J Biochem Technol (2025) 16(2): 33-40
https://doi.org/10.51847/JrmPvIA6dK
ISSN: 0974-2328

Chlorophytum Comosum in Hepatoprotection: A Novel Approach to Managing Toxic Liver Damage

Nuriiat Yahyaevna Magomedova, Patimat Muslimovna Magomedova, Patimat Magomedovna Pashaeva*, Aishat Gitinovna Magomedova, Indira Akhmedovna Amagaeva, Patimat Rasulovna Mukhidinova, Murad Rustamovich Shakhbanov, Ramazan Akhmedovich Abdulpatakhov

Received: 28 February 2025 / Received in revised form: 16 May 2025, Accepted: 20 May 2025, Published online: 25 June 2025

Abstract

This research investigates the therapeutic potential of aqueous *Chlorophytum comosum* extract in managing bilirubin metabolism disturbances in laboratory animals with experimentally induced toxic hepatitis. The study compared the efficacy of three treatment approaches: *Chlorophytum comosum* extract monotherapy, standard vitamin therapy (including vitamins B_1, B_2, B_6, B_{12}, PP, E, and C), and a combination of both treatments. The experiment involved four groups of Chinchilla breed rabbits, with toxic hepatitis induced by a single subcutaneous injection of carbon tetrachloride (CCl_4). Blood samples were collected daily to measure total and direct bilirubin levels using the «Lakhema» test method. Key findings revealed that CCl_4 intoxication significantly increased bilirubin levels, primarily affecting direct bilirubin. The highest bilirubin concentrations were observed on the 4th day in untreated rabbits. By the tenth day of the research, the combination therapy group notably showed the most effective reduction in bilirubin levels. The research highlights the potential of *Chlorophytum comosum* extract as a promising hepatoprotective agent, showing comparable efficacy to standard vitamin therapy and demonstrating additive effects when combined. These findings suggest that *Chlorophytum comosum* extract could serve as a valuable adjunct in managing toxic liver injuries, offering a natural alternative to conventional treatments. The study emphasizes the importance of further research into the hepatoprotective properties of plant-based remedies, particularly in addressing liver damage caused by environmental toxins and industrial pollutants. The results contribute to the growing body of evidence supporting the therapeutic potential of natural compounds in liver disease management.

Nuriiat Yahyaevna Magomedova, Patimat Muslimovna Magomedova, Patimat Magomedovna Pashaeva*, Aishat Gitinovna Magomedova, Indira Akhmedovna Amagaeva, Patimat Rasulovna Mukhidinova, Murad Rustamovich Shakhbanov, Ramazan Akhmedovich Abdulpatakhov
Department of Medicine, Faculty of Therapy, Dagestan State Medical University, Makhachkala, Russia.

***E-mail:** publab@bk.ru

Keywords: *Chlorophytum comosum* extract, Acute toxic hepatitis, Bilirubin fractions, Hepatoprotection

Introduction

Liver damage due to acute exogenous intoxications represents a significant clinical challenge, affecting more than 30% of patients with various forms of poisoning (Berumen *et al*., 2021; Torgersen *et al*., 2024). The global increase in environmental pollution and industrial activities has led to a rise in hepatotoxic exposures (Di Martino *et al*., 2023; Cunningham *et al*., 2024). Various industrial and agricultural toxins enter the human body through air and food, causing widespread liver damage (Alengebawy *et al*., 2021; Siddiqui *et al*., 2023).

Toxic liver injury can result from exposure to numerous chemicals, including pharmaceuticals, when accidentally ingested or administered (Philips *et al*., 2023; Jaeschke & Ramachandran, 2024). Industrial accidents and occupational hazards often lead to hepatotoxicity due to improper handling or accidental exposure to toxic substances (Gurley *et al*., 2022). Among these substances, carbon tetrachloride (CCl_4) is particularly noteworthy due to its widespread industrial use as a solvent for oils, fats, and rubber, as well as in fat and alkaloid extraction processes (Unsal *et al*., 2020; Fareed *et al*., 2024). The metabolic transformations of CCl_4 form the basis of its potent hepatotoxic effect, making it a relevant model for studying liver damage mechanisms (Márquez-Quiroga *et al*., 2022). When metabolized in the liver, CCl_4 generates toxic metabolites that disrupt cellular function and integrity, leading to liver injury (Shi *et al*., 2023).

The poor effectiveness of current liver damage treatment methods calls for the investigation of other therapeutic modalities. In recent decades, there has been growing interest in natural compounds with hepatoprotective properties (Sadovoy *et al*., 2017). Numerous studies have demonstrated the beneficial effects of various plant-derived extracts in protecting liver function and aiding recovery from hepatotoxicity (Mittal *et al*., 2025). Among natural compounds with potential hepatoprotective properties, *Chlorophytum comosum* (spider plant) has gained particular attention due to its rich biochemical composition and traditional medicinal use (Azami *et al*., 2022).

Chlorophytum comosum contains a complex mixture of bioactive compounds that contribute to its therapeutic potential (Adhami *et al*., 2021). The plant is particularly rich in flavonoids, which are known for their antioxidant and anti-inflammatory properties. Additionally, it contains coriic acids, mucilages, resins, and essential vitamins (C, PP, and E), all of which play crucial roles in liver protection and regeneration (Rzhepakovsky *et al*., 2022). The plant's long history of usage in traditional medicine, especially in Tibetan hepatitis treatment, offers a solid basis for current scientific research (Vakele *et al*., 2022). Its multifaceted chemical composition suggests a potential mechanism of action that involves several therapeutic pathways (Padayachee *et al*., 2021). Flavonoids may help reduce oxidative stress and inflammation, while vitamins contribute to cellular repair and metabolic support (Kavya *et al*., 2024). The unique combination of active components in *Chlorophytum comosum* makes it a promising candidate for hepatoprotective therapy (Adi Wicaksono *et al*., 2023). Flavonoids and coriic acids may help stabilize cell membranes and inhibit lipid peroxidation, while mucilages and resins could support detoxification processes (Zhang *et al*., 2024). The presence of essential vitamins further enhances its potential to support liver function and regeneration (Imtiaz *et al*., 2024). This diverse biochemical profile, combined with its historical medicinal use, justifies further investigation into *Chlorophytum comosum* as a potential therapeutic agent for liver protection (Zia-Ur-Rehman *et al*., 2023). Its ability to address multiple aspects of liver damage through different mechanisms of action makes it an attractive candidate for developing new hepatoprotective treatments.

This study focuses on investigating the therapeutic potential of *Chlorophytum comosum* extract in managing liver damage induced by toxic agents. By examining its effects on bilirubin metabolism, we aim to contribute to the development of novel, natural approaches to liver protection and recovery. The research is particularly timely given the increasing prevalence of liver diseases worldwide and the need for safe, effective, and accessible treatment options. Understanding the mechanisms by which natural compounds like *Chlorophytum comosum* extract can protect liver function may open new avenues for managing liver damage caused by environmental and industrial toxins.

Materials and Methods

The study was conducted in strict accordance with international guidelines for laboratory animal care and use. The experimental protocol was approved by the institutional ethics committee (Protocol No. 13-24/2024).

Experimental Animals

Male Chinchilla breed rabbits aged 5–6 months and weighing between 2.5 and 3 kilograms were selected for the study. The animals were randomly divided into four experimental groups, with each group containing six rabbits. All animals were housed under standardized conditions with controlled temperature, humidity, and lighting to minimize external influences on the experimental results (Nair & Jacob, 2016).

Experimental Design

The study employed a controlled experimental design to investigate the effects of different treatment modalities on liver function. The groups were defined as follows: the control group received no treatment following CCl_4 exposure, while the other groups received either *Chlorophytum comosum* extract, vitamin therapy, or a combination of both treatments.

Induction of Toxic Hepatitis

Toxic hepatitis was induced by administering a single subcutaneous injection of carbon tetrachloride (CCl_4) at a dose of 0.2 milliliters per kilogram of body weight. This dosage was selected based on preliminary studies to ensure reproducible liver damage while avoiding lethality. The injection was performed under aseptic conditions to prevent any secondary infections.

Treatment Administration

The *Chlorophytum comosum* extract was administered orally via a feeding tube three times daily at a dose of 2 milliliters per kilogram of body weight, starting three hours after CCl_4 administration. Vitamin therapy included a combination of vitamins B_1, B_2, B_6, B_{12}, PP, E, and C, administered daily at specific times to optimize absorption and efficacy (Wald *et al*., 2022).

Sample Collection and Processing

Blood samples were collected daily from the marginal ear vein using the Zapadnyuk method (Thompson *et al*., 2002). The procedure was performed under strict aseptic conditions to prevent contamination. Serum was obtained by refrigerating the blood for 20 minutes and then centrifuging it at 3000 revolutions per minute for 15 minutes. The resulting serum was stored under controlled temperature conditions until analysis.

Biochemical Analysis

Bilirubin levels were determined using the «Lakhema» test method, which is based on the diazo reaction of bilirubin with diazotized sulfanilic acid (Berska *et al*., 2020). This method allows for the measurement of both total bilirubin (including unconjugated and direct fractions) and direct bilirubin separately, providing valuable insights into liver function and bile production.

Statistical Analysis

Statistical analysis was performed using Student’s t-test for comparison between groups and the small sample method for intra-group analysis. Outliers were identified and excluded using the Chauvenet criterion. Statistical significance was set at $p < 0.05$ to ensure reliable interpretation of the results.

Quality Control

Rigorous quality control measures were implemented throughout the study to ensure data reliability. These included regular calibration of laboratory equipment, use of certified reagents, duplicate measurements for critical parameters, and blinded sample analysis to minimize potential biases. All laboratory procedures adhered strictly to established standard operating procedures.

Results and Discussion

Toxic liver damage induced by a single administration of CCl_4 resulted in significant alterations in bile formation intensity and composition, accompanied by severe disturbances in pigment metabolism. This was evidenced by elevated levels of bilirubin fractions in the blood serum of rabbits. However, the increase was not uniform for total and direct bilirubin.

Analysis of the obtained data revealed that total bilirubin levels relative to control values (intact animals) increased by approximately 50% across all study groups just 3 hours after CCl_4 administration. Direct bilirubin levels showed an even more pronounced elevation, exceeding baseline values by over 280%. This indicated a significant increase in blood bilirubin concentration, primarily due to direct bilirubin (Macías-García *et al*., 2019).

The elevated levels of conjugated bilirubin in the blood suggested impaired cellular bilirubin excretion into bile ducts and difficulties with bile outflow through intrahepatic ducts. Twenty-four hours after CCl_4 administration, total bilirubin levels in all groups (control without treatment, *Chlorophytum comosum* extract group, vitamin therapy group, and combination therapy group) were approximately 1.8 times higher than normal, while direct bilirubin levels were three times higher ($p < 0.001$), as shown in **Table 1**.

On the second day of the experiment, regardless of therapy, all rabbit groups showed a significant increase in both total and direct bilirubin levels compared to control values, approximately 180% and 460% respectively. These levels were also 50% higher than the previous day's measurements (Gondo & Haryanti, 2024; Makhoahle, 2024; Naseri & Sasani, 2024; Temirbekova *et al*., 2024; Wang, 2024).

By the third day of the study, total and direct bilirubin levels continued to increase significantly ($p < 0.001$) across all four rabbit groups, with an average increase of 100% and 80% compared to day two, and 370% and 1000% compared to intact animal values. Notably, groups two, three, and four showed the highest concentration of bilirubin fractions on the third day following the administration of CCl_4 (Alsharif *et al*., 2023; Cirik *et al*., 2023; Govindaraj *et al*., 2023; Muthuvignesh *et al*., 2023; Zharashueva *et al*., 2024).

On the fourth day of the study, the control group of rabbits without therapy showed the highest concentration of bilirubin fractions, exceeding normal values six-fold for total bilirubin and twelve-fold for direct bilirubin. Statistical analysis of data from the fourth day revealed that only group one's indicators significantly differed from the other groups ($p < 0.05$). No significant differences were observed between groups two, three, and four, with total and direct bilirubin levels remaining consistently elevated.

A turning point occurred after the fifth day of the study. From days five to ten, a gradual decrease in bilirubin fractions was observed in all four groups. During this period, bilirubin fraction levels in groups two, three, and four were significantly lower ($p < 0.05$) than those in the untreated control group one.

These findings suggest that while initial exposure to CCl_4 caused severe liver damage and significant disturbances in bilirubin metabolism, the applied therapies showed promising results in reducing bilirubin levels over time, with the most significant improvements observed after the fifth day of treatment (Guerra Ruiz *et al*., 2021; Qadri *et al*., 2025).

Table 1. Serum bilirubin levels (μmol/L) in rabbits with experimental toxic liver damage

Time	Control (no treatment after CCl_4 administration)		*Chlorophytum comosum* extract (Group 2)		Vitamin therapy (Group 3)		Combined therapy (Group 4)	
	Total bilirubin	Direct bilirubin	Total bilirubin	Direct bilirubin	Total bilirubin	Direct bilirubin	Total bilirubin	Direct bilirubin
3 hours	7,8 ±0,80	6,4 ±0,76	7,5 ±0,85	6,4 ±0,67	7,6 ±0,73	6,2 ±0,73	7,9 ±0,67	6,1 ±0,58
1 day	9,4+ 1,2	8,7 ±1,09	9,7 ±0,92	7,8 ±0,87	10,0±0,98	8,4 ±0,96	10,6 ±0,97	7,9 ±0,89
2 days	14,1 ±1,17	11,9+1,32	12,5 ±1,27	11,1 ±1,21	14,8 ±1,76	13,1 ±1,46	14,8 ±1,76	12,7±1,80
3 days	23,6±2,13	21,1±2,38	24,0 ±1,93	22,7±1,78	25,9±1,54	22,3 ±1,36	23,3 ±1,43	18,6 ±1,29
4 days	31,4 ±2,54	29,1 ±2,41	20,9 ±2,13	18,2 ±2,08	22,0±2,14	20,1 ±2,05	23,8±2,17	21,4±2,12
5 days	26,0 ±2,31	24,3 ± 2,33	16,9±2,18	14,1 ±2,13	21,4±2,19	17,6±2,17	24,3 ±2,21	17,2 + 2,10
6 days	25,3 ±2,1	23,1± 2,12	15,1±1,91	12,3±2,2	18,6±1,48	15,8±2.1	17,6±1,82	13,2±1,91
7days	23,3 ±2,10	22,1 ±2,18	12,7 ±2,01	10,8+1,92	16,8 ±2,01	12,1 ±2,14	13,8 ±2,03	11,2 ±1,93
8 days	21,8 ± 1,93	20,0±2,12	7,5 ±1,87	6,1 ±1,87	13,1 ±1,69	8,3 ±1,96	8,9 ±1,93	6,8 ±1,87
9 days	20,4 ±1,87	18,3 ±2,27	5,6±1,34*	4,3 ±1,63	9,0± 1,34	6,8±1,89	5,4±1,84*	4,3+1,82
10 days	17,1 ±1,74	15,2 ±2,82	5,2+ 1,91*	4,1 ±1,58	5,2 ±1,23*	4,1 ±1,78	5,1 ±1,73*	4,0+ 1,78

Notes. Control (intact animals): total bilirubin - 5.1±0.98, direct bilirubin - 2.14±0.02

* - P > 0.05 – relative to control (intact animals)

It is noteworthy that the total bilirubin levels in the second group treated with *Chlorophytum comosum* extract and the fourth group receiving a combination of *Chlorophytum comosum* extract and vitamin therapy had already returned to normal levels of intact

animals by the ninth day of the study. By the tenth day of our research, in the first group of animals, total bilirubin still exceeded normal values by 235%, and direct bilirubin by 600%.

The indicators of the second, third, and fourth groups regarding total and direct bilirubin content were at approximately the same level, showing no significant differences among themselves. Total bilirubin on the tenth day varied within normal limits across all study variants, while direct bilirubin decreased by 440% from its peak value and remained approximately 90% above normal levels (Ahmad *et al*., 2022; Dhanasekar *et al*., 2022; Saravanakumar *et al*., 2022; Du *et al*., 2023; Thazha *et al*., 2023).

Although the obtained direct bilirubin values were still far from normal, the observed reduction in bilirubin fractions in the three therapy groups compared to the first control group without therapy indicated the effective impact of aqueous *Chlorophytum comosum* extract and vitamins on bilirubin fraction concentrations in experimental toxic hepatitis (Ramírez-Mejía *et al*., 2024).

The data revealed that the aqueous extract of *Chlorophytum comosum*, unlike vitamin injections used in liver toxicity therapy, exhibited more pronounced hepatoprotective properties (Ern *et al*., 2023; Hossain *et al*., 2023; Kukreti *et al*., 2023; Ali *et al*., 2025). This was evidenced by total bilirubin levels, which remained at a significantly high level relative to normal values in the third vitamin therapy group on the ninth day of the study. In contrast, both the *Chlorophytum comosum* extract alone in the second group and combination with vitamins contributed to a significant reduction in total bilirubin to normal values.

The combined use of vitamins and *Chlorophytum comosum* extract at a dose of 2 ml per 1 kg of body weight did not show significant changes in the concentration of studied bilirubin fractions compared to vitamin therapy alone. **Figures 1 and 2** show that by the tenth day of the study, each therapy variant could be used as an independent method for restoring bilirubin fraction levels.

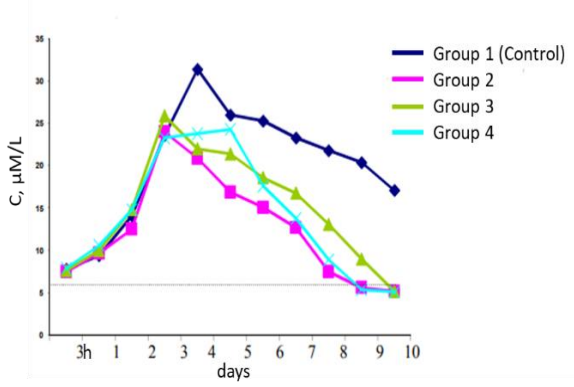

Figure 1. Dynamics of total bilirubin content in the blood serum of rabbits with toxic liver damage in various study options

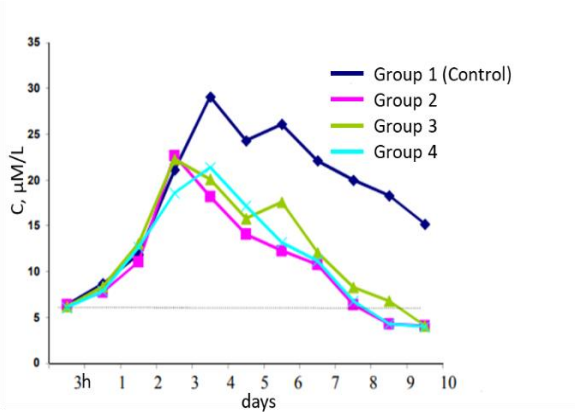

Figure 2. Dynamics of direct bilirubin content in the blood serum of rabbits with toxic liver damage in various study options

Given the demonstrated high activity, it may be appropriate to consider increasing the dosage of the aqueous *Chlorophytum comosum* extract for further research into its effects on blood bilirubin fractions in toxic hepatitis (Adetunji *et al*., 2021; Huzio *et al*., 2022; Almohmadi *et al*., 2024).

These findings suggest several important conclusions. First, the superior efficacy of *Chlorophytum comosum* extract compared to vitamin therapy alone indicates its potent hepatoprotective properties (Lister *et al*., 2020; Tedyanto *et al*., 2023). Second, the lack of additive effect from combining extract and vitamin therapy suggests that the extract can be used as a monotherapy (Flores-Estrada *et al*., 2023; Syarifah *et al*., 2023; Feng *et al*., 2024). Third, the significant reduction in bilirubin levels in treated groups compared to the control group demonstrates the therapeutic potential of *Chlorophytum comosum* extract in managing liver damage (Ayenew & Wasihun, 2023; Miao *et al*., 2023; Ferdjioui *et al*., 2024).

Future research should focus on optimizing the dosage regimen and exploring the long-term effects of *Chlorophytum comosum* extract therapy. Additionally, investigating the specific mechanisms underlying its hepatoprotective effects could provide valuable insights into developing new approaches to managing liver damage (Chakrabarty *et al*., 2022; Latief *et al*., 2023).

Conclusion

The conducted research has demonstrated that a single subcutaneous administration of carbon tetrachloride (CCl_4) at a dose of 0.2 ml per kilogram of body weight induces toxic hepatitis, which is accompanied by a statistically significant increase in bilirubin fractions in the blood serum of experimental animals. This finding confirms the potent hepatotoxic effect of CCl_4 and its ability to disrupt normal liver function. The study has revealed that both combined therapy involving vitamin treatment and aqueous Chlorophytum comosum extract, as well as monotherapy with either of these agents, effectively reduces the level of bilirubin fractions in cases of experimental toxic liver damage. Importantly, the reduction in bilirubin levels occurs to a similar extent regardless of the treatment modality employed, indicating

comparable efficacy of both therapeutic approaches. Throughout the 10-day observation period, no statistically significant differences were found in the concentration levels of bilirubin fractions between the compared groups of rabbits receiving various forms of therapy (groups 2, 3, and 4). This suggests that the therapeutic effect is consistent across different treatment modalities and does not depend on the specific combination of therapeutic agents used.

A particularly noteworthy finding is the statistically significant difference ($p < 0.05$) observed on the 10th day of the study between the concentration of bilirubin fractions in the control group without therapy (group 1) and the groups receiving various forms of treatment (groups 2, 3, and 4). This difference demonstrates the therapeutic efficacy of the applied interventions. By the 10th day of the study, a statistically significant ($p < 0.05$) reduction in total bilirubin levels to normal values was observed in groups 2, 3, and 4 of rabbits receiving therapy, in contrast to the control group without therapy. This finding underscores the effectiveness of both Chlorophytum comosum extract and vitamin therapy in restoring normal bilirubin metabolism and indicates their potential as viable treatment options for managing toxic liver damage.

These conclusions suggest that aqueous Chlorophytum comosum extract, either alone or in combination with vitamin therapy, represents a promising therapeutic approach for managing toxic hepatitis, offering comparable efficacy to traditional vitamin therapy while providing additional benefits through its unique biochemical composition.

Acknowledgments: None

Conflict of interest: None

Financial support: None

Ethics statement: All studies were conducted in compliance with the ethical standards and principles of the Helsinki Declaration. The experimental protocol was approved by the institutional ethics committee (Protocol No. 13-24/2024).

References

Adetunji, O. A., Olugbami, J. O., Adegoke, A. M., Gbadegesin, M. A., & Odunola, O. A. (2021). Reno-hepatoprotective and antidiabetic properties of methanol leaf extract of *Laportea aestuans* in Wistar rats. *Journal of Evidence-Based Integrative Medicine, 26*, 2515690X211017464. doi:10.1177/2515690X211017464

Adhami, S., Farooqi, H., Abdin, M. Z., Prasad, R., & Malik, A. A. (2021). Chemical profiling of *Chlorophytum comosum* (Thunb.) Jaques by GC-MS/LC-ESIMS and its antiproliferative effects on human carcinoma cell lines. *Anticancer Agents in Medicinal Chemistry, 21*(13), 1697–1707. doi:10.2174/1871520620666201123085300

Adi Wicaksono, W., Reisenhofer-Graber, T., Erschen, S., Kusstatscher, P., Berg, C., Krause, R., Cernava, T., & Berg, G. (2023). Phyllosphere-associated microbiota in the built environment: Do they have the potential to antagonize human pathogens? *Journal of Advanced Research, 43*, 109–121. doi:10.1016/j.jare.2022.02.003

Ahmad, S., Khan, T. M., Ayub, F., Mubarak, N., Khaliel, A. M., Elhanish, A. A., Telb, A., Alnafoosi, F. N., Suleiman, A., Baig, M. R., et al. (2022). Meta-analysis of urinary tract infections among patients with chronic kidney disease. *Bulletin of Pioneer Research in Medical and Clinical Sciences, 1*(2), 7–27. doi:10.51847/KZV1W3ahoN

Alengebawy, A., Abdelkhalek, S. T., Qureshi, S. R., & Wang, M. Q. (2021). Heavy metals and pesticides toxicity in agricultural soil and plants: ecological risks and human health implications. *Toxics, 9*(3), 42. doi:10.3390/toxics9030042

Ali, A. H. A., Siddiqui, M. A., Alghamdi, S. K., Alenazey, A. F., Alharbi, B. M., Almutairi, T. H., & Almutairi, S. S. (2025). Hepatoprotective properties of olive extract on methotrexate-induced liver damage. *Pakistan Journal of Biological Sciences, 28*(3), 162–168. doi:10.3923/pjbs.2025.162.168

Almohmadi, N. H., Aldhalmi, A. K., Zahran, M., Alhassani, W. E., Felemban, S. G., El-Nabtity, S. M., & Shaheen, H. M. (2024). Hepatoprotective efficacy of *Lagenaria siceraria* seed oil against experimentally carbon tetrachloride-induced toxicity. *Open Veterinary Journal, 14*(8), 2016–2028. doi:10.5455/OVJ.2024.v14.i8.31

Alsharif, S. B., Bahanan, L., Almutairi, M., Alshammry, S., & Khalifa, H. (2023). Retrospective assessment of dental implant-related anatomical structure perforations using cone beam computed tomography. *Annals of Dental Specialty, 11*(1), 21–30. doi:10.51847/jEyOudiF94

Ayenew, K. D., & Wasihun, Y. (2023). Hepatoprotective effect of methanol extract of *Agave americana* leaves on paracetamol-induced hepatotoxicity in Wistar albino rats. *BMC Complementary Medicine and Therapies, 23*(1), 99. doi:10.1186/s12906-023-03931-y

Azami, A. I., O'Neill, K., Pirro, S., & Ghazal, H. (2022). The complete genome sequence of *Chlorophytum comosum* (Asparagaceae, Asparagales), the spider plant. *Biodiversity Genomes, 2022*, 10.56179/001c.55588. doi:10.56179/001c.55588

Berska, J., Bugajska, J., & Sztefko, K. (2020). Newborns' bilirubin concentration determined by different methods in relation to hematocrit and albumin level. *Journal of Medical Biochemistry, 39*(2), 171–177. doi:10.2478/jomb-2019-0030

Berumen, J., Baglieri, J., Kisseleva, T., & Mekeel, K. (2021). Liver fibrosis: pathophysiology and clinical implications. *WIREs Mechanisms of Disease, 13*(1), e1499. doi:10.1002/wsbm.1499

Chakrabarty, N., Chung, H. J., Alam, R., Emon, N. U., Alam, S., Kabir, M. F., Islam, M. M., Hong, S. T., Sarkar, T., Sarker, M. M. R., et al. (2022). Chemico-pharmacological screening of the methanol extract of *Gynura nepalensis* D.C. deciphered promising antioxidant and hepatoprotective potentials: evidenced from in vitro, in vivo, and computer-aided studies. *Molecules, 27*(11), 3474. doi:10.3390/molecules27113474

Cirik, V. A., Aksoy, B., & Bulut, E. (2023). Studying the

relationship between the attitude towards gender roles of parents and the quality of parent-child relationship in nurses. *Journal of Integrative Nursing and Palliative Care, 4*, 30–37. doi:10.51847/90pkztCQgl

Cunningham, M., Gupta, R., & Butler, M. (2024). Checkpoint inhibitor hepatotoxicity: pathogenesis and management. *Hepatology, 79*(1), 198–212. doi:10.1097/HEP.0000000000000045

Dhanasekar, P., Rajayyan, J. S., Veerabadiran, Y., Kumar, K. S., Kumar, K. S., & Chinnadurai, N. (2022). Evaluation of alum and purification process of water by coagulation method. *Bulletin of Pioneer Research in Medical and Clinical Sciences, 1*(2), 1–6. doi:10.51847/R8GyfOmMDh

Di Martino, V., Verhoeven, D. W., Verhoeven, F., Aubin, F., Avouac, J., Vuitton, L., Lioté, F., Thévenot, T., & Wendling, D. (2023). Busting the myth of methotrexate chronic hepatotoxicity. *Nature Reviews Rheumatology, 19*(2), 96–110. doi:10.1038/s41584-022-00883-4

Du, X., Dong, Q., Sun, L., Chen, X., & Jiang, J. (2023). Studying the relationship between depression and internal stigma in mothers of children with cerebral palsy. *Journal of Integrative Nursing and Palliative Care, 4*, 17–22. doi:10.51847/9WQmf9zDW1

Ern, P. T. Y., Quan, T. Y., Yee, F. S., & Yin, A. C. Y. (2023). Therapeutic properties of *Inonotus obliquus* (Chaga mushroom): a review. *Mycology, 15*(2), 144–161. doi:10.1080/21501203.2023.2260408

Fareed, M. M., Khalid, H., Khalid, S., & Shityakov, S. (2024). Deciphering molecular mechanisms of carbon tetrachloride-induced hepatotoxicity: a brief systematic review. *Current Molecular Medicine, 24*(9), 1124–1134. doi:10.2174/0115665240257603230919103539

Feng, T., Li, S., Wang, P., Zhu, D., Xu, Z., Wang, L., Li, A., Kulyar, M. F., & Shen, Y. (2024). Hepatoprotective effects of *Radix Bupleuri* extract on aflatoxin B1-induced liver injury in ducks. *Ecotoxicology and Environmental Safety, 283*, 116781. doi:10.1016/j.ecoenv.2024.116781

Ferdjioui, S., Belhattab, R., Ouhida, S., Khither, H., Saoudi, S., & Mayouf, N. (2024). Hepatoprotective activity of *Mentha rotundifolia* aqueous extract against hepatocellular damage induced by CCL4 in rats. *Natural Product Research*, 1–6. doi:10.1080/14786419.2024.2387252

Flores-Estrada, J., Cano-Martínez, A., Vargas-González, Á., Castrejón-Téllez, V., Cornejo-Garrido, J., Martínez-Rosas, M., Guarner-Lans, V., & Rubio-Ruíz, M. E. (2023). Hepatoprotective mechanisms induced by spinach methanolic extract in rats with hyperglycemia—An immunohistochemical analysis. *Antioxidants, 12*(11), 2013. doi:10.3390/antiox12112013

Gondo, H. K., & Haryanti, E. (2024). Higher placental activin-A (ACV-A) and inhibin-A (INH-A) in preeclampsia placenta mother compare to diabetic mother. *Journal of Advanced Pharmacy Education & Research, 14*(3), 15–17. doi:10.51847/QVCQHO6GxQ

Govindaraj, A., Paulpandian, S. S., & Shanmugam, R. (2023). Effect of chlorhexidine and fluoride varnish on the incidence of white spot lesion in orthodontic patients. *Annals of Dental Specialty, 11*(1), 35–39. doi:10.51847/RgSlwwnDkR

Guerra Ruiz, A. R., Crespo, J., López Martínez, R. M., Iruzubieta, P., Casals Mercadal, G., Lalana Garcés, M., Lavin, B., & Morales Ruiz, M. (2021). Measurement and clinical usefulness of bilirubin in liver disease. *Advances in Laboratory Medicine, 2*(3), 352–372. doi:10.1515/almed-2021-0047

Gurley, B. J., McGill, M. R., & Koturbash, I. (2022). Hepatotoxicity due to herbal dietary supplements: past, present, and the future. *Food and Chemical Toxicology, 169*, 113445. doi:10.1016/j.fct.2022.113445

Hossain, K. N., Islam, M. S., Rahman, S. H., Sarker, S., Mondal, M., Rahman, M. A., Alhag, S. K., Al-Shuraym, L. A., Alghamdi, O. A., Islam, M. T., et al. (2023). In vitro antioxidant and in vivo hepatoprotective properties of *Wissadula periplocifolia* extract. *ACS Omega, 8*(49), 47001–47011. doi:10.1021/acsomega.3c06614

Huzio, N., Grytsyk, A., Raal, A., Grytsyk, L., & Koshovyi, O. (2022). Phytochemical and pharmacological research in *Agrimonia eupatoria* L. herb extract with anti-inflammatory and hepatoprotective properties. *Plants, 11*(18), 2371. doi:10.3390/plants11182371

Imtiaz, H., Khan, S. A., Hassan, A., Khan, A. R., Khurshid, G., Khan, Z. A., & Sajjad, Y. (2024). Insight into physiological and biochemical markers against formaldehyde stress in spider plant (*Chlorophytum comosum* L.). *Environmental Science and Pollution Research International, 31*(51), 61305–61319. doi:10.1007/s11356-024-35314-2

Jaeschke, H., & Ramachandran, A. (2024). Acetaminophen hepatotoxicity: paradigm for understanding mechanisms of drug-induced liver injury. *Annual Review of Pathology, 19*, 453–478. doi:10.1146/annurev-pathmechdis-051122-094016

Kavya, P., Theijeswini, R. C., & Gayathri, M. (2024). Phytochemical analysis, identification of bioactive compounds using GC-MS, in vitro and in silico hypoglycemic potential, in vitro antioxidant potential, and in silico ADME analysis of *Chlorophytum comosum* root and leaf. *Frontiers in Chemistry, 12*, 1458505. doi:10.3389/fchem.2024.1458505

Kukreti, N., Chitme, H. R., Varshney, V. K., Abdel-Wahab, B. A., Khateeb, M. M., & Habeeb, M. S. (2023). Antioxidant properties mediate nephroprotective and hepatoprotective activity of essential oil and hydro-alcoholic extract of the high-altitude plant *Skimmia anquetilia*. *Antioxidants, 12*(6), 1167. doi:10.3390/antiox12061167

Latief, U., Kaur, M., Dar, S. H., Thakur, S., Per, T. S., Tung, G. K., & Jain, S. K. (2023). Preparation and characterisation of liposomes of *Bergenia ciliata* extract and evaluation of their hepatoprotective activity. *Journal of Pharmaceutical Sciences, 112*(1), 328–335. doi:10.1016/j.xphs.2022.07.013

Lister, I. N. E., Ginting, C. N., Girsang, E., Nataya, E. D., Azizah, A. M., & Widowati, W. (2020). Hepatoprotective properties of red betel (*Piper crocatum* Ruiz and Pav) leaves extract towards H_2O_2-induced HepG2 cells via anti-inflammatory, antinecrotic, antioxidant potency. *Saudi Pharmaceutical Journal, 28*(10), 1182–1189. doi:10.1016/j.jsps.2020.08.007

Macías-García, D., Méndez-Del Barrio, C., Jesús, S., Labrador, M. A., Adarmes-Gómez, A., Vargas-González, L., Carrillo, F., Gómez-Garre, P., & Mir, P. (2019). Increased bilirubin levels in Parkinson's disease. *Parkinsonism & Related Disorders, 63*, 213–216. doi:10.1016/j.parkreldis.2019.01.012

Makhoahle, P. M. (2024). The increased use of medicinal plants necessitates guidance on issues relating to normal flora. *Journal of Advanced Pharmacy Education & Research, 14*(3), 26–30. doi:10.51847/OmnVqBhaTi

Márquez-Quiroga, L. V., Arellanes-Robledo, J., Vásquez-Garzón, V. R., Villa-Treviño, S., & Muriel, P. (2022). Models of nonalcoholic steatohepatitis potentiated by chemical inducers leading to hepatocellular carcinoma. *Biochemical Pharmacology, 195*, 114845. doi:10.1016/j.bcp.2021.114845

Miao, W., Huang, R., Huang, X., Gao, F., Leng, X., & Li, Q. (2023). Physicochemical properties and in vivo hepatoprotective effect of polysaccharides from grape pomace. *Antioxidants, 12*(2), 394. doi:10.3390/antiox12020394

Mittal, G., A, P., Dhali, A., Prasad, R., S, Y., Nurani, K. M., & Găman, M. A. (2025). Plant extracts with antioxidant and hepatoprotective benefits for liver health: a bibliometric analysis of drug delivery systems. *World Journal of Gastroenterology, 31*(18), 105836. doi:10.3748/wjg.v31.i18.105836

Muthuvignesh, N., Jei, J. B., & Balasubramaniam, M. (2023). Tooth supported overdenture in old patient with denture characterization–A case report. *Annals of Dental Specialty, 11*(1), 16–20. doi:10.51847/s9fuIqCHoR

Nair, A. B., & Jacob, S. (2016). A simple practice guide for dose conversion between animals and humans. *Journal of Basic and Clinical Pharmacy, 7*(2), 27–31. doi:10.4103/0976-0105.177703

Naseri, B., & Sasani, S. (2024). Stem rust, planting date, wheat maturity and genetic resistance, weather and productivity. *World Journal of Environmental Biosciences, 13*(4), 1–6. doi:10.51847/2njt2p8YQ0

Padayachee, B., Odun-Ayo, F., & Reddy, L. (2021). Apoptotic effect of *Bulbine natalensis* and *Chlorophytum comosum* in myelogenous leukemia K562 cell line. *Brazilian Journal of Biology, 84*, e251336. doi:10.1590/1519-6984.251336

Philips, C. A., Valsan, A., Theruvath, A. H., Ravindran, R., Oommen, T. T., Rajesh, S., Bishnu, S., & Augustine, P. (2023). Ashwagandha-induced liver injury—A case series from India and literature review. *Hepatology Communications, 7*(10), e0270. doi:10.1097/HC9.0000000000000270

Qadri, S. S., Javaid, D., Reyaz, A., Ganie, S. Y., & Reshi, M. S. (2025). Liver disorders and phytotherapy. *Toxicology Reports, 14*, 102047. doi:10.1016/j.toxrep.2025.102047

Ramírez-Mejía, M. M., Castillo-Castañeda, S. M., Pal, S. C., Qi, X., & Méndez-Sánchez, N. (2024). The multifaceted role of bilirubin in liver disease: a literature review. *Journal of Clinical and Translational Hepatology, 12*(11), 939–948. doi:10.14218/JCTH.2024.00156

Rzhepakovsky, I. V., Areshidze, D. A., Avanesyan, S. S., Grimm, W. D., Filatova, N. V., Kalinin, A. V., Kochergin, S. G., Kozlova, M. A., Kurchenko, V. P., Sizonenko, M. N., et al. (2022). Phytochemical characterization, antioxidant activity, and cytotoxicity of methanolic leaf extract of *Chlorophytum comosum* (green type) (Thunb.) Jacq. *Molecules, 27*(3), 762. doi:10.3390/molecules27030762

Sadovoy, V. V., Selimov, M., Shchedrina, T., & Nagdalian, A. A. (2017). Nutritional supplement for the control of diabetes. *Journal of Excipients and Food Chemicals, 8352017*, 1843.

Saravanakumar, V., Masi, C., Neme, I., Arjun, K., & Dinakarkumar, Y. (2022). Geographical comparison of phytoconstituents in *Euphorbia hirta*: a pilot study in Ethiopia and India. *Bulletin of Pioneer Research in Medical and Clinical Sciences, 1*(2), 34–41. doi:10.51847/ErNYBrhrFF

Shi, Y., Shi, L., Liu, Q., Wang, W., & Liu, Y. (2023). Molecular mechanism and research progress on pharmacology of ferulic acid in liver diseases. *Frontiers in Pharmacology, 14*, 1207999. doi:10.3389/fphar.2023.1207999

Siddiqui, S. A., Khan, S., Tariq, T., Sameen, A., Nawaz, A., Walayat, N., Oboturova, N. P., Ambartsumov, T. G., & Nagdalian, A. A. (2023). Potential risk assessment and toxicological impacts of nano/micro-plastics on human health through food products. *Advances in Food and Nutrition Research, 103*, 361–395. doi:10.1016/bs.afnr.2022.07.006

Syarifah, A. N., Suryadi, H., Hayun, H., Simamora, A., & Mun'im, A. (2023). Detoxification of comfrey (*Symphytum officinale* L.) extract using natural deep eutectic solvent (NADES) and evaluation of its anti-inflammatory, antioxidant, and hepatoprotective properties. *Frontiers in Pharmacology, 14*, 1012716. doi:10.3389/fphar.2023.1012716

Tedyanto, C. P., Wihanto, L., & Hendrata, A. P. (2023). Hepatoprotective effect of dried red jujube fruit extract against acetaminophen-induced acute hepatotoxicity. *Cureus, 15*(1), e33272. doi:10.7759/cureus.33272

Temirbekova, S., Afanaseva, Y., & Najodov, B. (2024). Monograph “Eniology, ecology and diversity” about ecological disaster. *World Journal of Environmental Biosciences, 13*(4), 29–33. doi:10.51847/RBEtnusE0h

Thazha, S. K., Cruz, J. P., Alquwez, N., Scaria, B., Rengan, S. S., & Almazan, J. U. (2023). Studying the attitude and knowledge of nursing students towards the physical restraint use in patients. *Journal of Integrative Nursing and Palliative Care, 4*, 1–5. doi:10.51847/cFz2ew4AK8

Thompson, M. D., Taylor, S. M., Adams, V. J., Waldner, C. L., & Feldman, E. C. (2002). Comparison of glucose concentrations in blood samples obtained with a marginal ear vein nick technique versus those from a peripheral vein in healthy cats and cats with diabetes mellitus. *Journal of the American Veterinary Medical Association, 221*(3), 389–392. doi:10.2460/javma.2002.221.389

Torgersen, J., Mezochow, A. K., Newcomb, C. W., Carbonari, D. M., Hennessy, S., Rentsch, C. T., Park, L. S., Tate, J. P., Bräu, N., Bhattacharya, D., et al. (2024). Severe acute liver injury after hepatotoxic medication initiation in real-world data. *JAMA Internal Medicine, 184*(8), 943–952. doi:10.1001/jamainternmed.2024.1836

Unsal, V., Cicek, M., & Sabancilar, İ. (2020). Toxicity of carbon tetrachloride, free radicals, and the role of antioxidants. *Reviews on Environmental Health, 36*(2), 279–295. doi:10.1515/reveh-2020-0048

Vakele, Y., Odun-Ayo, F., & Reddy, L. (2022). In vitro antioxidant and cytotoxicity activities of selected indigenous South African medicinal plants. *African Health Sciences, 22*(1), 395–403. doi:10.4314/ahs.v22i1.48

Wald, E. L., Badke, C. M., Hintz, L. K., Spewak, M., & Sanchez-Pinto, L. N. (2022). Vitamin therapy in sepsis. *Pediatric Research, 91*(2), 328–336. doi:10.1038/s41390-021-01673-6

Wang, D. (2024). An overview on the marine benthic dinoflagellates effects on human and environment. *World Journal of Environmental Biosciences, 13*(4), 7–13. doi:10.51847/QwZpooC6ZV

Zhang, K., Wang, Y., Zhang, Y., & Shan, X. (2024). Codon usage characterization and phylogenetic analysis of the mitochondrial genome in *Hemerocallis citrina*. *BMC Genomic Data, 25*(1), 6. doi:10.1186/s12863-024-01191-4

Zharashueva, E. B., Mirzayeva, A. K., Iakovleva, A. N., Dyshnieva, N. A., Dudurgova, A. T., Utovka, O. V., Strelchuk, S. V., & Dekkusheva, R. M. (2024). Sanitary and hygienic assessment of the dressing material modified with silver nanoparticles. *Journal of Advanced Pharmacy Education and Research, 14*(3), 9-14. doi:10.51847/J10C8y3UWQ

Zia-Ur-Rehman, M., Mubsher, A., Rizwan, M., Usman, M., Jafir, M., Umair, M., Alharby, H. F., Bamagoos, A. A., Alshamrani, R., & Ali, S. (2023). Effect of farmyard manure, elemental sulphur and EDTA on growth and phytoextraction of cadmium by spider plants (*Chlorophytum comosum* L.) under Cd stress. *Chemosphere, 313*, 137385. doi:10.1016/j.chemosphere.2022.137385