RESEARCH PAPER

Evaluation of the Hepatoprotective Activity of Myricetin against Cisplatin-Induced Liver Injury in Rats

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ABSTRACT

Objective: The present study aimed to evaluate the protective effect of Myricetin on Cisplatin induced hepatotoxicty in experimental rats.

Methods: Rats were randomly divided into five groups. Hepatotoxicity was induced by cisplatin at 7.5 mg/kg dose and serum AST, ALT, total bilirubin and albumin, hepatic hydroxy proline (HP), reduced glutathione (GSH) and malondialdehyde (MDA), cytokines were measured.

Results: In the present study we found that, Cisplatin in rats showed decreased in body and increased liver weight, while treatment with Myricetin showed normal body and liver weight. Serum AST, ALT, total bilirubin, HP, GSH, MDA and cytokines were increased Cisplatin rats. Myricetin treated rats showed reduction in the oxidative stress as well as inhibited the release of cytokines in dose dependent manner and showed protection against hepatotoxicity.

Conclusion: The study concludes that, Myricetin has protective effect against the hepatotoxicity induced by cisplatin.

Keywords: *Cisplatin; Hepatotoxicty; ALT; oxidative stress; Myricetin; Cytokine.*
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INTRODUCTION

Cisplatin is a widely used antineoplastic agent in the treatment of metastatic cancers and various solid tumours. Despite its strong therapeutic efficacy, its clinical application is often restricted due to dose-dependent toxicity(1). Higher doses of cisplatin, although more effective in suppressing tumour growth, are associated with severe adverse effects, including irreversible damage to the liver and other vital organs. The drug is also known to accumulate in hepatic tissue, particularly following high or repeated administration, which further contributes to its toxic profile(2).

Cisplatin-induced hepatotoxicity has been strongly linked to oxidative stress mechanisms. One of the proposed pathways involves the increased expression of CYP2E1, a key enzyme responsible for the generation of reactive oxygen species (ROS). This excessive production of ROS leads to cellular damage, lipid peroxidation, and impairment of normal hepatic function. Even low-dose repeated exposure to cisplatin has been reported to induce liver toxicity, likely due to progressive accumulation within hepatic tissue(3,4).

In addition to oxidative stress, reactive nitrogen species (RNS) also play a crucial role in cisplatin-induced liver injury. Species such as peroxynitrite ($ONOO^-$), peroxynitrous acid (HONOO), nitrogen dioxide radical (NO_2•), and related reactive intermediates contribute to nitrosative stress, exacerbating cellular damage. These RNS are derived from nitric oxide (NO•), which is synthesized by nitric oxide synthase (NOS) enzymes that catalyze NO production(5-7).

Given these mechanisms, there is growing interest in identifying natural compounds with antioxidant and hepatoprotective properties to mitigate cisplatin-induced toxicity. Myricetin, a naturally occurring flavonoid, has been reported to exhibit strong antioxidant, anti-inflammatory, and cytoprotective effects. However, its potential protective role against cisplatin-induced hepatotoxicity has not been fully explored(8,9).

Therefore, the present study aimed to investigate the protective effect of myricetin against cisplatin-induced hepatotoxicity in rats.

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MATERIALS AND METHODS

Animals

The experimental protocol was approved by the Ethical Committee of TVES's Hon'ble Loksevak Madhukarrao Chaudhari College of Pharmacy, Faizpur (652/PO/Re/S/02/CPCSEA). Male Wistar rats (180–200 g) were procured from Crystal Biological Solutions, Pune, India. Animals were housed in the Animal Care Facility under standard laboratory conditions, maintained at a temperature of 23 ± 1 °C, relative humidity of 65%, and a 12 h light/dark cycle. Animals had free access to standard pellet diet and water ad libitum. All experimental procedures were conducted in accordance with the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), India.

Drugs and Chemicals

Cisplatin (Cytoplatin-50, Cipla) was purchased from a local pharmacy. Glycitein was obtained from Sigma-Aldrich, India. ELISA kits for interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-α), and interleukin-1 beta (IL-1β) were procured from Bioscience, Mumbai, India. Reagents such as sodium chloride (NaCl), potassium chloride (KCl), and biochemical assay kits for aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) were also obtained from Bioscience, Mumbai.

Instruments and Equipment

The study utilized standard laboratory instruments including a micropipette, microplate reader, UV-spectrophotometer, centrifuge, analytical balance, pH meter, vortex mixer, homogenizer, microscope with camera system, and metabolic cages. A digital balance was used for dosing and body weight measurements.

Experimental Design: Cisplatin-Induced Hepatotoxicity in Rats

Thirty male Wistar rats were randomly divided into five groups (n = 6 per group):

Group I (Normal control): Received 1 mL normal saline intraperitoneally.

Group II (Control): Received cisplatin (3 mg/kg, i.p.) on day 10.

Group III (Myricetin 50): Received myricetin (50 mg/kg) + cisplatin (3 mg/kg, i.p.).

Group IV (Myricetin 100): Received myricetin (100 mg/kg) + cisplatin (3 mg/kg, i.p.).

Group V (Myricetin 150): Received myricetin (150 mg/kg) + cisplatin (3 mg/kg, i.p.).

Myricetin was administered daily up to day 28, while cisplatin was administered on day 10 of the experiment via the intraperitoneal route.

Induction of Hepatotoxicity

Hepatotoxicity was induced by a single intraperitoneal injection of cisplatin (3 mg/kg, diluted in distilled water up to 1 mL) on the 10th day of the experiment(10).

Body Weight Measurement

Body weight of all animals was recorded on days 0, 7, 14, 21, and 28 using an analytical balance. At the end of the experiment, animals were sacrificed and kidney weights were recorded.

Sample Collection

Blood samples were collected from all animals and centrifuged at 10,000 rpm for 10 min to separate serum. The serum was stored at −20 °C until biochemical analysis.

Biochemical Analysis(11,12)

Blood Urea Nitrogen (BUN)

BUN levels were estimated spectrophotometrically according to the manufacturer's protocol. Serum samples were diluted (1:4), incubated with urease reagent, followed by alkaline hypochlorite solution. Absorbance was measured at 620 nm using a microplate reader, and concentration was calculated using a standard curve.

Serum Creatinine

Serum creatinine was estimated using picric acid (Jaffe's method). Absorbance changes were recorded after reaction with sodium hydroxide and picric acid. Creatinine concentration was calculated using standard calibration.

Estimation of Oxidative Stress Markers

Kidney tissue (10% homogenate) was prepared in ice-cold phosphate buffer (50 mM, pH 7.4). The homogenate was centrifuged at 2000 g for 10 min at 4 °C, and the supernatant was used for analysis of malondialdehyde (MDA), reduced glutathione (GSH), catalase (CAT), and superoxide dismutase (SOD).

Total Protein Estimation

Protein concentration in tissue homogenate was determined by the Bradford method using Coomassie Brilliant Blue G-250. Absorbance was measured at 595 nm, and results were expressed as mg/g tissue.

Lipid Peroxidation (MDA Assay)

Lipid peroxidation was measured by estimating malondialdehyde (MDA) levels using thiobarbituric acid reactive substances (TBARS) assay. Absorbance of the pink chromogen was measured at 532 nm, and results were expressed as ng/mg protein(13).

Reduced Glutathione (GSH) Estimation

GSH levels were determined using DTNB reagent. After precipitation with trichloroacetic acid and centrifugation, absorbance was measured at 412 nm. Results were expressed as ng/mg protein.

Catalase Activity

Catalase activity was determined by measuring the decomposition rate of hydrogen peroxide (H_2O_2). The decrease in absorbance was recorded at 240 nm, and results were expressed as U/mg protein.

Superoxide Dismutase (SOD) Activity
SOD activity was estimated based on inhibition of nitroblue tetrazolium (NBT) reduction. Absorbance was measured at 560 nm, and enzyme activity was expressed as U/mg protein.

Nitrite Estimation (Griess Assay)
Nitrite levels were determined using Griess reagent. After incubation, absorbance was measured at 540 nm using a microplate reader, and concentrations were calculated from a standard curve.

Cytokine Estimation (ELISA)
Levels of TNF-α, IL-1β, and IL-6 were measured using a sandwich ELISA technique according to manufacturer instructions. Absorbance was recorded at 450 nm, and cytokine concentrations were calculated using standard curves.

RESULTS

Effect of Myricetin on body weight and liver weight
Body weight of Cisplatin treated group increased throughout the treatment periods as compared to normal groups. In group treated with Myricetin 150 mg/kg shows same pattern of increase in body weight like normal group. Myricetin treated with 50 mg/kg has no effect on body weight as compared to control group (P< 0.005). Liver weight of animal was measured at the end of study and we found that increase in liver weight in control group as compared to normal group (P< 0.001). Myricetin treated with 150 mg/kg showed most prominent effect on liver weight as compared to control group (P< 0.005) shown in table 1.

Table 1: Effect of Myricetin on body weight and liver weight

Group	Body weight (gm)		Liver weight (gm)
	0 Day	28 day	
Normal Control	192.5± 6.21	201.4±6.05	5.51 ± 0.6
Disease Control	184.7± 4.05	149.4±7.25	7.84 ± 0.6$^{###}$
T1	191.2±6.41	208.5±6.48	7.62 ± 0.8
T2	183.8±5.18	211.5±5.41	7.43 ± 0.7**
T3	185.8±6.15	213.7±5.14	5.89 ± 0.8***

Data were expressed as mean ± SEM, analysed using one way analysis of variance, *p<0.05, **P<0.01, ***P<0.001 compared to control rats and ##P<0.01, ###P<0.001 is compared with normal group.

Effect of Myricetin on Serum Aspartate Aminotransferase (AST)
A significant increase in serum AST levels was observed in the cisplatin-treated control group when compared with the normal group (P < 0.005), indicating hepatocellular injury. Treatment with myricetin at 50 mg/kg showed no significant effect on AST levels. However, administration of myricetin at doses of 100 and 150 mg/kg significantly reduced AST levels compared to the cisplatin control group (P < 0.005), suggesting hepatoprotective activity (Figure 1).

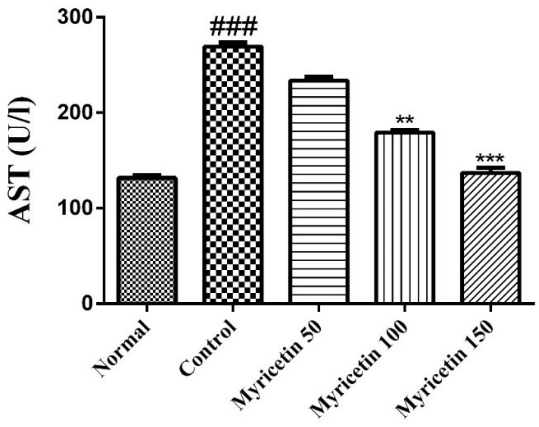

Figure 1: Effect of Myricetin on serum AST. Values are expressed as mean ± SEM (n = 6). Statistical significance was determined by one-way ANOVA followed by Dunnett's test. ###P < 0.01 vs Normal; *P < 0.01 vs Control.

Effect of Myricetin on Serum Alanine Aminotransferase (ALT)
Serum ALT levels were significantly elevated in cisplatin-treated rats compared to the normal group, indicating hepatic dysfunction. Treatment with myricetin resulted in a dose-dependent reduction in ALT levels. Doses of 100 and 150 mg/kg significantly decreased ALT levels compared to the cisplatin control group (P < 0.005) (Figure 2).

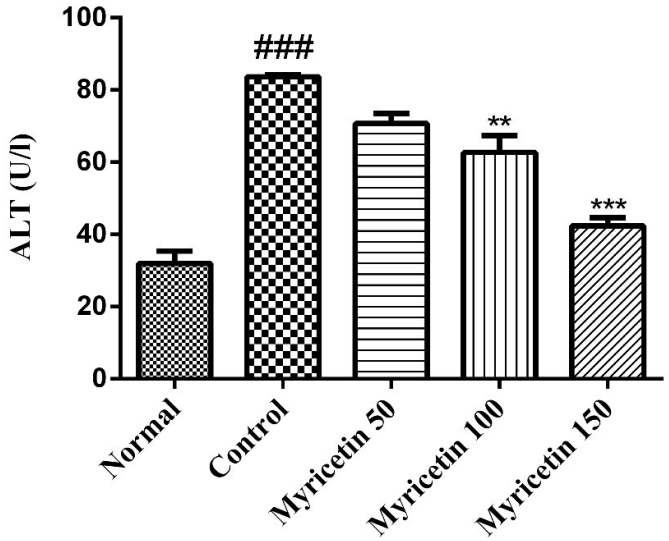

Figure 2: Effect of Myricetin on serum ALT. Values are expressed as mean ± SEM (n = 6). Statistical significance was determined by one-way ANOVA followed by Dunnett's test. ###P < 0.01 vs Normal; *P < 0.01 vs Control.

Effect of Myricetin on Serum Alkaline Phosphatase (ALP)

Cisplatin administration significantly increased serum ALP levels compared to the normal group (P < 0.005). Treatment with myricetin significantly reduced ALP levels, with the 150 mg/kg dose showing the most pronounced effect compared to the control group (Figure 3).

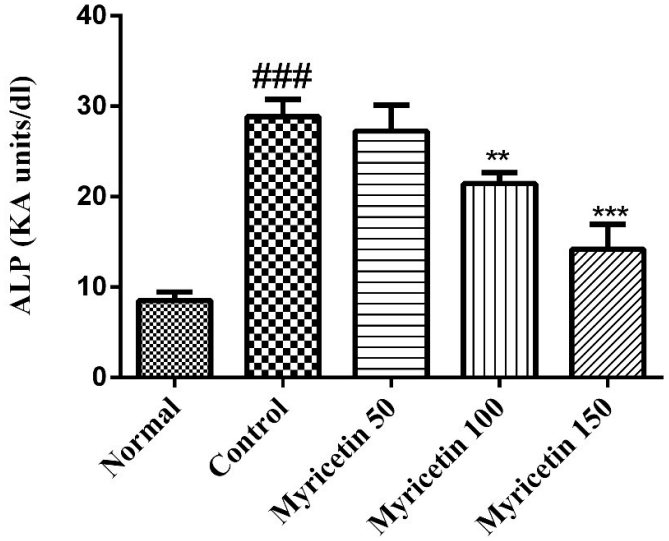

Figure 3: Effect of Myricetin on serum ALP. Values are expressed as mean ± SEM (n = 6). Statistical significance was determined by one-way ANOVA followed by Dunnett's test. ###P < 0.01 vs Normal; *P < 0.01 vs Control.

Effect of Myricetin on Serum Total Bilirubin

Total bilirubin levels were markedly elevated in cisplatin-treated rats compared to normal animals (P < 0.005). Myricetin treatment significantly reduced bilirubin levels in a dose-dependent manner, with the 150 mg/kg group showing the most significant improvement (Figure 4).

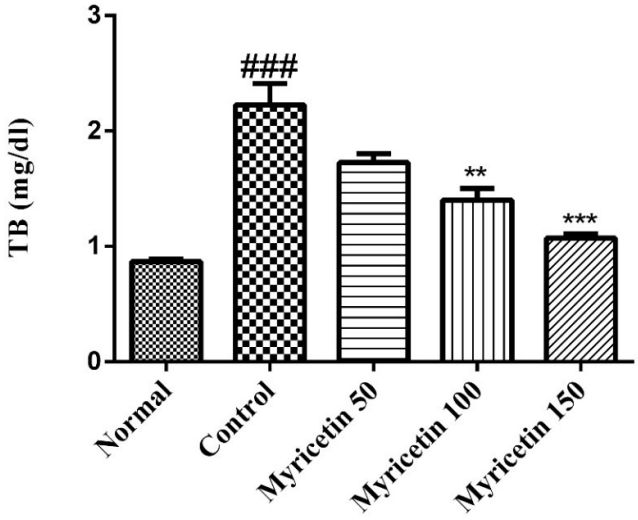

Figure 4: Effect of Myricetin on serum total bilirubin. Values are expressed as mean ± SEM (n = 6). Statistical significance was determined by one-way ANOVA followed by Dunnett's test. ###P < 0.01 vs Normal; *P < 0.01 vs Control.

Effect of Myricetin on Serum Hydroxyproline

Hydroxyproline levels were significantly elevated in cisplatin-treated rats, indicating hepatic fibrosis. Treatment with myricetin significantly reduced hydroxyproline levels in a dose-dependent manner, with the 150 mg/kg dose producing the greatest reduction (P < 0.005) (Figure 5).

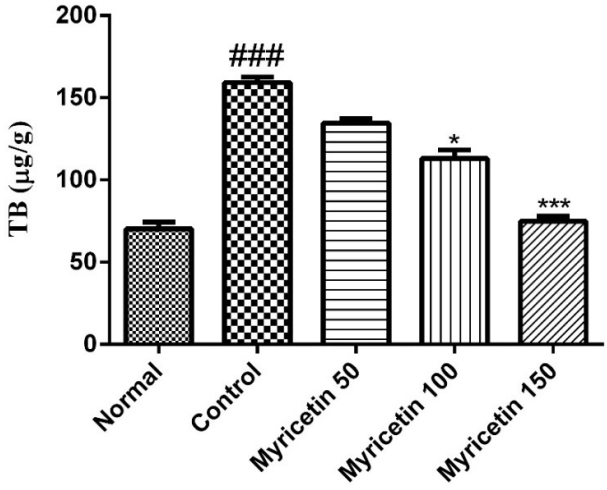

Figure 5: Effect of Myricetin on serum hydroxyproline. Values are expressed as mean ± SEM (n = 6). Statistical significance was determined by one-way ANOVA followed by Dunnett's test. ###P < 0.01 vs Normal; *P < 0.01 vs Control.

Effect of Myricetin on Pro-inflammatory Cytokine IL-6, IL-1β and, TNF-α

Cisplatin treatment significantly increased serum IL-6 levels compared to the normal group, indicating enhanced inflammatory response. Myricetin administration significantly reduced IL-6 levels, with 150 mg/kg restoring values close to normal. Serum IL-1β levels were significantly elevated in the cisplatin group. Treatment with myricetin (50, 100, and 150 mg/kg) significantly reduced IL-1β levels in a dose-dependent manner, with the highest dose showing maximum effect. A significant increase in TNF-α levels was observed in cisplatin-treated rats compared to normal controls. Myricetin treatment (100 and 150 mg/kg) significantly reduced TNF-α levels, suggesting an anti-inflammatory effect (Figure 6).

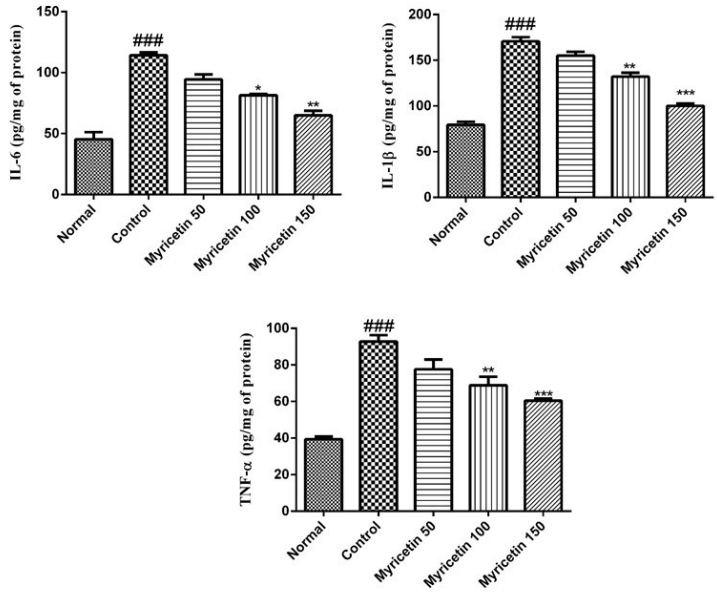

Figure 6- Effect of Myricetin on Pro-inflammatory Cytokine IL-6, IL-1β and, TNF-α

Values are expressed as means ± SEM, n = 06. Statistical significance was determined by one-way ANOVA followed by the Dunnet test: Compared with Normal ###P < 0.01, Compared with Control

Effect of Myricetin on oxidative stress

Cisplatin administration significantly decreased SOD activity compared to normal rats. Treatment with myricetin significantly increased SOD levels in a dose-dependent manner, indicating restoration of antioxidant defense.GSH levels were significantly reduced in cisplatin-treated animals. Myricetin administration significantly restored GSH levels in a dose-dependent manner compared to the control group. Catalase activity was significantly reduced following cisplatin administration. Treatment with myricetin significantly increased catalase activity in all treated groups, with the highest effect observed at 150 mg/kg. Cisplatin significantly increased MDA levels, indicating enhanced lipid peroxidation. Myricetin treatment significantly reduced MDA levels in a dose-dependent manner compared to the cisplatin control group (Figure 7).

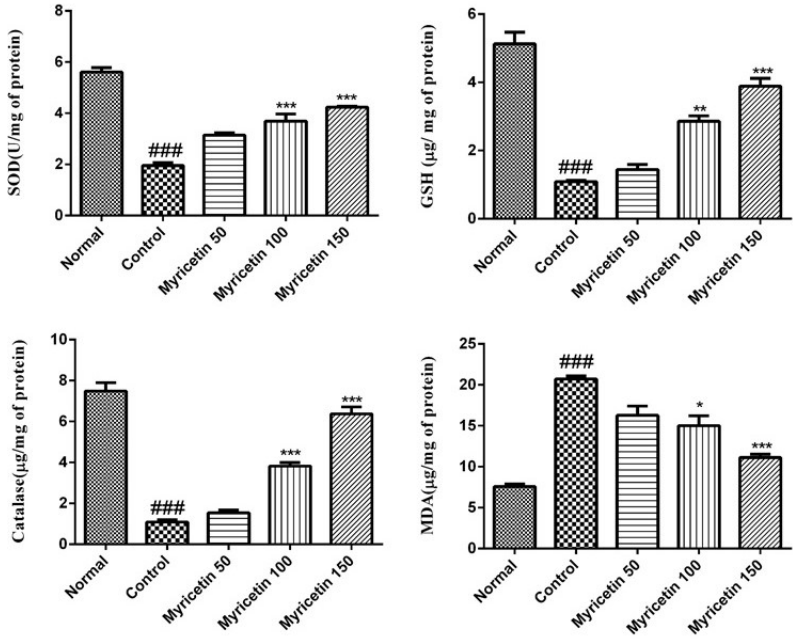

Figure 7- Effect of Myricetin on oxidative stress

Values are expressed as means ± SEM, n = 06. Statistical significance was determined by one-way ANOVA followed by the Dunnet test: Compared with Normal ###P < 0.01, Compared with Control

DISCUSSION

The present study investigated the hepatoprotective potential of myricetin against cisplatin-induced hepatic injury in rats. Cisplatin, a potent chemotherapeutic agent, is well known for its dose-limiting toxicity affecting multiple organs, including the liver. In the current study, cisplatin administration produced marked hepatotoxicity, as evidenced by significant elevations in serum liver function biomarkers (AST, ALT, ALP, and total bilirubin) along with increased hydroxyproline levels, indicating hepatic fibrosis. These biochemical alterations confirm that cisplatin induces substantial structural and functional liver damage, consistent with previous reports (14,15).

Elevated serum transaminases (AST and ALT) are classical indicators of hepatocellular injury, reflecting leakage of enzymes from damaged hepatocytes into the circulation. In the present study, cisplatin significantly increased AST and ALT levels, suggesting membrane damage and loss of hepatic cellular integrity. Similarly, increased ALP and bilirubin levels further indicate impairment in bile flow and hepatic excretory function. Treatment with myricetin significantly attenuated these elevations in a dose-dependent manner, suggesting stabilization of hepatocyte membranes and improvement in liver function(16).

Hydroxyproline, a biochemical marker of collagen deposition and fibrosis, was significantly elevated in cisplatin-treated animals, indicating progression toward fibrotic changes in hepatic tissue. Myricetin treatment markedly reduced hydroxyproline levels, suggesting inhibition of extracellular matrix accumulation and antifibrotic potential. These findings indicate that myricetin may help in preventing cisplatin-induced progression from hepatocellular injury to fibrosis.

Inflammation plays a central role in cisplatin-induced hepatotoxicity. In the present study, cisplatin significantly elevated pro-inflammatory cytokines, including TNF-α, IL-1β, and IL-6. These cytokines are key mediators of inflammatory signaling and contribute to hepatocyte apoptosis, necrosis, and progression of liver injury. Myricetin administration significantly suppressed the levels of these cytokines, indicating a strong anti-inflammatory effect. This suggests that myricetin may inhibit cytokine-mediated inflammatory cascades involved in cisplatin toxicity.

Oxidative stress is a major mechanism underlying cisplatin-induced organ toxicity. In the present study, cisplatin administration resulted in a significant increase in malondialdehyde (MDA) levels, indicating enhanced lipid peroxidation and membrane damage. Concurrently, antioxidant defense systems were severely compromised, as evidenced by decreased levels of superoxide dismutase (SOD), catalase, and reduced glutathione (GSH). These alterations confirm that cisplatin induces severe oxidative stress in hepatic tissue.

Treatment with myricetin effectively restored antioxidant status by increasing SOD, catalase, and GSH levels, while simultaneously reducing MDA levels. This indicates that myricetin exerts strong free radical scavenging activity and enhances endogenous antioxidant defense mechanisms. The observed effects may be attributed to the well-documented antioxidant properties of flavonoids, which can neutralize reactive oxygen species and protect cellular components from oxidative damage.

Overall, the results of the present study demonstrate that myricetin provides significant protection against cisplatin-induced hepatotoxicity through multiple mechanisms, including antioxidant, anti-inflammatory, and antifibrotic actions. The dose-dependent improvement observed in biochemical parameters further supports its therapeutic potential. The hepatoprotective effect of myricetin may be attributed to its ability to modulate oxidative stress pathways, suppress pro-inflammatory cytokine production, and stabilize cellular membranes.

In conclusion, myricetin shows promising potential as a protective agent against cisplatin-induced liver injury. Further studies involving molecular mechanisms and clinical evaluation are warranted to validate its efficacy and safety in translational settings.

REFERENCES

1. Alqudah, A., Qnais, E., Bsieso, Y. and Alotaibi, B.S., 2026. Cirsimaritin attenuates cisplatin-induced hepatotoxicity via modulation of oxidative stress and NF-κB/Akt signaling pathways in rats. Toxin Reviews, 45(2), pp.204-214.
2. Gazwi, H.S., Zaki, A.H., Abd Allah, N.A., Gomaa, A.T., Milošević, M., Al-Rejaie, S.S., Mohany, M. and Yassien, E.E., 2024. Mitigation of cisplatin-induced hepatotoxicity by Salvia officinalis: Attenuation of oxidative damage and inflammation in rats. Free Radical Biology and Medicine, 222, pp.62-71.
3. Satyam, S.M., Bairy, L.K., Rehman, A., Farook, M., Khan, S., Nair, A.A., Binu, N.N., Yehya, M. and Khan, M.M., 2024. Dapagliflozin: a promising strategy to combat cisplatin-induced hepatotoxicity in Wistar rats. Biology, 13(9), p.672.
4. Aboraya, D.M., El Baz, A., Risha, E.F. and Abdelhamid, F.M., 2022. Hesperidin ameliorates cisplatin induced hepatotoxicity and attenuates oxidative damage, cell apoptosis, and inflammation in rats. Saudi journal of biological sciences, 29(5), pp.3157-3166.
5. Martins, N.M., Santos, N.A.G.D., Curti, C., Bianchi, M.D.L.P. and Santos, A.C.D., 2008. Cisplatin induces mitochondrial oxidative stress with resultant energetic metabolism impairment, membrane rigidification and apoptosis in rat liver. Journal of Applied Toxicology: An International Journal, 28(3),

pp.337-344.

6. Lu, Y. and Cederbaum, A.I., 2006. Cisplatin-induced hepatotoxicity is enhanced by elevated expression of cytochrome P450 2E1. Toxicological Sciences, 89(2), pp.515-523.
7. Palipoch, S., Punsawad, C., Koomhin, P. and Suwannalert, P., 2014. Hepatoprotective effect of curcumin and alpha-tocopherol against cisplatin-induced oxidative stress. BMC complementary and alternative medicine, 14(1), p.111.
8. Yang, Y.L., Liu, M., Cheng, X., Li, W.H., Zhang, S.S., Wang, Y.H. and Du, G.H., 2019. Myricitrin blocks activation of NF-κB and MAPK signaling pathways to protect nigrostriatum neuron in LPS-stimulated mice. Journal of neuroimmunology, 337, p.577049.
9. Tikent, A., Laaraj, S., Bouddine, T., Chebaibi, M., Bouhrim, M., Elfazazi, K., Alqahtani, A.S., Noman, O.M., Hajji, L., Rhazi, L. and Elamrani, A., 2024. Antioxidant potential, antimicrobial activity, polyphenol profile analysis, and cytotoxicity against breast cancer cell lines of hydro-ethanolic extracts of leaves of (Ficus carica L.) from Eastern Morocco. Frontiers in Chemistry, 12, p.1505473.
10. Cagin, Y.F., Erdogan, M.A., Sahin, N., Parlakpinar, H., Atayan, Y., Polat, A., Vardi, N., Yildiz, A. and Tanbek, K., 2015. Protective effects of apocynin on cisplatin-induced hepatotoxicity in rats. Archives of medical research, 46(7), pp.517-526.
11. Nimbalkar, V. and Vyawahare, N., 2021. L-carnitine ameliorates bile duct ligation induced liver fibrosis via reducing the nitrosative stress in experimental animals: preclinical evidences. Heliyon, 7(11).
12. Kalkan, N.S. and Gökçimen, A., 2026. Protective structural and enzymatic roles of catechin and gallic acid against nephrotoxicity and hepatotoxicity ınduced by cisplatin. Scientific Reports, 16(1), p.9046.
13. Sonawane, V.K., Mahajan, U.B., Shinde, S.D., Chatterjee, S., Chaudhari, S.S., Bhangale, H.A., Ojha, S., Goyal, S.N., Kundu, C.N. and Patil, C.R., 2018. A chemosensitizer drug: disulfiram prevents doxorubicin-induced cardiac dysfunction and oxidative stress in rats. Cardiovascular toxicology, 18(5), pp.459-470.
14. Kedderis, G.L., 1996. Biochemical basis of hepatocellular injury. Toxicologic pathology, 24(1), pp.77-83.
15. Abou Seif, H.S., 2016. Physiological changes due to hepatotoxicity and the protective role of some medicinal plants. Beni-suef University journal of basic and applied sciences, 5(2), pp.134-146.
16. Mir, M., Arab, M.R., Shahraki, M.R., Mashhadi, M.A., SHAHRAKI, S.M., SARGOLZAEI, A.F. and Karimfar, M.H., 2015. Toxic effects of cisplatin on hepatocytes and liver enzymes of rats.