sativa Leaves Extract ZnO NPs Effect on the Adverse Effects of Creatine-Induced Liver Injury

Ashwaq Kadhem Obeid[1], Rawaa Hamid Abdulshahed[2], Tuqa Sabbar Rahi [3] Marwa Nasr Jawad [4], Hawraa Ahmed Hashim[3]

[1]Department of Biology, College of Education for Pure Sciences, University of Kerbala, Kerbala, Iraq.
[2]Directorate of Education of Kerbala, Ministry of Education, Kerbala, Iraq.
[3] College of Veterinary Medicine, University of Kerbala, Kerbala, Iraq.
[4]Quality Assurance and University Performance Department, University of Karbala, Karbala, Iraq.

Corresponding author: ashwaq.kadhem@uokerbala.edu.iq
rawaa.hamid@s.uokerbala.edu.iq , tuqa.s@uokerbala.edu.iq

Received:26/9/2025 **Accepted:** 25/11/2025 **Published:** 15/12/2025

***Abstract*— Treatment with medicinal plants occupied a large place in medical and pharmaceutical sciences and became a safe source for the pharmaceutical industry at the beginning of the current century, as attention was paid to using them in the programs of the World Health Organization (WHO) despite the great development in the fields of chemistry, pharmacy and the chemical drug industry, as it indicated Recent studies have shown the effect of medicinal plants as antioxidants, an alternative to medications and chemical treatments Creatine monohydrate supplements are among the most popular nutritional supplements in the world Creatine synthesis occurs naturally in the liver, kidneys, and pancreas using three amino acids: arginine, glycine, and methionine, to be stored within the skeletal muscles, which represents 95% of the total of this storage and can be found in the form of free creatine 40% or phosphorylated creatine 60%. Internally Creatine supplements have been used in bodybuilding. This study aimed to assess the anti-inflammatory effects of Eruca sativa leaves extract ZnO nanoparticles on the liver of male rats exposed to the to the high dose of Creatine. In this investigation, a total of 48 male rats were utilized. The research encompassed two experimental trials. The initial study involved 24 rats over a 30-day period to determine the optimal concentration of the zinc oxide nanoparticles of Eruca sativa. The concentrations used were 20, 40, and 60 mg/kg.BW., all of which were deemed safe for use. The second experiment aimed to assess the impact of the nano-extract at the chosen concentration (60 mg/kg.BW.) on the toxicity caused by creatine dosing (4 g/kg) over a 60-day period. The rats were divided into four groups:The experiment involved the administration of 1 ml of a physiological solution with a concentration of 0.09% (G1). According to the experimental protocol, the animals were administered a zinc oxide nanoparticle of Eruca sativa at a concentration of 60 mg/kg (G2). A dosage of creatine monohydrate (4 g/kg) was administered to the animals (G3). (G4): This group serves as the preventative group, and its animals were administered a zinc oxide nanoparticle of Eruca sativa at a dosage of 60 mg/kg, followed by a treatment of creatine at a dosage of 4 g/kg one hour later. the results of the study showed that there was no significant difference (P≥0.05) between the G2 and G1 in the AST, ALT and ALP. Respectively, an increase in AST, ALT and ALP was recorded in G3 compared to G1. The results of the histological results in the current study showed in G2 showed similarity to normal tissue, as it consists of a central vein and a regularity of the hepatic cords composed of polygonal hepatic cells and spherical nuclei with the presence of hepatic sinusoids. also did not notice any histological changes When compared with G1, G3 showed irregularity of the hepatic cords with slight dilatation of the central vein and congestion in the hepatic sinusoids with congestion in the central vein and the presence of slight degeneration of hepatic cells in some areas of the liver and necrosis of hepatic cells also showed infiltration of inflammatory cells compared to G1, G4 showed that The tissue is closer to normal, with regularity of the hepatic cords and a slight expansion of the sinusoids and the central vein compared to the group treated with creatine and G1. In conclusion, the results of this article revealed positive clinical and histopathological effects of Eruca sativa leaves extract ZnO NPs effect on the adverse effects of Creatine - induced liver injury.**

***Keywords* —** Eruca sativa, Creatine, Nano-zinc oxide, Liver injury.

INTRODUCTION

There is a growing trend among gym clients to incorporate nutritional supplements into their routines, often without the direct oversight of a healthcare professional. Furthermore, the out-of-control use of dietary supplements may also result in adverse health consequences, inclusive of changes in renal and liver feature. The examiner conducted by (1), encompassed a sample of 594 adults who engage in regular fitness center usage. The average age of the contributors changed into 37 ± 14 years, with 55.2% of them being girl. The research became carried out in a municipality situated inside the southern region of Brazil. A survey was performed with a purpose to check the usage of dietary supplements. A pattern of the look at population changed into assessed for indicators that suggest liver function, including aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP), as well as markers that indicate renal characteristic, including creatinine and urea. Binary logistic regression became implemented to the facts, considering changes for sex, training and age. The occurrence of nutritional complement intake was located to be 36. Zero%. Individuals who used the dietary supplements on the gym showed a better incidence of modifications in AST and urea tiers. These findings emphasize the importance of using nutritional dietary supplements efficaciously, specially under the steering of equipped professionals, to reduce ability risks.

It is normally stated that creatine monohydrate pills are a few of the most popular nutritional dietary supplements on a global scale (2). Although creatine dietary supplements have been first diagnosed in 1832, their trendy attractiveness and recognition did not arise until the Nineteen Nineties. This may be ascribed to the endorsement of two Olympic gold medalists who credited the use of creatine supplements as a contributing thing to their athletic accomplishments (3,4).

Following this, an enormous frame of studies has been undertaken to take a look at the effectiveness and safety of integrating a dietary routine that incorporates creatine supplementation. The motivation for this observes stemmed from preliminary apprehensions concerning the safety of utilizing those dietary supplements, which emerged in 1998 subsequent to the fatalities of three wrestlers who had ingested this complement for the duration of their aggressive education (Centers for Disease Control and Prevention 1997).

The impact of creatine supplementation at the liver tissue of seventy-two male albino rats become investigated in a look at performed by using, A dosage of five grams of creatine become supplied to the rats for periods of 1 week and 8 weeks. The findings of the observe indicated that the administration of creatine supplements led to a disturbance in hepatic feature. In the treated institution, there was proof of the infiltration of inflammatory leukocytes and the occurrence of liver necrosis. The presence of cell infiltration became located inside the portal canals, wherein those cells moved into necrotic liver lobules due to inadequate blood deliver (5). A fifty two-day examine became finished on a cohort of 59 male rats. The rats have been administered a creatine dose ranging from zero.1/2 to 0.05 mg/kg. The investigation discovered that the hepatic cells exhibited necrosis, observed by means of the presence of inflammatory cells and infiltration of mononuclear cells, resulting inside the growth of the sinusoids (6). The utilization of electron microscopy in the examination of the liver established that rats subjected to creatine treatment had larger hepatocytes, as well as a damaged endoplasmic reticulum and inflated mitochondria. The pattern contained fragmented organelles that had been surrounded by means of a membrane. Furthermore, a community improvement of droplets become found, comprising lipids of various sizes. The compactness of the nucleus turned into detected (7). Reactive radicals primarily target the liver, namely the parenchyma cells, which constitute the primary cellular component of the liver. These cellular entities are susceptible to oxidative stress resulting from hepatic damage (6).

Recent research has proven proof of the effectiveness of medicinal plants as feasible substitutes for conventional prescription drugs and chemical treatment options in phrases of antioxidant houses. Recent scientific studies have substantiated the therapeutic effectiveness of many botanical substances possessing antioxidant skills. Consuming end result has been shown to mitigate the severity of some diseases, mainly most cancers, and reduce the probability of chronic ailments in people. Medicinal vegetation possesses a mess of biologically energetic compounds, that have the potential to offer therapeutic benefits with ultimate efficacy and minimum damaging reactions. The identity of over 21,000 vegetation utilized globally for medicinal reasons in the control of many sicknesses and malignancies has been carried out by means of the World Health Organization (8,9).

Numerous botanical species possess highly powerful bioactive constituents that have notable therapeutic properties in both human and animal organisms. Numerous studies have demonstrated that the foliage of the watercress plant, for instance, exhibits a significant proportion. The composition of the substance comprises many bioactive compounds, namely proteins (36%), carbohydrates (28%), tannins (14.3%), glycosides (6%), saponins (7.4%) and alkaloids (11%). The moisture content in the leaves rises to around 90.7%. The increased amount of humidity positively impacts the reduction of detrimental chemical concentrations, specifically acid (10,11). The leaves possess erucic acid, a nutritional component that can be ingested by humans. Furthermore, the foliage also encompasses secondary metabolic byproducts, like flavonoids and phenols, which exhibit noteworthy biological properties (12,13).

The eruca sativa plant possesses medicinal homes that show off anti-inflammatory outcomes, rendering it a feasible therapeutic alternative for a range of ailments along with colitis, breathing tract infections, digestive gadget problems and diarrhea. The oil extract derived from watercress has been hired for the motive of promoting hair development and as a healing intervention for wounds and burns. Due to its antioxidant capabilities, it plays a vital role in protecting the liver from oxidative damage. The leaves of watercress have the capacity to mitigate the presence of free radicals due to their antioxidant properties (14,15).

A laboratory observe was carried out on male rats to take a look at the outcomes of antioxidants present within the Eruca

sativa plant on liver and kidney tissue that were subjected to xylene, a recognized hepatotoxic chemical. The administration of watercress extract containing xylene to a set of seventy rats led to huge development, as evidenced by way of a extensive discount in the concentrations of AST, ALP and ALT. Furthermore, there is a rise in the concentrations of GSH and an augmentation in GPx hobby, leading to the healing of these impairments to a nation that closely resembles the regular circumstance. The research findings indicated that the amelioration of toxicity become attributed to the antioxidant residences of Eruca sativa extract (16).

Studies research turned into undertaken to look at the outcomes of nano-zinc oxide at doses of 10 and 30 mg/kg B.W on rats that have been subjected to thiols, a substance identified for its capability to induce liver tissue harm. The findings of the studies indicated that the liver cords had usual characteristics, with moderate expansion and congestion determined in the sinusoids, in addition to decreased congestion inside the imperative vein. Moreover, the tissue displayed a heightened similarity to its inherent circumstance because of the uniform agency of the hepatic cords. The reduction of imperative venous congestion is finished thru a modest expansion of the sinusoids (17). This study aimed to assess the anti-inflammatory effects of Eruca sativa leaves extract ZnO nanoparticles on the liver of male rats exposed to the harmful effects of Creatine.

MATERIALS AND MTHODS

Operation with laboratories in of Al-Furat Al-Awsat Technical University. Ethical approval No. 151LBI04002. The male albino Wistar rats were utilized in this work. The conducted a study with a total of 48 rats, with weights ranging from 200-250 grams and ages ranging from 10-12 weeks. These rats were obtained from the animal house of the College of Pharmacy - University of Karbala. The study was conducted between January 11, 2022, and February 15, 2023.

The research encompassed two experimental trials. The initial step involved identifying the optimal concentration of the nano-extract derived from eruca sativa leaves (20, 40, 60 mg/kg) that yielded the highest efficacy, while ensuring safety for usage. The antioxidant activity of the nano-extract was assessed by measuring the levels of ALT, AST and ALP in the blood serum of rats. In the second experiment, the nano-extract was evaluated for its role in mitigating the toxicity caused by High dose of creatinine (4g/Kg), using a concentration chosen based on the results of the first experiment (60 mg/kg).

Experiment 1

The initial experiment employed a total of 24 adult male rats weighing between 200 and 250 grams. These rats were divided into four equal groups and administered doses for a duration of 30 days.

- The saline nutritional solution was administered to the control group at the time of the experiment.
- The initial group of participants was administered an oral dose of eruca sativa leaves extract ZnO nanoparticles (20 mg/kg) following its dissolution in 1 ml of distilled water.
- The second group of participants received an oral dose of eruca sativa leaves extract of ZnO nanoparticles (40 mg/kg) after dissolving it in 1 ml of distilled water.
- The oral administration of eruca sativa leaves extract ZnO NPs (60 mg/kg) was administered to the third extract group, following its dissolution in 1 ml of distilled water.

Experiment 2

According to the findings of the initial experiment, a dosage of 60 mg/kg of nano-zinc oxide extract derived from eruca sativa leaves was deemed appropriate for assessing its efficacy in mitigating hepatic, renal and reproductive toxicity induced by exposure to creatine monohydrate (4 g/kg) over a 60-day duration. The experimental animals were allocated into 24 adult rats, which were randomly assigned to four groups, each consisting of six individuals. The animals were treated according to the following protocol:

- Experimental group (G1): Throughout the experiment, a volume of 1 ml of a physiological solution with a concentration of 0.09% was administered.
- The experimental group (G2) received a single daily dose of ZnO NPs of eruca sativa leaves at a concentration of 60 mg/kg. The nano-extract was dissolved in 1 ml of distilled water.
- Creatine group: (G3) The animals received a single daily dose of creatine monohydrate (4 g/kg) after dissolving it in 2 cc of distilled water.
- The experimental group (G4) received a single daily dose of ZnO NPs of eruca sativa leaves as a preventive measure. The animals in this group were administered a nano-extract of watercress at a concentration of 60 mg/kg, which was dissolved in 1 ml of distilled water. One hour later, a dose of creatine was administered. 4 grams per kilogram after being dissolved in 2 milliliters of distilled water.

Preparation of Plant Extract

The plant extract was prepared following a (18) method, with some modifications made. Using fresh watercress leaves from the markets, the leaves were carefully collected and washed with tap water to remove any dirt. Afterward, the samples were rinsed multiple times with distilled water, dried in a shaded area, and then finely ground using an electric grinder to obtain the powder is carefully sifted and stored in a container away from direct sunlight. Measure out 5 grams of the substance and carefully transfer it into a glass beaker. Then, pour 400 milliliters of distilled water into the beaker. Continuously stir and let it sit for 12 hours. After that, it undergoes filtration using multiple layers of gauze. The solution is collected and placed in test tubes, just like a materials scientist would do. For the centrifuge device operating at a speed of 1200 rpm. To eliminate any remaining biological materials and fibers, the filtrate is carefully dried in an oven at a temperature of 40 degrees Celsius. This process results in the formation of a greenish-brown powder, which is then stored in an opaque glass bottle at a low temperature.

Preparation of Nano-zinc Oxide Extract

The synthesis of zinc oxide nanoparticles was conducted

following the methodology outlined in (19), with some modifications. The experimental protocol entailed the introduction of 6 grams of aqueous extract powder into a 500-milliliter glass beaker containing 100 milliliters of distilled water. Subsequently, 0.1 grams of zinc acetate were added to the mixture. In order to attain a pH 7, it is necessary to introduce diluted ammonia into every 100 ml of solution by means of continuous stirring using a magnetic stirrer set at a speed of 200 revolutions per minute. The procedure should be maintained at a temperature of 37℃ for a duration of 24 hours, or until the color transitions from a light green hue to a darker shade of green. The purification of the solution was enhanced through the process of filtering with No. 1 (Whatman) filter paper. Following this, the impurities were separated using the process of centrifugation, which involved rotating the mixture at a speed of 4500 revolutions per minute for a period of 30 minutes. Subsequently, the sediment obtained was subjected to two thorough rinses using distilled water, followed by drying at a temperature of 50 degrees Celsius. Zinc oxide nanoparticles are synthesized using an oven, resulting in the formation of a gray powder.

Statistical Analysis

Using the t-test and a significance threshold of ($P \leq 0.05$), the statistical tool Graph Pad Prism 8.0 was utilized. The information was displayed as mean ± SD.

Result and Discussion

The results of the study showed in Table (1) that there was no significant difference ($P \geq 0.05$) between the eruca sativa leaves extract ZnO NPs (60mg/kg) group in the AST, ALT and ALP compared to Control. And showed increase in AST, ALT and ALP was recorded in Creatine (4 gm/kg) group compared to Control. Also showed significant decrease in level ALT and ALP compared to Creatine (4 gm/kg) group.

Table 1. The protective role of nano-extract of Eruca sativa (60 mg/kg) against creatine-induced toxicity on liver enzymes in male albino rats.

Group	AST	ALT	ALP
Control	106.76 ± 2.17 B	10.00 ± 1.54 C	158.00 ±3.40 C
eruca sativa leaves extract ZnO NPs (60mg/kg)	102.25 ± 3.04 B	9.80 ± 0.67 C	165.17 ± 4.75 C
Creatine (4 gm/kg)	116.00 ± 3.40 A	21.10 ± 1.06 A	244.00 ±11.29 A
eruca sativa leaves extract ZnO NPs (60mg/kg)+ Creatine (4 gm/kg)	112.66 ± 6.62 A	16.20 ± 3.37 B	214.00 ± 1.46 B
LSD	5.0198	2.3597	7.7193

Histopathological Examination

The histological abnormalities observed in the liver tissue of male rats were determined using microscopic inspection in our present investigation.

The histological sections of the control group, as depicted in Figure (1), exhibited a typical histological composition. The examination revealed the presence of conventional hepatocytes and the arrangement of hepatic cords towards the central region of the lobule housing the central vein. Additionally, the cells displaying polyhedral shapes exhibited acidic cytoplasm. Some hepatic cells have eosinophilic and spherical nuclei, with the presence of many nuclei. These nuclei are interspersed with sinusoids, which are arranged towards the central vein.

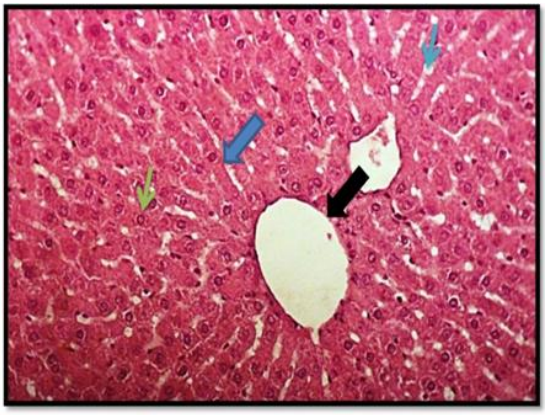

Figure 1. A cross-section of the rat liver tissue of the G1. It is noted that there is a normal central vein (←) and the organization of the hepatic cords ( ) and the liver cells and their nuclei ( ) with the presence of normal sinusoids (→) (E & H 200X).

The liver of rats that were administered a nano-extract of eruca sativa leaves at a dosage of 60 mg/kg exhibited histological characteristics that were comparable to those of normal tissue. These characteristics included the presence of a central vein and a regular arrangement of hepatic cords composed of polygonal hepatic cells and spherical nuclei, along with the existence of hepatic sinusoids. No histological alterations were seen in comparison to the control group. Figure 2.

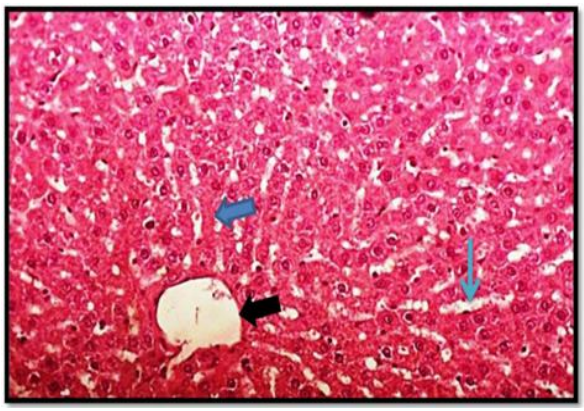

Figure 2. A cross-section of rat liver tissue in the group treated with nano-extract of eruca sativa leaves (60 mg/kg), in which

the presence of a normal central vein ( ) and regularity of the hepatic cords ( ) are noted, with the presence of sinusoids ( ) (E & H 200X).

The liver of rats in the third group, which were administered a dosage of creatine (4 g/kg), exhibited histological findings. These findings included irregularities in the hepatic cords, slight dilation of the central vein, congestion in the hepatic sinusoids, and the presence of slight degeneration of hepatic cells in certain regions of the liver. Additionally, necrosis of hepatic cells was observed, accompanied by the infiltration of inflammatory cells. Figure (3,4).

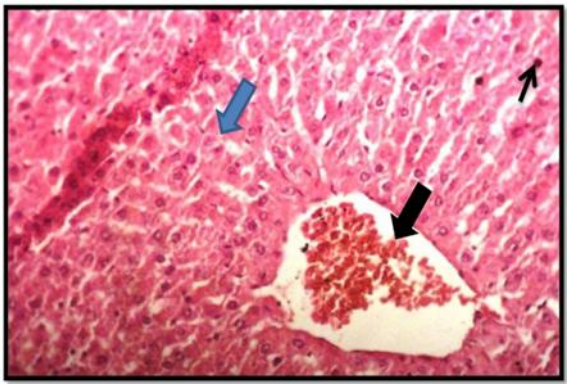

Figure 3. A cross-section of rat liver tissue in the group treated with creatine (4 g/kg) , in which congestion and dilatation of the central vein ( ), severe irregularity of the hepatic cords ( ), and necrosis of hepatic cells ( ) (E & H 200X).

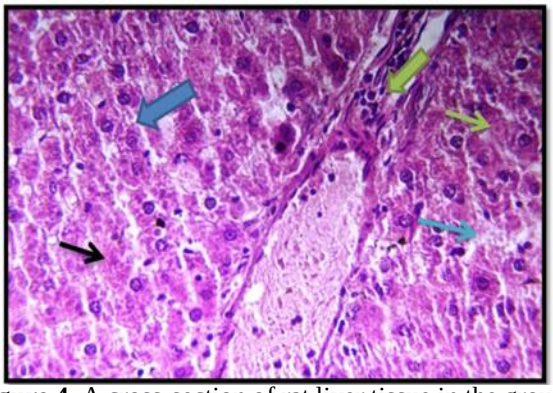

Figure 4. A cross-section of rat liver tissue in the group treated with creatine (4 g/kg), showing infiltration of inflammatory cells ( ), and severe irregularity of the hepatic cords ( ), with expansion and congestion of the hepatic sinusoids ( ), and necrosis of the hepatic cells ( ) With hepatocellular degeneration ( ) (E & H 400x).

In the present investigation, Figure (5) depicts a segment of the hepatic tissue within the cohort that received a dosage of 60 mg/kg of eruca sativa leaf nano-extract in conjunction with 4 g/kg of creatine. The hepatic cords have a higher degree of regularity, while the sinusoids and central vein display a modest enlargement.

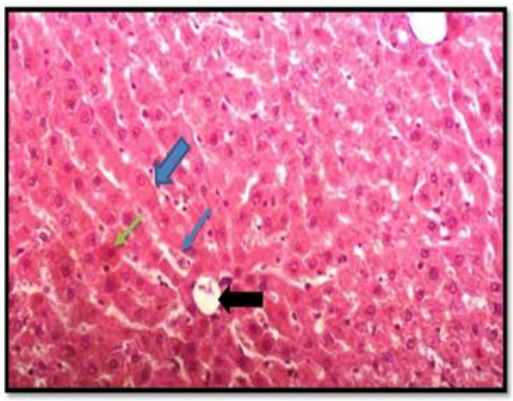

Figure 5. A cross-section of rat liver tissue in the preventive group treated with nano-extract of eruca sativa leaves (60 mg/kg) with creatine (4 g/kg). It is noted that the tissue is closer to normal with a normal central vein ( ) and regularity of the hepatic cords ( ) and liver cells and their nuclei ( ) with sinusoids ( ) (E & H 200X) .

The observed increased levels of liver enzymes in the experimental group treated with creatine were consistent with a previous investigation conducted by (5) involving 72 male albino rats that were administered a dosage of 5 grams of creatine for periods of one and eight weeks. The researchers made the observation that the administration of creatine supplements had a significant effect on liver tissue, leading to a disturbance in liver function. The presence of free radicals induces oxidative stress, which then leads to an increase in the levels of ALT, ALP, and AST, ultimately resulting in lipid peroxidation. The effectiveness of the enzymes indicated above can be improved as a result of the breakdown of hepatic cells. The occurrence of hepatocellular injury results in the enhanced release of these enzymes in comparison to the typical state, and the release and efficacy of these enzymes escalate in direct correlation with the extent of the injury. Liver disease has the potential to result in an elevation of various liver disorders and diseases, along with the liberation of these enzymes into the circulatory system, hence posing a risk of toxicity (16, 21).

The increase in these enzymes within the serum is ascribed to the destruction of cellular membranes, leading to their subsequent release into the circulatory system. The enzymes ALT and AST, which can be involved in the transfer of amino companies, are at once linked to hepatic activities. As a end result, the quantity of those substances in the bloodstream serves as a reliable indicator of the overall functioning of the frame's organs, with a unique emphasis at the liver. The frequent distribution of the 2 enzymes is determined in the liver, heart, skeletal muscle groups, crimson blood cells and kidneys (21). The size of the ALP enzyme content material inside the bloodstream offers large insights into the physiological functioning of the body's organs, with a particular emphasis at the liver. Cholangiocytes, that are regularly seen within the intrahepatic bile ducts, as well as inside the bone and placenta, incorporate this enzyme (22).

The found decrease in liver enzyme pastime in the group that acquired watercress extract A (referred to as the preventive organization) in evaluation to the creatine institution may be

attributed to the preventive plant's capacity to guard liver cellular membranes from oxidative damage and promote the removal of unfastened radicals. The located reduction can be ascribed to the anti-inflammatory traits of the bioactive compounds covered on this botanical specimen, which efficaciously inhibit the proliferation and unfold of inflammatory cells. In addition, the leaves comprise bioactive chemicals, especially erucin and erysolin, as well as phenols, which exhibit hepatoprotective consequences through the facilitation of liver cell regeneration and reduction of liver enzymes (16,23,24).

The results of our current inquiry align with a prior analysis (25) that analyzed a sample of 72 male rabbits. The objective of this study was to evaluate the influence of nano-zinc characteristics on different organs and their associated parameters. The findings demonstrated a beneficial impact on hepatic enzymes, which can be ascribed to the participation of zinc in many biochemical processes and physiological functions. Zinc has a crucial role in facilitating the optimal functioning of structural proteins, hormones and enzymes that are required for the processes of growth and differentiation.

In this investigation, albino Wistar rats were utilized as subjects to assess the impact of antioxidants found in the Eruca sativa plant on liver and kidney tissue that had undergone damage due to xylene, a well-documented hepatotoxic and nephrotoxic substance. Seventy rats were administered a watercress extract containing xylene, resulting in a notable decrease in the concentrations of creatinine, ALP, AST , MDA, uric acid and urea. Furthermore, an increase in glutathione levels and an augmentation in the activity of glutathione peroxidase are observed, and these deficiencies ultimately revert to a state that closely resembles the typical condition. The findings indicate that the antioxidant capabilities of the Eruca sativa extract were responsible for reducing the toxicity (16).The findings of a research conducted by (26) indicate that the administration of a 250 mg/kg aqueous extract of watercress leaves to white rats, both prior to, during, and following exposure to oxidative stress caused by the pesticide malathion, led to notable improvements in the blood parameters analyzed, as well as enhancements in the organization and structure of the liver, kidney, and thyroid gland tissues. A significant increase in several parameters, such as total body weight, relative thyroid weight, T3.74 hormone concentration, catalase levels, albumin levels, high-density lipoprotein concentration in blood serum, hemoglobin levels, red blood cell count, packed blood volume, and lymphocyte count, was observed when comparing the experimental group with the positive control group that received malathion treatment. A significant decrease in the concentrations of thyroid-stimulating hormone, liver function enzymes (ALP, ALT, AST), as well as urea, creatine, and MDA was observed in the group treated with malathion, in comparison to the control group. When comparing the group that had malathion treatment.

The liver assumes the principal role in the metabolic process of detoxification, wherein the body engages in the elimination of a substantial amount of harmful substances through the breakdown of unwanted compounds (27).

Histological analysis of the cohort subjected to zinc oxide nano-extract of watercress yielded comparable findings to those observed in the control group. The results are consistent with a prior investigation (16) that assessed the effectiveness of watercress leaf extract on 70 egg-laying rats subjected to xylene, a substance that caused harm to the liver and kidneys. The research findings indicate that the extract derived from watercress leaves had the capacity to mitigate liver damage induced by the bioactive compounds present in the plant. The liver tissue exhibited a restoration of its typical structure, notable absence of degeneration, and consistent arrangement of the hepatic cords.

E. sativa extract may have hepatoprotective effects by inhibiting the cytochrome P450 oxygenase enzyme system (28). Nevertheless, research has demonstrated that glucosinolates undergo conversion into isothiocyanates, thereby initiating the activation of metabolic enzymes that play a vital role in detoxification and the protection against stress. Oxidative Glucosinolate A is characterized by the presence of a sulfur compound that encompasses electron-donating S-S bonds. These bonds play a crucial role in promoting the liberation of molecules that possess the ability to hydrolyze hydroperoxides, such as alkyl hydroperoxides, H_2O_2 and other free radicals (29).

CONCLUSION

Nano-extract of eruca sativa leaves lead to protective role to histopathological and clinical improvements in the liver rats dosed with creatine

Acknowledgments

The authors thank the College of Education for pure sciences, University of Karbala, Karbala, Iraq.

Conflict of interest

The authors declare that there is no conflict of interest.

REFERENCES

1) Schlickmann, D. S., Molz, P., Brand, C., Dos Santos, C., da Silva, T. G., Rieger, A., ... & Franke, S. I. R. (2022). Liver and kidney function markers among gym users: the role of dietary supplement usage. British Journal of Nutrition, 128(4), 704-711.

2) Gualano B, Artioli GG, Lancha Junior AH. Suplementação de creatina e metabolismo de glicose: efeitos terapêuticos ou adversos? Revista Brasileira de Medicina do Esporte 2008;14:478.842.

3) Anderson, O. Creatine propels British athletes to Olympic gold medals: Is creatine the one true ergogenic aid. Run. Res. News 1993, 9, 1–5.

4) Hansson, G.K.; Robertson, A.K.; Söderberg-Nauclér, C. Inflammation and atherosclerosis. Annu. Rev. Pathol. 2006, 1, 297–329. [CrossRef]

5) Souza RA, Miranda H, Xavier M et al. Effects of high-dose creatine supplementation on kidney and liver responses in sedentary and exercised rats. J Sports Sci Med 2009;8: 672–81.

6) Tarnopolsky, M. A., J. M. Bourgeois, R. Snow, S. Keys, B. D. Roy, J. M. Histological assessment of intermediate-

and long-term creatine monohydrate supplementation in mice and rats. Kwiecien, and J. Turnbull.(2003) Am J Physiol Regul Integr Comp Physiol 285: R762–R769, 2003; 10.1152/ajpregu.00270.200

7) Wyss M and Kaddurah-Daouk R. (2000)Creatine and creatinine metabolism. Physiol Rev 80: 1107–1213.

8) Jamshidi-Kia, F., Lorigooini, Z., & Amini-Khoei, H. (2017). Medicinal plants: Past history and future perspective. Journal of herbmed pharmacology, 7(1), 1-7.

9) Am Ende, D. and am Ende, M. T. (2019). Chemical engineering in the pharmaceutical industry: an introduction. Chemical Engineering in the Pharmaceutical Industry: Drug Product Design, Development, and Modeling, 1-17.

10) Khoobchandani; M., Ojeswi; B.K., Ganesh; N., Srivastava; M.M., Gabbanini; S., Matera; R., Iori; R. and Valgimigli; L. (2010).

11) Muhammad Muhammad, Wajih Younis, and Abdullah, Muhammad Hamid (2013). Extracting and separating some active compounds in watercress and studying their biological effectiveness. Anbar University Journal of Pure Sciences. Volume 7. Issue 3.

12) Aabdul-jabbar RS (2018) Polyphenol and Flavonoid Contents and Antioxidant Activity in Freshly Consumed Rocket (Eruca sativa). IOP Conf. Series: Materials Science and Engineering 454 012158. https://doi.org/10.1088/1757-899X/454/1/01215.

13) AL-Musawi, R. S., Ali, A. H., Al-Majdi, K., & Al Gayar, S. (2022). Development of a convolutional neural network joint detector for non-orthogonal multiple access uplink receivers. EUREKA: Physics and Engineering, (4), 170-178.

14) Barlas, N.; T.; Irget, M.; E and Tepecik, M, (2011). Mineral content of the rocket plant (Eruca sativa). African J. of Biotechnology, 10(64): 14080- 14082.

15) Alam, M.; S.; Kaur, G.; Jabbar, Z.; Javed, K and Athar, M, (2007). Eruca sativa seeds posess antioxidant activity and exerta protective effect on mercuric chloride induced renal toxicity. Food Chem Toxical.; 45(6): 910-920.

16) Boukarine, R., Hamdi, L., & Khelili, K. (2023). Therapeutic Effects of Rocket Leaves (Eruca sativa) against Hepato-Renal Toxicity Caused by Xylene in Wistar Rats. Pakistan Journal of Zoology, 55(3).

17) Daoud, N.M., Aly, M.S., Ezzo, O.H. et al. Zinc oxide nanoparticles improve testicular steroidogenesis machinery dysfunction in benzo[α]pyrene-challenged rats. Sci Rep 11, 11675 (2021). https://doi.org/10.1038/s41598-021-91226-y

18) Hernandez, M ; Lopez, R. ; Abanas, R.M.;V. and Arias, A.(1994).Antimicrobial activity of visnea mocanera leaf extracts.J.Ethno pharma cology,41;115-119.

19) Upadhyaya, H., Shome, S., Sarma, R., Tewari, S., Bhattacharya, M.K., Panda, S.K.,(2018). Green synthesis, characterization and antibacterial activity of ZnO nanoparticles. Am. J. Plant Sci. 9, 1279–1291.

20) Schilling, B.K., Stone, M.H., Utter, A., Kearney, J.T., Johnson, M., Coglianese, R., Smith, L., O'bryant, H.S., Fry, A.C., Starks, M., Keith, R. and Stone, M.E. (2001). Creatine supplementation and health variables: a retrospective study. Medicine and Science in Sports and Exercise 33, 183-188.

21) Bennett, J. & plum, F. (1996). Textbook of Medicine. 20th Ed., 1, W. B. Saunders company Philadelphia. P. 610.

22) Ramos-Tovar, E., & Muriel, P. (2020). Free radicals, antioxidants, nuclear factor-E2-related factor-2 and liver damage. Journal of Applied Toxicology, 40(1), 151-168.

23) Bajilan, S. I. (2011). Effect of the aqueous extract of rocket (Eruca sativa L.) leaves on the histological structure of some organs in male mice. Journal of the college of basic education, 17(70), 13-21.

24) Lamy,E.;Shoder,J.;Paulus,S.;Brenk,P.;Stahi,T.andSa ndermann,V.M.(2008).Antigenotoxic proprieties of Eruca sativa (Rocket plant),erocin and erysolin in human hepatoma (HePG2) cells towards benzo(a)pyrene and their mode of action .Food and Cham.Toxicol.46(7):2415-24210.

25) Abdel-Wareth, A. A., Al-Kahtani, M. A., Alsyaad, K. M., Shalaby, F. M., Saadeldin, I. M., Alshammari, F. A., ... & Ahmed, A. E. (2020). Combined supplementation of nano-zinc oxide and thyme oil improves the nutrient digestibility and reproductive fertility in the male Californian rabbits. Animals 10 (12): 2234.

26) Kamush Safa,M.(2014). The effect of aqueous extract of Eruca sativa leaves on thyroid functions and some physiological parameters in male albino rats treated with malathion. University of Al-Qadisiyah, College of Education. M. S. Thesis.

27) Guyton, A. C.; and Hall, J. E. (2001). Reproductive and hormonal function of male (and the pineal). In: Texbook of medical physiology.Guyton, A.C., and , Hal , J. E(eds) 1st ed Aharcourt Publishers International company, philadephia,London-Toronto-Montreal-SydneyTokyo.:1003-1015.

28) Hanlon, N., Coldham, N., Sauer, M.J. and Ioannides, C., 2008. Up-regulation of the CYP1 family in rat and human liver by the aliphatic isothiocyanates erucin and sulforaphane. Toxicology, 252: 92–98. https:// doi.org/10.1016/j.tox.2008.08.002.

29) Barillari, J., Canistro, D., Paolini, M., Ferroni, F., Pedulli, G.F., Iori, R. and Valgimigli, L., 2005. Direct antioxidant activity of purified glucoerucin, the dietary secondary metabolite contained in rocket (Eruca sativa Mill.) seeds and sprouts. J. Agric. Fd. Chem., 53: 2475–2482. https://doi.org/10.1021/ jf047945a.