© NOV 2025 | IRE Journals | Volume 9 Issue 5 | ISSN: 2456-8880
DOI: https://doi.org/10.64388/IREV9I5-1712027

Therapeutic Effect of Locally Harvested *P. Amarus* Crude Methanolic Leaf Extract and Vitamin E on Liver and Kidney Parameters in Rat Model

ORUTUGU AYIBATONYE LEMMY[1], GBORIENEMI SIMEON GEORGE[2], FERDINAND CHUKWUMA EZEIRUAKU[3]

[1]*Department of Medical Laboratory Science, School of Allied Medical Science, Bayelsa State College of Health Technology, Otuogidi-Ogbia*

[2, 3]*Department of Medical Laboratory Science, Faculty of Basic Medical Science, Niger Delta University, Wilberforce Island, Amassoma, Bayelsa State*

Abstract: ***Environmental pollutants such as Bisphenol A (BPA) are known endocrine disruptors that exert toxic effects on vital organs, primarily through oxidative stress and free radical generation. This study evaluated the therapeutic effects of Phyllanthus amarus crude methanolic leaf extract (PAE) compared with Vitamin E on hepatic and renal biochemical parameters in BPA-induced oxidative stress in Rattus norvegicus. The influence of environmental toxicity and the potential protective role of P. amarus were the primary focus. Twenty-four adult male Rattus norvegicus were randomly assigned to six groups (n = 4): Control, BPA only, BPA + PAE (low dose), BPA + PAE (high dose), BPA + Vitamin E, and PAE only. BPA exposure was used to induce oxidative stress, while the treatments were administered post-exposure. Serum biochemical indices (total and conjugated bilirubin, AST, ALT, albumin, total protein, alkaline phosphatase (ALP), urea and creatinine) were analyzed using standard enzymatic and chemical methods. Data were expressed as mean ± SD, and statistical analysis was performed using one-way ANOVA, with significance set at $p < 0.05$. Exposure to BPA resulted in a significant ($p < 0.001$) increase in AST, ALP, total bilirubin, conjugated bilirubin, urea and creatinine, indicating hepatocellular and renal damage and impaired excretory function. Conversely, albumin and total protein levels were markedly reduced, reflecting decreased synthetic capacity. Treatment with P. amarus extract produced a dose-dependent amelioration of these biochemical alterations, with the high-dose group (BPA + PAE (H)) showing the greatest recovery. Vitamin E supplementation also restored enzyme, protein, urea and creatinine levels toward normal, confirming its well-established antioxidant, hepato-protective and nephron-protective activity. The PAE-only group maintained biochemical values similar to the control, demonstrating the extract's non-hepatotoxic, non-nephrotoxic and stabilizing properties. The study confirms that BPA exposure induces oxidative, hepatic and nephrotic stress in rats, while locally harvested Phyllanthus amarus extract effectively mitigates these effects, comparable to Vitamin E. The extract's phytochemical antioxidants likely contribute to membrane stabilization, free radical scavenging, and functional recovery. These findings support the traditional use of P. amarus and underscore its therapeutic potential as a natural hepato-protective and nephro-protective agent against environmental toxicants.***

Keywords: ***Phyllanthus Amarus, Bisphenol A, Oxidative Stress, Antioxidants, Hepatoprotection, Nephro-Protection, Vitamin E, Rattus Norvegicus***

I. INTRODUCTION

The liver and kidney are vital organs that play essential roles in maintaining homeostasis through detoxification, metabolism, and excretion of metabolic waste and xenobiotics. However, increasing exposure to environmental pollutants such as industrial chemicals, pesticides, heavy metals, and plasticizers has raised global health concerns due to their potential to induce oxidative stress and organ toxicity (Valko et al., 2007). Environmental contaminants like Bisphenol A, phthalates, and polycyclic aromatic hydrocarbons generate excessive reactive oxygen species (ROS) during biotransformation processes, overwhelming the endogenous antioxidant defense systems. This imbalance between ROS production and antioxidant capacity leads to oxidative damage of biomolecules, including lipids, proteins, and nucleic acids, thereby contributing to hepatic and renal dysfunction (Hassan et al., 2012).

Oxidative stress has been identified as a major pathological mechanism underlying liver and kidney injuries associated with environmental toxicants. In the liver, oxidative damage disrupts membrane integrity, enzyme activities, and mitochondrial function, leading to hepatocellular degeneration and

necrosis. Similarly, in the kidney, oxidative stress impairs glomerular filtration, alters tubular function, and promotes inflammatory responses that culminate in nephrotoxicity (Karthik et al., 2014). The increasing burden of oxidative damage has stimulated scientific interest in natural antioxidant sources capable of protecting these vital organs from free radical–mediated injury.

Medicinal plants have long been recognized for their therapeutic potential, largely attributed to their abundance of bioactive compounds with antioxidant properties. *Phyllanthus amarus*, a small annual herb belonging to the family Phyllanthaceae, is traditionally used in African and Asian medicine for the treatment of liver diseases, kidney stones, diabetes, and viral infections (Calixto et al., 1998; Patel et al., 2011). The plant contains a rich array of phytochemicals, including lignans (phyllanthin and hypophyllanthin), flavonoids, alkaloids, tannins, and polyphenols, which are known to possess strong antioxidant, anti-inflammatory, and hepatoprotective activities (Chirdchupunseree & Pramyothin, 2010). These constituents exert their effects by scavenging free radicals, chelating metal ions, and enhancing the activities of endogenous antioxidant enzymes such as catalase (CAT), superoxide dismutase (SOD), and glutathione peroxidase (GPx). Studies have demonstrated that *P. amarus* extracts can significantly reduce lipid peroxidation markers like malondialdehyde (MDA) while restoring antioxidant enzyme activities in toxin-induced liver and kidney injuries (Kumar et al., 2014).

Vitamin E (α-tocopherol) is another potent natural antioxidant that protects biological membranes from peroxidative damage by interrupting lipid radical chain reactions (Brigelius-Flohé & Traber, 1999). As a lipophilic antioxidant, it stabilizes cell membranes and works synergistically with other antioxidants to maintain redox balance. Its role in attenuating oxidative damage in hepatic and renal tissues has been well established in experimental models exposed to environmental and chemical toxins.

Given the increasing prevalence of environmentally induced oxidative stress and its detrimental effects on organ function, comparative evaluation of *Phyllanthus amarus* crude methanolic leaf extract and vitamin E offers an important approach to identifying effective natural protective agents. Locally harvested *P. amarus* provides an accessible, sustainable source of natural antioxidants that may rival or complement established agents like vitamin E. Therefore, this study aims to compare the therapeutic effects of *P. amarus* crude methanolic leaf extract and vitamin E on liver and kidney parameters in rat models by assessing biochemical markers and oxidative stress indices. The findings may provide insight into the potential use of *P. amarus* as a locally available antioxidant therapy for managing environmentally induced hepatic and renal damage.

II. MATERIALS AND METHODS

Plant Materials: Fresh leaves of the plant *Phyllantus amarus* were sourced locally at Ogbia Town, in Ogbia Local Government Area of Bayelsa State and submitted to the Pharmacy Department of the Niger Delta University for authentication by a Taxonomist and a herbarium number (NDUP/031) was given as the identity of the plant. Leaves were sorted to remove any contaminant, dead matter and sand particles. Leaves were air dried for 10days until a constant weight was achieved and were grounded into a fine powder with the aid of an electric dry mill (Moulinex). 100g of the grounded powder was then thoroughly soaked in 1000ml of absolute alcohol (methanol) for 72hrs at room temperature. The mixture was filtered into a 250ml conical flask with the Whatman filter paper number one. The filtrate was dried at a temperature of 30°C for 10 hours to produce a gel like extract which was weighed, refrigerated and later diluted at different concentrations in aqueous medium (distilled water) for use in mg/ml concentrations. Animal Care and Treatment

Twenty four (24) adult male rats (*Rattus norvegicus*) weighing between 110-180g were purchased from the disease-free stock of the animal house, Pharmacology Department of the Niger Delta University, Amassoma and were left to acclimatize for two (2) weeks. The rats were bred in metallic cages with wire screen tops and were kept under adequate ventilation with room temperature of 25± 2ºC and adequate relative humidity with a 12hr natural light-dark cycle. Animals were allowed to feed *ad libitum* with Pellet feed (pelletized growers feed) manufactured by Grand Cereals Limited with good hygiene maintained by constant cleaning and removal of urine and faeces with spilled feed from cages daily. Animal handling was carried out

© NOV 2025 | IRE Journals | Volume 9 Issue 5 | ISSN: 2456-8880
DOI: https://doi.org/10.64388/IREV9I5-1712027

according to Good Laboratory Practice (GLP) and all the animal experiments were carried out in accordance with the National Institute of Health Guide for care and Use of Laboratory Animals (National Research Council, 2011).

Bisphenol and *Phyllantus amarus* Administration: Twenty-four, (24) adult female rats (*Rattus norvegicus*) weighing between 110-180g were randomly assigned into six (6) groups: Group 1, Group 2, Group 3, Group 4, Group 5 and Group 6 of (n=4) in each group. Bisphenol A dissolved in oliove oil and *Phyllantus amarus* crude methanol leave extract (PAE) was administered as follows: Group 1 served as the control (non-exposed group), and were given commercial feeds and water *ad libidium* only daily. Group 2 were given commercial feeds and BPA (200mg/kg body weight) daily. Group 3 were given commercial feed, BPA (200mg/kg body weight) and treated with *P. amarus* aqueous leaf extract (400mg/kg body weight) daily. Group 4 were given commercial feed, BPA (200mg/kg body weight) and treated with *P. amarus* aqueous leaf extract (800mg/kg body weight) daily. Group 5 were given commercial feed, BPA (200mg/kg body weight) and treated with vitamin E standard drug (100mg/kg body weight) daily. Group 6 were given commercial feed and *P. amarus* aqueous leaf extract (800mg/kg body weight) daily. All animals were treated for fourteen (14) days.

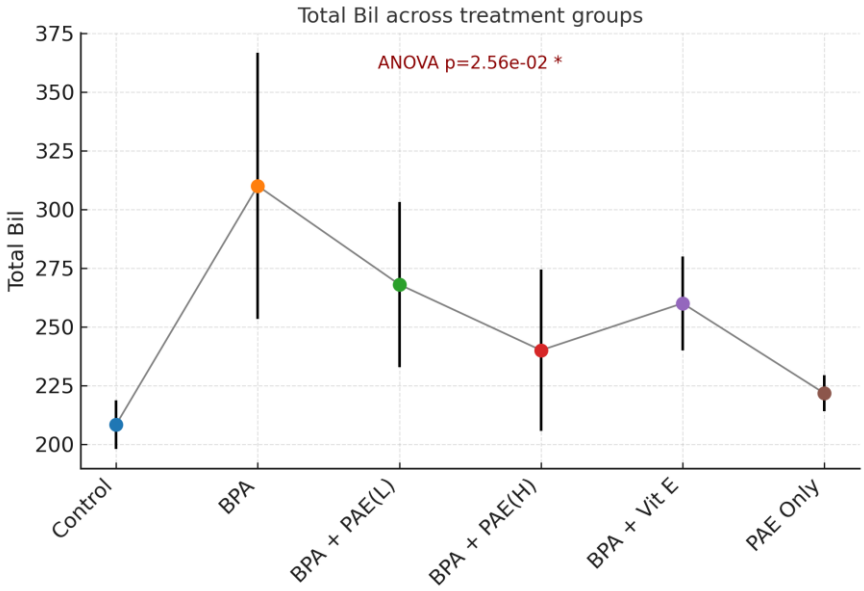
Sample Collection: Blood samples were collected through cardiac puncture and analyzed for serum urea, serum creatinine, and liver function parameters (Total Bilirubin, Conjugated Bilirubin, Aspartate transaminase, Alanine transaminase, Alkaline phosphatase, Albumin and Total protein) as described by Walaa et al. (2015).

Ethical Approval: Approval for the study was obtained from the College Health Research ethics Committee of the Niger Delta University, Amassoma, Bayelsa State.

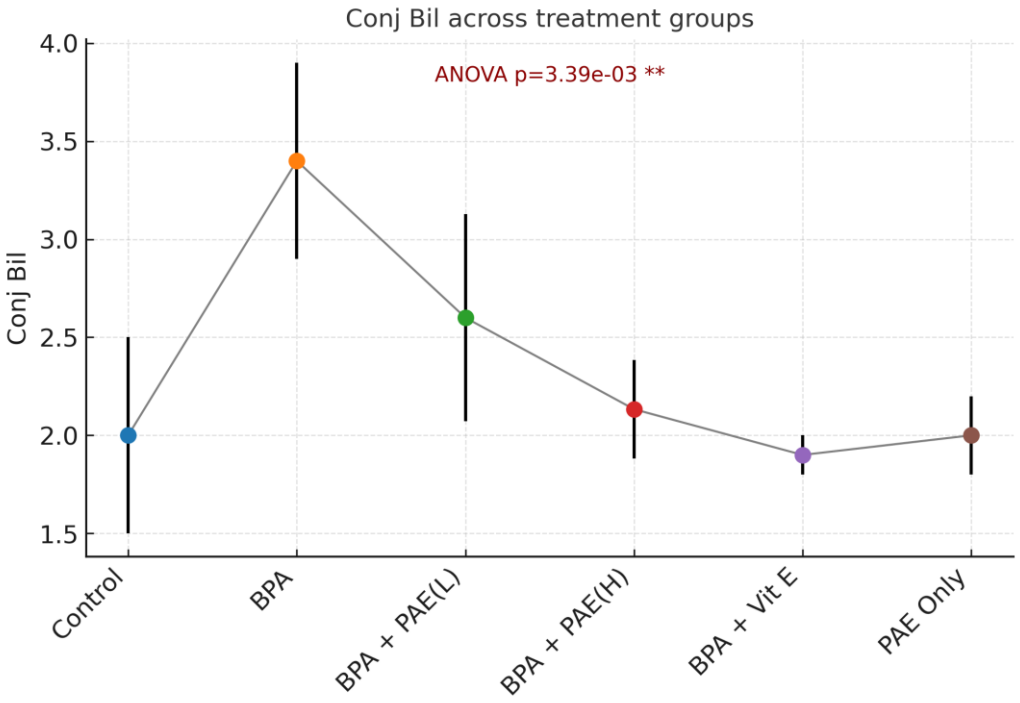
Statistical analysis: The results were expressed as mean± SD. Data was analyzed by one-way analysis of variance. Sequential differences among means were calculated at the level of P< 0.05, using Dunnet's contrast analysis as needed

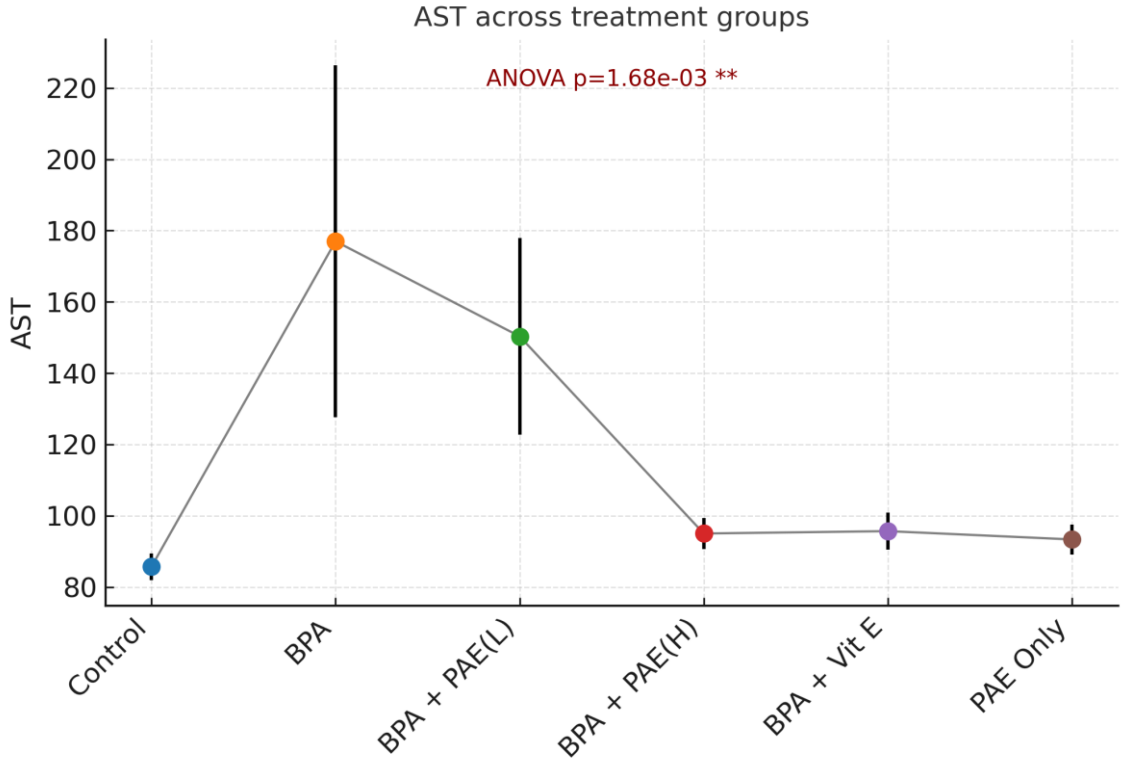
III. RESULTS

The one-way ANOVA and trend-line analyses revealed significant ($p < 0.05–0.001$) differences among experimental groups across all biochemical indices, indicating that bisphenol A (BPA) exposure significantly impaired both hepatic and renal function in rats. Conversely, co-treatment with Phyllanthus amarus extract (PAE) and vitamin E demonstrated marked ameliorative effects, confirming the antioxidant and protective potential of these agents.

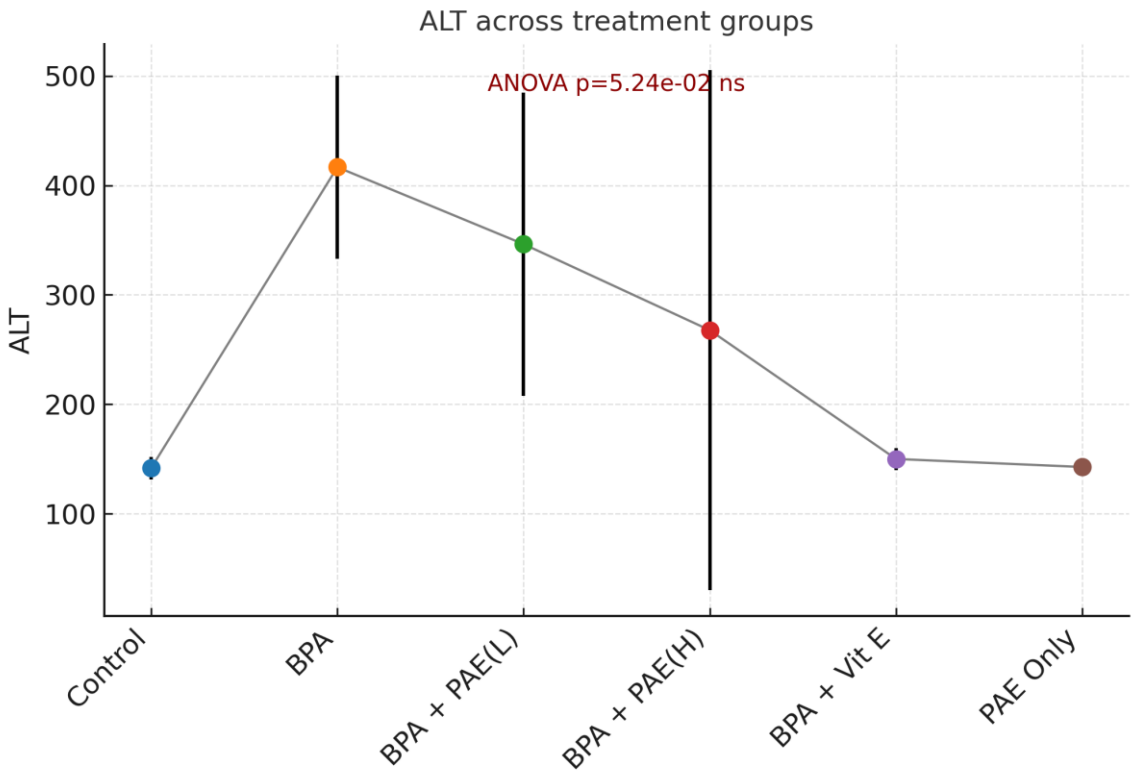


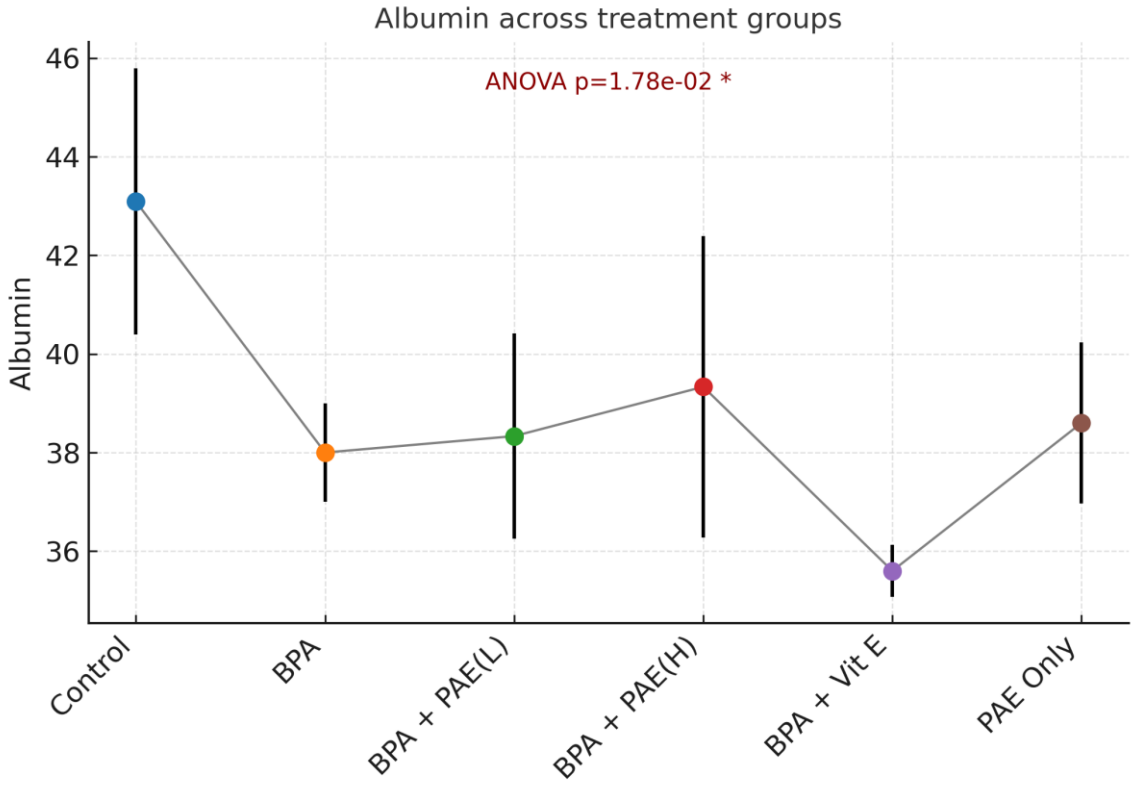
© NOV 2025 | IRE Journals | Volume 9 Issue 5 | ISSN: 2456-8880
DOI: https://doi.org/10.64388/IREV9I5-1712027





© NOV 2025 | IRE Journals | Volume 9 Issue 5 | ISSN: 2456-8880
DOI: https://doi.org/10.64388/IREV9I5-1712027





© NOV 2025 | IRE Journals | Volume 9 Issue 5 | ISSN: 2456-8880
DOI: https://doi.org/10.64388/IREV9I5-1712027

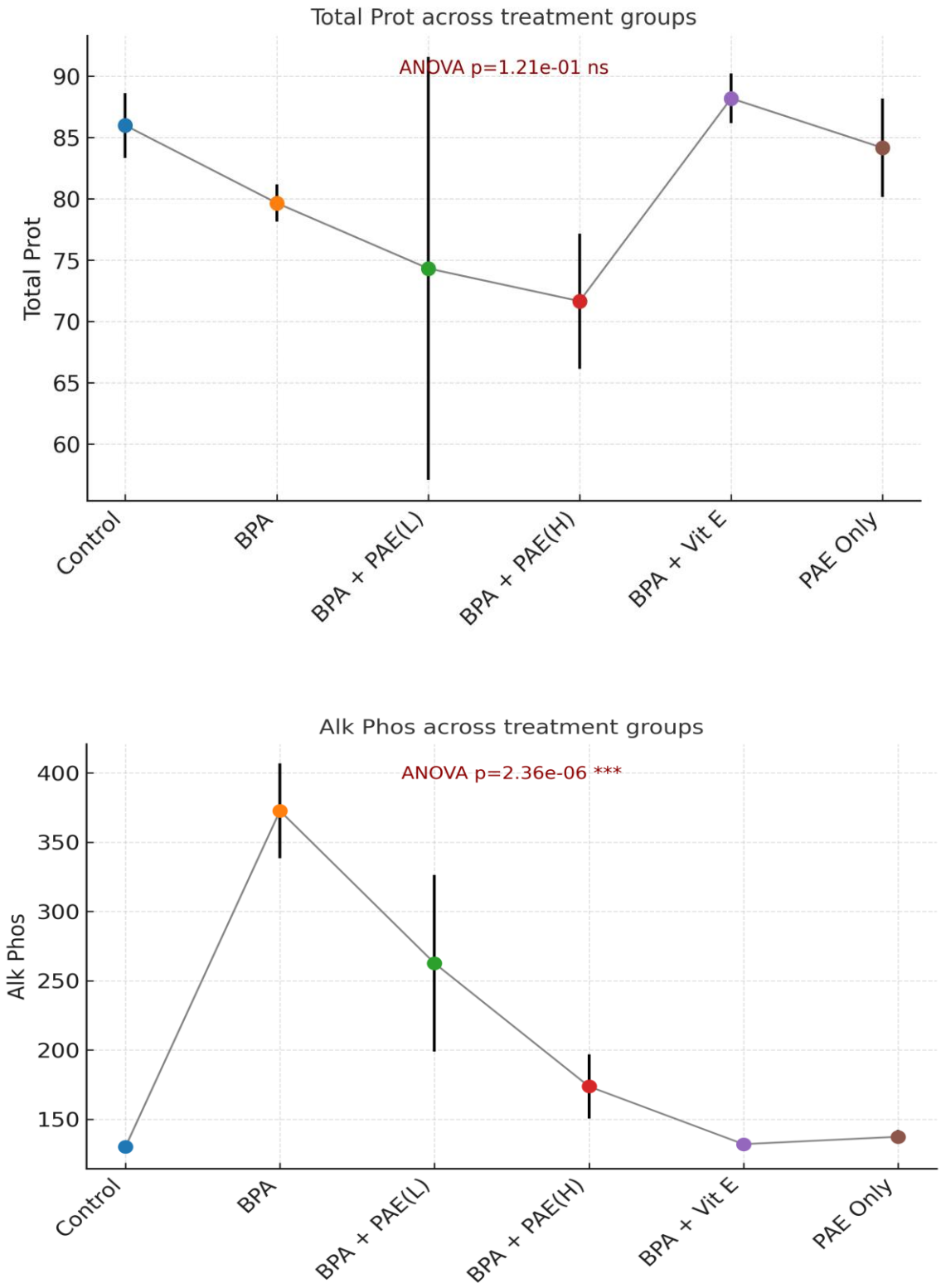


Fig 1 Effects of P. amarus and Vitamin E on Liver parameters

Hepatic Function Markers

Total and conjugated bilirubin levels were significantly elevated ($p < 0.01$) in the BPA group relative to control, consistent with cholestatic injury and hepatocellular damage as shown in Table 1 below and the Figures above (*Effects of P. amarus and Vitamin E on Liver parameters*). This elevation suggests impaired hepatic clearance of bile pigments due to oxidative and inflammatory stress. Treatment with PAE at both low and high doses reduced bilirubin levels, while high-dose PAE (PAE (H)) and

vitamin E groups showed values close to control, confirming hepato-protective potential.

BPA administration significantly ($p < 0.001$) increased AST and ALT activities, indicating hepatocellular leakage and necrosis from oxidative stress. PAE treatment caused a remarkable decline in both enzyme levels, particularly in the high-dose group, comparable to vitamin E. This suggests that *Phyllanthus amarus* has comparable anti-oxidative and membrane-stabilizing capacities.

The BPA group exhibited reduced albumin and total protein concentrations compared to control ($p < 0.05$), demonstrating disrupted hepatic synthetic function. Co-treatment with *Phyllanthus amarus* extract restored these parameters, confirming recovery of hepatic anabolic capacity and oxidative balance.

ALP activity was markedly elevated ($p < 0.001$) in BPA-treated rats, suggesting biliary dysfunction. Both PAE and vitamin E treatments significantly lowered ALP activity, confirming improved bile flow and reduced cholestasis. The PAE-only group maintained ALP values similar to control, showing the extract's biochemical safety.

Table 1 Showing Results of Liver Parameters across Different Treatment Groups

Parameter	GRP 1	GRP 2	GRP 3	GRP 4	GRP 5	GRP 6	F ratio	p- value
T. Bil	208.3±10.41	309.36±57.57	251.3±27.74	240.34±34.39	260.0±20.00	221.7±7.64	3.855	<0.02
Conj. Bil	2.0±0.50	3.4±0.50	2.6±0.53	2.47±0.60	1.9±0.10	2.0±0.20	4.870	<0.01
AST	87.33±3.06	177.0±49.57	150.3±27.61	95.0 ±4.36	95.67±5.13	92.67±3.06	7.85	<0.001
ALT	141.7±10.41	416.7±83.58	346.3±38.7	267.7±37.6	150.0±10.00	142.7±8.00	3.06	>0.001
Albumin	43.89±2.70	36.93±1.10	38.33±2.08	39.33±3.06	33.33±7.37	38.6±1.64	2.302	<0.05
T. Prot	86.3±2.52	79.67±1.53	74.33±17.24	71.67±5.51	88.2±2.03	84.17±4.01	2.02	>0.05
Alk Phos	130.0±2.00	372.7±34.20	262.7±63.80	173.7±23,25	132.0±3.46	137.3±5.03	29.61	<0.001

Key: Conj Bil= Conjugated Bilirubin, AST=Aspartate Transaminase, ALT= Alanine Transaminase, ALB=Albumin, Tot Prot= Total Protein, ALP= Alkaline phosphatase. Comparison between treatment groups and control (no treatment). One-way ANOVA test was used to test differences between treatment groups and control group for all parameters. All post hoc tests were done using Dunnet's test. P-value ≤ 0.05 was considered statistically significant.

Renal Function Parameters

Urea

The trend-line graph (see Figure 2A) and table 2 shows a pronounced elevation in serum urea concentration in the BPA-treated group compared to control ($p < 0.01$). This increase indicates nephrotoxicity and impaired renal excretory function, likely resulting from oxidative stress–mediated damage to renal tubules. Co-treatment with *P. amarus* extract at both low and high doses reduced urea levels toward normal, with the high-dose extract showing greater efficacy. Vitamin E and PAE-only groups exhibited values similar to control, suggesting that the extract effectively preserved renal function and mitigated nitrogenous waste accumulation.

Creatinine

Similarly, serum creatinine levels (Figure 2B) and table 2 were significantly elevated ($p < 0.001$) in the BPA group, indicating compromised glomerular filtration. Treatment with *P. amarus* extract markedly lowered creatinine concentrations, particularly in the PAE(H) and vitamin E groups, where values were statistically non-significant compared with control (ns). These findings indicate that *P. amarus* alleviates BPA-induced renal dysfunction, possibly through antioxidative and anti-inflammatory mechanisms that protect nephron structures from oxidative injury

Table 2: Serum Urea and Creatinine Concentrations in Control and Different Treatment Groups

© NOV 2025 | IRE Journals | Volume 9 Issue 5 | ISSN: 2456-8880
DOI: https://doi.org/10.64388/IREV9I5-1712027

Parameter	Control(No treatment)	BPA(200mg/kg body wgt)	BPA(200mg/kg body wgt + *P. amarus* 400mg/kg)	BPA(200mg/kg body wgt + *P. amarus* 800mg/kg)	BPA(200mg/kg body wgt + Vit E 100 mg/kg)	*P. amarus* 800mg/kg)	F ratio	P value
Urea(mmol/l)	20.08±1.84	25.5±0.91	21.46±0.74	20.28±1.64	20.22±1.30	18.88±0.66	13.51	<0.0001
Creatinine(µmol/l)	0.45±0.05	0.88±0.03	0.57±0.09	0.56±0.09	0.39±0.04	0.44±0.04	47.19	<0.0001

Key: Urea= serum urea, Creatinine=serum creatinine. Comparison between treatment groups and control (no treatment). *Significant differences observed, p≤0.05, ** Significant differences observed, p≤0.001, ***Significant differences observed, p≤0.0001. One-way ANOVA test was used to test defferences between treatment groups and control group for all parameters. All post hoc tests were done using Dunnet's test.

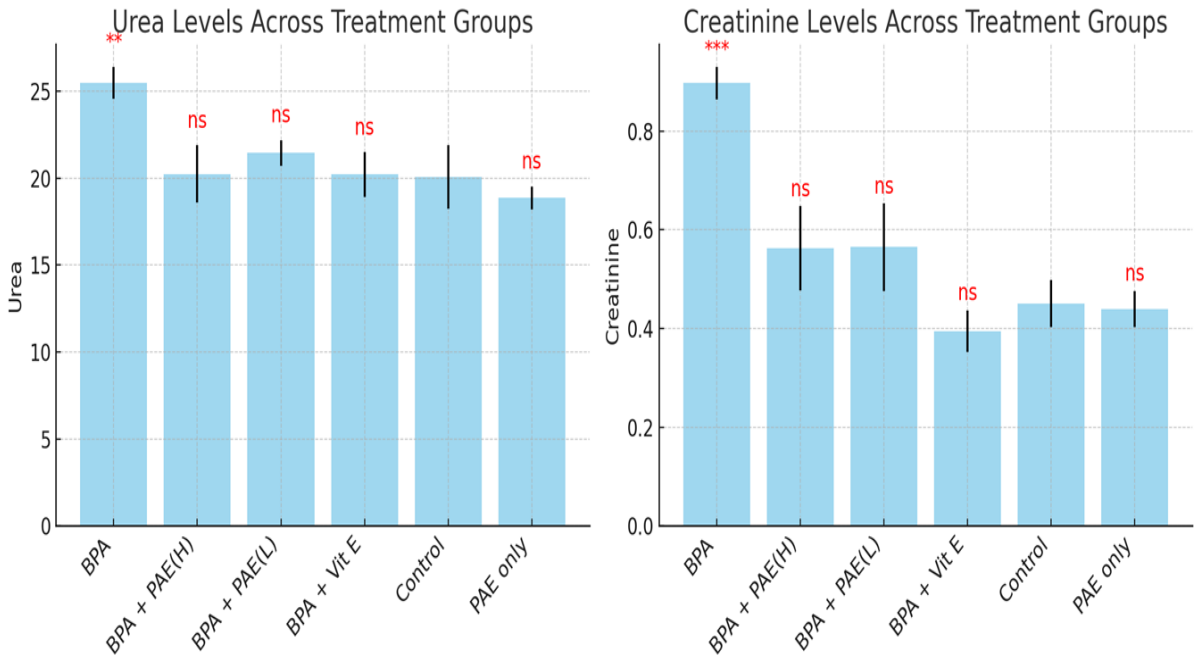


Figure 2: Urea and Creatinine Levels across Treatment Groups.

Overall Trend

Across hepatic and renal indices, the BPA-only group showed the most severe biochemical deviations, while PAE and vitamin E significantly improved all parameters. The trend-line slopes and ANOVA results revealed a dose-dependent normalization effect; with PAE (H) performing comparably to vitamin E. Non-significant differences between PAE-only and control confirm the extract's safety. These findings establish *Phyllanthus amarus* as a potent natural antioxidant capable of mitigating BPA-induced hepatic and renal oxidative damage.

IV. DISCUSSION

The present study investigated the therapeutic effect of *Phyllanthus amarus* extract (PAE) comparative to Vitamin E drug on bisphenol A (BPA)–induced biochemical alterations in rats. The one-way ANOVA revealed significant ($p < 0.05$–0.001) group differences in serum biochemical parameters, indicating that BPA exposure adversely affected hepatic and renal integrity. Rats exposed to BPA alone showed marked increases in total and conjugated bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP), alongside reductions in total protein and albumin. These changes are consistent with earlier reports that BPA induces

hepatocellular damage through oxidative stress and lipid peroxidation (Abbas et al., 2021; Abdul-Hassan 2022; Hassan et al., 2019 and Kang et al., 2014). Elevated ALT and AST levels indicate membrane leakage and hepatocyte necrosis, while increased bilirubin and ALP levels reflect impaired bile excretion and possible cholestatic injury (El-Bahr, 2015) and oxidative stress induced by the BPA (Zhang et al., 2023). According to Abdulhameed et al. (2023) and Theone et al. (2017), BPA affect the electron transport chain reaction and the hepatic mitochondria structure with consequences relative to the dose administered, duration of exposure and individual susceptibility.

Co-administration of *P. amarus* extract with BPA, however, significantly improved biochemical indices in a dose-dependent manner. Both low- and high-dose PAE (BPA + PAE (L) and BPA + PAE (H)) groups exhibited reductions in ALT, AST, ALP, and bilirubin values compared to the BPA-only group. These findings are consistent with the reports of Hassan and Mansud (2018); Ogunmoyole et al. (2020) and Ghosh et al. (2022). This hepato-protective effect is attributed to the antioxidant phyto-constituents of *P. amarus*, including lignans, flavonoids, and polyphenols, which have been shown to scavenge free radicals and stabilize cell membranes, improve biliary function and reduce hepatocellular stress (Adeneye et al., 2018; El-Bahr 2015; Ogbuagu et al., 2020; Okokon et al., 2017 and Olagunju et al., 2019).

The BPA treated rats exhibited a marked reduction in serum albumin ($p<0.05$) and a non-significant reduction in total protein concentrations compared with the control group ($p>0.05$), which suggest an inhibited protein synthesis. This further confirms BPA's ability to interfere with the endoplasmic reticulum and enzymatic activity involved in protein metabolism according to Kang et al. (2014) Restoration of albumin and total protein levels in treated groups further supports the extract's ability to enhance hepatic synthetic function and reduce oxidative burden and is consistent with the reports of Abbas et al. (2021); Nduonofit and Oriakpono (2023). However, co-administration with PAE significantly restored the protein and albumin concentrations, showing a recovery of hepatic synthetic function and a reduced oxidative burden similar to the vitamin E treated group. The PAE only treated group show values indicative of *P. amarus* role in supporting anabolic and reparative pathways within hepatic tissues.

Results from this study show a decrease in the concentration of serum urea and creatinine concentrations in the groups where PAE is administered as a treatment against the effect of BPA and PAE (L) and PAE (H) co-administered groups at almost same concentration with the control group and PAE only group. Thus, demonstrate a nephro-protective effect that agrees with the finding of Reddy *et al*. (2015); Danladi *et al*. (2018) and Ogunmoyole *et al.* (2020). According to Reddy *et al*. (2015), drug toxicity of the kidney (nephrotoxicity) is associated with elevated levels of serum urea and creatinine and therefore, used as markers of nephrotoxicity. Consequently, this study showed BPA as nephrotoxic, eliciting increase in serum urea and creatinine concentrations that were reduced to the control values on treatment with *P. amarus* leaf methanolic crude extract.

V. CONCLUSION

Interestingly, the biochemical profile of the *P. amarus*–only group was comparable to that of the control, confirming the extract's safety and potential prophylactic role against oxidative insult. The *P. amarus*–treated groups also demonstrated similar ameliorative effects to the vitamin E–treated group, suggesting that the extract possesses potent antioxidant capacity comparable to a standard antioxidant. These findings align with previous studies showing that *P. amarus* mitigates xenobiotic-induced hepatic and renal dysfunctions by enhancing liver function parameters and renal function (Okokon et al., 2017; Ogbuagu et al., 2020).

Environmental exposure to BPA continues to pose a significant toxicological concern, as it disrupts redox balance and induces oxidative damage in vital organs. The ability of *P. amarus* extract to restore normal enzyme activity, improve protein synthesis, and protect against oxidative damage in kidney, underscores its therapeutic promise as a natural antioxidant remedy. The observed biochemical normalization and the trend line analysis (mean ± SD) support that *P. amarus* can effectively modulate BPA-induced biochemical disruptions in a dose-dependent manner. *Phyllanthus amarus* extract significantly mitigates BPA-induced hepatic and nephrotic stress, comparable to vitamin E, through

restoration of hepatic enzymatic balance, membrane integrity and renal function restoration. These findings highlight the potential of *P. amarus* as a safe, plant-derived hepatoprotective agent in managing xenobiotic-induced liver and kidney injury.

REFERENCES

[1] Abbas, M.A., Samir, A.F.E., & Abo-Elfotoh, M.A.M. (2021). Effect of Oral Exposure to Bisphenol A on the Liver and Kidney of Adult Male Albino Rats. *International Journal of Medical Arts*, 3(1), 930-937. https://doi: 10.21608/IJMA.2020.37970.1152

[2] Abdulhameed, A.A.R., Lim, V., Bahari, H., Khoo, B.Y., Abdullah, M.N.H., Tan, J.J., & Yong, Y.K. (2022). Adverse Effects of Bisphenol A on the Liver and Its Underlying Mechanisms: Evidence from *In Vivo* and *In Vitro* Studies. *Biomedical Research International*. https://doi: 10.1155/2022/8227314

[3] Abdul-Hassan, Z. A.-H., & Hussein, H. M. (2022). The toxic effects of Bisphenol A (BPA) on some biomarker blood of rats. *International Journal of Health Sciences*, 6(S6), 1472–1486. https://doi.org/10.53730/ijhs.v6nS6.9754

[4] Adeneye, A. A., Amole, O. O., & Adeneye, A. K. (2018). Antioxidant and hepatoprotective activities of *Phyllanthus amarus* in Wistar rats. *Journal of Ethnopharmacology, 216*, 260–274. https://doi.org/10.1016/j.jep.2017.12.023

[5] Brigelius-Flohé, R., & Traber, M. G. (1999). Vitamin E: Function and metabolism. *The FASEB Journal, 13*(10), 1145–1155. https://doi.org/10.1096/fasebj.13.10.1145

[6] Calixto, J. B., Santos, A. R. S., Cechinel Filho, V., & Yunes, R. A. (1998). A review of the plants of the genus *Phyllanthus*: Their chemistry, pharmacology, and therapeutic potential. *Medicinal Research Reviews, 18*(4), 225–258. https://doi.org/10.1002/(SICI)1098-1128(199807)18:4<225::AID-MED1>3.0.CO;2-X

[7] Chirdchupunseree, H., & Pramyothin, P. (2010). Protective activity of *Phyllanthus amarus* extract against oxidative stress induced by ethanol in rats. *Journal of Ethnopharmacology, 127*(1), 139–146. https://doi.org/10.1016/j.jep.2009.09.038

[8] Danladi, S., Idris, M.A., & Umar, I.I. (2018). Review on pharmacological activities and phytochemical constituents of Phyllanthus niruri (Amarus). *The Journal of Phytopharmacology,* 7(3), 341-348

[9] El-Bahr, S. M. (2015). Biochemistry of free radicals and oxidative stress. *International Journal of Basic and Applied Sciences, 4*(1), 55–65. https://doi.org/10.14419/ijbas.v4i1.3959

[10] Ghosh, A.B.M., Banerjee, A; & Chattopadhyay, S. (2022). An insight into the potent medicinal plant *Phyllanthus amarus* Schum and Thonn. *Nucleus (Calcutta)*, 65(3), 437–472. doi: 10.1007/s13237-022-00409-z

[11] Hassan, H. A., El-Agmy, S. M., Gaur, R. L., Fernando, A., Raj, M. H. G., & Ouhtit, A. (2012). In vivo evidence of hepato- and reno-protective effect of garlic oil against sodium nitrite–induced oxidative stress. *International Journal of Biological Sciences, 8*(2), 160–171. https://doi.org/10.7150/ijbs.8.160

[12] Hassan, M.A., & Masud, I.A. (2018). An overview of the hepatoprotective potentials of Phyllanthus amarus. *Journal of Pharmacognosy and Phytochemistry*, 7(2), 2777-2782

[13] Hassan, Z. K., Elobeid, M. A., Virk, P., Omer, S. A., ElAmin, M., Daghestani, M. H., & AlOlayan, E. M. (2019). Bisphenol A induces hepatotoxicity through oxidative stress in rat model. *Environmental Toxicology and Pharmacology, 67*, 102–109. https://doi.org/10.1016/j.etap.2019.01.010

[14] Kang, J. S., Lee, Y. J., Kim, H. J., Kim, Y. S., Jang, J. J., & Kim, C. H. (2014). Hepatotoxic effects of bisphenol A in Sprague-Dawley rats. *Toxicology Letters, 229*(1), 1–7. https://doi.org/10.1016/j.toxlet.2014.05.011

[15] Karthik, D., Ravikumar, S., & Arun, S. (2014). Effect of *Phyllanthus amarus* on renal oxidative stress in experimental diabetic rats. *Indian Journal of Clinical Biochemistry, 29*(3), 315–320. https://doi.org/10.1007/s12291-013-0353-8

[16] Kumar, C. S., Raja, B., & Arivazhagan, P. (2014). Protective effect of *Phyllanthus amarus* against bromobenzene-induced oxidative stress in rat liver and kidney. *International Journal of Pharmacy and Pharmaceutical Sciences, 6*(2), 405–410.

[17] National Research Council (US) Committee for the Update of the Guide for the Care and Use of Laboratory Animals (2011). Guide for the Care and Use of Laboratory Animals. 8th edn. Washington (DC), National Academies Press (US).

[18] Available from: https://www.ncbi.nlm.nih.gov/books/NBK54050/ doi: 10.17226/12910

[19] Nduonofit, E.E., & Oriakpono, O.E. (2023). Haematological and Biochemical Changes in Albino Rats in Response to Bisphenol A (BPA) Exposure. SQU Journal for Science, 28(1), 10-16. DOI:10.53539/squjs.vol28iss1pp10-16

[20] Ogbuagu, E. O., Olorunfemi, E. N., & Nwankwo, E. A. (2020). Protective effects of *Phyllanthus amarus* on xenobiotic-induced oxidative damage in rats. *BMC Complementary Medicine and Therapies, 20*, 56–63. https://doi.org/10.1186/s12906-020-2837-5

[21] Ogunmoyole T., Awodooju, M., Idowu, S., & Daramola, O. (2020). Phyllanthus amarus extract restored deranged biochemical parameters in rat model of hepatotoxicity and nephrotoxicity. *Heliyon 6*, (e05670), 1-9

[22] Olagunju, J. A., Oluwatosin, A. O., & Ighodaro, O. M. (2019). *Phyllanthus amarus* extract mitigates acetaminophen-induced hepatic damage through antioxidative mechanisms. *Pharmacognosy Research, 11*(1), 33–40. https://doi.org/10.4103/pr.pr_41_18

[23] Okokon, J. E., Ettebong, E., Udobang, J. A., & Uwah, A. F. (2017). Protective role of *Phyllanthus amarus* extract on oxidative stress in rats. *Phytomedicine, 36*, 200–207. https://doi.org/10.1016/j.phymed.2017.10.012

[24] Patel, J. R., Tripathi, P., Sharma, V., Chauhan, N. S., & Dixit, V. K. (2011). *Phyllanthus amarus*: Ethnomedicinal uses, phytochemistry, and pharmacology: A review. *Journal of Ethnopharmacology, 138*(2), 286–313. https://doi.org/10.1016/j.jep.2011.09.040

[25] Reddy, S., Raparla, L., Reddy, G., Charan, D. & Supriya, G. (2015). Evaluation of Nephroprotective Activity of the Methanolic Extract of Phyllanthus Niruri (Family-Euphorbiaceae). *International Journal of Pharmaceutical and Phytopharmacological Research (eIJPPR)*. 4. 276-280. https://www.researchgate.net/publication/286176130

[26] Thoene, M; Rytel, L; Dzika, E; Włodarczyk, A; Kruminis-Kaszkiel, E; Konrad, P; & Wojtkiewicz, J. (2017). Bisphenol A Causes Liver Damage and Selectively Alters the Neurochemical Coding of Intrahepatic Parasympathetic Nerves in Juvenile Porcine Models under Physiological Conditions. *International Journal of Molecular Science,* 18(12), 2726-2735.

[27] Valko, M., Rhodes, C. J., Moncol, J., Izakovic, M., & Mazur, M. (2007). Free radicals, metals and antioxidants in oxidative stress–induced cancer. *Chemico-Biological Interactions, 160*(1), 1–40. https://doi.org/10.1016/j.cbi.2005.12.009

[28] Walaa M.S. A., Walaa A. M., & Nabil, T.M. (2015). Bisphenol A Toxicity in Adult Male Rats: Hematological, Biochemical and Histopathological Approach. *Global Veterinaria*, 14 (2): 228-238. DOI: 10.5829/idosi.gv.2015.14.02.9332

[29] Zhang, T; Huang, G; Wang, T; Chen, J; Zhou, X & Shi, W. (2023). Urinary bisphenol A exposure in relation to liver function abnormalities among U.S. adults: results from the National Health and Nutrition Examination Survey, 2003-2016. *International Journal of Molecular Science*, 18 (12), 2726. doi.org/10.1101/2023.10.01.23296398.