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Full-length Research Article

Chemo-Intervention of *Paullinia pinnata* Methanol Leaf Extract on Ethylene Glycol Monomethyl Ether–Induced Toxicity in Wistar Rats

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Summary: *Paullinia pinnata* (PP) is a medicinal vine used folklorically as a result of this attribute to treat various ailments. Ethylene glycol monomethyl ether (EGME) is a solvent of wide application and is toxic. This study is designed to elucidate the potential of *P. pinnata* methanol leaf extract in preventing the deleterious effect of EGME in the liver and kidney. The leaves of *P. pinnata* were extracted after defatting by Soxhlet extraction using absolute methanol. As a sequel to our previous study, seventy adult male Wistar rats were weight-matched into seven groups (n=10). Groups I and II served as controls and received distilled water and 10% dimethyl sulfoxide, respectively. Group III received EGME (200 mg/kg) only. Groups IV-VII were co-treated with EGME (200 mg/kg) and PP at 25, 50, 75 and 100 mg/kg doses, respectively. The administration was done by oral gavage daily for 14 consecutive days. On day 15, the animals were euthanized by cervical dislocation and the liver and kidneys were excised. Sections of the liver and kidney were fixed in 10% formalin for histology. The remainder of the liver and kidney were homogenized in Tris-HCl/KCl buffer and the supernatant was used for liver function and kidney function assays using standard laboratory techniques and ion selective electrode, respectively. EGME significantly ($p<0.05$) increased the activities of alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase and gamma glutamyl transferase in the liver, while the concentration of sodium ion was reduced, but that of chloride-, potassium-, calcium-, phosphate- ions, urea, uric acid and creatinine was increased in the kidney. Lesions were observed in the EGME only and EGME + PP (25 mg/kg) groups and not in the other co-administered groups. The methanol leaf extract of *Paullinia pinnata* prevented the perturbations of EGME at moderate doses in the liver and kidney.

Keywords*: Paullinia pinnata, ethylene glycol monomethyl ether, liver, kidney.*

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INTRODUCTION

Paullinia pinnata (PP) is a medicinal climber used folklorically as a result of this attribute to treat various diseases topically and via ingestion. Some of the folkloric applications include treatment of whooping cough, fever, as an emetic, rickets and management of gynaecological challenges (Burkill, 2000). Some of these uses have been supported by scientific demonstrations. These include antimicrobial, anti-cancer, anti-typhoid, and antioxidant manifestations (Adeyemo-Salami, 2020). Ethylene glycol monomethyl ether (EGME) is a solvent that is employed widely domestically and industrially and has been shown to be toxic to various organs upon exposure (Adeyemo-Salami, 2021). Aberrations in liver function as a result of exposure to EGME have been reported by Takei *et al*. (2010) and Bendjeddou and Khelili (2014). Given that investigations to ameliorate the toxic effect of EGME is of interest, as an extension to our previous observation of the effect of *P. pinnata* methanol leaf extract on the toxic effect of EGME on enzymatic and non-enzymatic antioxidant parameters in the liver and kidney (Adeyemo-Salami *et al*., 2024), we assessed the effect on the functions of these organs.

This study is therefore aimed at unraveling the result of exposure to EGME and the effect of *P. pinnata* methanol leaf extract on the damage caused by EGME on the function of the liver and kidney.

MATERIALS AND METHODS

Plant material: *P. pinnata* leaves were collected and authenticated at the Herbarium of Forestry Research Institute of Nigeria (F.R.I.N.), and the specimen identification FHI 106555 was assigned. The leaves were processed using the method of Adeyemo-Salami and Makinde (2013). Briefly, rinsed, air-dried and pulverized leaves of *P. pinnata* were defatted using n-hexane and then extracted using absolute methanol in a Soxhlet extractor. A 14% yield of the plant was realized with absolute methanol as the extract.

Ethical Approval: Ethical approval was sought and granted by the Animal Care and Use Research Ethics Committee of

the University of Ibadan, Nigeria, and the number UI-ACUREC/ APP/ 10/2016 /003 was assigned.

Experimental Animal and Care: Seventy (70) adult male Wistar rats weighing 140- 190g were obtained from the Department of Veterinary Anatomy, University of Ibadan, Oyo State, Nigeria, and were weight-matched into seven groups of ten animals each. They were acclimatized for a week in standard laboratory cages and given feed (Breedwell Feed, Nigeria) and tap water ad libitum at the Animal house of the Department of Biochemistry of the same University. The 12hour light/dark cycle was maintained.

Plate 1.
Paullinia pinnata Linn. Leaves

Experimental Design: The following treatment protocol was adopted and all administrations were done by oral gavage daily for 14 consecutive days:
Group I- distilled water
Group II- 10% dimethyl sulfoxide (DMSO) (vehicle for PP)
Group III- EGME (200 mg/kg) only constituted with distilled water
Group IV- EGME (200 mg/kg) + PP (25 mg/kg)
Group V- EGME (200 mg/kg) + PP (50 mg/kg)
Group VI- EGME (200 mg/kg) + PP (75 mg/kg)
Group VII- EGME (200 mg/kg) + PP (100 mg/kg)
The weight of the animals was monitored weekly. On day 15, the animals were euthanized by cervical dislocation and the liver and kidneys were excised and weighed. The liver and kidney were homogenized in Tris-HCl/KCl buffer and the supernatant was stored at -20^{0}C until time for biochemical analyses which were liver function (albumin, total bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma glutamyl transferase (GGT)) using Randox kits (U.K.), and electrolytes (sodium, potassium, and chloride ions) were analyzed using ISE SFRI Medical Diagnostics 4000 (France) while the other kidney function parameters (urea, creatinine, calcium ion, phosphate ion, and uric acid) were analyzed using Architect plus c4000 Chemistry Analyser (Abbott, USA).Sections of the liver and kidney were fixed in 10% formalin and subjected to histology. These tissues were processed for histopathology examination using a routine paraffin-wax embedded method by dehydrating using different grades of alcohol, de-alcoholizing in xylene, embedding in paraffin wax, and then rehydrating using alcohol. Sections of 5 micrometer thickness were stained with hematoxylin and eosin. The slides were then examined using a light microscope for lesions and were evaluated by a pathologist at the Department of Veterinary Anatomy, University of Ibadan, Nigeria.

Statistical Analysis: All data are expressed as mean ± standard error of mean and analyzed using one-way analysis of variance. P-values less than 5% were taken to be significant and post-hoc test was carried out using Bonferroni's multiple comparison test.

RESULTS

Figure 1 shows that there was decrease in weight gain in the groups treated with EGME only (from 17% to 10%) and EGME+ PP (25 mg/kg) (from 20% to 15%) after the first week of administration while the weight of the animals in the other groups increased with that in the EGME+ PP (75 mg/kg) being the least.

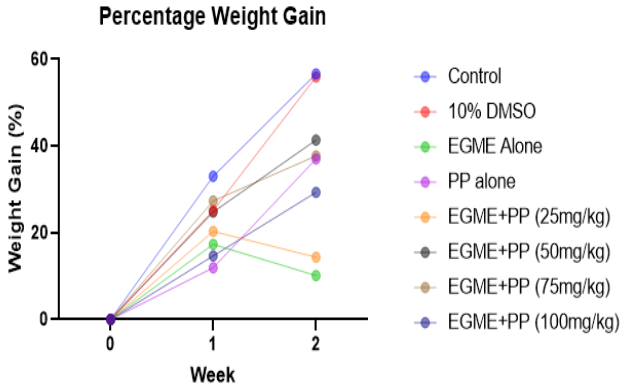

Figure 1:
Percentage weight gain over the period of the study

Table 1:
Effect on relative organ weight of animals co-treated with EGME And *P. pinnata*

Dose	Relative organ weight (%)	
	Kidney	Liver
Control	0.74±0.03	4.10±0.24
10% DMSO	0.64±0.10	3.65±0.24
EGME	0.26±0.02*	2.11±0.25*
EGME + PP (25mg/kg)	0.23±0.02*	2.02±0.44*
EGME + PP (50mg/kg)	0.72±0.11	3.64±0.42
EGME + PP (75mg/kg)	0.67±0.05	3.62±0.20
EGME + PP (100mg/kg)	0.72±0.09	3.52±0.20

Note: n=10; *- significantly differs from control at $p < 0.05$; all data are mean ± standard error of mean

Treatment with EGME only caused a significant ($p < 0.05$) reduction in the relative weight of the kidney and liver compared to the control. However, co-treatment with EGME and *P. pinnata* methanol leaf extract at 50, 75 and 100 mg/kg doses did not affect the relative weight of the organs except at the 25 mg/kg dose compared to the control (Table 1).

Table 2:
The influence of co-administration of EGME and *P. pinnata* on non-enzymatic liver function parameters

Dose	Albumin (g/dL)	Total bilirubin (mg/dL)
Control	3.94 ± 0.14	0.18 ± 0.03
10% DMSO	3.32 ± 0.14	0.26 ± 0.03
EGME (200 mg/kg)	2.40 ± 0.33[a]	0.69 ± 0.03[a]
EGME+PP (25 mg/kg)	1.82 ± 0.57[a,b]	0.57 ± 0.05[a]
EGME+PP (50 mg/kg)	4.31 ± 0.16[b]	0.25 ± 0.02[b]
EGME+PP (75 mg/kg)	3.31 ± 0.24[b]	0.16 ± 0.02[b]
EGME+PP (100 mg/kg)	3.16 ± 0.29[b]	0.22 ± 0.03[b]

Note: *n=10; all data are mean ± standard error of mean; a - significantly different from control at $p < 0.05$; b- significantly different from EGME group at $p < 0.05$*

Treatment with EGME only, significantly ($p < 0.05$) reduced the level of albumin and significantly ($p < 0.05$) increased the level of bilirubin in the liver in comparison with the control. The level of albumin in the groups co-administered with EGME and *P. pinnata* at 50, 75 and 100 mg/kg doses were significantly ($p < 0.05$) elevated when compared to the EGME only group but not with the control, except at the 25 mg/kg dose. The level of bilirubin was significantly ($p < 0.05$) reduced in the groups co-administered with EGME and *P. pinnata* methanol leaf extract at 50, 75 and 100 mg/kg doses when compared to the EGME only group but not with the control, except at the 25 mg/kg dose (Table 2).

Table 3 shows that administration of EGME only, significantly ($p < 0.05$) elevated the activities of ALT, AST, ALP and GGT in the liver compared with the control. Co-administration with EGME and *P. pinnata* at 50, 75 and 100 mg/kg doses significantly ($p < 0.05$) douced the activities of the enzymes when compared with the EGME only group and not the control, except at the 25 mg/kg dose.

Table 3:
The effect of co-administration of EGME and *P. pinnata* on certain enzymatic liver function biomarkers

DOSE	ALT (U/l)	AST (U/l)	ALP (U/l)	GGT (U/l)
Control	51.17 ±3.00	8.00 ±0.26	38.09 ±1.95	8.89 ±0.42
EGME (200 mg/kg)	74.40 ±1.29[a]	16.35 ±0.58[a]	101.00 ±1.64[a]	15.39 ±0.80[a]
EGME+PP (25 mg/kg)	66.50 ±1.50[a]	15.50 ±1.50[a]	112.10 ±10.00[a]	22.42 ±1.84[a,b]
EGME+PP (50 mg/kg)	46.50 ±2.50[b]	8.25 ±0.34[b]	48.76 ±3.54[b]	7.11 ±0.89[b]
EGME+PP (75 mg/kg)	58.00 ±1.87[b]	9.18 ±0.56[b]	37.44 ±1.18[b]	7.74 ±0.26[b]
EGME+PP (100 mg/kg)	57.80 ±1.99[b]	9.51 ±0.14[b]	39.83 ±1.10[b]	11.63 ±0.31[b]

Note: n=10; all data are mean ± standard error of mean; a - significantly different from control at $p < 0.05$; b- significantly different from EGME group at $p < 0.05$; ALT- alanine aminotransferase; AST- aspartate aminotransferase; ALP- alkaline phosphatase; GGT- gamma glutamyl transferase

Except for sodium ions, treatment with EGME only significantly ($p < 0.05$) increased the concentrations of potassium, chloride, calcium and phosphate ions and similarly, the concentrations of uric acid, urea and creatinine in the kidney in comparison with the control. Co-administration with EGME and *P. pinnata* at 50, 75 and 100 mg/kg doses resulted in significant ($p < 0.05$) increase in sodium ion level and significant ($p < 0.05$) decrease in the concentrations of potassium, chloride, calcium and phosphate ions, and that of uric acid, urea and creatinine in comparison to the EGME only group and not the control, except at the dose of 25 mg/kg (Table 4).

Table 4:
The influence of co-administration of EGME and *P. pinnata* on certain parameters for kidney function

DOSE	Na^+ (mmol/L)	K^+ (mmol/L)	Cl^- (mmol/L)	Urea (mg/dL)	Creatinine (mg/dL)	Ca^{2+} (mg/dL)	PO_4^{2-} (mg/dL)	Uric Acid (mg/dL)
Control	25.00 ±1.08	66.07 ±1.84	61.00 ±0.93	42.01 ±1.14	0.11 ±0.01	1.15 ±0.10	9.48 ±0.43	16.90 ±1.41
10% DMSO	25.67 ±0.88	75.85 ±0.65	65.33 ±1.45	51.64 ±0.98	0.18 ±0.02	1.40 ±0.06	11.54 ±0.37	19.25 ±0.75
EGME (200 mg/kg)	10.67 ±0.66[a]	92.83 ±2.82[a]	117.30 ±6.36[a]	71.21 ±1.19[a]	0.22 ±0.02[a]	1.77 ±0.09[a]	20.15 ±0.92[a]	26.75 ±1.25[a]
EGME+PP (25 mg/kg)	10.00 ±0.00[a]	102.00 ±0.00[a]	120.00 ±0.00[a]	53.50 ±0.00[a]	0.20 ±0.00[a]	1.70 ±0.00[a]	17.70 ±0.00[a]	20.00 ±0.00[a]
EGME+PP (50 mg/kg)	23.25 ±1.55[b]	66.40 ±1.20[b]	59.00 ±0.91[b]	40.93 ±2.24[b]	0.15 ±0.01[b]	1.12 ±0.06[b]	10.33 ±0.32[b]	14.48 ±0.51[b]
EGME+PP (75 mg/kg)	29.50 ±1.85[b]	69.37 ±1.27[b]	62.50 ±2.78[b]	38.52 ±2.31[b]	0.12 ±0.01[b]	1.13 ±0.09[b]	11.13 ±0.40[b]	14.43 ±0.56[b]
EGME+PP (100 mg/kg)	28.00 ±0.91[b]	70.18 ±2.70[b]	65.67 ±1.20[b]	50.42 ±1.92[b]	0.12 ±0.01[b]	1.18 ±0.09[b]	11.34 ±0.18[b]	16.80 ±0.40[b]

Note: n=10; all data are mean ± standard error of mean; a - significantly different from control at $p < 0.05$; b- significantly different from EGME group at $p < 0.05$; Na^+-sodium ion; K^+-potassium ion; Cl^--chloride ion; Ca^{2+}-calcium ion; PO_4^{2-}-phosphate ion

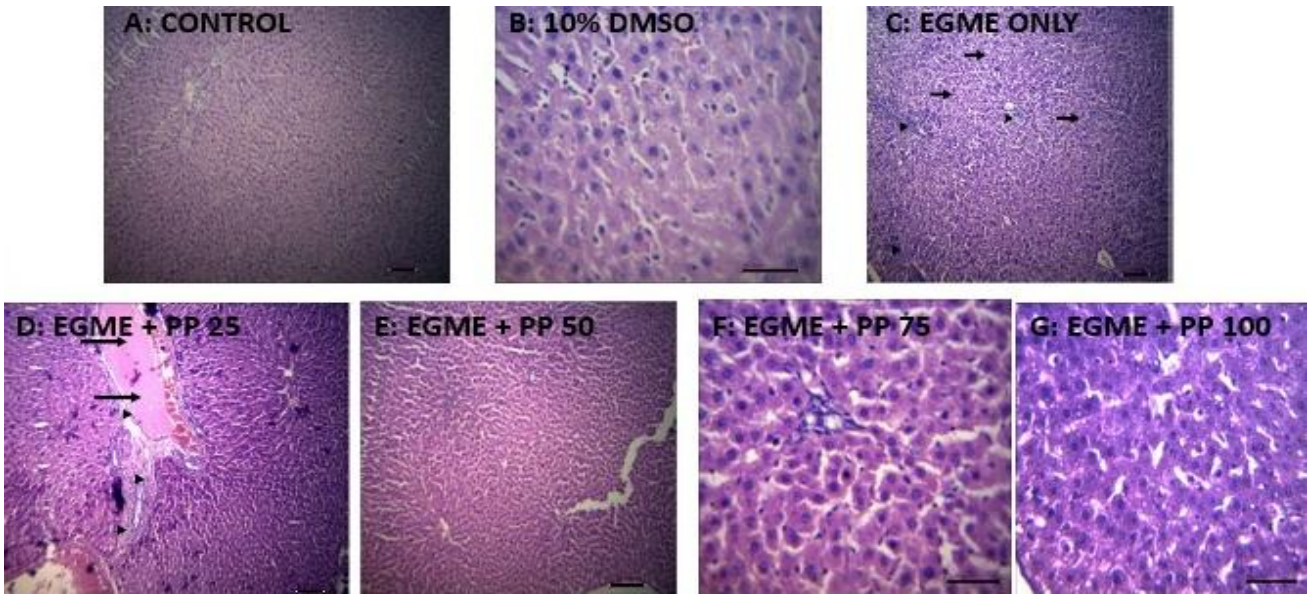

Plate 2:
Photomicrographs of the liver sections showing the effect of co-administration of EGME and *P. pinnata*: - A, B, and E - G - No lesions; **C**-There is a moderate to severe diffuse hydropic degeneration and necrosis of hepatocytes, there is also a diffuse lymphocytic cellular infiltration; **D-** Severe portal congestion with a mild to moderate periportal cellular infiltration by neutrophils and macrophages. The periportal connective tissue is also prominent.

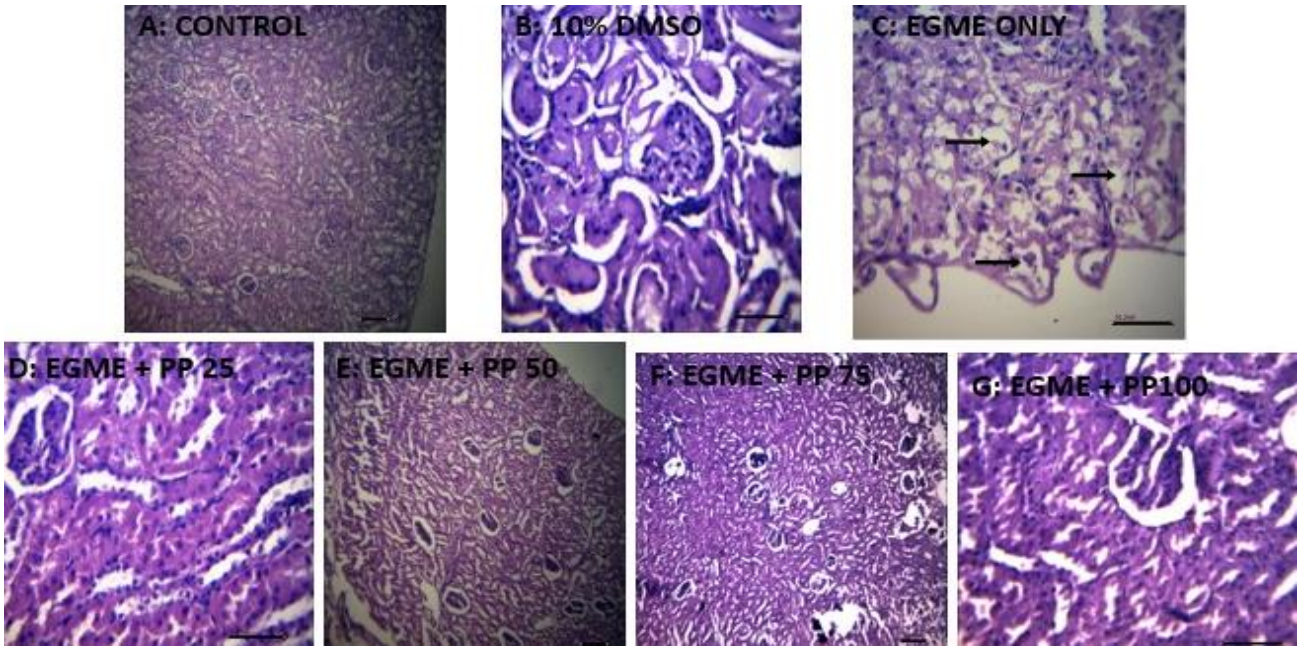

Plate 3:
Photomicrographs of the kidney sections showing the effect of co-administration of EGME and *P. pinnata*:- A, B and D - G- No lesions; **C**-There is a severe diffuse tubular degeneration and necrosis, especially below the capsule

DISCUSSION

The investigation showed that co-treatment with *P. pinnata* methanol leaf extract barred the perturbations of EGME in the liver and kidney at moderate doses.

The percentage weight gain in the EGME only treated group and that co-administered with EGME and *P. pinnata* methanol leaf extract at 25 mg/kg dose was reduced. Similarly, the relative organ weight had the same presentation. These are signs of toxicity, revealing that *P. pinnata* methanol leaf extract did not prevent the deleterious effect of EGME at that dose. In the groups co-administered with EGME and *P. pinnata* methanol leaf extract at 50, 75 and 100 mg/kg doses, the percentage weight gain and relative organ weights of the liver and kidney were not affected. This implies that at those doses the *P. pinnata* methanol leaf extract barred the adverse effect of EGME.

Albumin is a protein produced in the liver that assists with the transportation of fatty acids in the plasma including a host of other functions (Soeters and de Leeuw, 2021). In the macrophage-monocyte system, bilirubin is generated by the hydrolysis of haemoglobin to biliverdin and subsequently to bilirubin. Bilirubin is then transported via the plasma to the liver from which bilirubin diglucuronide is formed and subsequently released into the bile. Hence, bilirubin level serves as an indicator of liver and bile tract function (Washington and Hoosier, 2012). Administration of EGME lowered the albumin level and elevated the bilirubin level in

the liver. Co-administration with *P. pinnata* prevented the effect at 50, 75 and 100 mg/kg doses with the exception of the co-administration at the 25 mg/kg dose. This shows that the deleterious effect of EGME was douced at those doses, and indicates that the function of the liver is preserved and enhanced in the presence of the toxicant.

The activities of alanine aminotransferase, aspartate aminotransferase alkaline phosphatase, and gamma-glutamyl transferase are all indicators of the function of the liver. Alanine aminotransferase (ALT), formerly known as serum glutamate pyruvate transaminase (SGPT), functions in a transamination reaction by catalyzing the transfer of an α –amino group between α-ketoglutarate and alanine to generate glutamate and pyruvate, respectively. ALT is found in serum and organs with it being most abundant in the liver (Washington and Hoosier, 2012). It may be elevated in the light of biliary duct and liver damage, hepatitis, myopathy and congestive heart failure (Washington and Hoosier, 2012). Aspartate aminotransferase (AST), formerly known as serum glutamate oxalate transaminase (SGOT), is an enzyme that catalyzes the transamination reaction between α-ketoglutarate and aspartate to form glutamate and oxaloacetate respectively. With the exception of the bone, AST is found in all tissues and is highest in the skeletal muscle and liver. AST activity is elevated after neoplasia, trauma, infection, bruising and necrosis of the liver or muscle (Washington and Hoosier, 2012). Elevated activities of ALT and AST in the EGME only group tend to point to the fact that there is liver damage. Alkaline phosphatase is a metalloenzyme which is membrane bound, and is made up of three isozymes which are tissue specific. One of the isozymes is abundant in the hepatic tissue (Sharma *et al*., 2014). At high optimum pH (pH 9-10), it catalyzes the hydrolysis of monophosphate esters (in molecules such as proteins and nucleotides) with the concomitant release of inorganic phosphate (Sharma *et al*., 2012; Washington and Hoosier, 2012). Gamma-glutamyl transferase (GGT) has multiple catalytic functions including the transfer of gamma-glutamyl moiety to amino acids and short peptides and hydrolysis of reduced glutathione (GSH) to cysteinylglycine and gamma-glutamyl moiety in GSH conjugate metabolism (Anadon *et al*., 2014). Elevated GGT in the serum is an indicator of hepatobiliary insult including cholestasis and biliary effect, although it is also expressed in the bile ducts, kidney and pancreas. Also, it may be a biomarker of severe adverse drug reactions (Anadon *et al*., 2014). The EGME only treated group presented increased activities of ALP and GGT. This evidently suggests that there is insult on the function of the liver which may involve hepatobiliary dysfunction and cholestasis, characterized by reduced or paused bile flow which leads to the accumulation of bile in the liver and bloodstream, resulting in itching and jaundice (Cleveland Clinic, 2022). Co-administration with EGME and *P. pinnata* significantly reduced the toxic effect at 50, 75 and 100 mg/kg doses, except at the 25 mg/kg dose, on the activities of ALT, AST, ALP and GGT. Thus, showing that *P. pinnata* methanol leaf extract has the capacity to enhance liver function, in the light of exposure to EGME, at moderate doses. This observation is akin to the report of Bardi *et al*. (2014) where they administered thioacetamide to Sprague Dawley rats and co-treatment with *Andrographis paniculata* ethanol leaf extract reduced the effect. Moreover, this is similar to the documentation of Abdou *et al*. (2012) who showed that sesame oil barred the effect of cypermethrin on the liver function parameters and the antioxidant parameters in rats.

Sodium, potassium, chloride, calcium, and phosphate ions are all electrolytes found in the kidney. The kidney helps to maintain balance in the concentrations of these electrolytes. They help maintain water balance, regulate nerve and muscle function and acid-base balance (Lewis, 2021). With the exception of sodium ion, the concentrations of all the other electrolytes were elevated upon administration of EGME only and this was prevented upon co-treatment with *P. pinnata* at the doses of 50, 75 and 100 mg/kg with the exception of the 25 mg/kg dose. This is in tandem with Marhoume *et al*. (2021) who observed that co-administration with polyphenol-rich extracts of *Rubia tinctorum* reduced the effect of ethylene glycol and ammonium chloride on the electrolytes.

Urea, also called blood urea nitrogen (BUN) when measured in the blood, is also a non-protein nitrogenous waste product that is a byproduct of protein metabolism and an index for renal function because it is excreted from the body via the kidney (Salazar, 2014). Creatine supplies the muscles with energy and creatinine is the non-protein nitrogenous waste product of creatine. Creatinine is removed from the body by the kidney. Therefore it is a measure of the function of the kidney (Salazar, 2014). Uric acid is the final product of oxidation in purine metabolism which is excreted by the kidney (Giordano *et al*., 2015). It has been shown that elevated levels of urea, creatinine, and uric acid are associated or may be associated with impaired kidney function which plays a key role in the excretion of these waste products (Salazar, 2014; Giordano *et al*., 2015; Gounden *et al*., 2021). The most common renal vascular disease or damage is nephrosclerosis which is characterized by damage to blood vessels, glomeruli and tubulointerstitium (Vaidya and Aeddula, 2024). Therefore, the elevated levels of these products which was caused by the administration of EGME only and was barred by co-administration with *P. pinnata* at 50, 75 and 100 mg/kg doses but not at the 25 mg/kg dose, again shows that *P. pinnata* methanol leaf extract has the capacity to protect the kidney against damage from EGME, at moderate doses. These observations were similar to that of Romi *et al*. (2017) who reported an increase in the plasma levels of urate and creatinine upon administration of urate which was prevented by treatment with allopurinol, and that of Ogundipe *et al*. (2016) where aqueous leaf extract of *Ocimum gratissimum* was used to reverse the effect of gentamicin on the urine and plasma levels of urea and creatinine. Also, it is akin to the demonstrations of Abdou *et al*. (2012) who showed that sesame oil barred the perturbations in the kidney upon exposure to cypermethrin in rats. Therefore, co-administration with EGME and *P. pinnata* methanol leaf extract at 50, 75 and 100 mg/kg doses circumvented the reduced concentration of Na+ and increased concentrations of K+, Cl-, Ca2+, PO42-, urea, creatinine and uric acid caused by exposure to EGME, except at the dose of 25 mg/kg. Thus showing that *P. pinnata* methanol leaf extract protect the kidney from damage as a result of exposure to EGME. All of these results were supported by the histopathology report where varying lesions were observed in the liver and kidney for the EGME only treated group and

the group co-administered with EGME and *P. pinnata* methanol leaf extract at 25 mg/kg. This shows that *P. pinnata* methanol leaf extract had the capacity to protect the organs at 50, 75 and 100 mg/kg doses. The limitation of the study is that it was conducted using animals. Primate and human studies may be necessary to support the findings.

In conclusion, *Paullinia pinnata* methanol leaf extract protects the liver and kidney from the deleterious effect as a result of exposure to EGME, at moderate doses

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REFERENCES

Abdou, H.M., Hussien, H. and Yousef, M.I. (2012). Deleterious effects of cypermethrin on rat liver and kidney: Protective role of sesame oil. *J. Environ. Sci. Health* B 47 (4): 306-314.

Adeyemo-Salami, O.A. (2020). The medicinal properties of *Paullinia pinnata* Linn. leaves. *Int. J. Phytomed*. 12 (2): 019-025.

Adeyemo-Salami, O.A. (2021). Recent trends in ethylene glycol monomethyl ether research. In: Bhowmik, P.K. (ed.). New Innovations in Chemistry and Biochemistry. Vol. 6, Chapter 9, Book Publishers International, U.K., pp. 110-123.

Adeyemo-Salami, O.A., Kolade, D.S. and Akande, L.O. (2024). Investigation into the potential of *Paullinia pinnata* (Linn.) methanol leaf extract against toxicity by ethylene glycol monomethyl ether in Wistar rats. *NJBMB* 39 (2): 106-112.

Adeyemo-Salami, O.A. and Makinde, J.M. (2013). Acute and sub- acute toxicity studies of the methanol extract of the leaves of *Paullinia pinnata* (Linn.) in Wistar albino mice and rats. *Afr. J. Med. Med. Sci*. 42 (1): 81- 90. PMID: 23909098.

Anadon, A., Castellano, V. and Martinez-Larranaga, M.R. (2014). Biomarkers of toxicology. In: Biomarkers of drug toxicity. Academic Press, U.S.A, pp. 593-607.

Bardi, D.A., Halabi, M.F., Hassandarvish, P., Rouhollahi, E., Paydar, M., Moghadamtousi, S.Z., Al-Wajeeh, N.S., Ablat, A., Abdullah, N.A. and Abdulla, M.A. (2014). Andrographis paniculata leaf extract prevents thioacetamide-induced liver cirrhosis in rats. *PLOS One*. 9, e109424.

Bendjeddou, M. and Khelili, K. (2014). The toxic effect of the ethylene glycol monomethyl ether (EGME) in male rabbit. *Ann. Biol. Res.* 5(3): 8-15.

Burkill, HM. (2000):.The useful plants of West Tropical Africa. Families S-Z. Royal Botanic Gardens, Kew.

Cleveland Clinic (2022). Cholestasis. https://my.clevelandclinic.org/health/diseases/ 24554-cholestasis (Accessed April 1, 2025).

Giordano, C., Karasik, O., King-Morris, K. and Asmar, A. (2015). Uric acid as a marker of kidney disease: Review of the current literature. *Dis. Markers*. 2015: 382918.

Gounden, V. Bhatt, H. and Jialal, I. (2021). Renal function tests. StatPearls Publishing, U.S.A.

Lewis III, J.L. (2022). Overview of electrolytes. https://www.msdmanuals.com/home/hormonal-and-metabolic-disorders/electrolyte-balance/overview-of-electrolytes.

Marhoume, F.Z., Aboufatima, R., Zaid, Y., Limami, Y., Duval, R.E., Laadraoui, J., Belbachir, A., Chait, A. and Bagri, A. (2021). Antioxidant and polyphenol-rich ethanolic extract of Rubia tinctorum L. prevents urolithiasis in an ethylene glycol experimental model in rats. *Molecules* 26: 1005.

Ogundipe, D.J., Akomolafe, R.O., Sanusi, A.A., Imafidon, C.E., Olukiran, O.S. and Oladele, A.A. (2016). Effects of two weeks administration of *Ocimum gratissimum* leaf on feeding pattern and markers of renal function in rats treated with gentamicin. *Egypt. J. Basic Appl. Sci*. 3: 219-231.

Romi, M.M., Arfian, N., Tranggono, U., Setyaningsih, W.A. and Sari, D.C. (2017). Uric acid causes kidney injury through inducing fibroblast expansion, Endothelin-1 expression, and inflammation. *BMC Nephrol*. 18: 326.

Salazar, J.H. (2014). Overview of Urea and Creatinine. Lab. Med. 45: e19-20.

Sharma, U., Pal, D. and Prasad, R. (2014). Alkaline Phosphatase: An overview. *Indian J.Clin. Biochem*. 29: 269-278.

Sharma, U., Singh, S.K. Pal, D., Khajuria, R., Mandal, A.K. and Prasad, R. (2012). Implication of BBM lipid composition and fluidity in mitigated alkaline phosphatase activity in renal cell carcinoma. *Mol. Cell. Biochem*. 369: 287-293.

Soeters, P.B. and de Leeuw, P.W. (2021). The underlying metabolism of hypoalbuminemia and its clinical effects. In: Reciprocal translation between pathophysiology and practice in health and disease. Academic press, U.S.A, pp. 151-165.

Takei, M., Ando, Y., Saitoh, W., Tanimoto, T., Kiyosawa, N., Manabe, S., Sanbuissho, A., Okazaki, O., Iwabuchi, H., Yamoto, T., Adam, K.P., Weiel, J.E., Ryals, J.A., Milburn, M.V. and Guo, L. (2010). Ethylene glycol monomethyl ether-induced toxicity is mediated through the inhibition flavoprotein dehydrogenase enzyme family. *Toxicol. Sci*. 118 (2): 643-652.

Vaidya, S.R. and Aeddula, N.R. (2024). Chronic Kidney Disease. https://www.ncbi.nlm. nih.gov/books/NBK535404/ (Accessed April 1, 2025).

Washington, I.M. and Hoosier, G.V. (2012). Clinical Biochemistry and Hematology. In: Suckow, M.A., Steven, K.A. and Wilson, R.P. (eds.). The laboratory rabbit, guinea pig, hamster and other rodents. *Elsevier, U.S.A*, pp.63-68.