Research Article

PROCEEDING OF 9TH INTERNATIONAL SCIENTIFIC CONFERENCE, COLLEGE OF VETERINARY MEDICINE UNIVERSITY OF BASRAH, NOV. 6-7, 2024, IRAQ.

BASRAH JOURNAL OF VETERINARY RESEARCH, 2025, 24(S1):32-44.
https://bjvr.uobasrah.edu.iq/

Assessment of Nanosilymarin's Therapeutic Efficacy in Mitigating CCl4-Induced Hepatotoxicity in Rats

Nisreen Yasir Jasim, Rashad Fadhil Ghadhban.
Department of Physiology, Pharmacology and Biochemistry, College of Veterinary Medicine, University of Basrah, Iraq.

Corresponding Author Email Address: pgs.nisreen.yasir@uobasrah.edu.iq
ORCID ID: https://orcid.org/0000-0002-5792-1199
DOI: https://doi.org/10.23975/bjvr.2025.155288.1159

Received: 20 Nov. 2024 Accepted: 16 May 2025

Abstract

Drug and chemical substances are common causes of liver dysfunction, including acute hepatitis and liver failure. Carbon tetrachloride (CCl4) is widely used as a model to study hepatic toxicity. Nanosilymarin (S-CsNPs), with its antioxidant properties, has emerged as a potential therapeutic agent for liver injury. This study aims to evaluate the therapeutic effect of (S-CsNPs) on hepatotoxicity. The study involved 30 adult female albino rats, randomly divided into five groups. The first group served as the negative control and received no treatment. The second group received carbon tetrachloride (CCl4) intraperitoneally at a dose of 3 mL/kg twice weekly for four weeks. The third group was the untreated group, which also received CCl4 as described but did not receive any subsequent treatment. The fourth group was treated with silymarin at a dose of 50 mg/kg, administered orally once daily for three weeks following CCl4 exposure. The fifth group received (S-CsNPs) at a dose of 1 mg/kg, administered orally once daily for three weeks after CCl4 administration. Liver function was assessed via enzyme markers (ALT, AST, ALP, GGT, and bilirubin), and oxidative stress was evaluated by measuring TNF-α, MDA, SOD, and GSH levels. The CCl4 group showed significant elevations in liver enzymes and oxidative stress markers compared to negative controls. Treatment with (S-CsNPs) significantly($P<0.05$) reduced ALT, AST, ALP, GGT, bilirubin, TNF-α, and MDA levels, while increasing SOD and GSH levels compared to CCl4, untreated and silymarin-treated groups. Nanosilymarin effectively reduced CCl4-induced liver damage, indicating its potential as a liver-protective agent.

Keywords: Silymarin, CCl4, hepatotoxicity,nanosilymarin, liver.

Introduction

One significant cause of liver dysfunction is drug-induced liver injury (DILI), which can manifest a wide range of symptoms, from mild and non-specific indicators like asymptomatic transaminitis to severe conditions such as acute hepatitis, chronic hepatitis, cholestasis, and liver failure. DILI can result from various prescription medications, herbal remedies, and dietary supplements, often leading to the withdrawal of the offending drug from the market)1,2). Liver injury induced by carbon tetrachloride (CCl4) is a widely used model for studying hepatic toxicity and its underlying mechanisms. Exposure to CCl4 can lead to various negative effects on liver function, resulting in conditions ranging from mild transaminitis to severe liver failure. In this context, nanosilymarin emerges as a promising therapeutic agent due to its antioxidant properties and potential protective effects. This study aims to assess the therapeutic efficacy of nanosilymarin in mitigating the toxic effects associated with CCl4 exposure. The research hopes to explore the therapeutic potential of nanosilymarin as a safe and effective option for addressing hepatic toxicity, contributing to the development of new therapeutic strategies for liver diseases.

Materials and Methods

The Silymarin (Milk Thistle P.E.) utilized in this study was procured from Xi'an Natural Field Bio-Technique Co., Ltd, China. Chitosan was obtained from Sigma-Aldrich, Germany. Sodium Carboxymethylcellulose powder (CMC-Na) was obtained from BDH Chemical Limited, Poole, England. Carbon Tetrachloride (CCl4) was supplied by Shanghai Macklin Biochemical Co., Ltd, China. Diagnostic kits for assessing serum levels of various parameters were sourced from FUJIFILM, Japan.

Preparation of Nanosilymarin

The nanosilymarin was prepared by silymarin loaded on chitosan using the ionic gelation method, and the necessary tests such as UV-Visible spectroscopy, Fourier transformation infrared spectroscopy (FTIR) (Shimadzu, Japan), Scanning Electron Microscope (SEM), Atomic Force Microscopy (AFM) and X-ray diffraction (XRD) were performed to confirm its characteristics in the Ministry of Science and Technology, Directorate of Environment and Water in Iraq As previously described in my published study in Frontiers in Health Informatics Journal (3).

Animals Management

The study was conducted at the College of Veterinary Medicine, University of Basrah, in the animal house of the Department of Physiology. A total of 30 adult female albino rats (*Rattus rattus*), weighing approximately 200 ± 20g and aged 8 to 10 weeks, were used. Prior to the experiment, the rats underwent a two-week adaptation period. They were housed in groups of six in individual plastic cages measuring 15x35x50 cm. The animals were provided with a standard pellet diet from the Institute for Public Accuracy, available *ad libitum*, and had unrestricted access to water. The rats were maintained under controlled environmental conditions,

with a temperature of 22-25°C and a 12-hour light-dark cycle.

Experimental Groups Assignments:

1. Negative Control Group: No treatment or exposure to CCl4.

2. CCl4 Group: Rats will receive CCl4 injections (two doses per week) via intraperitoneal (i.p.) route for 4 weeks.

3. Untreated Group: Rats will receive CCl4 injections under the same protocol as the CCl4 group and will be left untreated.

4. Silymarin Treated Group: Rats will receive CCl4 injections (two doses per week) via intraperitoneal (i.p.) route for 4 weeks, followed by oral administration of free silymarin 50 mg/kg daily for 3 weeks.

5. Nanosilymarin Treated Group: Rats will receive CCl4 injections (two doses per week) via intraperitoneal (i.p.) route for 4 weeks, followed by oral administration of nanosilymarin 1 mg/kg daily for 3 weeks.

Procedure for Inducing Hepatotoxicity Using CCl4:

CCl4 Standard Volumetric Solution, Molecular Weight (MW): 153.82 g/mol, Purity: HPLC ≥ 99.0% from Shanghai Macklin Biochemical Co., Ltd, China was administrated following the protocol established by (4), CCl4 (30% solution dissolved in olive oil) will be administered via intraperitoneal injection (i.p.) at a dosage of 3 ml/kg body weight (Twice doses/week for 4 weeks).

Treatment of Silymarin and Nanosilymarin (S-CsNPs):

Silymarin was administered at a dosage of 50 mg/kg body weight, prepared as described by (5), by dissolving it in a 0.5% sodium carboxymethyl cellulose (CMC-Na) solution to form a suspension. The Nanosilymarin (S-CsNPs) that was prepared as previously described in my published study (3) was followed. Dosage: 1 mg/kg. Both treatments (Silymarin and S-CsNPs) will be administered orally via gavage once daily for 3 weeks, following the CCl4 intoxication period.

Blood samples collection

At the end of the experiment, 24 hours after the last dose administration, the rats were anesthetized with chloroform. Blood was collected by cardiac puncture using a 5 ml disposable syringe according to the method of (6). The collected blood was placed in gel tubes and centrifuged for 20 minutes at 1000 rpm to extract the serum then moved to Eppendorf tubes and kept at -20°C for biochemical analysis.

Biochemical Analysis

Conducting Tests Using the Auto Analyzer, the DRI-CHEM system from FUJIFILM, following the manufacturer's guidelines.

Liver Enzyme assessment:

Liver function markers were measured by assessing liver enzymes (ALP, ALT, AST ,and GGT) and total bilirubin (7).

Principle: DRI-CHEM NX500:

DRI-CHEM from FUJIFILM was a dry chemistry analyzer that can perform multiple test parameters of Clinical Chemistry. It had

a built-in auto-pipetting system that required no calibration and no water, providing easy preparation and maintenance. The new DRI-CHEM NX500 delivers results using a simple 3-step procedure. It's a quick and easy operation. The main principle of dry chemistry is based upon the reflectance spectrophotometry. In dry chemistry, slides are dry, multilayered analytical elements coated on polyester supports. A small amount of sample is deposited onto the slide and evenly distributed to all of the layers. The spreading layer contains the appropriate substrate and other components needed for the reaction. The analyte in the sample catalyzes the reaction sequence to yield products that absorb light at wavelengths in various regions (340 – 680nm), diffuse into the underlying layer, was monitored by reflectance spectrophotometry. The test types were colorimetric, enzymatic endpoint, two-point or multi-point rate, or potentiometric. The rate of change in reflection density is converted to the enzymatic activity or the amount of colored complex formed which is proportional to the analytic concentration in the sample (8).

Hepatic Oxidant markers and Anti-Oxidant Parameters

The levels of TNF-α, SOD, GSH, and MDA were measured using commercially available ELISA assay kits from Wuhan Fine Biotech Co., Ltd, China. The specific catalog numbers for each kit are (TNF-α: Cat. No. EH0302, SOD: Cat. No. EH4706-1, GSH: Cat. No. EU2547, MDA: Cat. No. EH4174) All assays were performed according to the manufacturer's instructions of (Fine. Test. China). ELISA System, microplate reader system (Paramedical, Italy) and Washer (Biokit, USA)the main instruments were used in these tests.

Statistical analysis

The Statistical Package for the Social Sciences (SPSS, version 11.0) was used to analyze the data. A one-way ANOVA with LSD post hoc analysis was employed to determine significant differences between group means (9).

Results

Liver enzymes

The Results illustrates the effects of nanosilymarin (S-CsNPs) on liver enzyme levels in female rats subjected to CCl4-induced hepatotoxicity. The liver enzymes measured include ALT, AST, ALP, GGT, and total bilirubin. The group treated with CCl4 showed significant($P<0.05$) elevations in all liver enzymes, indicating hepatocellular injury. Specifically, ALT, AST, ALP, and GGT levels were markedly increased, with total bilirubin also elevated, confirming impaired liver function. In contrast, the group treated with S-CsNPs exhibited enzyme levels comparable to the negative control group, indicating that the S-CsNPs effectively restored liver function. Enzyme levels in the nanosilymarin group were significantly ($P<0.05$) lower than the untreated group and the CCl4 group, demonstrating the therapeutic efficacy of S-CsNPs in mitigating liver damage caused by CCl4. This was comparable to the performance of the silymarin treatment group, with no significant differences between the two treatments.

Tab (1): Effect of S-CsNPs on liver enzymes in female Rat

	parameters (Mean ± SD) No=6				
Groups	**ALT (U/L)**	**AST (U/L)**	**ALP (U/L)**	**GGT (U/L)**	**Total Bilirubin (mg/dl)**
Negative control	46.50±12.30C	116.16±2.71C	34.16±10.94C	3.75±0.30C	0.12±0.05C
CCl4	88.66±5.39B	181.16±5.77B	71.16±7.13B	14.63±0.42B	0.42±0.09B
Untreated	112.00±5.40A	211.33±3.32A	100.66±4.13A	17.15±0.89A	0.69±0.07A
Silymarin(50mg)	48.00±2.36C	120.33±3.32C	38.33±1.63C	4.75±0.15C	0.13±0.02C
S-CsNPs 1 mg	44.50±1.04C	119.33±1.21C	35.66±1.03C	4.33±0.10C	0.12±0.02C
LSD	7.33	11.66	10.45	2.4	0.13

***The different letters show significant differences at (P<0.05),**

S-CsNPs=Silymarin-chitosan nanoparticles

Hepatic Oxidant markers and Anti-Oxidant Parameters

Effect of S-CsNPs on TNF-α and MDA

The results show the effect of S-CsNPs on Tumor Necrosis Factor-alpha (TNF-α) and Malondialdehyde (MDA) levels in the liver of female rats with CCl4-induced hepatotoxicity. The group treated with CCl4 exhibited significant increases in both TNF-α and MDA levels, indicating severe inflammation and oxidative stress in the liver. TNF-α and MDA levels in this group were notably higher compared to the control and treated groups (S-CsNPs and silymarin).

On the other hand, the group treated with S-CsNPs showed a substantial reduction in both TNF-α and MDA levels compared to the untreated and CCl4 groups, indicating an anti-inflammatory effect and a reduction in oxidative stress. The levels of TNF-α and MDA in this group were similar to those in the silymarin-treated group, with no significant differences between the two treatments.

Tab (2): Effect of S-CsNPs on TNF-α and MDA.

Groups	parameters (Mean ± SD) No=6	
	TNF-α (pg/ml)	MDA (ng/ml)
Negative control	13.12±1.91 B	63.93±11.25 C
CCl4	50.41±5.26 A	402.26±38.92 B
Untreated	53.37±5.10 A	471.72±82.98 A
Silymarin(50mg)	11.65±1.90 B	63.52±27.62 C
S-CsNPs 1 mg	9.56±0.94B	49.59±3.98C
LSD	5.95	37.28

***The different letters a show significant difference at (P<0.05),**

S-CsNPs=Silymarin-chitosan nanoparticles

Effect of S-CsNPs on GSH and Superoxide Dismutase

The result shows the effect of S-CsNPs on glutathione (GSH) and superoxide dismutase (SOD) levels in female rats with CCl4-induced liver damage. The CCl4 group exhibited a significant reduction in both GSH and SOD levels, indicating severe oxidative stress and compromised antioxidant defense. GSH and SOD levels were significantly($P<0.05$) lower in the CCl4 and untreated groups compared to the control group.

In contrast, the group treated with S-CsNPs demonstrated a notable ($P<0.05$) increase in both GSH and SOD levels compared to the untreated and CCl4 groups. The S-CsNPs group showed significantly higher GSH and SOD levels, with GSH levels almost restored to those of the negative control group and SOD levels showing a substantial improvement as well. These results were superior to those observed in the silymarin-treated group, where GSH and SOD levels were improved but not to the same extent as with S-CsNPs.

Tab (3): Effect of S-CsNPs on GSH and Superoxide Dismutase.

Groups	parameters (Mean ± SD) No=6	
	SOD (ng/ml)	GSH (ug/ml)
Negative control	6.73±0.50A	63.53±3.60 A
CCl4	2.29±0.34D	9.98±1.40C
Untreated	2.28±0.69D	9.18±1.39C
Silymarin(50mg)	3.33±0.26C	50.12±1.71 B
S-CsNPs 1 mg	4.22±0.29B	58.53±4.57 A
LSD	0.7	5.00

***The different letters a show significant difference at (P<0.05),**

S-CsNPs=Silymarin-chitosan nanoparticles

Discussion

Measurement of liver enzymes (ALT, AST and ALP) are used to assess liver function. In this study as showed in table (1), CCl4 administration significantly elevated these enzymes and total bilirubin levels, indicating liver damage and compromised cellular integrity, consistent with previous studies (10, 11,12). The elevation in liver markers like transaminases suggests cellular damage and enzyme leakage into the bloodstream (13,14). CCl4 toxicity, through GSH-Px depletion and lipid peroxidation, further increases AST, ALT, and ALP levels (15). Bilirubin, a byproduct of red blood cell breakdown, typically processed by the liver, rises when liver function is impaired. This inability to properly filter and excrete bilirubin suggests liver dysfunction and can indicate conditions such as hepatitis or cirrhosis (16). The results also showed a significant and meaningful decrease in liver enzymes and total bilirubin levels when administering silymarin at dose of 50 mg/kg of body weight, as well as nanosilymarin (S-CsNPs) at doses of 1 mg /kg. This decrease was compared to the injury group treated with CCl4 and the untreated group. This indicates the effectiveness of the treatment, as it effectively treated the damage induced by CCl4 and this is consistent with what the (17) presents in the review section of their study on the effect of silymarin as a treatment for liver diseases who noticed AST, ALT and GGT levels all fell significantly with silymarin therapy. The mechanism of Silymarin involves preserving the hepatocellular membrane's integrity and

inhibiting the penetration of toxins into the liver's interior, thereby preventing additional cellular damage. Additionally, Silymarin enhances ribosomal protein synthesis by activating nucleolar polymerase A (NPA), which initiates hepatocyte synthesis and promotes liver regeneration, this agreed with (18). As findings in results table (2) demonstrated that I.P exposure of CCl4 cause to significantly raised in pro-inflammatory cytokine (TNF-α) and oxidative marker MDA values compared to the normal control, with significantly diminished in these values in therapeutic groups (Silymarin and nanosilymarin) comparison to untreated rats group. This might probably be attributed to the poisoning with CCl4 cause to lipid peroxidation as revealed via the elevated value of MDA. The malondialdehyde (MDA) level in liver tissue was assessed as an indicator of lipid peroxidation in oxidative liver damage and is one of lipid peroxidative product and for several decades it has been used as a biomarker of lipid peroxidation. In addition, the increase of MDA has been considered a key feature in liver injury (19 ,20). Products of lipid peroxidation can lead to changes in biological membranes, resulting in serious cellular injury. An increase in the formation of MDA was observed in liver cells of rats exposed to CCl4, indicating detrimental effects on the cells (21). The increase in TNF-α levels after exposure to CCl4 may be associated with the inflammatory effects resulting from CCl4-induced tissue damage. TNF-α is secreted by various cell types, including immune cells such as adipose tissue, macrophages, and granulocytes, as well as hepatocytes. Therefore, the elevation in TNF-α levels could be part of the inflammatory response in the liver following exposure to CCl4. CCl4 induce an inflammatory response in hepatocytes with release of TNF-α. (22) found The increase in TNF-α levels in response to acute liver injury is attributed to its inflammatory effects, as it is regarded as one of the potent inflammatory cytokines crucial for the body's defense mechanism. Our findings indicate that TNF-α influences acute liver injury induced by CCl4 and the elevation its levels results from the stimulation of the acute phase inflammatory response, leading to the release of this mediator and the generation of reactive oxygen species through mitochondrial respiratory chain reactions which leading to lipid peroxidation and disruption in the proteins and DNA. On the other hand, increasing of cytokines releases will lead to increased inflammation development concomitantly with increased hazards of exposure this similar with the study that presented by (23). Also the results showed the reduction in MDA and TNF-α levels in both therapeutic groups (Silymarin and nanosilymarin) compared to the untreated group and infected group by CCl4 this decrease in malondialdehyde levels occurs after treatment the injured rats by CCl4 with silymarin which may be due to the antioxidant activity of silymarin and its ability to clear free radicals produced by CCl4 so confirms the antioxidant role of silymarin. Moreover, even at lower dose, nanosilymarin (1mg /kg) exhibited a marginally superior impact compared to higher dose of the silymarin extract (50mg /kg b.w), underscoring the efficacy of nanosilymarin despite its lower dosage,

which matches high concentration of the extract. Moreover, silymarin protects cellular membranes from oxidation by inhibiting lipid peroxidation, which otherwise impairs lipids within these membranes. It prevents the degeneration of cellular lipids, thereby protection membrane integrity and inhibiting oxidative damage. Also silymarin inhibits toxic compounds metabolism this agreed with (24) who indicates that silymarin inhibits metabolism of thioacetamide.

(25) The Silymarin reduces lipid peroxidation through two main mechanisms. Firstly, it diminishes the chemical reaction that stimulates carbon tetrachloride by cytochrome P-450 enzyme, thereby reducing the formation of free radicals of trichloromethyl and consequently minimizing the onset of lipid peroxidation. Secondly, it inhibits the chemical reactions that activate lipid peroxidation in cells, thereby decreasing the oxidative impact on cellular fats and preserving their integrity.

According to oxidative stress parameters, there was a significant drop in glutathione reductase GSH and SOD in the liver of CCl4-injected animals compared to the control group. This effect agrees with (26) study, when they investigated CCl4 efficacy on rat models too. CCl4 is considered capable of causing liver injury by generating highly reactive free radicals $CCl_3^{\bullet}$ and $CCl_3OO^{\bullet}$ through its biotransformation via the cytochrome P-450 system (27). These active radicals react synergistically with macromolecules, leading to a cascade of events including peroxidative degradation of membrane phospholipids and accumulation of lipid-derived oxidative products. These reactions cause liver damage and failure of antioxidant defense mechanisms (28). The values of SOD and GSH began to significantly increase upon treatment with silymarin50 mg/kg b.w and nanosilymarin 1 mg /kg compared to the group affected by CCl4 and the untreated group. The increase in SOD and GSH levels after treatment with silymarin (50 mg) and nanosilymarin (1 mg) can be explained in several ways. The treatment may reduce inflammation, improve liver function, and prevent the deterioration of antioxidant levels. The results indicate that Nanosilymarin exhibits significant therapeutic efficacy in improving liver functions and reducing oxidative stress, making it a promising option for treating liver toxicity. Nanosilymarin particles (S-CsNPs) possess unique physical properties, such as nanoscale size, which facilitate better absorption compared to conventional silymarin. These properties enhance S-CsNPs's ability to effectively reach targeted tissues, leading to a reduction in elevated liver enzyme levels (such as ALT, AST, ALP, and GGT) resulting from liver toxicity. Nanosilymarin (S-CsNPs) effectively alleviated oxidative stress and inflammation while enhancing endogenous antioxidants, suggesting a protective role against CCl4-induced hepatotoxicity. This effect is attributed to its improved cellular penetration and sustained therapeutic action. In conclusion, the data suggest that S-CsNPs provide significant Therapeutic effects, comparable to silymarin, in restoring liver enzyme levels to near-normal values after CCl4-induced hepatotoxicity

Conclusion

The present study demonstrated that nanosilymarin (S-CsNPs) possesses significant hepatoprotective and antioxidant properties against CCl_4-induced liver injury in female rats. Treatment with S-CsNPs resulted in marked improvement in liver enzyme levels (ALT, AST, ALP, GGT, and total bilirubin) and oxidative stress biomarkers (TNF-α, MDA, SOD, and GSH), restoring them near to normal levels. These therapeutic effects were superior or at least comparable to those of free silymarin, despite the lower administered dose. The enhanced efficacy of S-CsNPs is likely attributed to improved bioavailability and cellular uptake due to its nanoparticulate formulation. Thus, nanosilymarin represents a promising candidate for further preclinical and clinical investigations as a potent therapeutic agent for managing hepatotoxicity and liver diseases caused by chemical insults such as carbon tetrachloride.

Acknowledgment

The authors extend their heartfelt gratitude to the staff of the Ministry of Science and Technology, Directorate of Environment and Water, with special thanks to Dr. Labeeb Ahmed for his invaluable support in the preparation and characterization of nanoparticles. We are also deeply thankful to Dr. Mahesh Gopasetty, a liver surgeon and organ transplant specialist, and Dr. Divya K, a pathologist, Bangalore, India, for their insightful advice, assistance, and unwavering compassion throughout the course of this research.

Conflicts of interest

The authors declare that there is no conflict of interest.

Ethical Clearance

This work is approved by The Research Ethical Committee.

References

1. Holt M, Ju C. (2010). Drug-induced liver injury. *Handb Exp Pharmacol. (196):*3-27. DOI: https://doi.org/10.1007/978-3-642-00663-0_1
2. Singh, D., Cho, W. C., & Upadhyay, G. (2016). Drug-induced liver toxicity and prevention by herbal antioxidants: an overview. *Frontiers in physiology*, 6, 363. DOI: 10.3389/fphys.2015.00363
3. Jasim, N. Y. (2024). Comparative Study of Nanosilymarin Loaded on Chitosan versus Free Silymarin in CCl4-Induced Hepatotoxicity in Female Rats. *Frontiers in Health Informatics, 13*(2), 587-598. DOI: https://doi.org/10.52783/fhi.47
4. Khan, R. A., Khan, M. R., & Sahreen, S. (2012). Protective effect of Sonchus asper extracts against experimentally induced lung injuries in rats: a novel study. *Experimental and Toxicologic Pathology, 64*(7-8), 725-731
5. Wang L, Huang QH, Li YX, et al. (2018).Protective effects of silymarin on triptolide-induced acute hepatotoxicity in rats. *Molecular Medicine Reports, 17*(1), 789–800. DOI: https://doi.org/10.3892/mmr.2017.7958
6. Hoff, J.; Rlatg, L.V.T. (2000). Methods of Blood Collection in the Mouse: Lab

Animal. San Diego: TECHNIQUE. 10: 51-53.

7. Agrawal S, Dhiman RK, Limdi JK. (2016). Evaluation of abnormal liver function tests. *Postgraduate Medical Journal, 92*(1086), 223 234.DOI: https://doi.org/10.1136/postgradmedj-2015-133715.
8. FUJIFILM Corporation. (2016). *NX500E R2*(16:07-F1079-F9711). Printed in JAPAN.
9. Dugard P. (2014). Randomization tests: A new gold standard?. *Journal of Contextual Behavioral Science, 3*(1), 65–68. DOI: https://doi.org/10.1016/j.jcbs.2013.10.001.
10. Thanh TB, Thanh HN, Minh HPT, et al. (2015).Protective effect of Tetracera scandens L. leaf extract against CCl4-induced acute liver injury in rats. *Asian Pacific Journal of Tropical Biomedicine, 5*(3), 221–227.DOI: https://doi.org/10.1016/S2221-1691(15)30009-5)
11. El-Haskoury, R., Al-Waili, N., Kamoun, Z., Makni, M., Al-Waili, H., & Lyoussi, B. (2018). Antioxidant activity and protective effect of carob honey in CCl4-induced kidney and liver injury. *Archives of medical research, 49*(5), 306-313.
12. Baradaran, A., Samadi, F., Ramezanpour, S. S., & Yousefdoust, S. (2019).Hepatoprotective effects of silymarin on CCl_4-induced hepatic damage broiler chickensmodel.*ToxicologyReports,6,*788–794. DOI:https://doi.org/10.1016/j.toxrep.2019.07.011
13. Newairy, A. A., & Abdou, H. M. (2013). Effect of propolis consumption on hepatotoxicity and brain damage in male rats exposed to chlorpyrifos. *African Journal of Biotechnology, 12*(33), 5232–5243.DOI: https://doi.org/10.5897/AJB12.2797
14. Sher, M., Hussain, I., Khan, F. A., Afridi, H. H., Sher, W. M., Gulfam, N., … & Ahmad, Z. (2023). Effect of Silymarin Particle Size On Its Solubility And Oral Bioavailability, The Enhancement Of Pharmacological Actions.*Journal of Population Therapeutics and Clinical Pharmacology, 30*(18), 2527–2560. DOI: https://doi.org/10.53555/jptcp.v30i18.3484
15. Weber, L. W., Boll, M., & Stampfl, A. (2003). Hepatotoxicity and mechanism of action of haloalkanes: carbon tetrachloride as a toxicological model. *Critical Reviews in Toxicology, 33*(2), 105–136. DOI: https://doi.org/10.1080/713611034
16. Yap, C. Y., & Aw, T. C. (2010). Liver function tests (LFTs). *Proceedings of Singapore Healthcare*, *19*(1), 80-82.
17. Saller, R., Meier, R., & Brignoli, R. (2001). The use of silymarin in the treatment of liver diseases. *Drugs, 61*, 2035–2063. DOI: https://doi.org/10.2165/00003495-200161140-00003
18. Pradhan, S. C., & Girish, C. (2006). Hepatoprotective herbal drug, silymarin from experimental pharmacology to clinical medicine. *Indian journal of medical research*, *124*(5), 491-504.
19. Mateos, R., Lecumberri, E., Ramos, S., Goya, L., & Bravo, L. (2005). Determination of malondialdehyde (MDA) by high-performance liquid

chromatography in serum and liver as a biomarker for oxidative stress: Application to a rat model for hypercholesterolemia and evaluation of the effect of diets rich in phenolic antioxidants from fruits.*Journal of Chromatography B, 827*(1),76–82.DOI: https://doi.org/10.1016/j.jchromb.2005.06.035

20. Lien, D. T. P., Hoang, C. T. K., Hanh, N. T., Chu, D. X., Tram, P. T. B., & Toan, H. T. (2016). Hepatoprotective effect of silymarin on chronic hepatotoxicity in mice induced by carbon tetrachloride. *Journal of Pharmacognosy and Phytochemistry*, *5*(5), 262-266.
21. Balahoroğlu, R., Dülger, H., Özbek, H., Bayram, İ., & Şekeroğlu, M. R. (2008). Protective effects of antioxidants on the experimental liver and kidney toxicity in mice. *European Journal of General Medicine, 5*(3), 157–164. DOI: https://doi.org/10.29333/ejgm/82598
22. Dong, Y., Liu, Y., Kou, X., Jing, Y., Sun, K., Sheng, D., ... & Wei, L. (2016). The protective or damaging effect of Tumor necrosis factor-α in acute liver injury is concentration-dependent. *Cell&bioscience*, *6*,1-10 DOI: https://doi.org/10.1186/s13578-016-0074-x
23. Astiz, M., de Alaniz, M. J. T., & Marra, C. A. (2012). The oxidative damage and inflammation caused by pesticides are reverted by lipoic acid in rat brain. *Neurochemistry International, 61*(7), 1231–1241. DOI: https://doi.org/10.1016/j.neuint.2012.09.003
24. Papetti, A., Daglia, M., & Gazzani, G. (2002). Anti-and pro-oxidant activity of water soluble compounds in Cichorium intybus var. silvestre (Treviso red chicory). *Journal of Pharmaceutical and Biomedical Analysis, 30*(4), 939-945. DOI: https://doi.org/10.1016/S0731-7085(02)00473-9
25. Lettéron, P., Labbe, G., Degott, C., Berson, A., Fromenty, B., Delaforge, M., Larrey, D., & Pessayre, D. (1990). Mechanism for the protective effects of silymarin against carbon tetrachloride-induced lipid peroxidation and hepatotoxicity in mice: Evidence that silymarin acts both as an inhibitor of metabolic activation and as a chain-breaking antioxidant. *Biochemical Pharmacology, 39*(12), 2027–2034.DOI: https://doi.org/10.1016/0006-2952(90)90625-U
26. Abdel-Moneim, A. M., Al-Kahtani, M. A., El-Kersh, M. A., & Al-Omair, M. A. (2015). Free radical-scavenging, anti-inflammatory/anti-fibrotic and hepatoprotective actions of taurine and silymarin against CCl4 induced rat liver damage. *PloS one*, *10*(12), e0144509. DOI: https://doi.org/10.1371/journal.pone.0144509
27. Huo, H. Z., Wang, B., Liang, Y. K., Bao, Y. Y., & Gu, Y. (2011). Hepatoprotective and antioxidant effects of licorice extract against CCl4-induced oxidative damage in rats. *International Journal of Molecular Sciences*, *12*(10), 6529-6543. DOI: https://doi.org/10.3390/ijms12106529
28. Vuda, M., D'Souza, R., Upadhya, S., Kumar, V., Rao, N., Kumar, V., Boillat, C., & Mungli, P. (2012). Hepatoprotective and antioxidant activity of aqueous extract of Hybanthus enneaspermus against CCl_4-induced liver injury in rats. *Experimental and Toxicologic Pathology, 64*(7–8), 855–859. DOI: https://doi.org/10.1016/j.etp.2011.03.006

تقييم الفعالية العلاجية للنانوسليمارين في تخفيف السمية الكبدية المستحثة بـ CCl4 في الجرذان

نسرين ياسر جاسم , رشاد فاضل غضبان
فرع الفسلجة والأدوية والكيمياءالحياتية, كلية الطب البيطري, جامعة البصرة , البصرة, العراق.

الخلاصـــــــــــة

تعتبر الأدوية والمواد الكيميائية من الأسباب الشائعة التي تُحدث خللًا في وظائف الكبد، مثل التهاب الكبد الحاد وفشل الكبد .يُستخدم الكربون تيتراكلورايد (CCl4)على نطاق واسع كنموذج لدراسة السمية الكبدية .يُعد السليمارين، بخصائصه المضادة للأكسدة، عاملًا علاجيًا محتملًا لعلاج إصابات الكبد .الهدف الرئيسي من هذه الدراسة هو تقييم التأثير العلاجي للنانوسليمارين (S-CsNPs) في الجرذان المصابة بـ . CCl4 شملت الدراسة 30 جرذًا أبيض بالغًا من الإناث، تم تقسيمها عشوائيًا إلى خمس مجموعات .المجموعة الأولى اعتُبرت مجموعة السيطرة السالبة ولم تتلقَ أي علاج .أما المجموعة الثانية فقد حُقنت داخل البريتون بـ (CCl4) بجرعة 3 مل/كغم (مرتين أسبوعيًا لمدة أربعة أسابيع .المجموعة الثالثة كانت مجموعة غير معالجة، تلقت (CCl4) فقط كما في المجموعة الثانية دون تلقي علاج لاحق .المجموعة الرابعة عولجت بالسليمارين بجرعة 50ملغم/كغم عن طريق الفم يوميًا لمدة ثلاثة أسابيع بعد التعرض لـ CCl4 أما المجموعة الخامسة فقد تلقت (S-CsNPs) بجرعة 1 ملغم/كغم عن طريق الفم يوميًا لمدة ثلاثة أسابيع بعد إعطاء CCl. تم تقييم وظائف الكبد بقياس مستويات إنزيمات الكبد(ALT، AST، ALP ، GGT والبليروبين الكلي)، وتقييم الإجهاد التأكسدي عبر قياسTNF-α، MDA، SOD ، و GSH.أظهرت مجموعة CCl4 ارتفاعًا كبيرًا في إنزيمات الكبد ومؤشرات الإجهاد التأكسدي TNF-α) وMDA، وانخفاضًا معنويًا في SOD) و GSHمقارنةً بمجموعة السيطرة .بينما أدى العلاج بالنانوسليمارين إلى انخفاض ملحوظ في مستويات ALT،AST، ALP، GGT ، البليروبين،TNF-α ، وMDA، وارتفاع معنوي في SOD و GSHمقارنةً بالمجموعتين غير المعالجة والمعالجة بالسليمارين .تشير النتائج إلى التأثير العلاجي الفائق للنانوسليمارين، حيث أظهرت الدراسة فعاليته في تخفيف إصابة الكبد الناتجة عنCCl4 ، مما يجعله خيارًا علاجيًا واعدًا للسيطرة على أمراض الكبد.

الكلمات المفتاحية :سليمارين،CCl4 ، السمية الكبدية، النانوسليمارين، الكبد.