

Petrol Fumes Induced Liver Toxicity in Wistar Rats: The Ameliorative Potentials of *Rhizophora racemosa* stem bark, *Bridelia ferruginea* and *Emilia sonchifolia* leaves.

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Abstract

The ameliorative potential of aqueous leaf extracts of *Bridelia ferruginea* and *Emilia Sonchifolia*, alongside an aqueous stem bark extract from *Rhizophora racemosa* on liver toxicity in rats exposed to petrol fumes was evaluated in this study. 54 male rats of Wistar strain weighing between 200-250g were used in the study. Test groups were exposed to petrol fumes in a fume chamber for 4 hours daily followed by treatment with the extracts for 28 days. Liver function tests, tissue antioxidant assay and histological examination of the liver were carried out. In contrast to normal control group, rats exposed to petrol fumes exhibited a significant increase $p < 0.05$ in serum levels of Alanine amino transferase (ALT), Aspartate aminotransferase (AST), Alkaline phosphatase (ALP), Gamma glutamyltransferase (GGT), as well as liver tissue malondialdehyde. Liver tissue Superoxide dismutase (SOD), catalase (CAT) and Glutathione peroxidase (GPx) were significantly decreased compared to the normal control group. Changes were reversed to normal range following treatment with the extracts. The histological results showed adverse changes in the livers of the petrol exposed group. This was reversed by administration of the extracts. The aqueous extract of these plants may therefore be protective against toxicity resulting from petrol fumes. This research investigated the protective effects of aqueous leaf extracts of *Bridelia ferruginea* and *Emilia sonchifolia*, combined with an aqueous stem bark extract from *Rhizophora racemosa*, on petrol fume-induced liver toxicity in Wistar rats. A total of 54 male rats, each weighing between 200-250 g, were randomly assigned to experimental groups. The treatment groups were exposed to petrol fumes in a fume chamber for 4 hours daily and subsequently administered the plant extracts for 28 consecutive days. Biochemical assessments, including liver function tests and antioxidant enzyme assays, as well as histopathological examination of liver tissues, were conducted Relative to the normal control group, petrol fume exposure significantly $p < 0.05$ elevated serum activities of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma-glutamyl transferase (GGT), alongside increased hepatic malondialdehyde (MDA) levels. Conversely, hepatic antioxidant defenses, superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), were markedly reduced. Administration of the plant extracts restored these biochemical parameters toward normal values. Histological analysis further revealed pronounced hepatic alterations in the petrol-exposed group, which were markedly ameliorated following treatment with the extracts.

Keywords: Petrol, Liver toxicity, GGT, AST, ALP, ALT, antioxidants, plant extracts.

Introduction

Petrol, commonly known as gasoline or Premium Motor Spirit (PMS), is a critical energy source globally, powering industries and transportation systems. Derived from distilled crude oil, it consists of highly volatile hydrocarbon mixtures, often modified with performance-enhancing additives. While primarily used to fuel engines, its solvent properties make it valuable for oil and fat dissolution. Evaporative emissions release petrol fumes into the environment, posing inhalation risks during routine activities. Residential and commercial reliance on petrol-powered generators further escalates exposure risks. Occupations involving direct handling, such as refinery staff, auto mechanics, and fuel station workers, face heightened vulnerability due to prolonged contact (Mohsin *et al.*, 2022).

Chronic inhalation of petrol vapors, as demonstrated by Abubakar *et al.* (2015), alters blood hydrocarbon composition, reducing saturated hydrocarbons while increasing aromatic unsaturated variants. Animal studies confirm that prolonged exposure disrupts lipid metabolism, inflicts organ damage (particularly to the liver and kidneys), and deranges biochemical homeostasis (Uboh *et al.*, 2009; Owumi *et al.*, 2021). Petroleum derivatives are further associated with genotoxic, carcinogenic, neurotoxic, and immunotoxic effects across species (Alabi *et al.*, 2017). A primary toxicity mechanism involves oxidative stress, marked by elevated lipid peroxidation in circulation (Owagboriaye *et al.*, 2016). Occupational exposure also correlates with reproductive dysfunction (Mohsin *et al.*, 2022).

Medicinal plants have long been employed in disease management due to their rich repertoire of bioactive compounds (Azimkhanova *et al.*, 2021). Constituents like alkaloids, flavonoids, tannins, and glycosides underpin their antimicrobial and therapeutic efficacy (Tchamgoue *et al.*, 2024). The global demand for plant-based products spans pharmaceuticals, nutraceuticals, and cosmetics, reflecting their role in modern drug development. While developing nations rely heavily on herbal medicine for primary care (Mofokeng *et al.*, 2022), industrialized countries increasingly incorporate traditional remedies into mainstream healthcare (Sánchez *et al.*, 2020). Notably, many FDA-approved drugs, including certain chemotherapeutics, originate from plant-derived precursors.

Plants combat oxidative damage via endogenous antioxidants, which scavenge free radicals and shield biomolecules from degradation (Rodriguez-Casado, 2016; Juan *et al.*, 2021). Enzymes like superoxide dismutase (SOD) are pivotal in mitigating oxidative stress (Jena *et al.*, 2023). Dietary intake of antioxidant-rich plants has proven effective in managing chronic diseases linked to oxidative imbalance (Anand & Bharadvaja, 2022; Salehi *et al.*, 2020).

Emilia sonchifolia (lilac tassel flower) thrives in tropical climates, growing to ~40 cm with lyrate leaves that turn purple upon maturation. Its vibrant inflorescences range from lilac to white, and its fruits feature reddish-brown capsules with white trichomes (Hussain & Sharma, 2024). Phytochemical analyses reveal alkaloids, terpenoids, and flavonoids, among others (Neethu & Gangaprasad, 2018). Ayurveda employs it for inflammation, wounds, and hypertension (Saratale *et al.*, 2018), while in vitro studies validate its radical-scavenging capacity (Dominic *et al.*, 2014). Culturally significant in India and Vietnam, it treats conditions from eczema to snakebites (Dash *et al.*, 2015). Nigerian traditional medicine utilizes it for gastric ulcers (Edu *et al.*, 2017).

Bridelia ferruginea, a Phyllanthaceae shrub, is endemic to African ecosystems (Njamen *et al.*, 2012). Ethnomedicine exploits its antidiabetic, anti-inflammatory, and wound-healing properties

(Afolayan *et al.*, 2019). Pharmacological studies corroborate its efficacy against malaria, diarrhea, and microbial infections (Mahomoodally *et al.*, 2021), attributed to its alkaloid and flavonoid content (Yeboah *et al.*, 2022).

Rhizophora racemosa, a West African mangrove, grows up to 30 m with distinctive stilt roots (Ellison, 2010). Local names like *Angala* (Ijaw) reflect its cultural integration. Its flavonoid-rich bark and leaves treat gastrointestinal ailments (Ngeve *et al.*, 2016), while its smoke preserves food via antimicrobial action (Chiavaroli *et al.*, 2020).

Materials and Methods

Plant materials and preparation of extracts

Bridelia ferruginea and *Emilia sonchifolia* leaves were harvested from the Niger Delta University campus in Bayelsa State, Nigeria. Botanical authentication was performed by Prof. Kola Ajibesin (Department of Pharmacognosy, Niger Delta University). The collected leaves were rinsed with cold water and subsequently shade-dried for a period of two weeks. The desiccated leaves were then mechanically ground into a fine powder. An aqueous extraction was performed by macerating 100 g of each powdered sample in 1 L of distilled water for 72 hours, with periodic agitation. The resulting mixtures were filtered, and the filtrates were concentrated using a water bath maintained at 60°C. The final crude aqueous extracts were stored in refrigerated conditions in sealed containers until required for analysis.

Rhizophora racemosa stem bark were obtained from the Edema area of Ogbia Local Government in Bayelsa State, Nigeria. Prof. Kola Ajibesin from the Department of Pharmacognosy at Niger Delta University provided taxonomic confirmation of the plant material. The bark was segmented, cleaned with cold water, and air-dried in a shaded environment. Once desiccated, the material was mechanically ground into a fine powder. An aqueous extraction was then performed by macerating 100 g of the powder in 1 L of distilled water for 72 hours with occasional agitation. The mixture was filtered, and the resulting filtrate was concentrated using a water bath set at a constant 60°C. The final crude extract was stored in a sealed container under refrigeration to preserve its stability until further analysis.

Petrol/Chemical Reagents

The petrol used for this study were obtained from the Nigerian National Petroleum Corporation (NNPC) filling station Edepie, Yenagoa, Bayelsa State, Nigeria. Enzyme kits used for biochemical assays were procured from Randox™ Laboratories Ltd, Crumlin, Co, Antrim, United Kingdom. The rest of the chemicals used for the research work were purchased from Loba Chemie PVT LTD India.

Experimental Animals

Fifty-four male Wistar rats (200–250 g) were sourced from the Niger Delta University's Department of Pharmacology animal breeding facility. Prior to experimentation, the animals were housed in standard plastic cages for a two-week acclimatization period within the department's laboratory. Housing conditions included a 12-hour light/dark cycle, a temperature range of 20–25°C, and ad libitum access to both food and water.

Ethical Consideration

Ethical approval for this research was granted by the Research Ethical Committee of the College of Health Sciences at Niger Delta University, Wilberforce Island in Bayelsa State, Nigeria.

Experimental Design

For a 28-day study, 54 healthy male Wistar rats (9 groups of 6) were treated as follows: a negative control (water), a positive control (petrol fumes + water), six groups receiving petrol fumes plus one of three plant extracts (*E. sonchifolia*, *B. ferruginea*, *R. racemosa*) at 200 or 400 mg/kg, and a reference group (petrol fumes + Vitamin E, 200 mg/kg). All compounds were administered orally by gavage.

Exposure of Animals to Petrol Fumes

The exposure procedure was adapted from the Methods described by Uboh *et al.* (2005) and Owagboriaye *et al.* (2016). Rats were subjected to petrol fumes through inhalation within a fume chamber measuring 150 cm × 90 cm × 210 cm. To ensure adequate vapor saturation before exposure, 500 ml of petrol in 1000 ml beakers was placed inside the chamber one hour in advance. The animals were exposed to the fumes for 4 hours daily across 28 consecutive days. After each exposure period, they were promptly relocated to a petrol-free section of the laboratory to minimize extended inhalation of the vapors.

Sample Collection and Biochemical analysis

Blood was drawn for biochemical assessment according to a strict protocol. On days 0, 1, 7, 14, 21, and 28, animals were lightly anesthetized with chloroform, and blood was collected via the submandibular vein. To standardize the results and account for diurnal variations, all blood collections were conducted within a two-hour window. 24 hours post-exposure.

At the conclusion of the experiment (day 28), animals were anesthetized with chloroform before being sacrificed. Livers were harvested for antioxidant and histological studies.

ALT, AST, ALP and GGT were determined following the instructions in the biochemical kits inserts.

Biochemical Assays: Oxidative stress parameters were analyzed using the following referenced protocols. Superoxide dismutase (SOD) activity was determined according to Marklund and Marklund (1974). Catalase (CAT) activity was assessed based on the method of Aebi *et al.* (1974). Glutathione peroxidase (GPx) activity was evaluated using a coupled enzymatic assay system linked to glutathione reductase, as described by Lawrence and Burk (1976). Lipid peroxidation, expressed as malondialdehyde (MDA) concentration, was estimated using a modified version of the thiobarbituric acid (TBA) method by Armstrong and Al-Awadi (1991).

STATISTICAL ANALYSIS

Results are expressed as mean ± SEM. Statistical analysis was performed using one-way ANOVA followed by Tukey's post-hoc test (SPSS v20, IBM, USA), with $p < 0.05$ set as the threshold for significance.

Results

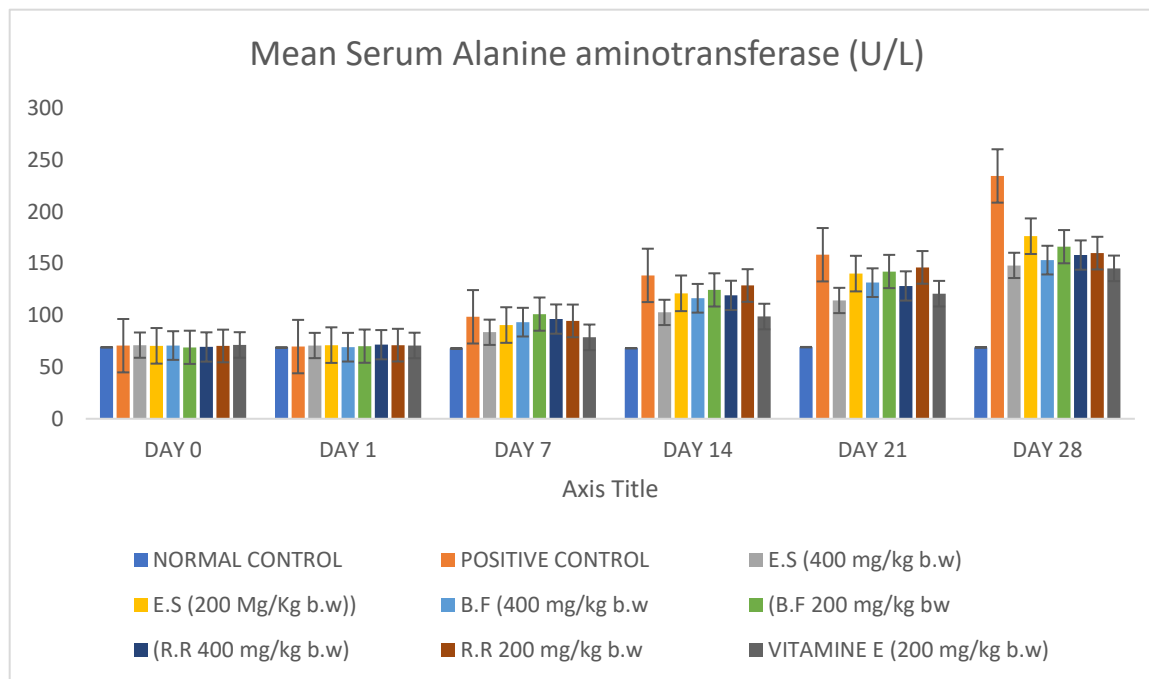


Figure 1. Serum alanine aminotransferase (ALT) activity in Wistar rats after a 28-day petrol fume exposure period and subsequent administration of aqueous extracts from Emilia sonchifolia (E.S.), Bridelia ferruginea (B.F.) and Rhizophora racemosa (R.R.). Data are represented as the mean $\pm$ standard error of the mean (SEM); n=6. A significant difference compared to the control is indicated at $p < 0.05$.

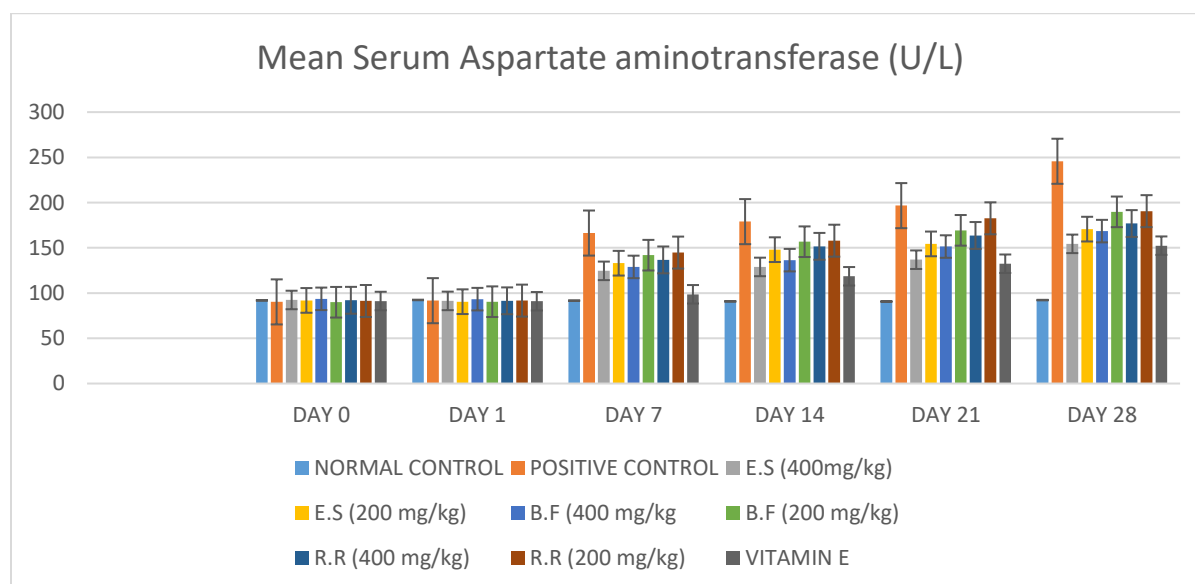


Figure 2: Serum aspartate aminotransferase (AST) activity in Wistar rats after a 28-day petrol fume exposure period and subsequent administration of aqueous extracts from Emilia sonchifolia (E.S.), Bridelia

ferruginea (B.F.) and Rhizophora racemosa (R.R.). Data are represented as the mean $\pm$ standard error of the mean (SEM); n=6. A significant difference compared to the control is indicated at $p < 0.05$.

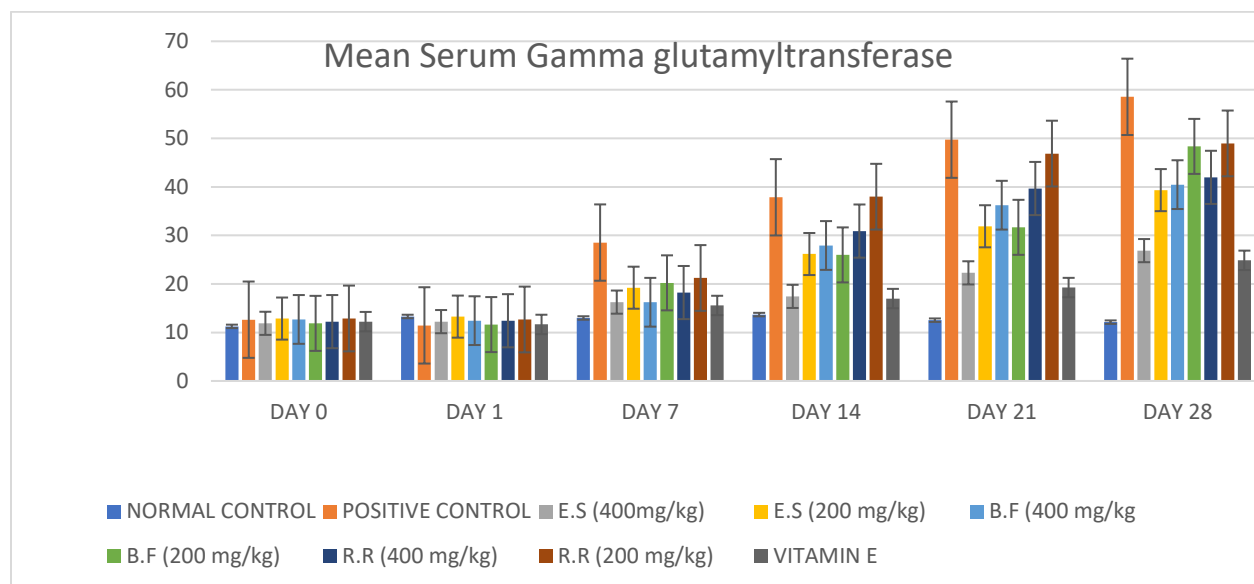


Figure 3. Serum gamma glutamyltransferase (GGT) activity in Wistar rats after a 28-day petrol fume exposure period and subsequent administration of aqueous extracts from Emilia sonchifolia (E.S.), Bridelia ferruginea (B.F.) and Rhizophora racemosa (R.R.). Data are represented as the mean $\pm$ standard error of the mean (SEM); n=6. A significant difference compared to the control is indicated at $p < 0.05$.

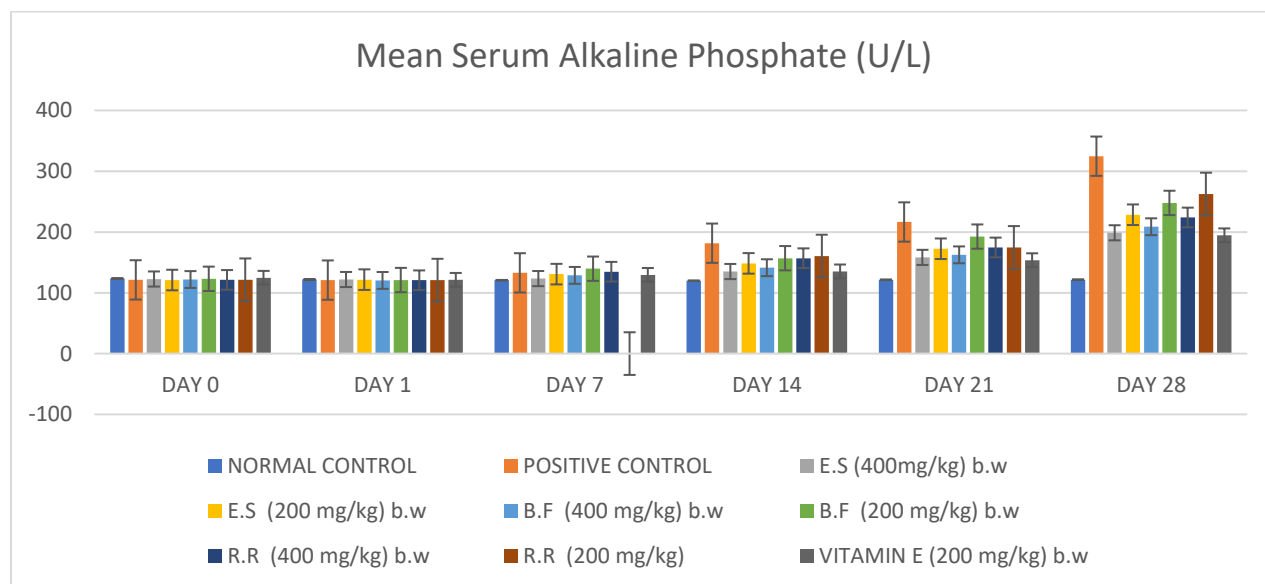
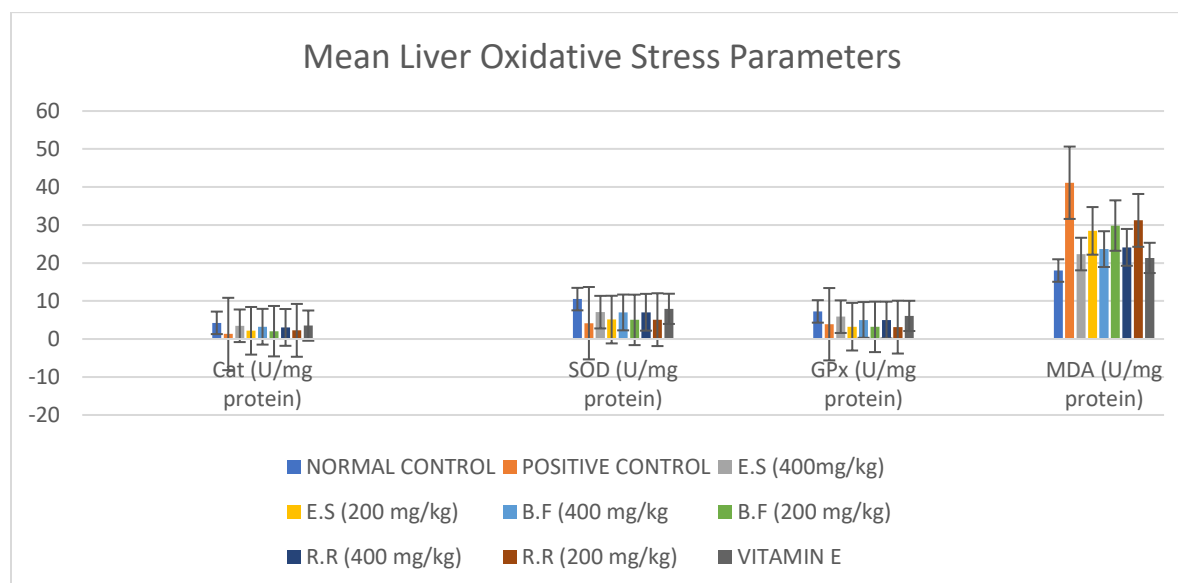


Figure 4: Serum alkaline phosphatase (ALP) activity in Wistar rats after a 28-day petrol fume exposure period and subsequent administration of aqueous extracts from Emilia sonchifolia (E.S.), Bridelia ferruginea (B.F.) and Rhizophora racemosa (R.R.). Data are represented as the mean $\pm$ standard error of the mean (SEM); n=6. A significant difference compared to the control is indicated at $p < 0.05$.

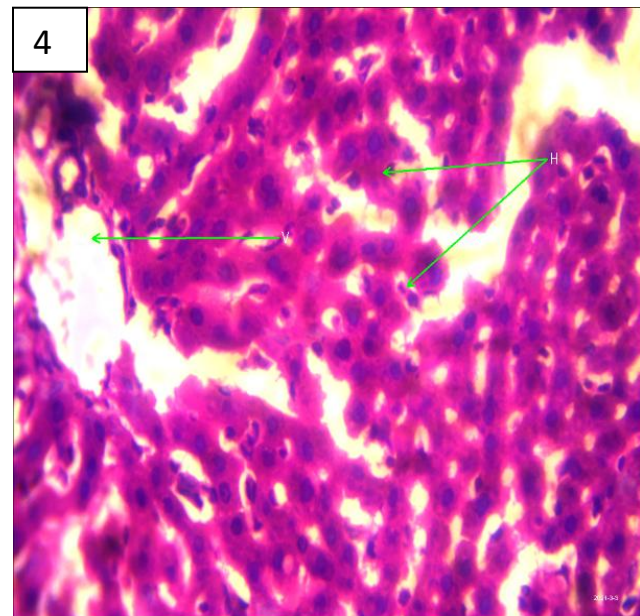
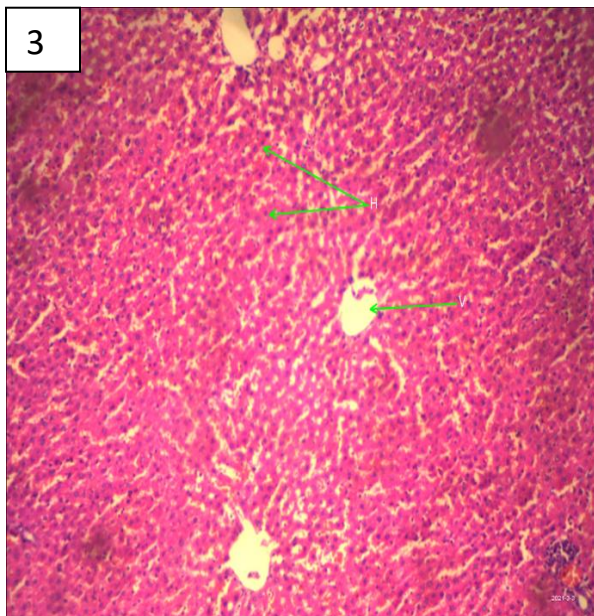
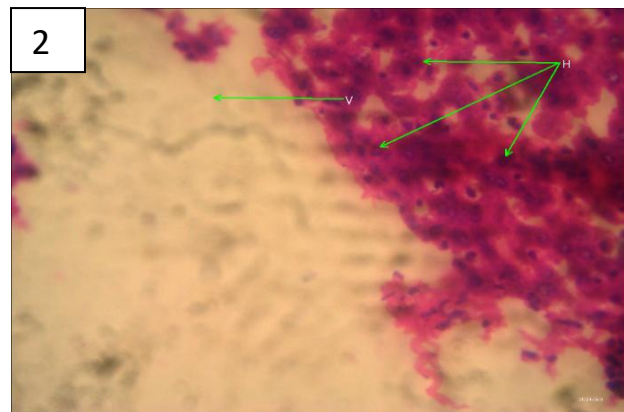
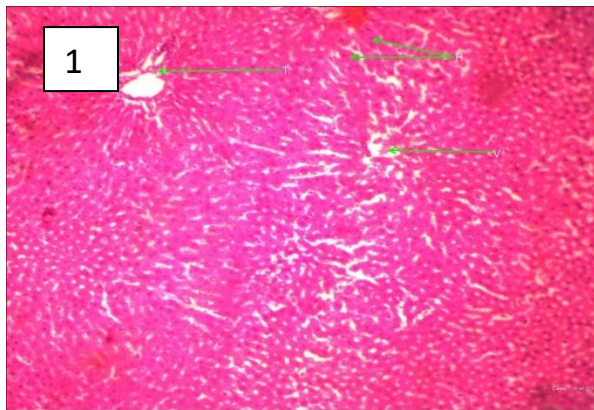


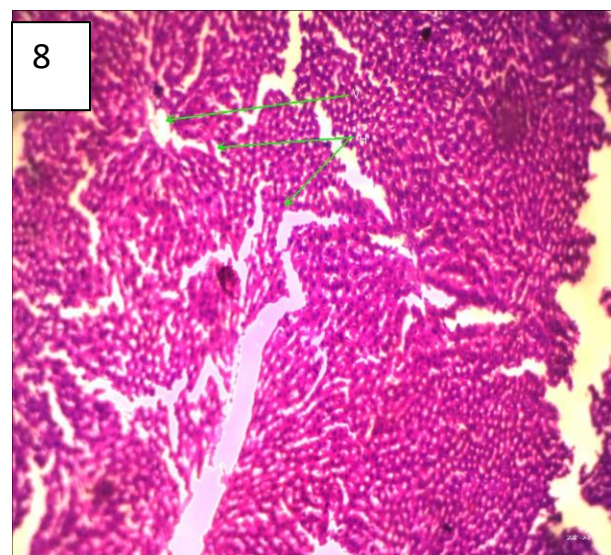
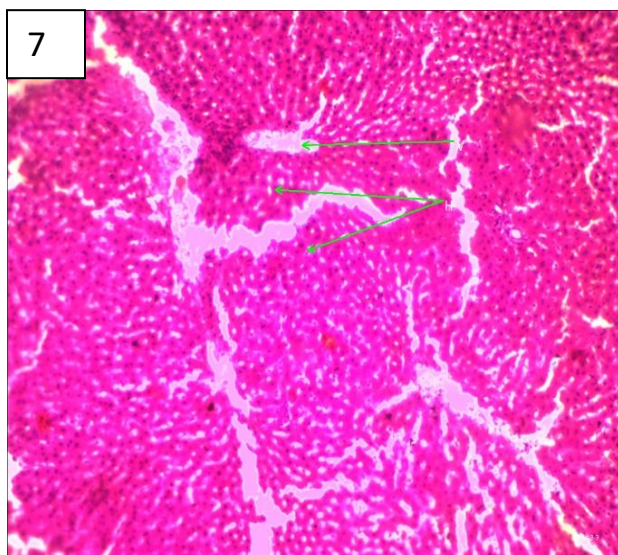
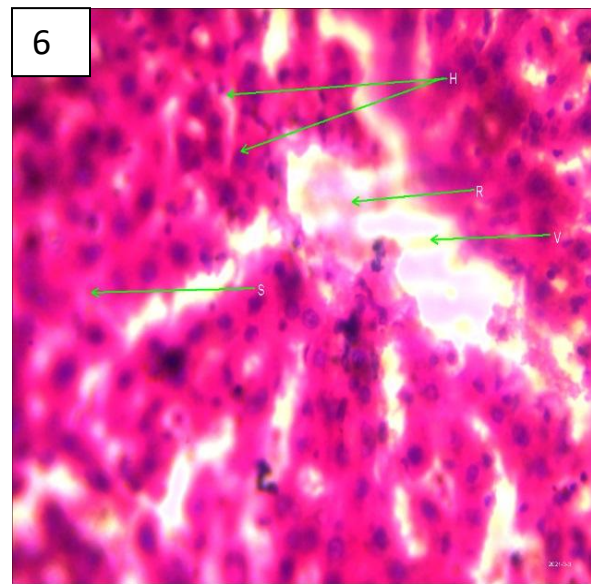
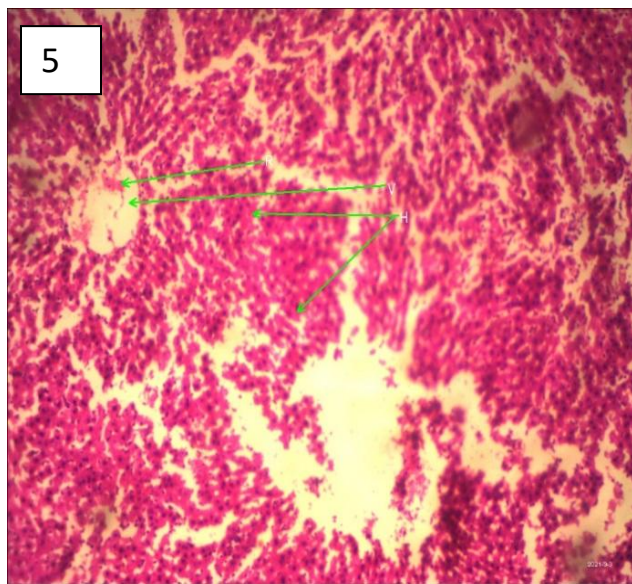
Hepatic antioxidant enzymes and lipid peroxidation after treatment. Effects of 28-day petrol fume exposure and subsequent administration of plant extracts on catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx) activities, and malondialdehyde (MDA) concentration. Data are mean $\pm$ SEM, $n=6$. A statistically significant difference from the control group is indicated at $p < 0.05$). Abbreviations: E.S., Emilia sonchifolia; B.F., Bridelia ferruginea; R.R., Rhizophora racemosa.

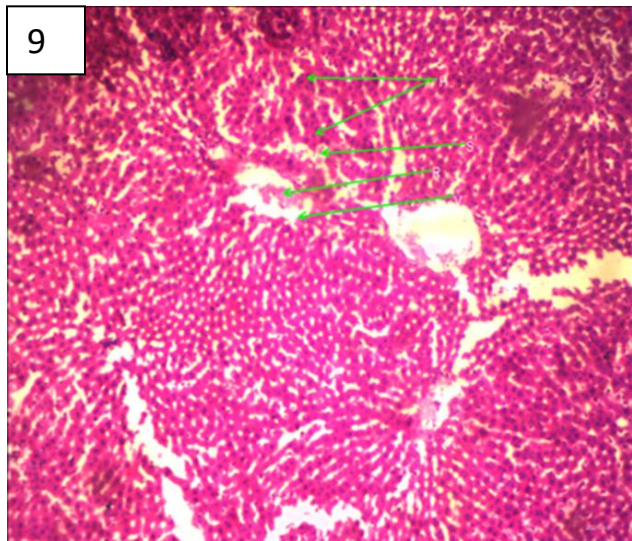
Histology of Liver Tissues

Histological sections of liver tissue from control and experimental rats were stained with hematoxylin and eosin (H&E) and examined at 400x magnification after a 28-day period of petrol fume exposure and treatment with aqueous plant extracts.

Plate 1 (Normal Control): Represents the baseline hepatic architecture, displaying well-organized rays of hepatocytes (H), a distinct central venule (V), and an intact portal tract (T). **Plate 2 (Positive Control - Petrol Fumes):** Reveals severe histopathological damage, characterized by a markedly enlarged central vein (V) and a highly disorganized arrangement of hepatocytes. **Plate 3 (Petrol + E.S. 200 mg/kg):** Exhibits mild architectural distortion of the hepatocyte (H) arrangement and central vein (V) structure. **Plate 4 (Petrol + E.S. 400 mg/kg):** Shows a moderate level of distortion within the parenchymal architecture (H) and around the central vein. **Plate 5 (Petrol + B.F. 200 mg/kg):** Demonstrates a moderately undifferentiated liver parenchyma (H), accompanied by slight congestion in the central vein (R) and visible sinusoids (S). **Plate 6 (Petrol + B.F. 400 mg/kg):** Presents a moderately undifferentiated parenchymal architecture (H) with an identifiable central vein (V). **Plate 7 (Petrol + R.R. 200 mg/kg):** Displays moderate distortion of the general liver architecture (H) and central vein. **Plate 8 (Petrol + R.R. 400 mg/kg):** Indicates mild vascular congestion (R), a disorganized arrangement of hepatocytes (H), visible sinusoids (S), and the central vein. **Plate 9 (Petrol + Vitamin E 200 mg/kg):** The architecture appears normal and comparable to the untreated control (Plate 1), showing well-defined hepatocyte rays (H), a central venule (V), and a portal tract (T).







Discussion

Petrol is a complex hydrocarbon blend primarily serving as fuel for internal combustion engines and as an industrial solvent. A significant body of research indicates that its composition includes hazardous compounds such as benzene, toluene, ethylbenzene, and xylene (BTEX), which are recognized for their considerable risks to human health (Soleimani, 2020). Due to its high volatility, petrol readily emits fumes that contribute to environmental chemical pollution. Inhalation exposure is linked to a spectrum of toxicological effects, encompassing damage to the liver (hepatotoxicity) and blood system (Zhang *et al.*, 2020), renal impairment, disruptions in lipid metabolism, and alterations in key biochemical pathways (Uboh *et al.*, 2009; Owumi *et al.*, 2021). Furthermore, evidence points to its potential for DNA damage, genetic mutations, cancer-causing potential, nervous system toxicity, and immune system impairment in humans and animal models (Rahul *et al.*, 2017).

The toxicity of petrol is primarily mediated through its biotransformation by cytochrome P450 enzymes, specifically the hepatic isoenzyme CYP2E1 (Gonza'lez-Jasso *et al.*, 2003). This metabolic process leads to an excessive generation of reactive oxygen species (ROS) (Dong *et al.*, 2019). Consequently, this surge in ROS disrupts the body's delicate oxidant-antioxidant balance, precipitating a state of oxidative stress (Vona *et al.*, 2021). This biochemical imbalance is a key mechanism underlying the subsequent cellular and physiological dysfunction observed.

The application of medicinal plants for the prevention and treatment of diseases has a long history in human societies (Azimkhanova *et al.*, 2021). This traditional use is supported by the discovery that plants synthesize a diverse array of bioactive compounds, including alkaloids, flavonoids, tannins, coumarins, glycosides, and vitamins. These phytochemicals exhibit defined physiological activities in living systems and possess efficacy against a variety of pathogens.

This study evaluated the therapeutic prospects of aqueous preparations from *Emilia sonchifolia* (E.S.) and *Bridelia ferruginea* (B.F.) on the livers of rats exposed to petrol fumes for 28 days, using multiple biochemical, antioxidant, and histological markers of liver injury. Exposure to petrol fumes led to significant elevations in serum ALT, AST, ALP and GGT, alongside marked

reductions in hepatic antioxidant enzyme activities, CAT, SOD and GPx, with corresponding increases in MDA, a marker of lipid peroxidation. These biochemical changes became observable after the 7th day of the experiment. The biochemical derangements were supported by histological evidence of hepatocellular distortion and vascular congestion.

The progressive increase in serum ALT, AST, ALP, and GGT activities in the Positive Control group (petrol fumes alone) indicated significant hepatocellular and hepatobiliary injury. ALT and AST elevations reflect hepatocellular membrane disruption and leakage of intracellular enzymes into circulation (Ostróžka-Cieślak 2024). ALP and GGT elevations are associated with cholestasis, oxidative stress, and hepatobiliary dysfunction (Thakur *et al.*, 2024; Youssef and Wu, 2024). These findings corroborate previous reports that inhalation of petroleum hydrocarbons induces oxidative stress, lipid peroxidation, and hepatic damage (Owumi *et al.*, 2021).

Parallel reductions in CAT, SOD, and GPx, and elevation of MDA, further confirm oxidative stress as a key mechanism of petrol fume-induced hepatotoxicity. The depletion of antioxidant enzymes impairs the liver's capacity to neutralize reactive oxygen species (ROS), exacerbating lipid peroxidation and hepatocellular injury (Allameh *et al.*, 2023).

Importantly, treatment with aqueous extracts of E.S., B.F., and R.R. at both 400 mg/kg and 200 mg/kg significantly ameliorated these petrol-induced biochemical and oxidative alterations in a dose-dependent manner. The higher doses (400 mg/kg) consistently demonstrated superior protective effects and ES appeared to be the most effective of the three plants. For instance, by day 28, ALT activities in rats treated with 400 mg/kg of E.S. (148.33 U/L), B.F. (153.44 U/L), and R.R. (158.34 U/L) were significantly lower than in the untreated Positive Control group (234.82 U/L). Similar dose-dependent reductions were observed for AST, ALP, and GGT.

Furthermore, the extracts significantly restored hepatic CAT, SOD, and GPx activities and reduced MDA levels, confirming their antioxidant properties. The protective effects are likely attributable to bioactive phytochemicals—flavonoids, polyphenols, terpenoids known to scavenge ROS and stabilize hepatocyte membranes (Gonfa *et al.*, 2025).

Vitamin E (200 mg/kg), a well-established antioxidant, served as a positive control and significantly reversed all biochemical and oxidative indices of liver injury, achieving comparable results to the plant extracts at higher doses. For instance, Vitamin E treatment resulted in normalization of GGT (24.86 U/L), ALT (145.44 U/L), and antioxidant enzymes, validating the efficacy of the plant extracts.

Histological analysis further corroborated these biochemical findings. Livers from petrol-exposed rats exhibited enlarged central veins, distorted hepatocyte architecture, and sinusoidal congestion. Conversely, extracts of E.S., B.F., and R.R. attenuated these histopathological lesions in a dose-dependent fashion, with the 400 mg/kg doses showing moderate improvements, and Vitamin E-treated livers exhibiting near-normal architecture.

These findings confirm that aqueous extracts of *Emilia sonchifolia*, *Bridellia ferruginea*, and *Rhizophora racemosa* confer significant hepatoprotective effects against petrol fume-induced liver injury through antioxidant mechanisms. Their efficacy was comparable to that of Vitamin E, a standard hepatoprotective agent. However, none of the treatments fully restored biochemical or histological parameters to baseline within 28 days, suggesting that extended treatment durations or combination therapies may be required for complete recovery.

Conclusion

These medicinal plants offer promising complementary therapies for mitigating hepatotoxicity induced by environmental pollutants. Further studies are warranted to isolate active constituents, elucidate mechanisms of action, and evaluate long-term efficacy and safety.

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CONFLICT OF INTEREST

There is no conflict of interest.

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