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Research Paper

Comparative histological study of hepatoprotective efficacy of Vitamin C and Platelet-Rich Plasma Against Carboplatin-Induced Liver Damage in Male Albino Rats

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ABSTRACT

Background: Carboplatin is an effective platinum-based chemotherapeutic agent; however, its use may be complicated by hepatotoxicity. Vitamin C (VC) and platelet-rich plasma (PRP) possess antioxidant and regenerative properties that may mitigate hepatic injury. To compare the individual and combined effects of vitamin C and PRP on carboplatin-induced histopathological liver injury in male albino rats.

Methods: Thirty adult male rats were split into five groups (6 per group): control; carboplatin alone; carboplatin plus vitamin C; carboplatin plus PRP; and carboplatin plus vitamin C and PRP. Carboplatin was administered intraperitoneally (60 mg/kg) on day 1. Vitamin C (100 mg/kg, intraperitoneally) was administered daily on days 0–7, and PRP (150 µL/rat, subcutaneously) was administered on days 0, 2, 4, and 6. PRP was prepared using double centrifugation. Hematoxylin and eosin-stained liver sections were examined microscopically.

Results: Carboplatin caused marked disruption of hepatic cords, severe hepatocellular swelling and necrosis, and central venous alterations in the rat liver. Vitamin C or PRP treatment individually largely preserved normal lobular cytoarchitecture, with appearances comparable to that of the controls. Combined treatment also produced predominantly normal architecture; however, focal mild zonal or vacuolar degeneration and hepatocellular necrosis persisted, indicating no superior protection.

Conclusion: Vitamin C and PRP attenuated carboplatin-induced hepatic histopathology in rats, whereas their combination provided incomplete protection without evident additive benefits. However, quantitative histological, biochemical, and dose-response studies are required before clinical translation.

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Introduction

Recent advancements in antineoplastic therapy have substantially improved clinical outcomes and patient longevity. However, these advancements are frequently compromised by systemic toxicities such as nephrotoxicity, cardiotoxicity, and hepatotoxicity [1]. Liver toxicity is considered a side effect of chemotherapy and immunosuppressants used in the field of cancer tumor treatment, such as methotrexate, platinum drugs such as oxaliplatin, etc. Liver damage can lead to cellular damage, including hepatic steatosis, necrosis, vascular injury, and cirrhosis [2].

Platinum-based chemotherapeutic drugs, comparable to cisplatin and carboplatin, are cytotoxic agents employed in the treatment of patients with cancer, such as lung and ovarian cancer. However, their benefits are limited, as are those of other platinum agents, because they cause cumulative toxicity, most notably nephrotoxicity, cardiotoxicity, and hepatotoxicity [3]. Although Carboplatin is effective in inducing apoptosis in malignant cells through DNA adduct formation and interference with DNA repair mechanisms [4] Its clinical utility is frequently compromised by severe systemic toxicities, including neurotoxicity, hepatotoxicity, gastrointestinal disturbances, and ototoxicity [5]. Oxidative stress is the fundamental mechanism underlying carboplatin-induced liver injury, leading to severe histopathological changes, including steatosis, tissue necrosis, and cholestasis [6].

Ascorbic acid (Vitamin C) is a potent component of the cellular antioxidant defense system. It has an anti-inflammatory function because it rids cells of reactive oxygen species that cause inflammation, which increases pro-inflammatory cytokines and liver fibrosis [7]. Furthermore, many studies have shown that ascorbic acid has a protective effect against many drugs that cause liver tissue damage through oxidative stress [8, 9].

Platelet-rich plasma (PRP) is an autologous biological product used clinically for its therapeutic properties, which include increased concentrations of autologous growth factors, secretory proteins, and cytokines that stimulate cell renewal, differentiation, and tissue regeneration [10]. Owing to its autologous origin, PRP exhibits a safety profile and contains many growth factors, such as Transforming Growth Factor beta-1 (TGF-β1), Epithelial Growth Factor (EGF), and Platelet-Derived Growth Factor (PDGF) [11]. Recently, PRP has gained clinical prominence as a cost-effective, enriched with bioactive proteins and growth factors, PRP significantly accelerates tender tissue reform and musculoskeletal regeneration [12]. Given that several toxicity mechanisms have been proposed for chemotherapy drugs, including carboplatin, such as the production of reactive oxygen species, and given that different researches have highlighted employ of vitamin C and platelet-rich plasma and their function in reducing them, the purpose of our investigate their efficacy individually or synergistically in damaged liver tissue and to investigate their protective or enhancing role in the pathological histopathological changes and Carboplatin induced hepatotoxicity.

Materials and Methods

Chemicals

Vitamin C was procured from Bayer (Germany). Carboplatin was obtained from Fresenius Kabi (India). All other chemicals were obtained from Sigma-Aldrich (USA).

Preparation stain powder

The stains were prepared according to Suvarna et al. (2019) [13].

Hematoxylin stain powder

Hematoxylin powder (4 g) was deliquesced in 25 mL of ethanol and added to a saturated ammonium alum solution (15 g/100 mL). The container was then covered with a gauze plug. This solution was then left for five days. Subsequently, it was filtered, glycerin was added, and 100 mL of alcohol was incorporated. The staining solution was exposed to light and air for 6 weeks and then filtered before use.

Eosin stain powder.

Eosin powder (1) g is dissolved in alcohol and then filtered before use.

Production of Platelet-Rich Plasma (PRP)

According to Gao et al. (2020), PRP was prepared by double centrifugation. Ten milliliters of whole blood were collected from rats via cardiac puncture. 0.5 mL of each blood specimen was isolated in EDTA tubes for total platelet count determination, while the remaining blood was placed in PRP tubes containing citric acid and dextrose solution (ACD). The samples were centrifuged at 2000 rpm for 5 min. Using another sterile tube, the liquid above was transferred; it was then centrifuged at 4000 rpm for 15 minutes, and PPP, representing two-thirds of the upper layer, was

isolated. The remaining bottom layer, representing 1/3 of the platelet-rich plasma, was thoroughly mixed, and 0.75 mL was separated for final platelet counting. To eliminate the membrane fragments of platelets from PRP, PRP was filtered via a 0.22 µm pore filter

Experimental design

Thirty adult male rats (190–205 g) were obtained from the National Center for Pharmaceutical Control and Research. Rats were split into five experimental groups (six per group) and placed in cages supplied with special food (*ad libitum*) and water. They were maintained under controlled temperature conditions (25:29°C) and acclimatized for one week under standard laboratory conditions.

1) First group (C): Rats (6) served as controls, and the remaining rat groups were injected intraperitoneally with a single dose of 60 mg/kg carboplatin (Ca) on the first day after being treated with other treatments (VC, PRP).

2) Second group(Ca): Rats (6) injected with intraperitoneal (IP) carboplatin (Ca) on the first day of the experiment.

3) Third group (VC+Ca): Rats (6) injected intraperitoneally with (100) mg/kg Vitamin C (VC) daily (0 -7).

4) Fourth group (PRP+Ca): Rats (6) injected subcutaneously (SC) with (150) µl /rat PRP extract on days (0, 2, 4, and 6).

5) Fifth group (VC+PRP+Ca): Rats (6) injected in intraperitoneal (IP) Rats injected intraperitoneally (IP) with 100 mg/kg (VC) on days (0-7) and subcutaneously with 150 µl/rat PRP extract on days (0, 2, 4, and 6). On the eighth day of the experiment, the experimental animals were sacrificed, and liver specimens were collected.

Histopathological study

The preparation of histological sections was based on [13] Liver specimens were collected after anesthesia and dissection and preserved for preparation of histological slides. It included fixation in 10% formalin for 18-24 hours. The samples were dehydrated by passing them through ethyl alcohol (70%, 80%, 90%, and 100%) for 30 min at each concentration. The samples were cleared in two phases with xylene for 30 min. For infiltration, specimens were placed in a 1:1 mixture of xylene and paraffin wax at the liquefaction point (58°C), then heated to 60°C for 1 hour, followed by filtration with Pure paraffin for 1 hour. The samples were embedded in special molds and left until the wax solidified, and then stored in a cool place. Sections of the molds were cut with a manual rotating microtome and then transferred to a water bath (45°C), then arranged on a hot plate (45°C), and stained with hematoxylin for 5-10 min. Then, the slides were stained with Eosin for two minutes. Histological specimens were photographed using novel microscopes with a digital camera. The pathologist was blinded to group allocation

Statistical processing

The data were analyzed using a one-way ANOVA, and the mean ± standard error was calculated in GraphPad Prism 6.

Results

The platelet Yield in PRP

The platelet concentration (plt) in PRP is approximately three times that of whole blood (Wb). as shown in Figure 1.

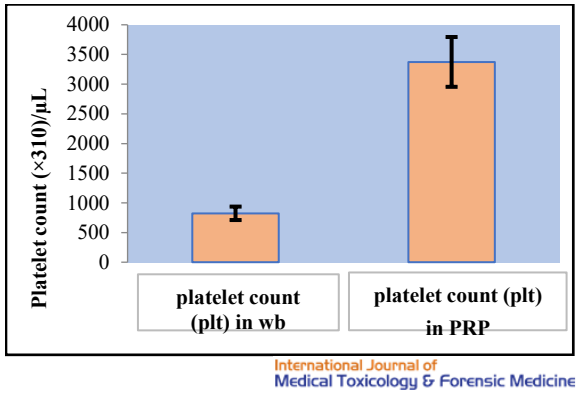

Figure 1. Platelet (Plt) total in PRP and in unfractionated whole blood (Wb) significant differences at ($p \leq 0.05$).

Histopathological Findings

Histopathological investigations of the liver of rats treated with carboplatin revealed marked zonal degenerative changes in the hepatic cords (Figure 5). The magnified figure in Figure 3 reveals marked disorganization of the hepatic cords and central veins. It prevents cellular swelling and hepatocyte necrosis. Further examination revealed marked disarrangement of the hepatic cords and central vein, as well as severe degeneration and necrosis of hepatocytes (Figures 6 and 7). Compared with the control group (Figures 2 and 4), the experimental groups showed altered hepatic cell cytoarchitecture. The carboplatin+ (Vitamin C) and PRP+ treatment groups showed normal cellular structure in the liver lobules, similar to the control group, in contrast to the histological changes, lesions, and injury observed in the carboplatin-only treatment

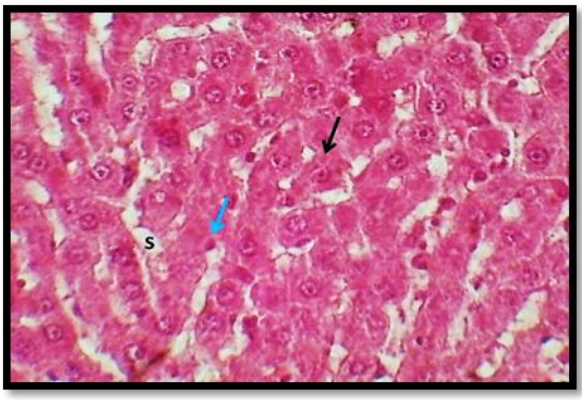

Figure 2. Section portion of liver (Control) manifest: Normal regular appearance of hepatocytes (Black arrow), kupffer cells (Blue arrow) & sinusoid (S). H&E stain.400x.

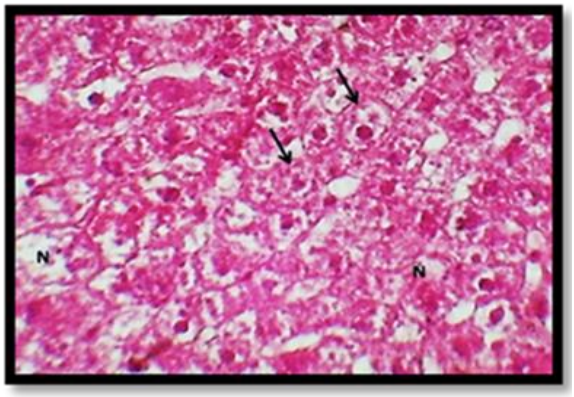

Figure 3. Section portion of liver (Induction group-2) manifest: cellular swelling (Arrows) and necrosis of hepatocytes (N). H&E stain.400x.

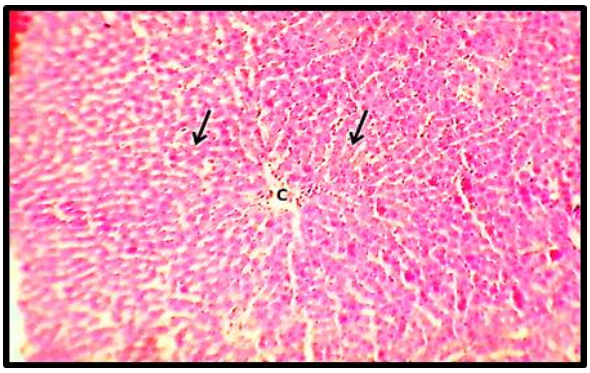

Figure 4. Section portion of liver (Control) manifest: Normal regular appearance of central vein (C & hepatic cords (Arrows). H&E stain.100x.

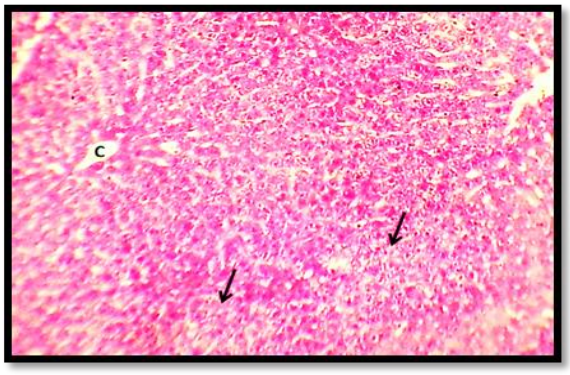

Figure 5. Section portion of liver (Induction group-2) manifest: A zonal degenerative change of the hepatic cords (Arrows). H&E stain.100x.

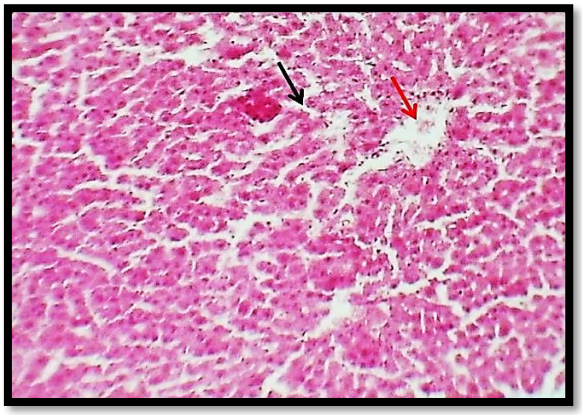

Figure 6. Section portion of liver tissue (Induction group-2) manifest: disarrangement of the central vein (Red arrow) & hepatic cords (Black arrow). H&E stain.100x.

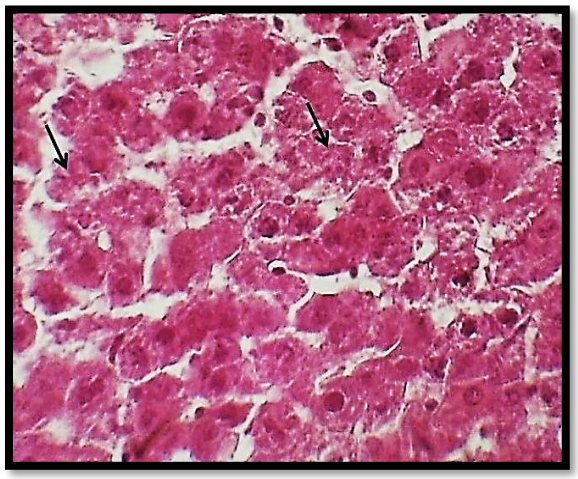

Figure 7. Section portion of liver tissue (Induction group-2) manifest: sever degeneration and necrosis of hepatocytes (Arrows). H&E stain.400x.

group, as illustrated in Figures 8-11.

Most histopathological images from the group treated with (Vitamin C and PRP) + carboplatin were similar to those observed in the control group, showing normal cells, in contrast to the control and carboplatin-treated groups (Figures 12 and 13). However, other images revealed minor degenerative changes, including vascular degeneration and intrahepatic necrosis

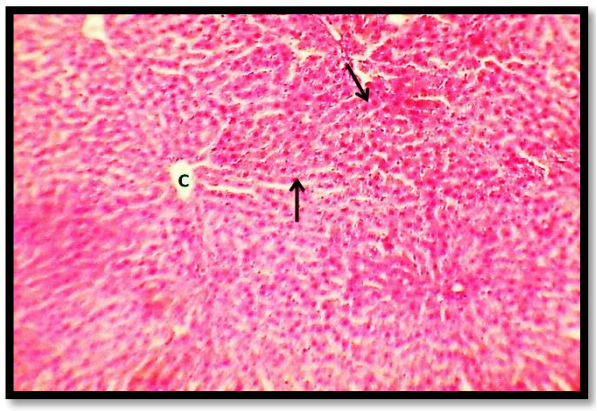

Figure 8. Section portion of liver tissue (Group 3) manifest: Normal orderly appearance of central vein (C & hepatic cords (Arrows). H&E stain.100x.

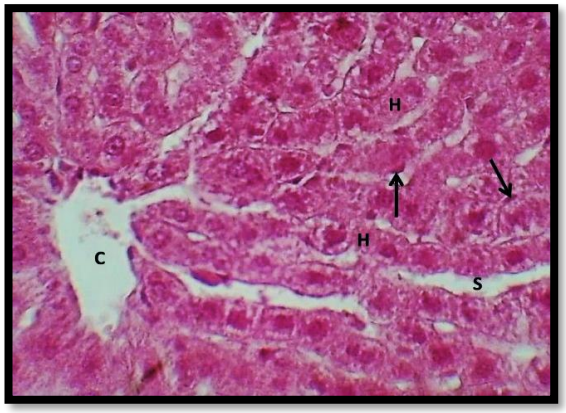

Figure 9. Section portion of liver tissue (Group 3) manifest: Normal orderly appearance of hepatocytes (H), kupffer cells (Black arrow) & sinusoid (S). H&E stain.400x.

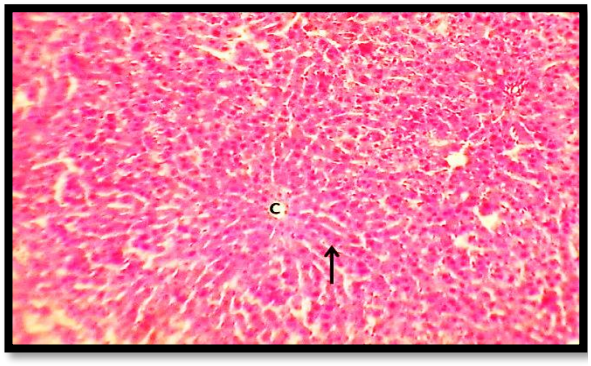

Figure 10. Section portion of liver tissue (Group 4) manifest: Normal orderly appearance of central vein (C & hepatic cords (Arrows). H&E stain.100x.

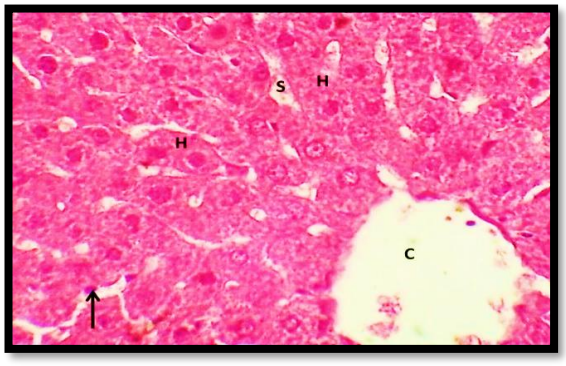

Figure 11. Section portion of liver tissue (Group 4) manifest: Normal appearance of hepatocytes (H), kupffer cells (Black arrow) & sinusoid (S). H&E stain.400x.

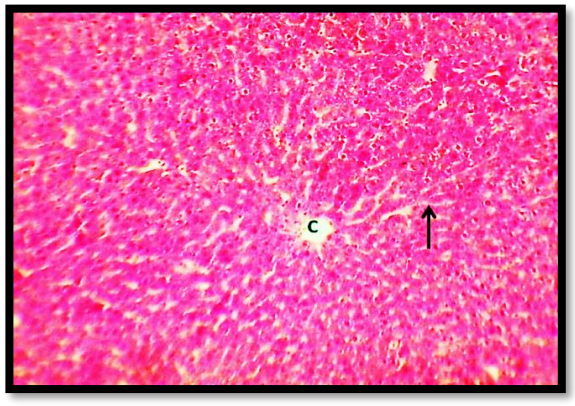

Figure 12. Section portion of liver liver tissue (Group 5) manifest: Normal appearance of central vein (C) & hepatic cords (Arrow). H&E stain.100x.

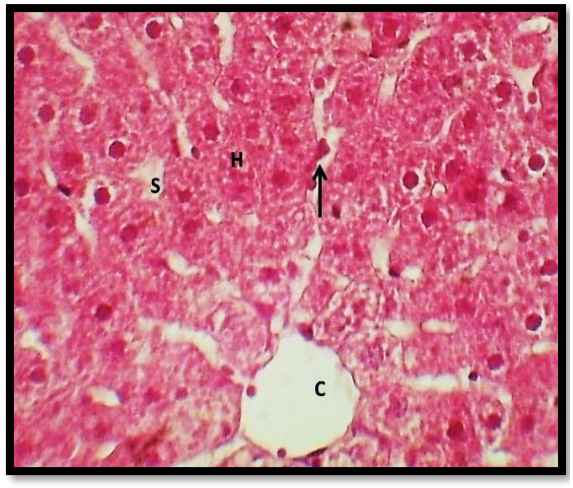

Figure 13. Section portion of liver tissue (Group 5) manifest: Normal regular appearance of hepatocytes (H), kupffer cells (Black arrow) & sinusoid (S). H&E stain.400x.

(Figures 14 and 15).

Discussion

The liver performs a vital function in the metabolic processes of toxins and remedies. Therefore, it is susceptible to injury from cytotoxic chemotherapy drugs that can produce liver toxicity [14, 15]. Our Histopathological findings confirmed that carboplatin administration provoked severe hepatic damage. Over the control group (Figure 4 and 5). Mechanistically,

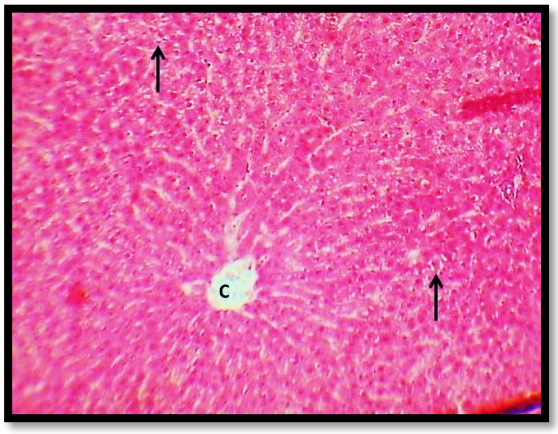

Figure 14. Section portion of liver tissue (Group 5) manifest: Normal orderly appearance of central vein (C) with mild zonal degenerative changes (Arrows). H&E stain.100x.

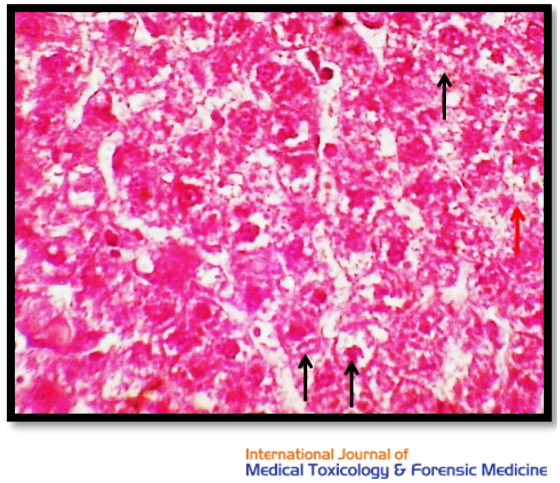

Figure 15. Section portion of liver tissue (Group 5) manifest: vacular degeneration of liver cells (Black arrows) & necrosis (red arrow). H&E stain.400x.

despite the strong antineoplastic activity of carboplatin, widely used in cancer treatment, its clinical application is often hindered by oxidative stress [16, 17].

However, co-administration of Vitamin C or PRP exhibited a significant hepatoprotective activity. As shown in Figures 8–11). The (VC+ Ca) and (PRP+ Ca) groups exhibited significant recovery of liver cell architecture; lobular structures were almost indistinguishable from those in the negative control group. This effect may be attributed to the strong antioxidant characteristics of vitamin C. Vitamin C is a biological reducing agent that can provide electron(s) to neutralize ROS or peroxides, thus preventing oxidative damage to cellular membranes [18]. Moreover, ascorbic acid is known to upregulate the activity of endogenous antioxidant enzymes, including Catalase, Glutathione Peroxidase, and SOD, thereby helping prevent the progression of liver fibrosis and inflammation [21, 19]. These findings align with [20] who reported that Vitamin C (VC) provides relative protection against drug-induced hepatotoxicity (e.g., Rifampicin) via modulation of the antioxidant defense system [21] Histological examinations, as shown in PRP+ Ca group Figure (10, 11), of the PRP therapy group showed a normal cellular structure of the liver lobules, similar to the control group, in contrast to the histological changes and damage observed in carboplatin therapy. PRP is a bio-concentrated autologous plasma system considered a regenerative therapy in medicine [22]. The study [24, 23] supports our findings regarding liver cell repair and regeneration, indicating that touch between blood platelets and liver cells stimulates the liberated of cytokines: insulin-like growth factor 1 (IGF-1), tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), hepatocyte growth factor (HGF), and eglufenac (EGF). These PRP cytokines promote platelet-stimulated hepatocyte proliferation. These pathways operate in diverse ways, including a positive effect on Kupffer cells, leading to an increase in platelet count and thus improved granular vascular endothelium in the liver [25]. Other results revealed minor degenerative changes, including vascular degeneration and intrahepatic necrosis in the PRP+VC+ Ca group (Figures 14 and 15). This may be due to several factors, including: VC may shift from its antioxidant role to that of Vitamin C ether via stimulating the production of free radicals [26]. Vitamin C and PRP compete for the same transporter proteins on the cell membrane, leading to impaired absorption of one or both and thus a lack of protective effect [27]. Platelets need to produce low, targeted levels of reactive oxygen species (ROS signaling) stimulating to stem cytes migration in addition to division. Vitamin C prior to PRP may disrupt this pathway [28]. PRP with vitamin C at a very low pH impairs platelets' ability to regulated release alpha-granules into the target tissue, rendering them ineffective [29].

Conclusion

Vitamin C and PRP reduced carboplatin-induced hepatic injury and preserved liver architecture in rats. Their synergistic effect may be partially enhanced compared to their individual use, as they act as inhibitors in some parts of the liver and as active agents in others, based on the reasons discussed in the results discussion above. These factors may lead to a shift in the synergistic effect from active to inhibitory. Quantitative dose-response studies incorporating biochemical and molecular endpoints are needed to determine the optimal use and translational relevance of these compounds. Different PRP dosages, measure cytokine levels identify the types of chromosomal

abnormalities resulting from carboplatin chemotherapy, and determine the protective effect of vitamin C or PRP through gene expression in liver tissue cells, particularly in cancer patients undergoing chemotherapy.

Ethical Approval

Ethical approval for this research was secured from the Ethics Board panel of the Iraqi Center for Cancer and Medical Genetics Research at Mustansiriyah University (Reference No. 4, dated June 30, 2026). All animal methodology was conducted in accordance with the committee's ethical recommendations and the standards of the National Panel for Research Ethics in Science and Technology. Every effort was made to protect animal dignity and welfare, apply the principles of replacement, reduction, and refinement, minimize pain and distress, maintain appropriate housing and biological conditions, and ensure that all procedures were performed by suitably trained personnel.

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No external funding was received for this research.

Conflicts of Interest

The authors report there are no competing interests to declare.

References

[1] Agrawal P, Jain M. The amelioration of side effects associated with chemotherapy. Curr Cancer Ther Rev. 2025;21:164–75. [DOI: 10.2174/0115733947274568231121173724]

[2] Mudd TW, Guddati AK. Management of hepatotoxicity of chemotherapy and targeted agents. Am J Cancer Res. 2021;11:3461–74. [Link]

[3] Griesinger F, Korol EE, Kayaniyil S, Schuler M, Eberhardt WEE, Murtaza G, et al. Efficacy and safety of first-line carboplatin- versus cisplatin-based chemotherapy for non-small cell lung cancer: a meta-analysis. Lung Cancer. 2019;135:196–204. [DOI: 10.1016/j.lungcan.2019.07.010]

[4] Stevens SM, McClelland CM, Trusheim JE, Bhatt A, Savino PJ, Liu GT, et al. Carboplatin-associated cranial neuropathy. J Neuroophthalmol. 2018;42:302–5. [DOI: 10.1080/01658107.2017.1419367]

[5] Stojanovska V, Sakkal S, Nurgali K. Platinum-based chemotherapy: gastrointestinal immunomodulation and enteric nervous system toxicity. Am J Physiol Gastrointest Liver Physiol. 2015;308:G223–32. [DOI: 10.1152/ajpgi.00212.2014]

[6] Cao S, Wang C, Ma H, Yin R, Zhu M, Shen W, et al. Genome-wide association study on platinum-induced hepatotoxicity in non-small cell lung cancer patients. Sci Rep. 2015;5:11556. [DOI: 10.1038/srep11556]

[7] Das SK, Nerune SM, Das KK. Antioxidant therapy for hepatic diseases: a double-edged sword. J Basic Clin Physiol Pharmacol. 2024;35:7–14. [DOI: 10.1515/jbcpp-2023-0156]

[8] Abdulrazzaq AM, Badr M, Gammoh O, Abu-Rish EY, Salim S, Hjh M, et al. Hepatoprotective actions of ascorbic acid, alpha lipoic acid and silymarin or their combination against acetaminophen-induced hepatotoxicity in rats. Medicina. 2019;55:181. [DOI: 10.3390/medicina55050181]

[9] Okereke UO, Mbah A, Nwosu IC, et al. Investigating the protective effects of ascorbic acid against paracetamol-induced liver toxicity in Wistar rats. Asian J Res Med Pharm Sci. 2024;13:1–8. [DOI: 10.9734/ajrimps/2024/v13i4269]

[10] Wu WS, Chen LR, Chen KH. Platelet-rich plasma (PRP): molecular mechanisms, actions and clinical applications in human body. Int J Mol Sci. 2025;26:10804. [DOI: 10.3390/ijms262110804]

[11] Pineda-Cortel MR, Suarez C, Cabrera JT, et al. Complexity of platelet-rich plasma: mechanism of action, growth factor utilization and variation in preparation. Plasmatology. 2024;18:26348535241277625. [DOI: 10.1177/26348535241277625]

[12] Ballesta FJG, Vásquez LNA, Borbón JR, et al. Management of platelet-rich plasma and stem cells versus conventional treatments in musculoskeletal injury repair: a systematic review. J Musculoskelet Surg Res. 2025;9:1–9. [DOI: 10.25259/JMSR_402_2025]

[13] Suvarna, SK, Layton C, Bancroft JD. Theory and practice of histological techniqueseighth. UK. Elsevier Health Sci. 2019;8:126-79. [Link]

[14] Hoofnagle JH, Björnsson ES. Drug-induced liver injury: types and phenotypes. N Engl J Med. 2019;381:264–73. [DOI: 10.1056/NEJMra1816149]

[15] Jaeschke H. Mechanisms of hepatotoxicity. Toxicol Sci. 2002;65:166–76. [DOI: 10.1093/toxsci/65.2.166]

[16] Kim SW, Paek J, Nam EJ, et al. The feasibility of carboplatin-based intraperitoneal chemotherapy in ovarian cancer. Eur J Obstet Gynecol Reprod Biol. 2010;152:195–9. [DOI: 10.1016/j.ejogrb.2010.05.033]

[17] Miyagi Y, Fujiwara K, Kigawa J, et al. Intraperitoneal carboplatin infusion may be a pharmacologically more reasonable route than intravenous administration as a systemic chemotherapy: a comparative pharmacokinetic analysis of platinum using a new mathematical model after intraperitoneal vs. intravenous infusion of carboplatin—a Sankai Gynecology Study Group (SGSG) study. Gynecol Oncol. 2005;99:591–6. [DOI: 10.1016/j.ygyno.2005.06.055]

[18] Adikwu E, Deo O. Hepatoprotective effect of vitamin C (ascorbic acid). Pharmacol Pharm. 2013;4:84–92. [DOI: 10.4236/pp.2013.41012]

[19] EL-Gendy KS, Aly NM, Mahmoud FH, et al. The role of vitamin C as antioxidant in protection of oxidative stress induced by imidacloprid. Food Chem Toxicol. 2010;48:215–21. [DOI: 10.1016/j.fct.2009.10.003]

[20] Awodele O, Akintonwa A, Osunkalu VO, et al. Modulatory activity of antioxidants against the toxicity of rifampicin in vivo. Rev Inst Med Trop São Paulo. 2010;52:43–6. [DOI: 10.1590/S0036-46652010000100007]

[21] Reddy AG, Soujanya S, Lakshman M, et al. Evaluation of the protective role of vitamin C in imidacloprid-induced hepatotoxicity in male albino rats. J Nat Sci Biol Med. 2013;4:63. [DOI: 10.4103/0976-9668.107262]

[22] Pavlovic V, Ciric M, Jovanovic V, et al. Platelet rich plasma: a short overview of certain bioactive components. Open Med. 2016;11:242–7. [DOI: 10.1515/med-2016-0048]

[23] Ohkohchi N, Murata S, Takahashi K. Platelet and liver regeneration. In: Davies J, editor. Tissue regeneration: from basic biology to clinical application. InTech; 2012. [DOI: 10.5772/25422]

[24] Gilgenkrantz H, Collin de l'Hortet A. New insights into liver regeneration. Clin Res Hepatol Gastroenterol. 2011;35:623–9. [DOI: 10.1016/j.clinre.2011.04.002]

[25] Takahashi K, Liang C, Oda T, Ohkohchi N. Platelet and liver regeneration after liver surgery. Surg Today. 2020 ;50(9):974-83. [DOI: 10.1007/s00595-019-01890-x]

[26] Timoshnikov VA, Kobzeva TV, Polyakov NE, et al. Redox interactions of vitamin C and iron: inhibition of the pro-oxidant activity by deferiprone. Int J Mol Sci. 2020;21:3967. [DOI: 10.3390/ijms21113967]

[27] Cao X, Yi Y, Ji M, et al. The dual role of vitamin C in cancer: from antioxidant prevention to prooxidant therapeutic applications. Front Med (Lausanne). 2025;12:1633447. [DOI: 10.3389/fmed.2025.1633447]

[28] Ranzato E, Martinotti S, Volante A, Burlando B. Platelet lysate promotes mesenchymal stem cell ROS production required for activation of cell migration. Cell Prolif. 2011;44(2):183–92. [DOI: 10.1111/j.1365-2184.2011.00744.x]

[29] Murphy S, Gardner FH. Effect of pH on platelet aggregation and the release reaction. Blood. 1975;46(2):209–18. [DOI: 10.1182/blood.V46.2.209.209]