RESEARCH PAPER

PROTECTIVE EFFECT OF PHYLLANTHUS AMARUS EXTRACT ON ACETAMINOPHEN-INDUCED HEPATOTOXICITY IN WISTAR RATS

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ABSTRACT

Background: Acetaminophen overdose is an established cause of drug-induced liver injury. Phyllanthus amarus is traditionally used for liver-related disorders and contains bioactive constituents, including phyllanthin and hypophyllanthin. This study evaluated a hydroalcoholic extract of the aerial parts of P. amarus in Wistar rats with acetaminophen-induced hepatotoxicity.

Methods: Leaves and stems were extracted by Soxhlet extraction using 70:30 ethanol–distilled water. Thirty Wistar rats were divided into five groups of six. Acetaminophen (2000 mg/kg) was administered during days 1–7; P. amarus (50 or 200 mg/kg) or Silymarin (35 mg/kg) was administered during days 8–14. Serum bilirubin, AST/SGOT, ALT/SGPT, ALP and total protein were assessed with liver histopathology.

Results: The toxic-control group showed higher bilirubin, AST/SGOT, ALT/SGPT and ALP values than the normal control. P. amarus treatment was associated with lower values, with the 200 mg/kg group showing a greater numerical response than the 50 mg/kg group. Histopathology showed comparatively better preservation of hepatic architecture at 200 mg/kg.

Conclusion: The hydroalcoholic P. amarus extract was associated with improvement in several biochemical and histopathological findings following acetaminophen exposure. The 200 mg/kg dose showed the more consistent response of the two tested extract doses.

Keywords: Phyllanthus amarus; acetaminophen; hepatotoxicity; hepatoprotection; hydroalcoholic extract; Silymarin; Wistar rats.

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INTRODUCTION

The liver performs major metabolic, synthetic, storage and detoxification functions and is therefore continuously exposed to drugs and other xenobiotics. Acetaminophen is widely used as an analgesic and antipyretic, but excessive exposure can cause hepatocellular injury. Increased formation of the reactive metabolite N-acetyl-p-benzoquinone imine, glutathione depletion, oxidative stress and mitochondrial injury contribute to this damage. [1–5]

Phyllanthus amarus Schum. & Thonn. has a long history of traditional use in liver-related disorders and has been investigated for antioxidant and hepatoprotective effects. Its phytochemical profile includes lignans such as phyllanthin and hypophyllanthin, together with flavonoids, tannins, terpenoids and other constituents. [6–10] Previous experimental studies have reported protective effects of P. amarus in chemically induced liver injury. [10–12] the present study therefore evaluated a hydroalcoholic extract of its aerial parts against acetaminophen-induced hepatotoxicity in Wistar rats, with Silymarin as the standard treatment.

MATERIALS AND METHODS

Plant material and extraction. Aerial parts comprising leaves and stems were powdered. Fifty grams were extracted in a Soxhlet apparatus with 500 mL of 70:30 ethanol–distilled water (350 mL ethanol and 150 mL distilled water). The extract was filtered through Whatman No. 1 paper, concentrated using a rotary vacuum evaporator and further dried on a water bath. The dried extract was stored in an amber-coloured airtight container at 4°C.

Phytochemical screening. The extract was qualitatively screened for alkaloids, flavonoids, tannins, saponins, glycosides, terpenoids, carbohydrates and proteins. Positive reactions were recorded for all groups except proteins.

Animals and experimental design. Thirty Wistar albino rats were divided into five groups (n=6). Group A received distilled water (0.9%) and served as normal control. Group B received

acetaminophen 2000 mg/kg during days 1–7. Groups C and D received P. amarus extract at 50 and 200 mg/kg, respectively, during days 8–14. Group E received Silymarin 35 mg/kg during days 8–14.

Ethics. The experiment was conducted after Institutional Animal Ethics Committee approval and according to prescribed ethical guidelines. IAEC approval/reference number: CAH/BIU/2026/015. At the end of the experimental period, the animals were subjected to terminal anesthesia and euthanasia using ether, following the laboratory's approved animal-handling procedure. All animal procedures were conducted with due consideration for animal welfare.

Assessment and statistics. Serum total bilirubin, AST/SGOT, ALT/SGPT, ALP and total protein were assessed at the end of the study, and liver tissue was examined histopathologically. Data were expressed as mean ± SEM (n=6). The thesis reports one-way ANOVA followed by Dunnett's multiple comparison test, with $P<0.05$ considered statistically significant.

RESULTS

Preliminary screening was positive for alkaloids, flavonoids, tannins, saponins, glycosides, terpenoids and carbohydrates and negative for proteins.

The biochemical findings are shown in Table 1. Acetaminophen produced the highest recorded AST/SGOT, ALT/SGPT and ALP values in the toxic-control group. P. amarus treatment was associated with lower values, with the 200 mg/kg group showing a greater numerical reduction than the 50 mg/kg group.

Parameter	Normal Control	Toxic Control	P. amarus 50 mg/kg	P. amarus 200 mg/kg	Silymarin 35 mg/kg
Total bilirubin (mg/dL)	0.45 ± 0.006	1.22 ± 0.011	1.20 ± 0.010	0.43 ± 0.006	0.46 ± 0.007
AST/SGOT (IU/L)	39.57 ± 0.386	66.50 ± 0.533	32.10 ± 0.310	21.65 ± 0.191	38.50 ± 0.372
ALT/SGPT (IU/L)	50.8 ± 0.476	137.20 ± 1.021	100.10 ± 0.885	47.50 ± 0.449	80.20 ± 0.610
ALP (IU/L)	211.33 ± 1.395	472.50 ± 2.499	301.20 ± 2.900	270.50 ± 1.934	265.50 ± 1.541
Total protein (g/dL)	6.95 ± 0.046	9.50 ± 0.063	8.30 ± 0.060	7.50 ± 0.056	6.57 ± 0.047

Table 1. Serum biochemical findings in the experimental groups. Values are mean ± SEM; n=6 animals/group. The final column gives the 200 mg/kg P. amarus value followed by the Silymarin value.

At 200 mg/kg, P. amarus produced total bilirubin of 0.43 ± 0.006 mg/dL, AST/SGOT of 21.65 ± 0.191 IU/L, ALT/SGPT of 47.50 ± 0.449 IU/L and ALP of 270.50 ± 1.934 IU/L. The corresponding Silymarin values were 0.46 ± 0.007 mg/dL, 38.50 ± 0.372 IU/L, 80.20 ± 0.610 IU/L and 265.50 ± 1.541 IU/L.

The overall biochemical pattern is illustrated in Figure 1.

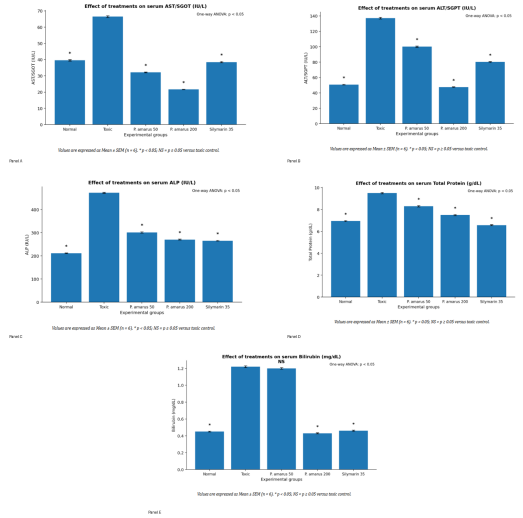


Figure 1. Serum biochemical findings across the experimental groups.

HISTOPATHOLOGY

The normal-control liver showed comparatively preserved architecture, whereas the toxic-control section showed marked architectural disturbance. The 50 mg/kg group showed partial improvement and the 200 mg/kg group showed comparatively better preservation. The Silymarin group also

showed relatively preserved hepatic architecture (Figure 2).

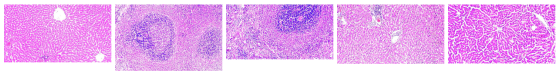


Figure 2. Representative histopathological sections of liver from the experimental groups.

DISCUSSION

The biochemical and histopathological findings together indicate that acetaminophen produced clear hepatic alterations in the toxic-control group. Bilirubin, AST/SGOT, ALT/SGPT and ALP were higher than in the normal control, while the liver sections showed corresponding structural disturbance. This agrees with the established use of acetaminophen as an experimental model of hepatic injury. [3–5]

P. amarus treatment was associated with lower bilirubin and enzyme values than the toxic control. The numerical response was more pronounced at 200 mg/kg than at 50 mg/kg across the main liver-associated parameters, and the histopathological observations followed the same general direction. Earlier studies have also reported hepatoprotective activity of P. amarus and have highlighted constituents such as Phyllanthus and hypophyllanthin. [7, 10–14]

The comparison with Silymarin varied by parameter. The 200 mg/kg group recorded lower AST/SGOT and ALT/SGPT values than Silymarin, whereas Silymarin showed a slightly lower ALP value; bilirubin values were close. Thus, the response was not uniform across all measures. The present experiment did not directly investigate molecular pathways or individual constituents, so such mechanisms remain literature-supported possibilities rather than findings demonstrated by this study.

CONCLUSION

The hydroalcoholic extract of the aerial parts of P. amarus was associated with improvement in several biochemical and histopathological findings following acetaminophen exposure. Among the tested extract doses, 200 mg/kg showed the more consistent numerical response. Further work using standardized extracts, quantitative phytochemical markers and detailed mechanistic and safety assessment would help define its hepatoprotective potential.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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