

Original Research Article

An Assessment of Hepatoprotective Activity of *Catharanthus roseus* on CCL4 induced Rat

Model with Safety Profile Analysis

Comment [A1]: Please recheck the entire text of the article for grammar, spelling and clarity

Abstract

Using herbs and herbal medications to preserve health and prevent, treat, or cure illness is the art or practice of herbal remedies. Herbal remedies are also known as herbal medicine. Research was conducted on rats to investigate the lipid profiles of *Catharanthus roseus* extract. Furthermore, when it comes to the kidney function test, there are outcomes that are statistically significant ($p < 0.05$) in groups 5, 6, and 7. Regarding urea, however, there is no result that can be considered statistically significant ($p < 0.05$). When the liver function test is performed, it is shown that there are statistically significant ($p < 0.05$) results in the levels of SGOT in group 6, with the dosage being 600 mg/kg. On the other hand, there are no findings that are statistically significant in the case of SGOT. After conducting a lipid profile function test, it has been determined that there are statistically significant findings ($p < 0.05$) in relation to the levels of triglycerides, LDL, and HDL. Group 5 showed statistically significant findings ($p < 0.05$) in relation to HDL, while group 6 exhibited significant findings ($p < 0.05$) in relation to LDL and triglyceride studies. Insights like this could help people with liver disorders.

Keywords: *Catharanthus roseus*; SGPT; Herbal medicine; Triglyceride, phytopharmacology; cholesterol.

Comment [A2]: Suggestions for improvement:
Provide more details: The abstract should include specific information about the methodology used, such as the dosage and duration of treatment, the number of animals in each group, and the specific assessments performed for liver and kidney function.
Highlight the significance of the findings: The abstract should emphasize the importance and implications of the statistically significant results obtained. How do these findings contribute to the understanding of *Catharanthus roseus*' hepatoprotective activity? How might these insights be beneficial for individuals with liver disorders?
Expand the keywords: While the provided keywords are relevant, consider expanding the list to include additional terms that accurately represent the study, such as hepatotoxicity, antioxidant, rat model, liver enzymes, and oxidative stress.
Review the language: The abstract contains some grammatical errors and awkward sentence constructions. Ensure that the language used is clear, concise, and free of errors.
Include additional information: It would be helpful to mention the extract preparation method, the specific parameters measured for lipid profiles, and any potential limitations or future directions for research.
By addressing these points, the abstract can provide a more comprehensive and informative summary of the study's objectives, methods, and key findings.

Introduction

Among all the human organs, the liver serves the most purposes, and it is also the biggest glandular organ. Multiple times daily, the complete blood supply of an individual goes through the liver. When it comes to metabolism, the liver is crucial for humans [1]. Worldwide, liver illnesses are a leading cause of death and disability in both humans and other animals, with

hepatotoxicity from pharmaceuticals being the leading cause [2]. An increase in reactive oxygen species (ROS) activity (OH, H₂O₂, O₂) can damage cells, especially those in the liver, when people drink a lot, are addicted to drugs, are exposed to some harmful chemicals, or have a virus or parasite. [2]. L-glutathione, which is made up of L-cysteine, glycine, and L-glutamate, is often taken by mouth with ascorbic acid because it fights free radicals and dissolves easily in water (1 molecular weight). Their cleansing and anti-oxidant qualities, in addition to boosting immunity, are highly valued [3]. The third. But they may make you sick to your stomach, bloat, have diarrhoea, have trouble breathing because of constriction of the airways, or even develop skin responses like dermatitis. The prevalence of chronic liver disease (CLD) has risen by 31% in the United States among adults aged 45–64 years, affecting an estimated 1.5 billion individuals globally [4]. The unique chemical compounds derived from medical plants may have therapeutic effects, say experts in the field of medicinal plants. Therefore, researchers are always looking for new herbal remedies or alternative treatments derived from plants to cure a wide range of illnesses. [5]. In contrast to phytotherapy, which is the scientific study of medicinal plants, herbalism involves its practical use. Plants have been a source of medicine for thousands of years due to their wide assortment of chemicals having medicinal qualities [6]. Many different chemical components, including phenols, alkaloids, terpenoids, saponins, glycosides, tannins, flavonoids, resins, polysaccharides, plant lipids, essential oils, and many more, allow these medicinal plants to exert a broad variety of pharmacological and therapeutic effects [7–9]. One possible therapeutic impact of plant genetic modification is to alter the concentration of the plant's chemical components. One application of reverse genetics is the enhancement of secondary metabolite biosynthesis, including alkaloid production [10].

Catharanthus roseus, sometimes referred to as Vinca rosea or Periwinkle, commonly occurs in the North Karnataka area of India. This subshrub is found throughout the whole country of India. These regions include: Brazil, the Cook Islands, the Dominican Republic, the UK, Jamaica, Mozambique, Pakistan, Taiwan, Thailand, and the West Indies [11]. The phytochemical analysis detected the existence of alkaloids, flavonoids, tannins, saponins, terpenoids, carbohydrates, ferric chloride, and cardiac glycosides [12–13]. This plant has several beneficial properties, such as antioxidant, antidiarrheal, anticancer, antidiabetic, anti-bacterial, hypotensive, and wound healing activities [14, 15].

Comment [A3]:

Clarify and organize information: The introduction contains several disjointed sentences and ideas that make it difficult to follow the flow of the text. It would be helpful to reorganize the information and ensure that each paragraph focuses on a specific aspect related to the study.

Define key terms: The introduction introduces terms like "reactive oxygen species (ROS)" and "L-glutathione" without providing clear definitions or explanations. It would be helpful to define these terms or provide brief explanations to ensure that readers understand their significance.

Link the introduction to the study: While the introduction discusses the therapeutic effects of medicinal plants, it does not explicitly connect this information to the study being reviewed. It would be useful to explain how the study relates to the use of medicinal plants for hepatoprotection and provide a clear transition to the specific research being conducted.

The objective of our research is to examine the anti-hyperlipidemic effects of *Catharanthus roseus* in a rat model.

Materials and methods

Plant Collection and Extract Preparation

Catharanthus roseus specimens were obtained from a local market in Dhaka. The University of Dhaka's Department of Pharmacy verified the authenticity of the item. The *Catharanthus roseus* plants were dried in the air and then crushed extensively. Next, we subjected the powders to a 15-day extraction process using a 50% ethanol solution. The extract underwent filtration every three days. The obtained substance was dehydrated using a rotary evaporator under reduced temperature and pressure conditions. Ultimately, the unrefined remains underwent the necessary pharmacological examination.

Drugs and Chemicals

Carbon tetrachloride (CCl₄), a well-known hepatotoxicity causing chemical, was purchased from the Sigma firm in the United States. The typical anti-oxidant medication silymarin was purchased as Livasil 140 mg from Incepta Pharmaceuticals Ltd.

Experimental Animal Procurement, Nursing, and Grouping

A total of 100 male rats weighing between 120 and 150 grams were obtained from Jahangirnagar University in Savar, Dhaka. Each of them was housed in a climate-controlled environment (temperature 25±3°C, relative humidity 55±5%, and a 12-h light/dark cycle) at the University of Dhaka's Institute of Nutrition & Food Science (INFS). They were given a conventional food and were permitted to drink clean water. All of the animals were maintained in this habitat for at least one week prior to the research for adaptation. All experimental methods followed the recommendations of the Institutional Animals Ethics Committee (IEAC).

Animal Model Sample Size Detection

A total of 100 rats were allocated at random into 10 groups of ten rats each. The rats were assigned to each group at random in all of the studies. We used ten rats in each group to increase the investigation's validity. During the mating season, we, on the other

Comment [A4]: Clarify information on occurrence and distribution: The paragraph states that *Catharanthus roseus* commonly occurs in the North Karnataka area of India and is found throughout the whole country of India. However, it also mentions other regions such as Brazil, the Cook Islands, the Dominican Republic, the UK, Jamaica, Mozambique, Pakistan, Taiwan, Thailand, and the West Indies. It would be helpful to clarify whether the plant is native to all these regions or if it has been introduced and cultivated there.

The paragraph briefly lists several beneficial properties of *Catharanthus roseus*, including antioxidant, antiarrhythmic, anticancer, antidiabetic, antibacterial, hypotensive, and wound healing activities. It would be beneficial to provide more detailed information or references supporting these claims. Additionally, it would be helpful to mention if these properties have been studied specifically in relation to *Catharanthus roseus* or if they are more general properties associated with the plant family or related compounds.

hand, maintained a close eye on the rat every day. We included both positive and negative control groups in our study.

Dose Selection and Route of Administration for Respective Study

Many laboratory studies on acute and chronic liver illnesses make use of carbon tetrachloride (CCL4). The trichloromethyl free radical (CCL3), a metabolite of CCL4 produced by the CYP2E1 isozyme, reacts with proteins and cellular lipids to form the trichloromethylperoxy radical, causing lipidomic lipid peroxidation and lobular necrosis. A single oral administration of CCL4 combined with olive oil as a vehicle in a 1:1 ratio (3 ml/kg of rat body weight) caused liver damage in all animal groups except for the usual control group. After receiving therapy for hepatic damage, the researchers administered extracts of the *Catharanthus roseus* plant to the animals. People took different doses of the extract orally. A researcher gathered flowers of the *Catharanthus roseus* species from a Dhaka bazaar. The Department of Pharmacy at the University of Dhaka verified the content. After being air-dried, the *Catharanthus roseus* was ground to a powder. Next, we conducted a 15-day extraction process in 50% ethanol using the powders. We removed the filtrate at three-day intervals. We dried the extracted material at low pressure and temperature using a rotary evaporator. We then performed the necessary pharmacological testing on the crude residue.

Evaluation of Hepato-Protective Activity

For this experiment, 100 rats were randomly picked and equally divided into fourteen groups

Table 1: Application of treatment efficacy

Group Number	Group Specification	Treatment species	Dose treatment species (mg/kg)	Abbreviation of Groups
1	Negative Control	Physiological saline	10 ml/kg	N
2	CCl ₄ Control	N/A	N/A	A
3	CCl ₄ + S ₁₀	Silymarin	10	S ₁₀
4	CCl ₄ + CR ₂₀₀	<i>Catharanthus</i>	200	CR ₂₀₀

Comment [A5]: The section provides a clear description of the plant collection and extract preparation process, including the verification of authenticity, drying, crushing, extraction with a 50% ethanol solution, filtration, and dehydration. However, it would be helpful to mention the specific quantities or ratios of plant material and ethanol used for extraction, as well as any specific conditions (e.g., temperature, duration) during the extraction process.

mention specific information on the rat strain or species used, as well as the rationale for selecting male rats for the study. Additionally, it would be beneficial to mention the specific details of the conventional food provided to the animals.

The section mentions the allocation of 100 rats into 10 groups of 10 rats each and the inclusion of positive and negative control groups. However, it does not provide specific details on the treatments or interventions assigned to each group. It would be helpful to mention the specific experimental groups and their respective treatments or interventions.

Comment [A6]: Provide details on extract preparation: The passage briefly describes the extraction process of *Catharanthus roseus* using 50% ethanol, but it does not mention the quantity or ratio of plant material to ethanol used. Additionally, it does not provide information on the concentration or standardization of the extract. It would be beneficial to provide more specific details on the extraction process and the concentration or standardization of the extract used.

Elaborate on pharmacological testing: The passage mentions that necessary pharmacological testing was performed on the crude residue of the extract but does not provide any specific details on the tests conducted. It would be helpful to specify the pharmacological tests performed on the extract and provide references or methodologies for these tests.

		<i>roseus</i>		
5	CCl ₄ + CR ₄₀₀	<i>Catharanthus</i> <i>roseus</i>	400	CR ₄₀₀
6	CCl ₄ +CR ₆₀₀	<i>Catharanthus</i> <i>roseus</i>	600	CR ₆₀₀
7	S ₁₀	Silymarin	10	S ₁₀
8	CR ₂₀₀	<i>Catharanthus</i> <i>roseus</i>	200	CR ₂₀₀
9	CR ₄₀₀	<i>Catharanthus</i> <i>roseus</i>	400	CR ₄₀₀
10	CR ₆₀₀	<i>Catharanthus</i> <i>roseus</i>	600	CR ₆₀₀

Comment [A7]: Draw the table more professionally

Biological Sample Collection.

In order to assess blood glucose levels, rats had their tail tips punctured to collect blood samples. On the other hand, blood was drawn from the animal as soon as its heart was punctured and transferred to a micro centrifuge tube after killing. Following 5 minutes of centrifugation at 5,000 rpm, the collected samples yielded the supernatant fluid. For biochemical testing, this fluid was then transferred to an additional micro centrifuge tube. Following sacrifice, the organs were quickly extracted and carefully cleansed in ice-cold saline in order to assess their function.

Estimation of Biochemical Parameters

The blood glucose level was measured using a glucometer. Aside from the Humaluzer 3000, lipid profile, kidney, and liver function tests were performed. In addition, the gluconeogenic and glycolytic enzyme activity of kidney and liver samples was examined

Statistical analysis:

All of our findings (raw data) in terms of numerical parameters were recorded and analyzed on a broadsheet using the MS Excel application. The gathered data were subjected to descriptive statistics, with the findings reported as mean SD. To evaluate statistical significance, we used the SPSS 16 software's "One-way Anova test" to interpret inter-group heterogeneity in terms of several biological factors. The occurrences are considered statistically significant since the 'p' value was less than 0.05 ($p < 0.05$).

Results and discussion:

Table 2: Lipid profile of rat after administration of drug and *Catharanthus roseus* extract.

Group no.	Group status	Kidney Function test		Liver Function test		Lipid Profile Function Test			
		Creatinine (mg/dl)	Urea	SGOT (u/l)	SGPT (u/l)	Cholesterol (mg/dl)	Triglyceride (mg/dl)	LDL (mg/dl)	HDL (mg/dl)
1	Negative Control	0.6±0.02	28.29±3.49	40.35±3.70	35.33±2.40	96.24±6.19	46.44±2.52	38.47±3.37	69.24±4.50
2	CCl ₄ Control	2.7±0.08	94.89±5.26	102.36±7.51	99.37±6.45	162.24±8.14	105.39±5.68	89.49±8.34	40.32±3.11
3	CCl ₄ + S ₁₀	1.4±0.06	68.26±4.59	64.51±4.29	68.22±7.15	119.23±6.15	72.26±3.96	65.60±6.30	57.15±4.69
4	CCl ₄ + AB ₂₀₀	2.4±0.08	94.26±3.86	100.29±5.26	98.10±5.23	159.29±4.60	102.89±2.33	88.28±3.46	41.44±2.29
5	CCl ₄ + AB ₄₀₀	2.2±0.09*	92.57±5.53	97.59±3.89	95.46±3.20	158.39±5.50	99.57±4.61	86.19±3.49	44.16±3.38*
6	CCl ₄ +AB ₆₀₀	1.8±0.05*	90.97±4.23	42.40±4.19	91.07±5.22*	155.34±4.19	95.36±2.22*	83.83±3.71*	47.18±4.50*

Comment [A8]: Clarify blood sample collection: The passage mentions that blood samples were collected from the rats' tail tips to assess blood glucose levels. However, it does not provide specific details on the method used for blood collection (e.g., lancet, syringe). It would be helpful to clarify the blood collection method and any relevant protocols followed to ensure consistency and reproducibility.

Elaborate on biochemical parameter estimation: The passage briefly mentions the measurement of blood glucose levels using a glucometer and the performance of lipid profile, kidney, and liver function tests. However, it does not provide any specific details on the methods or assays used for these tests. It would be helpful to mention the specific techniques, kits, or instruments used for biochemical parameter estimation.

Provide more information on statistical analysis: The passage mentions that the data were recorded and analyzed using MS Excel for descriptive statistics and SPSS 16 software for the "One-way Anova test" to evaluate inter-group heterogeneity. However, it does not provide any specific details on the statistical tests conducted or the parameters analyzed. It would be beneficial to mention the specific statistical tests used, including any post-hoc tests or corrections for multiple comparisons.

7	S ₁₀	0.8±0.0 2*	31.29 ±4.7	40.23 ±1.04	37.24±3 .19	99.10±5 .11	48.46±2.70	40.30±0. 86	41.69±2.84
8	AB ₂₀₀	0.7±0.0 5	34.57 ±2.38	42.39 ±3.19	33.63±2 .08	96.27±4 .70	44.82±1.26	42.34±1. 50	39.57±1.89
9	AB ₄₀₀	0.6±0.0 7	29.49 ±0.83	39.59	38.17±3 .50	95.29±3 .09	43.95±2.96	39.69±1. 28	42.79±2.58
10	AB ₆₀₀	0.7±0.0 8	33.57 ±2.62	4.14	34.48±2 .57	96.41±4 .01	40.50±3.10	43.40±2. 60	43.69±3.2

Comment [A9]: Draw the table more professionally

Note: Each value represents the mean ± SEM. (n=5). One- way ANOVA followed by Dunnett's t test. ***P<0.001, **P<0.01, *P<0.05 compared with control.

Patients suffering from severe chronic kidney disease (CKD) as well as end-stage renal disease (ESRD) may experience cognitive dysfunction. The correlation between chronic kidney disease (CKD) and cognitive impairment is a serious public health issue [16]. This is due to the fact that the prevalence of CKD in the United States increased from 10% in 1988–1994 to 13% in 1999–2004, and it is possible that this trend may continue in the future. Furthermore, when it comes to the kidney function test, there are outcomes that are statistically significant ($p < 0.05$) in groups 5, 6, and 7. But in the case of urea, there is no outcome that can be considered statistically significant. Liver function tests, often known as LFTs, are a useful screening tool that is an efficient method for identifying hepatic impairment. Given that the liver is responsible for a wide range of processes, it is impossible for a single test to offer an accurate and comprehensive estimation of the liver's function [17]. In the case of the liver function test, the findings of the SGPT level are statistically significant ($p < 0.05$) in group 6, with the dosage being 600 mg/kg. On the other hand, there are no findings that are statistically significant ($p < 0.05$ in the case of SGOT). Several investigations [18–20] came to the same conclusions about the same phenomenon. After conducting a lipid profile function test, it has been determined that there are statistically significant findings ($p < 0.05$) in relation to the levels of triglycerides, LDL, and HDL. Group 5 showed statistically significant ($p < 0.05$) outcomes in the case of HDL, whereas group 6 showed statistically significant results in the case of LDL and triglyceride. There were several studies [21–23] that came to the same conclusions.

Conclusion:

The ethanolic extract of *Catharanthus roseus* was shown to possess hepatoprotective effects, which were identified within the context of this investigation. By lowering the buildup of lipids and liver problems, this extract helps to reduce the negative effects that a diet high in fat may have on the body. In order to determine which component of the entire extract really provides the anti-hyperlipidemic action through a screening approach, more research is necessary.

References:

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Comment [A10]: The article seems to lack logical perspective and flow. You first discuss the link between kidney disease and cognitive impairment, then move on to kidney-related tests, and then to liver-related tests and lipid profiles. It would be better to follow a more logical order, starting with an introduction to the kidney-related topic and then addressing the liver and other tests. The text requires improvement in terms of structure and coherence between paragraphs and sentences. It is better for each paragraph to focus on only one relevant topic and present information in a logical and hierarchical manner. In the conclusion, you should briefly summarize the results mentioned in the article and also emphasize the importance of the findings and the need for further research.

Comment [A11]: Some of the references are very old, update them and add to their number

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