Contents lists available at UGC-CARE

International Journal of Pharmaceutical Sciences and Drug Research

[ISSN: 0975-248X; CODEN (USA): IJPSPP]

Available online at www.ijpsdronline.com

Research Article

Role of *Bougainvillea glabra* Stem Extract on Paracetamol and Alcohol-Induced Hepatotoxicity in Rats

Lakshminarayana Manjunath*, Vikas Jogpal

School of Medical and Allied Sciences G. D. Goenka University, Sohna, Gurugram, Haryana, India.

ARTICLE INFO

Article history:

Received: 27 August, 2023

Revised: 02 December, 2023

Accepted: 04 December, 2023

Published: 30 January, 2024

Keywords:

Bougainvillea glabra extract, Hepatoprotective, Paracetamol, Alcohol, Serum glutamic oxaloacetic transaminase, Serum glutamic pyruvic transaminase, Alkaline phosphatase, Total bilirubin.

DOI:

10.25004/IJPSDR.2024.160101

ABSTRACT

The current study investigates the *in-vivo* hepatoprotective effectiveness of *Bougainvillea glabra* stem extract against alcohol and paracetamol-induced hepatotoxicity in animal models. The alterations in liver enzymes including serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), alkaline phosphatase (ALP), and total bilirubin are studied in rats given *B. glabra* extract with paracetamol or alcohol to produce hepatotoxicity. The levels of glutathione and lipid peroxidation were also examined, and the outcomes were contrasted with silymarin as the reference. The acute toxicity studies presented the plant extract under category 5 of GHS system, which further motivated the studies for hepatoprotective activity. The induction of hepatotoxicity was confirmed with the elevated levels of serum and tissue biochemical by the administration of paracetamol and alcohol. Under paracetamol as a hepatotoxin, the animals with 200 and 400 mg/kg p.o demonstrated near figures for SGPT and SGOT of the group treated with silymarin with significance. The results were still more appreciative under alcohol as a hepatotoxin. In both cases, the group with 400 mg/kg p.o gave a promising result with the reduced inflammatory cells under histopathological studies.

Introduction

with more functions than any other human organ, the liver is the biggest glandular organ in the body. The whole blood supply of an individual travels through the liver numerous times each day; the liver is essential to human metabolism. Bile is produced by the liver, which also makes prothrombin, fibrinogen, and heparin, a mucopolysaccharide sulfuric acid ester that aids in preventing blood clots in the circulatory system.[1] The normal functioning of the liver is distracted by drug-induced liver injury (DILI) and is a chief regulatory as well as clinical challenge.[2] Drug-induced hepatotoxicity can present a wide range of malfunctions in the liver, from an asymptomatic increase of liver enzymes to uncontrollable hepatic failure.

Overdosing on paracetamol (PCM), commonly known as acetaminophen, can have serious adverse effects on the kidneys and liver.[3,4] Cytochrome P450 enzymes activate PCM and transform it into the hazardous metabolite N-acetyl-p-benzoquinoneimine (NAPQI), which results in oxidative stress and glutathione (GSH) diminution.[5,6] Chronic alcohol consumption is widely established to cause fatty liver, hepatomegaly, alcoholic hepatitis, fibrosis as well as cirrhosis. It has been suggested that endotoxin is what starts the chain of events that leads to alcohol-induced toxicity.[7] Although modern medicine has made enormous strides, there are still very few effective medications that can help the liver recover from injury or regenerate its cells. To treat a wide range of clinical liver disorders, several active plant extracts are

***Corresponding Author:** Mr. Lakshminarayana Manjunath

Address: School of Medical and Allied Sciences G. D. Goenka University, Gurugram, Haryana, India.

Email ✉: ml_nani82@yahoo.co.in

Tel.: +91-9741677544

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

often used.[8-11] To avoid any liver damage brought on by exposure to xenobiotics like alcohol and other narcotics and non-narcotics, the phytochemicals, which are organic components of several plants, offer protection against liver disorders caused by drugs and can be included in daily life. A pretreatment of methanolic extract of *Agave americana* leaves elevated the hepatocellular architecture for the paracetamol-intoxicated liver,[12] an ethanolic extract of *Moringa oleifera* bark had significantly reduced the levels of liver enzymes such as serum glutamic-oxaloacetic transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), Alkaline phosphatase (ALP) and total bilirubin, which was elevated by intake of paracetamol.[13] A similar observation is made for *Bacopa monnieri L.,*[14] *Rhazya stricta, Balanites aegyptiaca* and *Haplophylum tuberculatum*,[15] *Ziziphus oxyphylla* Edgew,[16] *Trichosanthes dioica*[17] and many other plants. Reports on extracts of *Avicennia marina,*[18] *Anogeissus acuminate,*[19] *Smilax china*[20] and several other plants are investigated to treat alcohol-induced hepatotoxicity. Numerous of these plants have also demonstrated their many therapeutic uses; however, the wealth of Indian herbs and plants for biomedical applications remains largely unexplored.

Bougainvillea glabra, commonly called as the paper flower from the family Nyctinaginacea, which consists of 14 species. The plant grows as a shrub as well as a climber in topical and sub-tropical gardens throughout the world.[21] The plant is reported to have several phytochemicals such as tannins, alkaloids, flavonoids, and beta-cyanins.[22,23] The leaves of *B. glabra* is reported to have anti-diarrhoeal action, anti-microbial activity and several pharmacological benefits.[24,25] However, the hepatoprotective activity of *B. glabra* stem extract remains unexplored and is attempted to tap in present work.

Though, plenty of modern (tricholine citrate, trithio-paramethoxy phenyl propene, essential phos-pholipids, pancreatin combined with l-ornithine l-aspartate, silymarin, and ursodesoxy cholic acid) as well as traditional herbal medications are available for liver diseases, most of which are ineffective and have potentially dangerous side-effects. Even in developed nations, the widespread usage of complementary and alternative medicine has increased which provides a platform for new herbal medications. Our previous publication explored the phytochemicals present in *B. glabra* stem extract, quantitatively and qualitatively.[26] The work also tapped the *in-vitro* antioxidant activity and hepatoprotective feature. The work confirmed the presence of several antioxidant phytochemicals such as flavonoids, tannins, phenols, steroids, and many other phytochemicals and their potency towards studied biomedical applications. The present work explores the *in-vivo* hepatoprotective efficacy of stem extract of *B. glabra* against paracetamol and alcohol-induced hepatotoxicity in animal models. The *B. glabra* extract-treated rats with paracetamol and alcohol-induced hepatotoxicity are examined for variations in the liver enzymes such as SGOT, SGPT, ALP and total bilirubin. The lipid peroxidation and glutathione (GSH) levels were also investigated and the results were compared with the standard, silymarin.

Materials And Methods

Plant Material Collection and Processing

Stems of *B. glabra* were gathered in and around Gurugram, Haryana during the flowering stage. All the leaves and flowers were removed; approximately 60 cm from the flowering end was selected. Then the selected part was shade dried for three weeks at room temperature. After sufficiently dried, stems were ground into a fine powder

Materials of the Study

All of the chemicals, reagents, and solvents utilized were of analytical quality and weren't previously purified.

Plant Extract Preparation

The plant extracts were created in accordance with earlier research. With the help of 200 mL of each solvent- pet ether, ethanol, and water in order of increasing polarity and 70% of the hydro-alcoholic combination, 20 g of finely powdered *B. glabra* stem material were successfully extracted. Every time, the stem sample was completely dried before using the other solvent. The extracted sample from the *B. glabra* stem was mixed, filtered, and evaporated to dryness using a hot water bath to achieve a yield of 1.5 g. The same sample was then stored in an airtight container and used for analysis.[15,16]

Animal Husbandry

The CPCSEA criteria for animal care and usage were followed in the conduct of this investigation. The test facility's Institutional Animals Ethical Committee (IAEC) gave the study its seal of approval and the reference number IEAC, SSCP/224/2021-22.

A wistar, male rats of age 8 to 10 weeks were considered for the study. The animals were accustomed to the laboratory environment for a minimum of 7 days, and they will be checked daily for clinical indicators. The animals were kept in typical laboratory settings with air conditioning, a sufficient supply of fresh air (air changes 12–15 per hour), a room temperature of 20 to 22°C, a relative humidity range of 49 to 63%, and a 12 hours cycle of light and darkness. Each animal was kept in a cage with a stainless steel mesh top grill that had a place to store pellet food and a water supply. Standard laboratory rodents were used to feed the animals, and unlimited access to reverse osmosis water was also supplied.

Acute Toxicity Studies

The dose for the main study was selected based on the acute toxicity study conducted as per OECD No 423.[26] Six

female rats were used in a limit test that was conducted in two steps at a dose of 2000 mg/kg/bw (three rats per step). In Step 1, rats were fasted overnight and received a single oral dose of the test drug by gavage at a dose of 2000 mg/kg body weight. Food was withheld for an additional 3 to 4 hours and seen for clinical symptoms and mortality for at least 24 hours, step 2 rats that had fasted overnight received the test item in a similar way to step 1 rats. For 14 days, mortality and clinical observations were tracked.

Hepatotoxicity Induction using Paracetamol

The experiment was carried out in male wistar rats. Animals were acclimatized for seven days prior to the study. Animals were grouped and treated as presented in Table 1 for a period of 7 days. Paracetamol was administered to all groups except group I daily at the dose of 2 g/kg p.o. Group III animals received the standard drug silymarin (200 mg/kg; p.o.) simultaneously for a period of 7 days, whereas the groups IV to VI animals received *B. glabra* stem extract at the dose of 100, 200, and 400 mg/kg, respectively. During this period of treatment, the rats were maintained on a standard pellet diet and water. All the animals were sacrificed 24 hours after the fasting of the last dose of paracetamol, i.e., on the 8^{th} day. Blood was collected under mild anesthesia allowed to clot and then subjected to centrifugation at 4000 rpm for 15 minutes. Biochemical parameters like SGOT, SGPT, ALP, total bilirubin, and direct bilirubin were measured.

Hepatotoxicity Induction using Alcohol

The experiment was carried out in male wistar rats. Animals were acclimatized for seven days prior to the study. Animals were grouped and treated as presented in Table 2 for a period of 11 days. Alcohol was administered to all groups except group I daily at the dose of 5 g/kg of 25% w/v; p.o. Group III animals received the standard drug silymarin (200 mg/kg; p.o.) simultaneously for a period of 11 days, whereas the groups IV to VI animals received *B. glabra* stem extract at the dose of 100, 200, and 400 mg/kg, respectively. During this period of treatment, the rats were maintained on a standard pellet diet and water. All the animals were sacrificed 24 hours after the last dose of alcohol, i.e., on the 12^{th} day. Blood was collected under mild anesthesia allowed to clot and then subjected to centrifugation at 4000 rpm for 15 minutes. Biochemical parameters like SGOT, SGPT, ALP, total bilirubin, and direct bilirubin were measured.

Assessment of Serum Biochemicals

Serum biochemical parameters such as SGPT, SGOT, ALP and TB were estimated using commercially available diagnostic kits for enzymatic biochemicals. The estimation procedure was followed according to the instructions given on the kits, ERBA Manheim IFCC Erba SGPT kit with code number 120207, ERBA SGOT KIT with code number 120204 and ERBA ALP kit with code number 120238.

Table 1: Grouping and treatment of the animals with paracetamol-induced hepatotoxicity

Group	*Group ID*	*Treatment*	*Total no. of animals*
1	Control	DM water	6
2	Positive control (Paracetamol)	Paracetamol 2 g/kg; p.o.	6
3	Paracetamol + *Silymarin*	Paracetamol 2 g/kg; p.o.+ silymarin (200 mg/kg; p.o.)	6
4	Paracetamol + *B. glabra* stem extract	Paracetamol 2 g/kg; p.o.+ *B. glabra* stem extract (100 mg/kg; p.o.)	6
5	Paracetamol + *B. glabra* stem extract	Paracetamol 2 g/kg; p.o.+ *B. glabra* stem extract (200 mg/kg; p.o.)	6
6	Paracetamol + *B. glabra* stem extract	Paracetamol 2 g/kg; p.o.+ *B. glabra* stem extract (400 mg/kg; p.o.)	6

Table 2: Grouping and treatment of the animals with alcohol-induced hepatotoxicity

Group	*Group ID*	*Treatment*	*Total no. of animals*
1	Control	DM water	6
2	Positive control (Alcohol)	Alcohol 5 mL/kg of 25% w/v; p.o.	6
3	Alcohol + *Silymarin*	Alcohol 5 mL/kg of 25% w/v; p.o.+ silymarin (200 mg/kg; p.o.)	6
4	Alcohol + *B. glabra* stem extract	Alcohol 5 mL/kg of 25% w/v; p.o.+ *B. glabra* stem extract (100 mg/kg; p.o.)	6
5	Alcohol + *B. glabra* stem extract	Alcohol 5 mL/kg of 25% w/v; p.o+ *B. glabra* stem extract (200 mg/kg; p.o.)	6
6	Alcohol + *B. glabra* stem extract	Alcohol 5 mL/kg of 25% w/v; p.o+ *B. glabra* stem extract (400 mg/kg; p.o.)	6

Assessment of Tissue Biochemical

Thiobarbituric acid (TBA) and malondialdehyde (MDA), a breakdown byproduct produced from several oxidized molecules, provide the basis for the assay. The resultant chromogen is measured at its highest absorbance wavelength, which is 532 nm. In a test tube, 0.1 mL of homogenate was added to a test tube along with 1-mL of TBA reagent, which contained 0.375% TBA, 15% tricarboxylic acid (TCA), and 0.25 N HCl in equal amounts.

The test tube was then placed in a boiling water bath for 30 minutes. The mixture was then centrifuged at 6000 rpm for 5 minutes after spending 10 minutes in crushed ice. Using absorbance for blank and the obtained solution, lipid peroxidation was determined.

An accurate measurement of the glutathione concentration in a sample can be obtained by measuring the absorbance of 5-thio-2-nitrobenzoic acid (TNB) at 412 nm. To precipitate proteins, 0.5 mL of homogenate is combined with 0.1 mL of 25% TCA and centrifuged at 4000 rpm for 5 minutes. The next step was combining 0.3 mL of the supernatant with 10 mM 5,5'-dithiobis-2-nitrobenzoic acid (DTNB) and 0.5 mL of 0.1 M phosphate buffer. After incubating this combination for 10 minutes, the absorbance at 412 nm was measured in comparison to acceptable blanks.

Histopathology

At the day of study termination, the livers were collected and weighed, and part of the liver was used for antioxidant activity and the remaining was immersed in a 10% formalin solution for a histopathology examination.

Statistics

The values were analyzed *via* GraphPad Prism 5 and the values were expressed in mean ± SEM. The mean values were compared by using one-way ANOVA followed by Dunnett's posttest.

Results And Discussion

Acute Toxicity Studies

The test item's minimal lethal dose (MLD) was greater than 2000 mg/kg body weight, according to the findings of acute oral toxicity research (Acute toxic class method) conducted on rats. According to OECD guideline no. 423, the test chemical can be classified under globally harmonized system (GHS) category 5 based on the observed MLD value. Based on this $1/5^{th}$, $1/10^{th,}$ and $1/20^{th}$ doses were selected for the efficacy study.

Paracetamol-induced Hepatotoxicity and its Treatment

Serum biochemicals

SGOT and SGPT are the standard liver enzyme markers to assess liver toxicity. The necrosis of liver cells leads to a major rise in these enzymes in blood serum. Administration of PCM significantly increased hepatocellular damage and is apparent from the increased levels of serum biochemical parameters, SGOT (191 U/L), SGPT (96 U/L), ALP (543 U/L) and bilirubin levels in group II animals when compared to the normal control, group I. A small amount of PCM is N-hydroxylated by the cytochrome P-450 enzyme to produce the extremely reactive and electrophilic intermediate NAPQI. It is normally removed through combination with glutathione, followed by additional metabolism to mercapturic acid and excretion into the urine. Yet, the metabolite, NAPQI is produced in quantities sufficient to decrease the hepatic glutathione following the use of high doses of PCM. The hepatocytes become extremely vulnerable to oxidative damage as a result, and NAPQI binds covalently to macromolecules, causing enzymatic systems to malfunction. The liver injury instigated by PCM overdose alters the transport function of the hepatocytes resulting in the leaking of plasma membrane, and hence increased levels of serum enzymes.[27,28]

The animals treated with considered *B. glabra* stem extract at three different doses (100, 200 and 400 mg/kg p.o) exhibited significant reduction in the above parameters. The measured levels of SGOT and SGPT for all tested groups are presented in Figs 1 and 2, respectively. Compared with the positive control, the groups IV, V and VI showed lesser levels with a significance *p < 0.05, **p < 0.01 and ***p < 0.001 compared to with positive control group. The standard drug silymarin treated group III also upturned the hepatotoxicity and the levels were lesser than the group III. A similar trend was observed for SGPT, wherein, group V and group VI showed a similar trend as of standard control group III with a significance of ***p < 0.001.

Along with SGPT and SGOT, ALP and total bilirubin would also play a great role in assessing hepatotoxicity. The estimated levels of same are presented in Figs 3 and 4. Like SGPT and SGOT, ALP and total bilirubin levels increased to 446.2 and 0.62, respectively with the administration of PCM, however decreased increased concentration of considered extract. Group VI with 400 mg/kg of *B. glabra* stem extract showed a significance factor equal to that of standard silymarin-treated group II for ALP. Nevertheless, total bilirubin was slightly higher for all three groups treated with extract, compared to the silymarin-treated group, with significance **p < 0.01 compared to positive control, group II.

Tissue biochemical

Lipid peroxidation and reduced glutathione are the two significant tissue biochemical parameters to assess

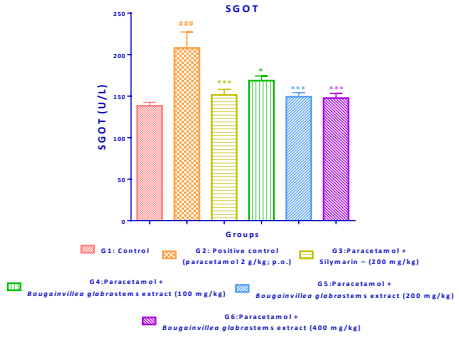

Fig. 1: Estimated levels of SGOT in considered groups for paracetamol induced hepatotoxicity and its treatment with *B. glabra* stem extract

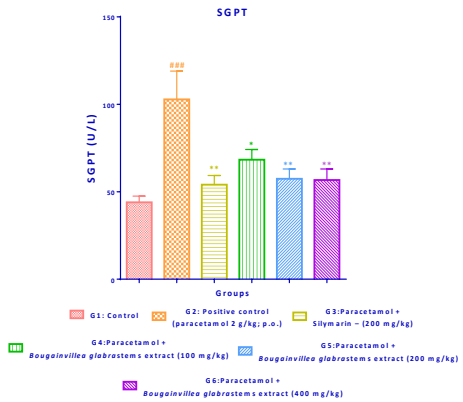

Fig. 2: Estimated levels of SGPT in considered groups for paracetamol induced hepatotoxicity and its treatment with *B. glabra* stem extract

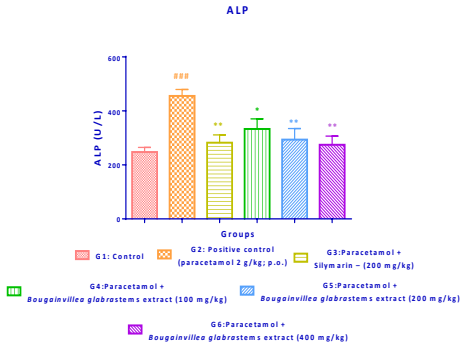

Fig. 3: Estimated levels of ALP in considered groups for paracetamol induced hepatotoxicity and its treatment with *B. glabra* stem extract

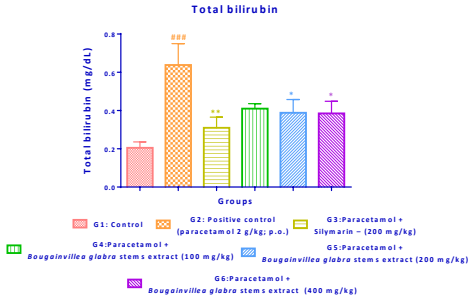

Fig. 4: Estimated levels of total bilirubin in considered groups for paracetamol induced hepatotoxicity and its treatment with *Bougainvillea labra* stem extract

the health of the liver. Oral intake of PCM in excess considerably increases the liver lipid peroxide levels by a fold, compared to control group, group I as in Fig. 5. With a statistical significance of $^{**}p < 0.01$, group VI administered with 400 mg/kg showed the same significance as of group III, treated with silymarin. In contrast, the reduced glutathione levels decreased with decreased extract concentration.

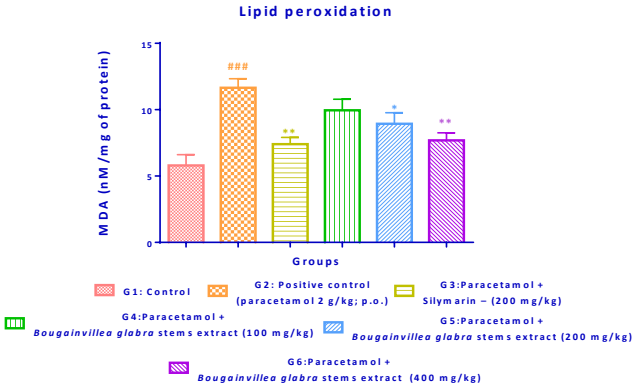

Fig. 5: Estimated levels of lipid peroxides in considered groups for paracetamol induced hepatotoxicity and its treatment with *B. glabra* stem extract

Tissue histopathology

Histopathological analysis of liver tissue sections from the normal control group revealed a healthy cellular arrangement characterized by well-defined hepatic cells, sinusoidal spaces, and a central vein (depicted in Fig. 6A). Conversely, the livers of paracetamol-treated rats in group 2 exhibited disrupted hepatic cell structure, including centrilobular necrosis, hyperplasia, vascular and cellular degeneration, polymorphonuclear aggregation, inflammation, and fatty degeneration (illustrated in Fig. 6B). Rats treated with silymarin (100 mg/kg) in group 3 showcased a significant decrease in fatty degeneration, as well as the absence of necrosis and inflammation (as shown in Fig. 6C). Remarkably, rats treated with varying doses (100–400 mg/kg) of *B. glabra* stem extract in groups 3, 4, and 5 displayed signs of protective effects. These included a noticeable reduction or absence of inflammatory cells, mitigated vascular congestion and degeneration, and reduced cellular degeneration, necrosis, and vacuole formation (depicted in Fig. 6 D–F).

Alcohol-induced Hepatotoxicity and its Treatment

Serum biochemical estimation

The work further investigates the efficacy of *B. glabra* stem extract in treating hepatotoxicity induced by ethanol. The above-said liver enzyme levels were estimated and compared among normal control, positive control and test groups. The alcohol-induced hepatotoxicity increases SGPT, and SGOT which is evident from Figs 7 and 8. Group II showed an estimated SGPT and SGOT levels of 93.2 and 96.8 U/L has reduced for the silymarin and other test groups. Though a considerable reduction in SGPT and SGOT levels is observed for test groups, the decrease in the levels could not reach the level of normal control and even for test groups. A similar trend is observed for ALP and TB as well (Figs 9 and 10). With an increased serum biochemical, it is understood that there might be hepatic duct blockage or an incomplete biliary obstruction. The levels decreased

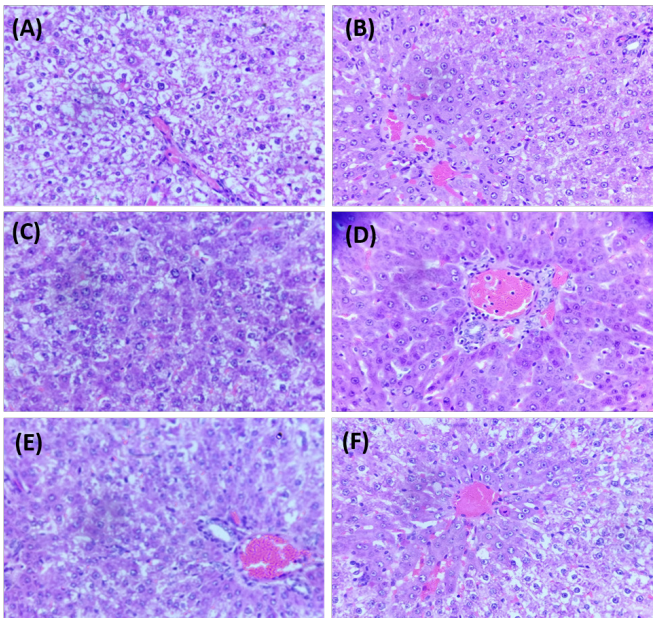

Fig. 6: Histopathalogical observation for paracetamol induced hepatotoxicity and its treatment with *B. glabra* stem extract

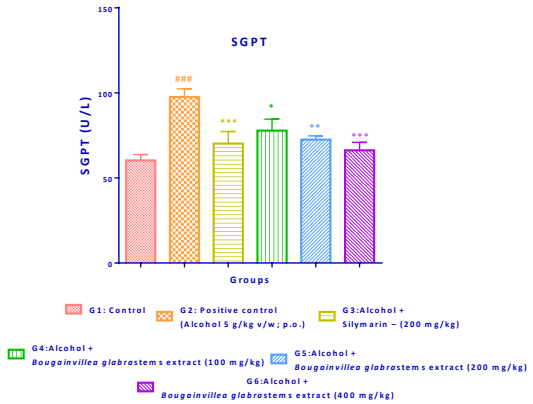

Fig. 7: Estimated levels of SGPT in considered groups for alcohol induced hepatotoxicity and its treatment with *B. glabra* stem extract

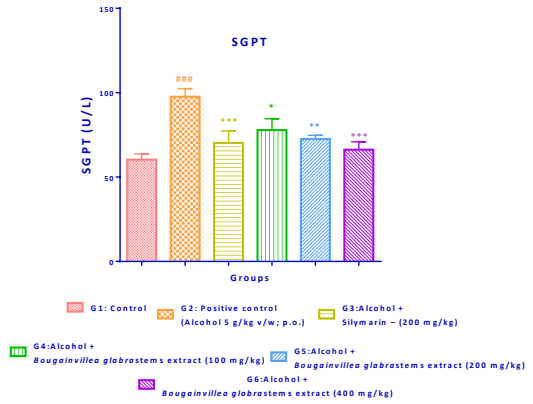

Fig. 8: Estimated levels of SGOT in considered groups for alcohol induced hepatotoxicity and its treatment with *B. glabra* stem extract

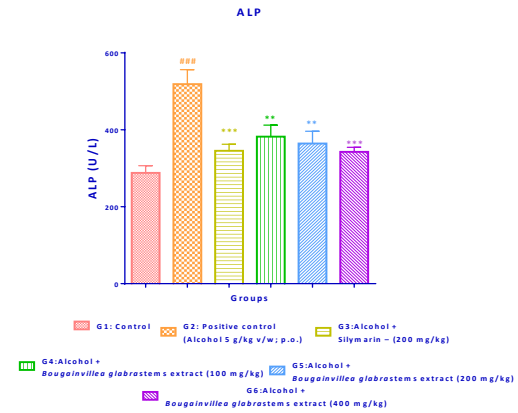

Fig. 9: Estimated levels of ALP in considered groups for alcohol induced hepatotoxicity and its treatment with *B. glabra* stem extract

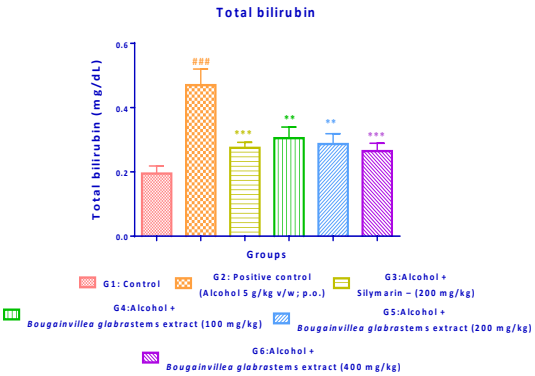

Fig. 10: Estimated levels of TB in considered groups for alcohol induced hepatotoxicity and its treatment with *B. glabra* stem extract

when treated with the leaf extract showing the reduced hepatic duct blockage.

Tissue biochemical estimation

The tissue biochemicals such as lipid peroxidation and reduced glutathione are estimated and recorded in Figs 11 and 12. Lipid peroxidative degradation of biomembrane causes the toxicity induced by ethanol. Such toxicity is also evidenced by reduced free radical scavenging activity of enzymes like GSH in ethanol-intoxicated test groups. Several living things contain large amounts of glutathione, a naturally occurring tripeptide and non-enzymatic biological antioxidant. The increased free radicals could damage the DNA of the cell and that further results in many other medical complications. It is well-known that a GSH deficit in living things can cause tissue damage and dysfunction.

The intervention of different doses of *B. glabra* stem extracts treated animals showed a significant decrease in the above parameters in alcohol-induced hepatotoxicity. Further administration of *B. glabra* stem extracts showed a decrease in LPO levels and increased GSH levels in the respective groups compared to positive control

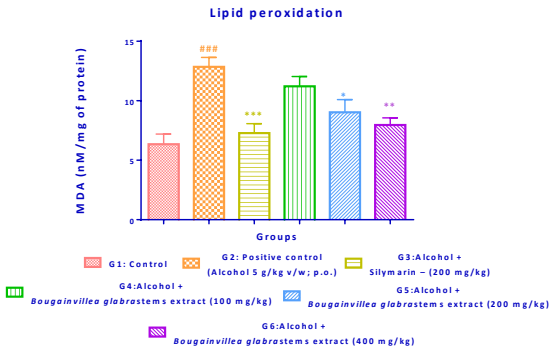

Fig. 11: Estimated tissue lipid peroxidation in considered groups for alcohol induced hepatotoxicity and its treatment with *B. glabra* stem extract

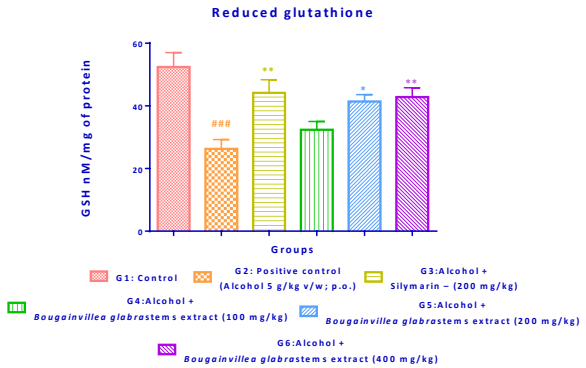

Fig. 12: Estimated reduced glutathione in considered groups for alcohol induced hepatotoxicity and its treatment with *B. glabra* stem extract

group animals. From the overall study, we can conclude the intervention of *B. glabra* stem extract showed a good hepatoprotective effect against alcohol-induced hepatotoxicity in rats.

Tissue histopathology

Histopathological analysis of liver sections from the normal control group revealed a healthy cellular framework characterized by well-defined hepatic cells, sinusoidal spaces, and a central vein (Fig. 13A). Conversely, in group 2 rats subjected to alcohol treatment, hepatocytes displayed noticeable swelling, accompanied by the occlusion of sinusoidal spaces (Fig. 13B). Additionally, in group 3, where rats were administered silymarin (100 mg/kg), liver sections demonstrated a significant reduction in fatty degeneration, along with the absence of necrosis and inflammation (Fig. 13C). Remarkably, in rats treated with varying doses (100–400 mg/kg) of *B. glabra* stem extract (groups 4, 5, and 6), liver sections exhibited indications of protection (Fig. 13D to 13F).

The work compares the results of two indirect hepatotoxins, paracetamol and alcohol. Both have caused specific biochemical lesions, which block the metabolic pathways resulting in variations in biochemical parameters, a first

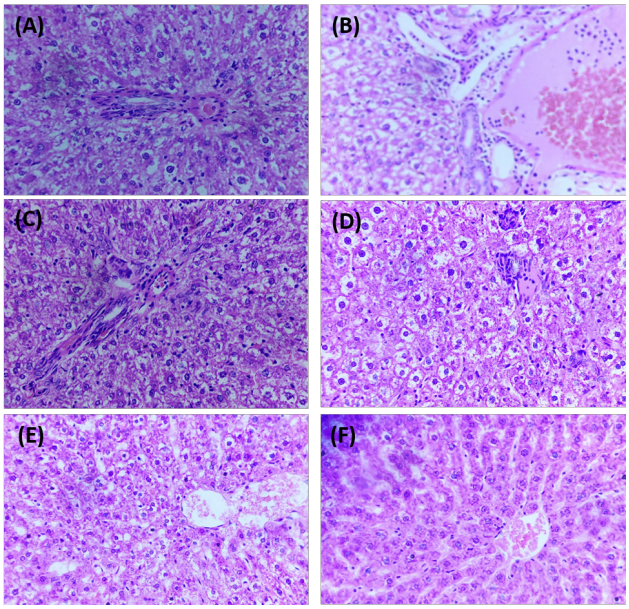

Fig. 13: Histopathalogical observation for alcohol induced hepatotoxicity and its treatment with *B. glabra* stem extract

step of hepatic disorders. However, the *B. glabra* stem extracts managed to balance the altered biochemicals due to the presence of effective phytochemical components.

Conclusion

The study's findings show that the aqueous extract of *B. glabra* stem extracts has hepatoprotective qualities. The antioxidant properties of the extract may be responsible for this ability. Paracetamol and alcohol successfully induced hepatotoxicity in the animals. The reduction in hepatotoxicity was confirmed in the treated groups with the reduction of elevated SGPT, SGOT, GSH, ALP and TB levels. To identify, isolate, characterize, and assess the active principle responsible for the plant's hepatoprotective action, more research is necessary. This investigation does not examine the toxicological properties of plants; thus, a toxicological assessment may be done.

References

1. Pandey S, Darunde D. Herbal drugs–an approach for the treatment of live disorders. International Journal Of Pharmacognosy. 2019; 6(5): 164-171. Availabe from: DOI: 10.13040/IJPSR.0975-8232. IJP.6(5).164-71
2. Parmar SR, Vashrambhai PH, Kalia K. Hepatoprotective activity of some plants extract against paracetamol-induced hepatotoxicity in rats. Journal of herbal medicine and toxicology. 2010; 4(2): 101-106.
3. Baponwa O, Amang AP, Mezui C, Koubala BB, Siwe GT, Vandi VL, Tan PV. Antioxidant mechanism of renal and hepatic failure prevention related to paracetamol overdose by the aqueous extract of Amblygonocarpus andongensis stem bark. BioMed Research International. 2022 Jul 21;2022: 1846558. Availabe from: doi: 10.1155/2022/1846558
4. Hussein RM, Kandeil MA, Mohammed NA, Khallaf RA. Evaluation of the hepatoprotective effect of curcumin-loaded solid lipid

nanoparticles against paracetamol overdose toxicity: Role of inducible nitric oxide synthase. Journal of Liposome Research. 2022 Oct 2;32(4):365-75. Available from: https://doi.org/10.1080/08982104.2022.2032737
5. Pingili RB, Pawar AK, Challa SR. Effect of chrysin on the formation of N-acetyl-p-benzoquinoneimine, a toxic metabolite of paracetamol in rats and isolated rat hepatocytes. Chemico-Biological Interactions. 2019 Apr 1;302:123-34. Available from: https://doi.org/10.1016/j.cbi.2019.02.014
6. Foudah AI, Alqarni MH, Soliman GA, Rahman RF, Çalışkan ÖA, Ganaie MA, Yusufoglu H. The Potential Hepatoprotective and Antioxidant Activities of Astragalus davisii against Paracetamol Induced Liver Damage in Rats. Journal of Pharmaceutical Research International. 2020 Sep 30;32(23):102-14. Available from: https://hdl.handle.net/11454/62873
7. Slevin E, Baiocchi L, Wu N, Ekser B, Sato K, Lin E, Ceci L, Chen L, Lorenzo SR, Xu W, Kyritsi K. Kupffer cells: inflammation pathways and cell-cell interactions in alcohol-associated liver disease. The American Journal of Pathology. 2020 Nov 1;190(11):2185-93. Availabe from: DOI: 10.1016/j.ajpath.2020.08.014
8. Ali SA, Sharief NH, Mohamed YS. Hepatoprotective activity of some medicinal plants in Sudan. Evidence-Based Complementary and Alternative Medicine. 2019 Dec 18;2019. Available from: doi: 10.1155/2019/2196315
9. Janghel V, Patel P, Chandel SS. Plants used for the treatment of icterus (jaundice) in Central India: A review. Annals of hepatology. 2019 Sep 1;18(5):658-72. Available from: DOI: 10.1016/j.aohep.2019.05.003
10. Maharaja P, Sengottuvel T, Aarthi A, Gopalasatheeskumar K. Review on Antioxidant and Hepatoprotective activity of Medicinal plants against Paracetamol Induced animal model. Research Journal of Pharmacognosy and Phytochemistry. 2020;12(2):114-9. Available from: DOI:10.5958/0975-4385.2020.00020.5
11. Baliga MS, Shivashankara AR, Venkatesh S, Bhat HP, Palatty PL, Bhandari G, Rao S. Phytochemicals in the prevention of ethanol-induced hepatotoxicity: A revisit. Dietary interventions in liver disease. 2019 Jan 1:79-89. Available from: https://doi.org/10.1016/B978-0-12-814466-4.00007-0
12. Ayenew KD, Wasihun Y. Hepatoprotective effect of methanol extract of Agave americana leaves on paracetamol induced hepatotoxicity in Wistar albino rats. BMC Complementary Medicine and Therapies. 2023 Dec;23(1):1-8. Available from: https://doi.org/10.1186/s12906-023-03931-y
13. Islam R, Alam MJ. Evaluation of liver protective activity of Moringa oleifera bark extract in paracetamol induced hepatotoxicity in rats. BioRxiv. 2019 Jan 7:513002. Available from: https://doi.org/10.1101/513002;
14. Karim R, Khan AF, Yeasmin R, Akter J, Akter T. An evaluation of hepatoprotective activity of aqueous and ethanolic extracts of Bacopa monnieri (L.) against paracetamol-induced hepatotoxicity in swiss albino mice. European j. biomed. pharm. Sci. 2020;7:393-401. Available from: https://www.ejbps.com/ejbps/abstract_id/6554
15. Ali BH, Bashir AK, Rasheed RA. Effect of the traditional medicinal plants Rhazya stricta, Balanitis aegyptiaca and Haplophylum tuberculatum on paracetamol-induced hepatotoxicity in mice. Phytotherapy Research. 2001 Nov;15(7):598-603. Available from: DOI: 10.1002/ptr.818
16. Awan AF, Akhtar MS, Anjum I, Mushtaq MN, Fatima A, Khan MU, Haider SI. Hepatoprotective effect of Ziziphus oxyphylla Edgew in paracetamol-induced hepatotoxic rat model. Pakistan journal of pharmaceutical sciences. 2020 Sep 1;33(5):2449-54. Available from: http://142.54.178.187:9060/xmlui/handle/123456789/13063
17. Billaha MM, Hasan MA, Sarker UR, Banik R, Hossen MI, Hasan MN. The ethanolic extract of Trichosanthes dioica leaves can ameliorate the liver damage in paracetamol induced liver toxicity in SD rats. Journal of Pharmaceutical Research International. 2019 Jan 23;25(1):1-6. Available from: DOI: 10.9734/JPRI/2018/46204
18. Vellimalai K, Kumar GD, Jayaseelan K. Hepatoprotective and antioxidant activity of ethanolic leaves extract of Avicennia marina against alcohol-induced liver toxicity in rats. Journal of Drug Delivery and Therapeutics. 2019 Aug 30;9(4-A):403-8. Available from: DOI https://doi.org/10.22270/jddt.v9i4-A.3500
19. Pal LC, Agrawal S, Gautam A, Chauhan JK, Rao CV. Hepatoprotective and antioxidant potential of phenolics-enriched fraction of Anogeissus acuminata leaf against alcohol-induced hepatotoxicity in rats. Medical Sciences. 2022 Mar 4;10(1):17. Available from: DOI: 10.3390/medsci10010017
20. Boby N, Lee EB, Abbas MA, Park NH, Lee SP, Ali MS, Lee SJ, Park SC. Ethanol-induced hepatotoxicity and alcohol metabolism regulation by GABA-enriched fermented smilax China root extract in rats. Foods. 2021 Oct 8;10(10):2381. Available from: DOI: 10.3390/foods10102381
21. Elumalai A, Eswaraiah MC, Lahari KM, Shaik HA. In-vivo screening of Bougainvillea glabra leaves for its analgesic, antipyretic and anti-inflammatory activities. Asian Journal of Research in Pharmaceutical Science. 2012;2(3):85-7. Available from: https://ajpsonline.com/AbstractView.aspx?PID=2012-2-3-1
22. Shivani M, Prathibha S, Sri BK, Chintagunta AD, Sampath NS, Kumar SJ, Kumar NS, Dirisala VR. Extraction of natural dye from and its bougainvillea glabra applications in food industries. Indian J Ecol. 2020;47(11):207-11.
23. Edwin E, Sheeja E, Toppo E, Tiwari V, Dutt KR. Efecto antimicrobiano, antiulceroso y antidiarreico de las hojas de buganvilla (Bougainvillea glabra Choisy). 2007; 48(2): 135-44. Available from: http://hdl.handle.net/10481/27961
24. Abarca-Vargas R, Petricevich VL. Bougainvillea genus: A review on phytochemistry, pharmacology, and toxicology. Evidence-based complementary and alternative medicine. 2018 Jun 24;2018. Available from: DOI: 10.1155/2018/9070927
25. Sahu N, Saxena J. Bougainvillea glabra a natural antioxidant: A review. Chemistry. 2012 Mar;46(2):4113-7.
26. Manjunath L, Jogpal V. Antioxidant activity of Bougainvillea glabra stem extract on various In-vitro experimental models. European Chemical Bulletin, 2023; 11(11): 47. Available from: doi: 10.48047/ecb/2022.11.11.472022.03/10/2023
27. Singh H, Prakash A, Kalia AN, Majeed AB. Synergistic hepatoprotective potential of ethanolic extract of Solanum xanthocarpum and Juniperus communis against paracetamol and azithromycin induced liver injury in rats. Journal of Traditional and Complementary Medicine. 2016 Oct 1;6(4):370-6. Available from: doi: 10.1016/j.jtcme.2015.07.005
28. Zimmerman HJ. Enzymes in hepatic disease. Diagnostic enzymology. 1970: 24-26.

HOW TO CITE THIS ARTICLE: Manjunath L, Jogpal V. Role of *Bougainvillea glabra* Stem Extract on Paracetamol and Alcohol-Induced Hepatotoxicity in Rats. Int. J. Pharm. Sci. Drug Res. 2024;16(1):1-8. **DOI:** 10.25004/IJPSDR.2024.160101