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THE ANTITOXIC EFFECT OF THE ROSUVASTATIN IN THE CYCLOPHOSPHAMIDE-INDUCED LIVER TOXICITY IN MALE RATS

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ABSTRACT

The study aims to examine the protective effect of rosuvastatin on liver toxicity caused by cyclophosphamide, including tissue, inflammatory markers, and oxidative damage. Twenty-four rats were separated into three distinct groups. The first group was the untreated group, which got no therapy; the second group received just a single dose of cyclophosphamide (150 mg/kg); and the third group received rosuvastatin (20 mg/kg) every day for two weeks. On the eighth day, they also received a single dose of cyclophosphamide. On the fifteenth day, the animals were anesthetized, and the liver's tissue was taken for histology and immunohistochemical analysis. Microscopically, the cyclophosphamide group showed liver cell necrosis, severe dilation of sinusoids, proliferation of inflammatory cells, and portal vein congestion. In the cyclophosphamide + rosuvastatin (C+R) group, the pathological effects were less severe compared to the cyclophosphamide group alone. TNF-α levels were significantly elevated in the cyclophosphamide group but decreased in the rosuvastatin pretreated group compared to the cyclophosphamide group. MDA levels were elevating in the cyclophosphamide group, whereas rosuvastatin treatment significantly prevented this. This study suggests that rosuvastatin has a potential protective effect by observing the anti-inflammatory, antioxidant, and anti-apoptotic effects in the cyclophosphamide-induced liver toxicity model.

Keywords: Histology, Inflammation, Oxidative damage, Cyclophosphamide.

INTRODUCTION

The inability to discover an alternative treatment agent for patients can lead to significant challenges, particularly concerning hepatotoxicity. The liver plays a crucial role in the elimination, metabolism, and detoxification of harmful substances, including medicinal products (Hassan *et al.*, 2020; Behairy *et al.*, 2024). This may limit the potential of therapeutic entanglement of the agent (Al-Allaf and Ashoo, 2021). Hepatotoxicity is one of the critical issues that affect general health in humans (Al-Allaf and Ashoo, 2014; Ali *et al.*, 2021a; Ali *et al.*, 2021b).

Cyclophosphamide is a well-established chemotherapy agent utilized in the treatment of cancer, autoimmune disorders, hematological conditions, and for marrow transplantation (Petri, 2004; Tsai-Turton *et al.*, 2007; Shokrzadeh *et al.*, 2014;

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Ahlmann and Hempel, 2016; Abdul Razak *et al.,* 2019; Al-Allaf *et al.,* 2022). This treatment was introduced as a cancer therapy in 1959 (Brock and Wilmanns, 1958). It remains important for hematological malignancies, including lymphoma and leukemia, as well as for epithelial tumors such as breast, ovarian, and lung carcinomas (Emadi *et al.,* 2009). The drug was approved in Germany for treating acute lymphoblastic leukemia (ALL), Hodgkin and non-Hodgkin lymphomas, chronic lymphoblastic leukemia, breast carcinoma, ovarian carcinoma, rhabdomyosarcoma, plasma-cytoma, and neuroblastoma (Baxter Oncology, 2015). Despite its use as an anticancer agent, the International Agency for Research on Cancer has classified it as a carcinogen in both humans and animals (IARC, 1987). The adverse effects of this medication, including hepatotoxicity, can limit its therapeutic use (Mok, 2000; Alnuaimi *et al.,* 2022). The exact mechanism of cyclophosphamide-induced liver injury remains unclear. Any hepatic impact can cause toxic effects on the liver, as the liver plays an important role in detoxification and maintaining metabolic balance. Hepatic cytochrome P450 enzymes metabolize cyclophosphamide, producing active metabolites like acrolein and phosphoramide mustard (Adnan *et al.,* 2009; Jeelani *et al.,* 2017). Most therapeutic effects of cyclophosphamide result from phosphoramide mustard, whereas acrolein causes necrosis and apoptosis (Zhu *et al.,* 2015; Steinbrecht *et al.,* 2020). Recently, several researchers have reported that some cyclophosphamide metabolites cause inflammation, oxidative damage, and apoptosis as the primary mechanisms of liver toxicity (Alqahtani and Mahmoud, 2016; Caglayan *et al.,* 2018; Al-Haithloul *et al.,* 2019; Alnuaimi and Alabdaly, 2023). Research is ongoing to find chemical or natural substances that can be co-administered with cyclopho-sphamide to reduce or limit its toxic effects on the liver.

On the other hand, the recent era of using some drugs beyond their original actions as cinnarizine, bosentan, and rosuvastatin (Attarbashee and Abu raghif, 2020; Attarbashee *et al.,* 2023; Mammdoh *et al.,* 2023) and that due to their antioxidant, or anti-inflammatory effects.

Rosuvastatin is one of the drugs used to treat high levels of harmful fats and cholesterol in the blood. It works by inhibiting the enzyme HMG-CoA reductase in the mevalonate pathway (Oda and Keane, 1999; Aljawad *et al.,* 2015; Abdeena *et al.,* 2019). This inhibition suppresses isoprenylation, responsible for regulating cell proliferation, inducing pro-inflammatory cytokines, and generating reactive oxygen species (Antonopoulos *et al.,* 2012; Abdel Daim, 2018). Recently, some articles have highlighted the benefits of using this drug to maintain liver function. Previous research has reported that rosuvastatin can effectively prevent liver damage induced by fipronil in male rats by alleviating oxidative damage and apoptosis markers (Arulpriya *et al.,* 2010).

The therapeutic impact of rosuvastatin on inflammatory and oxidative damage has been documented in several inflammatory diseases (Yamagata *et al.,* 2007; Hamzeh *et al.,* 2018). Therefore, this agent was suitable for detailed investigations against hepatotoxicity. The aim of this study is to investigate the protective impact of rosuva-statin on cyclophosphamide-induced liver toxicity by studying histological, inflam-matory, and oxidative damage markers.

MATERIALS AND METHODS

Ethical approval

The study was authorized by the institutional animal ethics committee at the College of Dentistry at the University of Mosul" (UoM.Dent/A, L12/22).

Drugs and chemicals

Rosuvastatin was obtained from Astra Zeneca, UK, and cyclophosphamide was

procured from Baxter, USA. Both medications were delivered to rats after freshly dissolved in a normal saline solution.

Experimental design

The study took place between November of 2023 and the end of June 2024. This study involved 24 male adult albino Wister rat species, weighing between 300-400g, and their ages were roughly two months. Following passive preliminary tests, all rats acclimated to their new surroundings. All techniques were achieved in accordance with the applicable regulations and recommendations.

Grouping of animals

The 24 rats were randomly allocated to three separate groups of eight in each group. Group 1 (control), G1 (n=8): the rats received normal saline solution during 15 days. Group 2, G2 (n=8): cyclophosphamide (induction group) underwent just one IP injection of cyclophosphamide, which was 150 mg/kg on the eighth day of the trial. Group 3, G3 (n=8): C+R (protected group) received rosuvastatin (20 mg/kg) orally once a day for an entirely of 14 days: 7 days preceding induction and 7 days post induction (Abdeena *et al.*, 2019; Mammdoh *et al.*, 2023) (Figure 1).

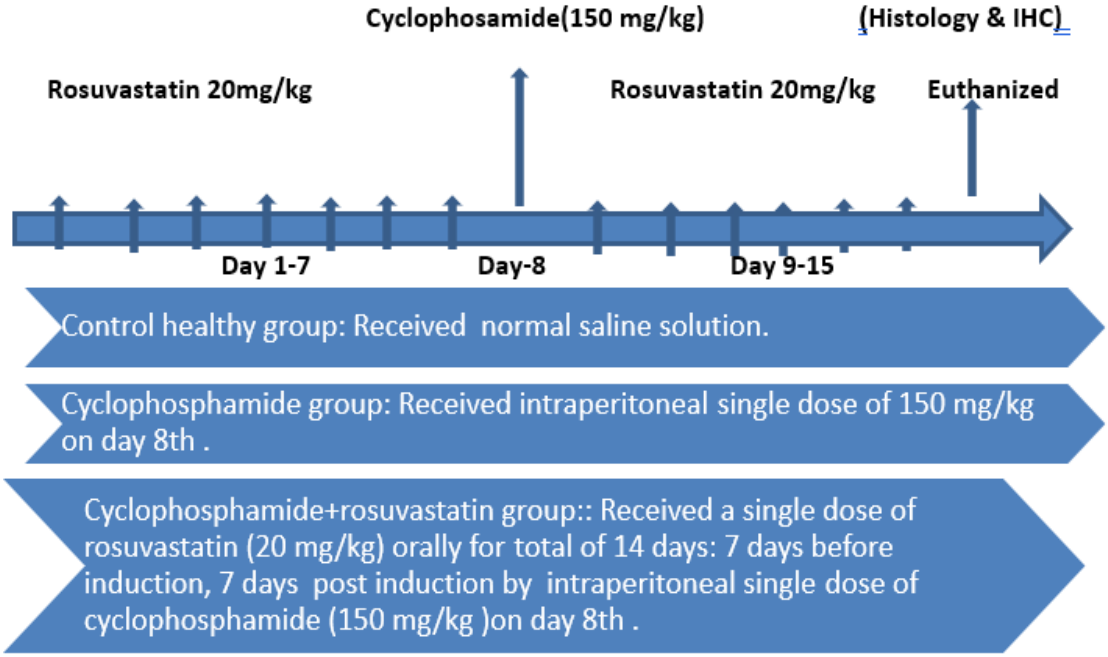


Figure 1: The experimental design

Preparation of animals.

The animals were housed in normal plastic cages with a cycle of twelve hours of light and darkness, a temperature range of (22 ± 2°C), humidity (30-50%), and air that was constantly changed utilizing a venting vacuum, and fresh water and regular chow meals were provided (ad libitum). Before initiating the study, we gave the rats a week to adjust to the animal house setting. To prevent coprophagy, rats had been randomly assigned to cages with large wire-mesh floors.

On day 15, the animals were euthanized using ketamine plus xylazine (80 mg per kg), and the liver tissue was removed and processed for histology and immunohisto-chemistry (Ali *et al.*, 2021a; Ali *et al.*, 2021b; Kadhim *et al.*, 2022; Ridha-Salman *et al.*, 2024a; Khorsheed *et al*. 2024; Luty et al. 2025).

Histopathological analysis

Dissected rat liver tissue is handled carefully and preserved immediately. The specimens were placed in 10% buffered (neutral) formalin. This slowly permeated the tissue, producing chemical and physical alterations that hardened and protected it for future processing. The specimen was secured for 6–24 hours. Through sequential cycles of ethanol solutions at increasing concentrations, specimens were dehydrated to pure, water-free alcohol. All concentrations of ethanol are miscible in water and gradually replace the specimen. Concentrations are increased gradually to prevent tissue distortion (Travlos, 2006; Yahiya *et al.,* 2023; Al-Jammas et al., 2023; Abbas, 2024; Ridha-Salman, 2024b; Alfakje and Al-Mashhadane, 2024; Al-Najjar and Al-Mashhadane, 2024). Samples of 4 mm thick are dehydrated as follows: 70%, then 80%, then 90%, then 95%, and at last 100% ethanol for two hours. Since wax and ethanol are incompatible, we cannot infiltrate the tissue with wax even though it is mostly waterless. We used xylene, a solvent that mixes with ethanol and paraffin wax. Xylene replaced ethanol in tissue, followed by melting paraffin wax (Weiss *et al.,* 2011; Abed-Mansoor and Abu-Raghif, 2022; Raheem, 2023; Thammer *et al*., 2025). Here are specimen-clearing protocols: Two hours of xylene. Infiltration with 65° paraffin wax is now possible for the tissue specimen: Wax for two hours. A wax "block" was created for microtome sectioning by completely infiltrating the specimen. An embedding center fills a mold with molten wax and places the specimen (Ali *et al.,* 2014; Oubaid *et al*., 2023a; Oubaid *et al*., 2023b). Appropriate sectioning is vertically parallel to the tissue's surface. A steel knife in a microtome cut 4 micrometer-thick tissue sections and mounted them on a glass slide for light microscopy (Weiss *et al.,* 2011). We stained with H&E, The most common histology and histopathology light microscopical stain. Eosin, an acidic dye, dyes the cytoplasm pink, while hematoxylin, an alkaline dye, attaches to nucleic acids in nuclei to color them blue (Weiss *et al.,* 2011).

Principle of IHC Test

This approach detects the ultimate outcome of the expression of genes (protein) in cells from the control, induction, and protection groups using specific antibodies that are polyclonal. The primary antibody is subsequently recognized by a second antibody with an identified label. The chemical utilized is DAB in chromogen solutions. A reaction that is positive will result in a precipitation of brown color at the antigen site in the investigated tissue (Kabiraj *et al.,* 2015; Ghazy and Abu Raghif, 2021; Kadhim and Al-Mosawi, 2021).

Immunohistochemical procedure

The staining systems of Abcam (UK) utilize a horseradish peroxidase-streptavidin complex for the staining of paraffin-embedded tissue slices. Four micrometer slices were cut from paraffin-embedded tissue blocks and placed on positively charged slides. The slides were placed in an oven with hot air maintained overnight at 40°C. “The slides were sequentially immersed in the following solutions at room temperature for a duration of 5 minutes: xylene; fresh xylene, absolute ethanol, 95% ethanol, 90% ethanol, 70% ethanol, 50% ethanol, and distilled water. The remaining procedures were conducted in a moistened chamber at ambient temperature. Prior to initiation, all components of the staining system were equilibrated to room temperature. Antigen retrieval was performed using a humid heat method at 95°-98° in a water bath with a 10 mM citric acid solution at pH 6.0 for 5 minutes, followed by a 20-minute period at ambient temperature. All samples were rinsed with running and purified water.

After five minutes in 1-3 drops of peroxidase block to inhibit endogenous peroxidase activity, then the samples were washed with phosphate buffer saline. The slides were then washed in PBS for two minutes on a shaking plate to remove excess water. After applying 1-3 drops of serum block, the specimens were incubated for 20 minutes and washed twice with PBS for three minutes. After two hours of incubation with the primary antibody, the samples were washed with PBS, twice for two minutes on a mixing plate, and excess fluid was removed from the slides. After incubating for 30 minutes in 1-3 drops of biotinylated secondary antibodies, the samples were rinsed with PBS and rinsed again for 2 minutes on a stir plate. The extra water was pulled off the slides. One to three drops of the HRP-streptavidin combination were added to the specimens, and incubated for thirty minutes. Double-washed with PBS for two minutes on a stirring plate. Excess water was eliminated from slides. One drop of 10x chromogen and 1.5 ml DAB substrate were mixed. A 10-minute incubation with one to three drops of DAB chromogen stained each slide mild brown. Stained sections were examined under a microscope after washing with deionized water. To counterstain slides, hematoxylin was applied for 5–10 seconds. Multiple deionized water changes cleaned the samples quickly. The slides were cleaned with tap water. After that, sections were dehydrated immediately, 1-2 drops of permanent mounting medium (DPX) were applied, a glass coverslip was placed (Wang *et al.,* 2012). "Semi-quantitative grading centered around positive staining evaluates immunohisto-chemistry. Score 0 means no stain, 1 means 25%, 2 means 26-50%, 3 means 51-75%, and 4 means 76-100%" (Manna *et al.,* 2019; Hassan *et al.,* 2022; Attarbashee *et al.,* 2023; Yahiya *et al.,* 2023).

Table 1: The antibodies used for immunohistochemical staining.

Primary antibody	Primary antibody supplier	Origin (catalog no.)	Dilution	Secondary antibody
Anti-Tumor necrosis factor alpha (TNF-α)	Abcam, UK	(Cat number: ab6671)	1:1000 dilution	Immunoperoxidase secondary detection kit (Staining System ab80436)-expose mouse and rabbit specific HRP/DAB Detection IHC kit (Abcam/ UK) and cat number: ab80436.
Anti-Malondialdehyde antibody (MDA)	Abcam, UK	Polyclonal rabbit antibody (Cat number: ab28364)	1:500 dilution	

Statistical analysis

The data was imported into the most pertinent version of the statistical software (SPSS 24). Both the mean and standard deviation were employed in descriptive statistical analysis. The outcomes were presented graphically and subjected to statistical analysis. In instances including more than two distinct groups, "a one-way analysis of variance (ANOVA) was conducted, followed by a Tukey HSD post hoc test" for pairwise comparisons. The significance threshold was set at $p<0.05$ (Nundy *et al.,* 2022).

RESULTS

Drug Effects on Proinflammatory Indicator (TNF-α)

The cyclophosphamide (induction group) showed significantly higher levels of inflammatory marker (TNF-α), compared to the control group (Figure 2A, B, C, D).

However, the C+R (protected group) had considerably ($p<0.05$) lower levels of TNF-α in comparison with cyclophosphamide (induction group) (Figure 2E, F) and Table (2).

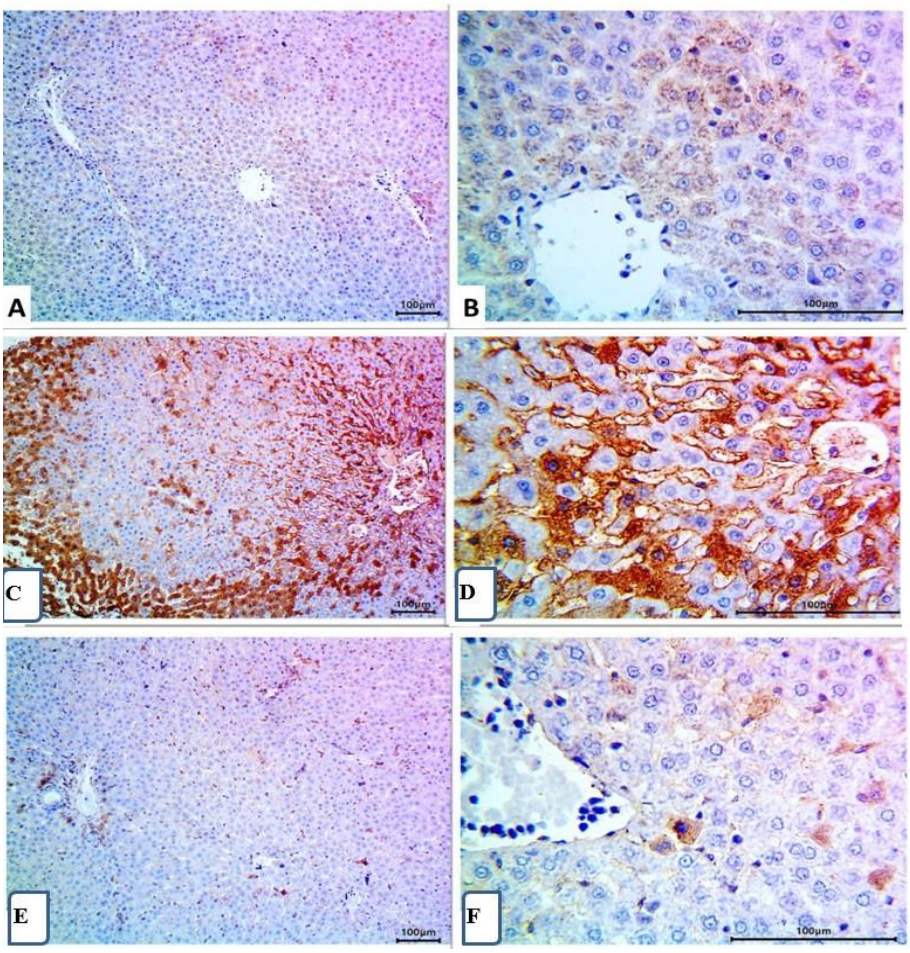


Figure 2: Shows the effect of the cyclophosphamide and rosuvastatin on liver TNF-α expression. A,B. Weak TNF-α expression (score 1+) in the control group of rat livers. C,D. the cyclophosphamide (induction group) shows a high positive TNF-α expression (score 4+). E, F. cyclophosphamide + rosuvastatin (protected group) exhibited weakly positive TNF-α expression (score 1+).

Table 2: Effect of cyclophosphamide and rosuvastatin on proinflammatory indicator (TNF-α) and oxidative marker (MDA).

Parameter score	Study groups (mean ± standard Error)		
	Control	**Cyclophosphamide (induction group)**	C+R **(protected group)**
TNF-α	1.00±0.0	4.00±0.0 [a]	1.5±0.189 [b]
MDA	0.0±0.0	3.5±0.189 [a]	1.5±0.189 [b]

Comparisons revealed by the letters, a: substantial versus control group; b: significant versus cyclophosphamide group.

Drug Effects on Oxidative Indicator (MDA)

Compared to the control group, the cyclophosphamide (induction group) had significantly ($p<0.05$) higher IHC levels for the oxidative biomarker (MDA), (Figure 3 A-D). C+R (protected group) had significantly ($p<0.05$) lower IHC levels of the oxidative marker than the cyclophosphamide (induction group) (Table 2) and (Figure 3 E, F).

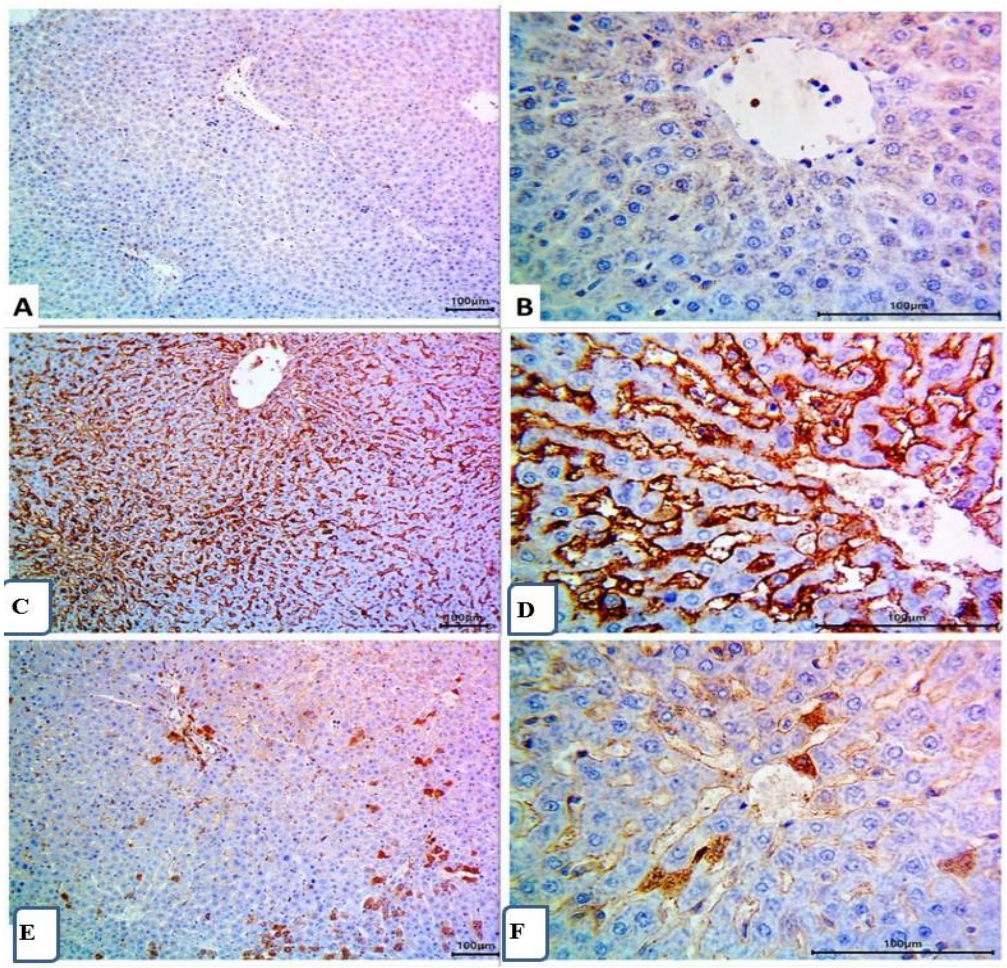


Figure 3: Shows the effect of cyclophosphamide and rosuvastatin on liver expression of MDA. A, B. negative expression (score 0) in the control group of rat liver. C, D. the cyclophosphamide (induction group) shows a high positive expression (score 4+). E, F. the C+R (protected group) exhibited moderately positive expression (score 2+).

Histopathological Findings:

Histological examination of hepatic tissue in the control group revealed mild congestion in the central vein, portal vein, and sinusoids, with slight vacuolar degeneration of some hepatocytes (Figure 4a, b). The cyclophosphamide (induction group) showed notable hepatocyte necrosis, severe sinusoidal dilatation, proliferation of inflammatory cells, and congestion of the portal vein, compared to the control group (Figure 4c, d). Moreover, the C+R, protected group showed less congestion in the central vein, and fewer degenerated hepatocytes, with overall less severe pathological changes compared to cyclophosphamide group (Figure 4e and 4f). Therefore, administrating rosuvastatin showed a significant ($p<0.05$) protective and beneficial effect, compared to cyclophosphamide group, which is comparable to that of the control group.

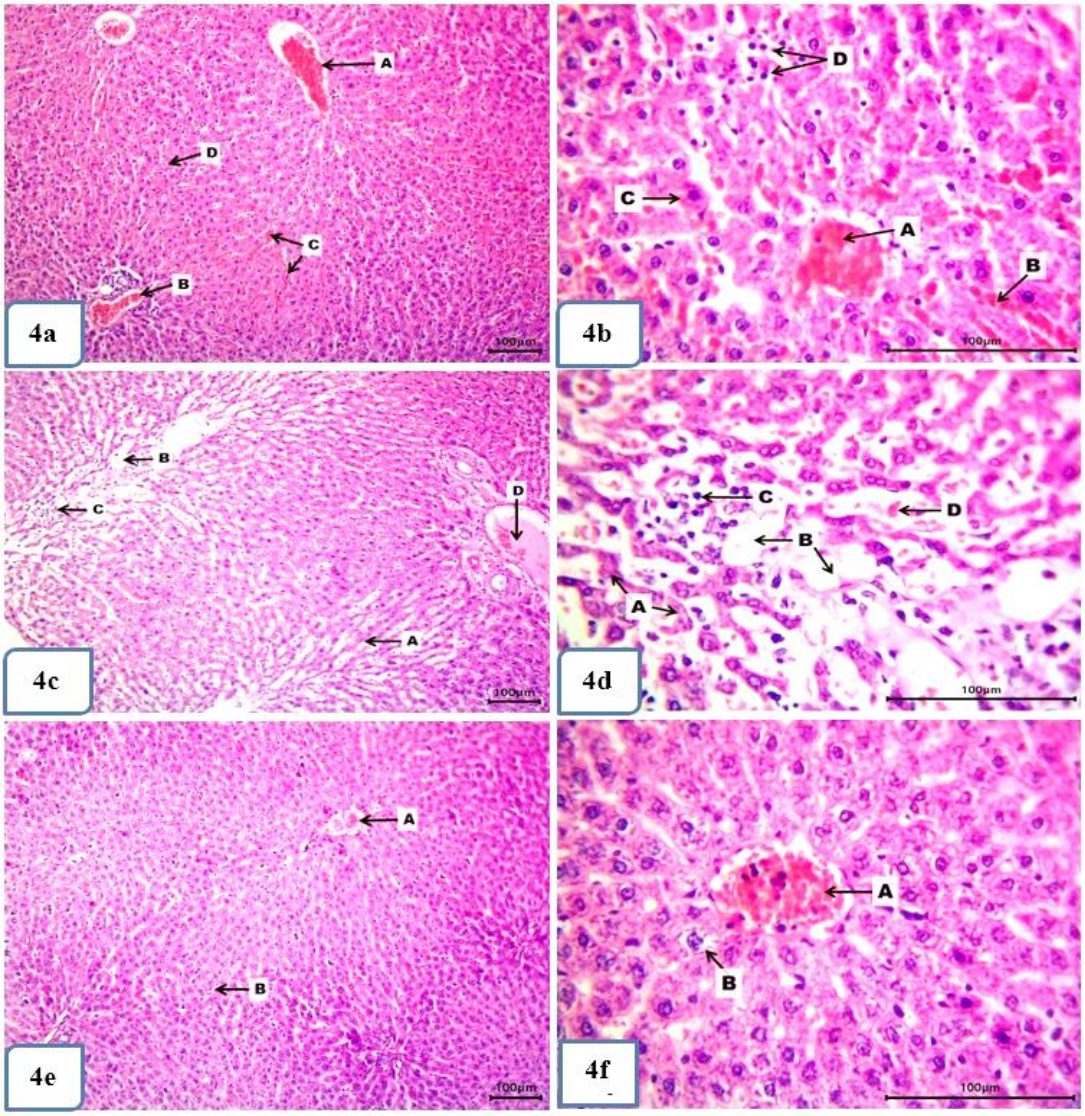
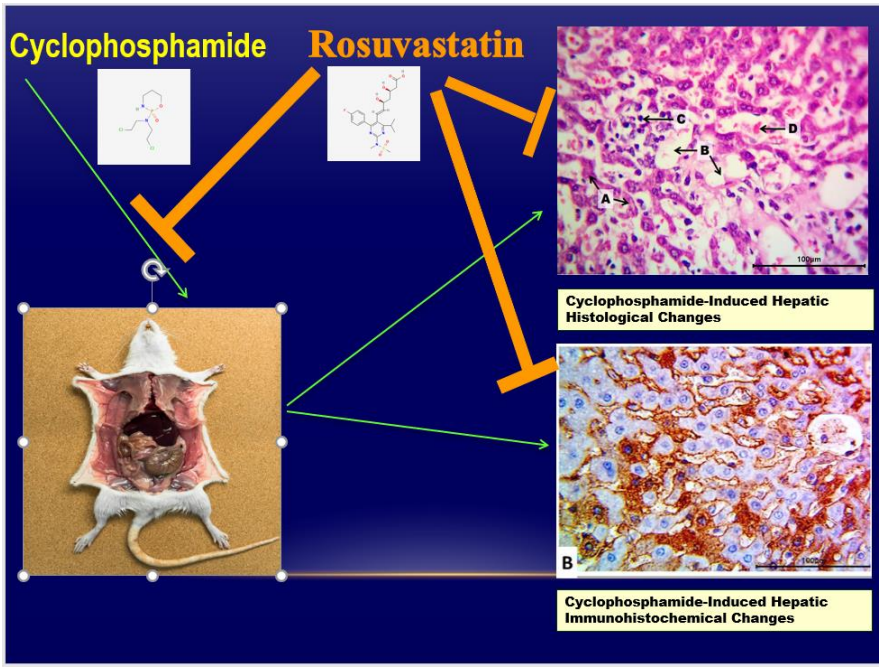


Figure 4: Effects of the cyclophosphamide and rosuvastatin on hepatic histological alterations: 4a, b. Histological section of rat liver from the untreated control group demonstrating the (A), central vein (B), and portal area (C) in their normal architecture of the hepatocytes. 4c, d. the cyclophosphamide (induction group) demonstrating hepatocytic necrosis (A), severe dilatation of the sinusoids (B), proliferation of inflammatory cells (C) and congested portal vein (D). 4e, f. the C+R group's liver tissue demonstrating congestion of the central vein (A) hepatocytes, and vacuolar degeneration (B), (H&E stain).

DISCUSSION

Cyclophosphamide is an antineoplastic medicine that is commonly used to treat a variety of disorders, including multiple sclerosis, rheumatoid arthritis (RA), and cancer. Its clinical implementation is restricted because of its various negative and hazardous consequences (Shokrzadeh *et al.*, 2014; Jiang *et al.*, 2017). Previous research has reported the protective effects of statins in liver toxicity models (Kocak *et al.*, 2015; Clarke *et al.*, 2016). However, no study has investigated whether statins can prevent cyclophosphamide-induced hepatotoxicity. The study found that cyclophosphamide administration dramatically raised the level of the inflammatory cytokine (TNF-α) compared to the control group. This rise in TNF-α level reflects a strong inflammatory response induced by cyclophosphamide. However, after treating

these rats with rosuvastatin, the TNF-α level significantly decreased (1.5 ± 0.189) compared to the cyclophosphamide-only group (4.00 ± 0.0), indicating an anti-inflammatory effect of rosuvastatin.



Graphical abstract

Cytokines such as TNF-α are key mediators in inflammation proceeding (Attarbashee *et al.,* 2023; Attarbashee *et al.*, 2025; Habbas *et al*., 2025). TNF-α is an inflammatory cytokine that helps regulate inflammation, apoptosis, and multi-plication, contributing to liver toxicity (Sternhufvud *et al.*, 2015). TNF-α aids in the development of liver damage. Previous research reported that TNF-α concentration affects protein actions. High doses of TNF-α are believed to cause lipopolysaccharide-induced liver damage (Aal-Aaboda *et al*., 2021). TNF-α levels remained constant during acetaminophen-induced liver injury (Zhao *et al.,* 2020; Qadri *et al.,* 2023). Naito *et al.* (2006) reported that rosuvastatin led to TNF-α inhibition, accompanied by a significant inhibition of intestinal inflammation.

The outcome showed that the level of malondialdehyde (MDA), an indicator of oxidative stress, significantly increased in the cyclophosphamide-treated group (3.5±0.189) compared to the control (0.0±0.0). After treating rats with rosuvastatin, the MDA level significantly decreased to (1.5±0.189) in the C+R-treated group, indicating an antioxidant effect of rosuvastatin. Experimental research has reported that free radicals in oxidative stress are the main mechanism in cyclophosphamide-induced hepatotoxicity (Frank *et al.,* 1996; Chabra *et al.,* 2014; Winterbourn *et al.,* 2015). Due to free radicals, oxidative stress is a crucial marker in mediating liver impairment. The oxidation of cyclophosphamide leads to the production of ROS and LPO in an inflammatory process, which damages liver cells, disrupts the redox cycle, and elevates LPO (Biaglow *et al.,* 1988; Selvakumar *et al.,* 2005). Improving LPO levels in experimental rats with MDA as the most common oxidized product (Haque *et al.,* 2003; Ridha-Salman *et al.,* 2024b; Shihab and Kadhim, 2023). Maheshwari *et al.* (2006) demonstrated that rosuvastatin significantly reduced oxidative stress by elevating glutathione levels and decreasing MDA levels in colitis models. Additionally, another study (Qasim *et al.,*

2021) confirmed that rosuvastatin significantly reduces oxidative stress by lowering MDA levels in rats.

Our histopathological study demonstrated that cyclophosphamide disrupted hepatic structure via hepatocyte necrosis, severe sinusoidal dilation, proliferation of inflammatory cells, and congestion of the portal vein. These pathogenic changes were consistent with prior research (Deaciuc *et al.,* 2001; Fouad *et al.,* 2014; Hamzeh *et al.,* 2018). Cyclophosphamide-induced lipid peroxidation and oxidative stress can cause damage to hepatic tissue, leading to disturbance in liver function (Selvakumar *et al.,* 2005). In this work, administering rosuvastatin to cyclophosph-amide-treated rats resulted in significant protection of hepatic tissue structure in comparison with the cyclophosphamide group.

In the C+R group, mild inflammatory changes are attributable to rosuvastatin's protective effect on the inflammatory process. Phosphoramide mustard triggers apoptosis via DNA cross-linking structure, whereas acrolein, a highly reactive chemical, provoked toxicity and the impairment of typical cell activity (Frew *et al.,* 2015). Free radicals that attach to DNA activate pro apoptotic biomarkers, leading to cell death (Hussein *et al.,* 2005; Khaleel *et al*., 2025a; Khaleel *et al*., 2025b). Cyclophosphamide caused liver apoptosis by increasing pro-inflammatory cytokines and diminishing anti-inflammatory cytokines. Antioxidant medications have been reported to prevent liver damage caused by cyclophosphamide (Shi *et al.,* 2014). Pre- and post-treatment with rosuvastatin, an antioxidant drug, 7 days pre and 7 days post cyclophosphamide injection ameliorated hepatocyte apoptosis. Other investigations revealed that rosuvastatin had anti-apoptotic properties (Wang *et al.,* 2020; Jo *et al.,* 2021; Ren *et al.,* 2022), which supported this finding.

CONCLUSION

The findings showed that cyclophosphamide promotes inflammatory response, oxidative stress, and apoptosis in rats. Rosuvastatin medication greatly lowers these side effects, indicating its efficacy as an anti-inflammatory, anti-oxidant, and anti-apoptotic agent. Rosuvastatin can reduce the harmful effects of cyclophosphamide by increasing cell protection and improving rat health.

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Conflict of Interest:
There is no conflict of interest to declare.

Availability of data and materials
Upon reasonable request, the author will provide data supporting the study's results.

Author Contribution Statement
The author, who oversaw the examination, supplied funding and sponsored supplies and rats for the study lab, completed the final copy of the document, calculated mathematical data, and used electronic reinforcement.

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التأثير المضاد للروزوفاستاتين في سمية الكبد المحدثة بالسايكلوفوسفاميد في ذكور الجرذان

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تهدف الدراسة إلى فحص التأثير الوقائي للروزوفاستاتين على سمية الكبد الناجمة عن السايكلوفوسفاميد، بما في ذلك الأنسجة وعلامات الالتهاب والأضرار التأكسدية. تم فصل أربعة وعشرين جرذا إلى ثلاث مجموعات ، كل منها مكونة من ثمانية. كانت المجموعة الأولى غير المعالجة (الضابطة)، والتي لم تحصل على أي علاج؛ تلقت المجموعة الثانية جرعة واحدة فقط من السايكلوفوسفامايد (١٥٠ ملغم/كغم)؛ وتلقت المجموعة الثالثة الروزوفاستاتين (٢٠ ملغم / كغم) يومياً لمدة أسبوعين. وفي اليوم الثامن، تلقوا أيضًا جرعة واحدة من السايكلوفوسفامايد. في اليوم الخامس عشر، تم تخدير الحيوانات، وأخذ أنسجة الكبد للتحليل النسيجي والكيميائي المناعي. أظهرت المقاطع النسيجية المرضية في مجموعة السايكلوفوسفامايد نخر خلايا الكبد، وتمدد شديد للجيوب، وانتشار الخلايا الالتهابية، واحتقان الوريد البابي. في مجموعة السايكلوفوسفامايد + الروزوفاستاتين، كانت التأثيرات المرضية الشاملة أقل حدة مقارنة بمجموعة السايكلوفوسفامايد وحدها. كانت مستويات TNF-α مرتفعة بشكل ملحوظ في مجموعة السايكلوفوسفامايد ولكنها انخفضت في مجموعة السايكلوفوسفامايد + الروزوفاستاتين. كانت مستويات MDA مرتفعة في مجموعة السايكلوفوسفامايد، في حين أدى علاج الروزوفاستاتين إلى تحسينها بشكل ملحوظ. تشير هذه الدراسة إلى أن عقار روزوفاستاتين له تأثير وقائي محتمل من خلال ملاحظة التأثير المضاد للالتهابات ومضادات الأكسدة ومضاد موت الخلايا المبرمج في نموذج سمية الكبد الناجم عن السايكلوفوسفامايد.