Trop J Nat Prod Res, July 2024; 8(7): 7820-7827 **ISSN 2616-0684 (Print)**
ISSN 2616-0692 (Electronic)

Tropical Journal of Natural Product Research

Available online at https://www.tjnpr.org

Original Research Article

Animal model assessment of HELLP Syndrome during Treatment with Methanol Plant Extracts of *Jatropha curcas, Alchonnea cordifolia,* and *Secamone afzelii*

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ARTICLE INFO

Article history:
Received 21 April 2023
Revised 08 May 2024
Accepted 19 May 2024
Published online 01 August 2024

ABSTRACT

In treating preeclampsia-induced wistar rats, this study examined the effects of methanolic plant extracts of *Jatropha curcas*, *Alchonnea cordifolia*, and *Secamone afzelii*, respectively, on the evaluation of HELLP syndrome. Fifteen sets of age-matched female Wistar rats were employed, with one serving as a control group. The Adriamycin Model was used to induce preeclampsia. The rats were then administered 50, 100, and 200 mg/kg of the extracts. Another group was administered methyl DOPA (at 10 mg/kg). At the end of the study, the arts were anesthetized and sacrificed humanely. Platelet counts, hemoglobin, and liver enzymes were measured following standard procedure. The study found that extracts of plant extracts did not cause any toxic effects on test animals, and there was no mortality at 5000 mg/kg. Aspartate transaminase levels increased during preeclampsia, but *J. curcas* and *A. cordifolia* extracts at low-to-moderate concentrations reduced these levels. Post-partum AST levels decreased from 60.7 U/l during preeclampsia to 25.3 - 39.2 U/l. There were no significant alterations in total protein levels ($p>0.05$). Preeclamptic Wistar rats treated with theextracts showed higher packed cell volume and platelet counts during preeclampsia. Upon administration of 100 mg/kg *J. curcas* and 200 mg/kg *S. afzelii*, the prognosis of preeclampsia was generally better after postpartum than during the third trimester.The study reveals that preeclampsia treatment with *J. curcas*, *A. cordifolia*, and *S. afzelii* extracts improves liver enzymes, total protein levels, packed cell volume, and platelet counts, suggesting potential therapeutic options.

***Keywords*:** HELLP Syndrome, Foetus, Preeclampsia, Plant Extracts, Pregnancy.

Introduction

One of the known illnesses afflicting pregnant women is preeclampsia (PE), which is typified by high blood pressure and an abundance of protein in the urine. According to Gizachew*et al*.,[1] it has a major impact on maternal and fetal disease and mortality worldwide. The only effective therapy for this condition, which mostly affects humans, is birthing during pregnancy. Although placental trophoblast cells from the fetus rebuild the mother's uterine arteries irregularly in most cases of PE, the disease is probably multifactorial.[2] Han*et al*.[2]stated that PE is a pregnancy-related illness that affects 6-8% of pregnancies worldwide. Swelling, proteinuria (≥0.3 g/day), and elevated blood pressure (≥140/90 mmHg) are the first symptoms. Symptoms can last up to six weeks after giving birth and often start around the 20th week of pregnancy. PE can progress to eclampsia, a severe illness marked by convulsions that might endanger the mother's and the unborn child's lives in rare circumstances.[3] Hemolysis, elevated liver enzymes, and low platelet count, or HELLP syndrome, is a well-known side effect linked to PE and eclampsia. But development may happen without regard to these circumstances.[4]Elçuk*et al*.[4] found that the prevalence of HELLP syndrome in pregnancies complicated by PE and eclampsia ranges from2.0 - 19.3 percent. HELLP syndrome can appear before, or after childbirth. happens in one-third of the instances throughout the postpartum phase. However, when HELLP syndrome appears after labor, pulmonary edema, as well as renal failure are more likely.[5] Individuals diagnosed with HELLP syndrome may exhibit a range of symptoms and indications, but none of which are unique to the illness, along with significant PE and eclampsia. HELLP syndrome patients may have consequences including disseminated intravascular coagulation (DIC), placental abruption, acute renal failure (ARF), pulmonary edema, liver hematoma, and retinal detachment. This is one of the reasons for the reports of higher rates of newborn and maternal death.[6] Restrictions to fetal growth or slower maturation may result from the disorder's impact on the blood arteries entering the placenta, which restricts the distribution of oxygen, nutrients, and blood to the developing foetus. HELLP syndrome, which is characterized by widespread hemolysis, increased levels of unbound adult hemoglobin (Hb), low platelet counts, and high levels of liver

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Citation: Atoe K, Idu M, Ikhajiagbe B, Bakre AG, Adeyemi O, Omenai SA, Egbo HO, Omozuwa SO and Edenya O.O. Animal model assessment of HELLP Syndrome during Treatment with Methanol Plant Extracts of *Jatropha curcas*, *Alchonnea cordifolia*, and *Secamone afzelii*. Trop J Nat Prod Res. 2024; 8(7): 7820 – 7827 https://doi.org/10.26538/tjnpr/v8i7.28

Official Journal of Natural Product Research Group, Faculty of Pharmacy, University of Benin, Benin City, Nigeria

enzymes, can develop from PE. Substantial dangers may result from this disorder affecting the mother as well as the child.[7] Although partial or inadequate HELLP syndrome comprises just a few of the triad's aspects (H, EL, or LP), a comprehensive identification of HELLP syndrome requires the presence of all three core criteria.[8,9] The woman and her unborn child are at great danger from HELLP syndrome, therefore it's important to think carefully about when and how to deliver the baby since several issues can occur and make diagnosis and treatment difficult. [10,11]

Numerous *in vitro* and animal models have been employed to investigate different aspects of preeclampsia (PE), particularly focusing on abnormal trophoblast invasion, vascular injury in the mother, and disrupted immune interactions between the mother and fetus.[12] Despite the slow pace of progress, research on the pathophysiology and treatment of PE continues to advance the field. There remains a critical need for new ideas, innovative disease models, and creative research approaches to effectively address this complex condition.[13] Thus, one of the most important objectives in the sector is the creation of innovative PE therapies. Only a mix of fundamental investigation employing experimental animals as well as human clinical studies will determine therapeutic targets for PE therapy. To identify possible biomarkers and pathogenic variables linked to the course of PE, human studies are essential.[5,14] Nevertheless, results from human research are sometimes correlational and might not clearly show cause-and-effect linkages, which makes it difficult to conduct a thorough analysis of the quantitative significance of time-dependent processes in the illness. Conversely, given its intrinsic drawbacks, animal model experiments allow scientists to carry out evidence of concept tests. These investigations[15,16] enable researchers to evaluate whether certain variables detected in women with PE can indeed generate hypertension and other symptoms of the condition.

Decreased platelets counts and elevated leukocyte counts are observed in women experiencing PE.[17] The number of lymphocytes increases throughout the third trimester. During pregnancy, especially in the initial trimester, complete monocytosis develops; however, as the baby develops, the severity of the condition decreases. In order to help prevent the expulsion of a fetal allograft, monocytes infiltrate the decidual tissue between the seventh and twentieth week of pregnancy, perhaps during PGE2-mediated immunosuppression. The proportion of monocytes to lymphocytes rises noticeably during pregnancy. In contrast to common assumption, basophil or eosinophil counts are not significantly changed during pregnancy.[18]PE has a major negative impact on pregnancies that has to be handled right away. There are several disadvantages to PE therapy as it is now provided. Antihypertensive drugs may benefit mothers even when there is a chance they might damage the fetus. Even when the fetus is still undeveloped, it is frequently suggested to give birth quickly in order to save the mother's life. There have been several fetuses reported to have Neonatal Respiratory Distress Syndrome (NRDS) cases. There have been suggestions for alternative treatment approaches, such as the use of plant extracts.[19,20]

Although, when used as prescribed, herbal treatments are usually seen to be safe, there have been very few instances when they have been linked to serious adverse effects. Misuse of herbs or possible drug interactions between herbal supplements and prescription drugs can put pregnant women in danger or seriously damage the developing fetus. The lack of strict laws governing herbal medications, in contrast to contemporary treatments, is concerning considering their increasing usage, particularly in pregnancy. Although there is little information on using certain herbs to treat PE, some may be able to control associated conditions including proteinuria and hypertension. When used improperly, herbal medicines can have unexpected side effects or seriously harms the developing fetus when used with pharmaceutical medication.[21] Compared to contemporary medications, herbal remedies are not subject to the same stringent standards, which poses safety concerns, especially when using them more often during pregnancy. While research on particular herbs in the treatment of PE is limited, some may be able to assist control symptoms associated with PE, such as proteinuria and high blood pressure. Herbs are used by Nigerians to treat a range of pregnancy-related ailments. Numerous plant extracts have been linked to the treatment of PE, such as *Secamone afzelii*, *Alchonnea cordifolia*, and *Jatropha curcas*.[21] Therefore, this study aimed to assess HELLP syndrome as a prognostic tool using animal model treated with methanolic plant extracts of *S. afzelii, A. cordifolia, and J. curcas*.

Materials and Methods

Collection and identification of plant samples

Fresh plant samples were collected in the month of January of 2019, from a farm that dealt with phytomedicinals in Benin City. This was the Frist Generation farms at Ward 6, Iguosula, Benin City. Upon collection, the plants were presented for sample identification at the Herbarium Unit of the Department of Plant Biology and Biotechnology of the University of Benin, Benin City, with the following voucher specimen numbers; *Secamone afzelii* (UBH-S566), *Alchonnea cordifolia (*UBH-A560), and *Jatropha curcas*(UBH-J404).The plant samples were thereafter washed thoroughly, and then rinsed in several changes of distilled water. They were then subjected to air drying, and thereafter ground into a powder using a kitchen blender (model - Panasonic® MX-GX1021WTZ). The powder samples were weighed, and thereafter, about 100 g of this sample was thoroughly extracted by submerging it in 200 ml of methanol. This was allowed to stay for twelve hours. Afterwards, the extracts that resulted were filtered through a 125-mm No. 42 Whatman Filter and kept ready for use in the laboratory.

Study design

The sets of Wistar rats used in this study were all females within he weight range of 200 to 256 g, amounting to a mean of 237 g. They were all age-matched (±3 days). The Wistar rats were then kept in a well-ventilatedsetting with daily variations in light and darkness during the month of May 2019. The rats were allowedunobstructed access to drinkable water, which was always replaced from a nearby tap. The pH range for the water offered to the rats was between 6.8 and 7.2, with a mean of 6.96. Additionally, a standard meal ration that consisted of 0.35 g NaCl, 20 g protein, and 1.17 g arginine per 100 g of food was provided daily to the experimental rats. Before the experiment started, they had a week to get used to their environment.

The wistar rats were thereafter split into fifteen (15) groups, each with six (6) rats, at random for this investigation. Whereas the first group was the control with no administration of treatment regimen, the other 15 groups were induced through the Adriamycin Model to become preeclamptic so that extracts as well as a standard drug would be administered (Table 1).

Table 1: List of various experimental and treatment groups in the current study

Study groups	Explanation of group settings
G1	Control (normotensive)
G2	Normotensive, administered *J. curcas*
G3	Normotensive, administered *A. cordifolia*
G4	Normotensive, administered *S. afzelii*
G5	Preeclamptic, only
G6	Preeclamptic, administered methyl DOPA (at 10 mg/kg)
G7	Preeclamptic, administered *J. curcas* (50 mg/kg)
G8	Preeclamptic, administered *J. curcas* (100 mg/kg)
G9	Preeclamptic, administered *J. curcas* (200 mg/kg)
G10	Preeclamptic, administered *A. cordifolia (*50 mg/kg)
G11	Preeclamptic, administered *A. cordifolia (*100 mg/kg)
G12	Preeclamptic, administered *A. cordifolia (*200 mg/kg)
G13	Preeclamptic, administered *S. afzelii* (50 mg/kg)
G14	Preeclamptic, administered *S. afzelii* (100 mg/kg)

G15	Preeclamptic, administered *S. afzelii* (200 mg/kg)

Induction of preeclampsia
Preeclampsia (PE) was induced in the female wistar rats following the Adriamycin Model as developed by Podjarny et al.[22]Following this protocol, the rats, under mild ether-based anesthesia, were administered Adriamycin (Adriablastina, Abic)intraperitoneallyat a dose of 3.5 mg/kg body weight.Injection was via the superficial femoral vein. Two weeks after the administration of Adriamycin, the rats when thereafter allowed to mate with selected fertile male counterparts for 4 days. To adequately indicate the onset of gestation, the vaginal smear was examined to show presence of spermatozoa.

Management of experimental animals
The care and management of the wistar rats were in accordance with laid down procedures and protocols.[23]The animal cages were cleaned whenever and where necessary.

Collection of vital organs for investigation
Upon reception of the last dosage of the various extracts, the rats were prepared to be humanely sacrificed. They had to be firstly anesthetized. This was done with aid of chloroform.Care was ensured during sacrifice of the rats in the study. Thereafter, organs of interest were collected following standard procedure and assayed accordingly.[23]

Determination of Liver Enzymes, Haematocrit and Platelet counts
Liver enzymes were measured using plasma, whereas haematocrit and platelet counts were measured from whole blood collected in an EDTA container after the animals were sacrificed. The Plasma was extracted from whole blood collected into a heparinized bottle, which was then centrifuged at 3000rpm for15minutes. The liver enzymes aspartate transaminase and alanine transaminase were measured using a spectrophotometer, and Randox Laboratory Limited provided the kits. The approach used was the standard operational assay. The haematocrit and platelet counts were measured using the Auto Haematology Analyzer Model XrHA640.

Ethical issues
Study was conducted after ethical approval was received from the Research and Ethics Committee of the Faculty of Life Sciences, University of Benin, Benin City;reference L519017, dated March 7, 2019.

Statistical analysis
The analysis of the data was done with SPSS version 20. Results presented showed mean values from 3 replications. Means were separated with aid of least significant different values at p = 0.05.

Results and Discussion

The study investigated the potential therapeutic effects of methanolic plant extracts of *Jatropha curcas*, *Alchornea cordifolia, and Secamone afzelii* on preeclamptic Wistar rats. This study sought to evaluate the effects of these extracts on liver function, hematological parameters, and prognosis based on HELLP syndrome criteria in preeclamptic rats. The study found that methanolic plant extracts did not pose acute toxicity, with zero mortality observed in test animals at doses up to 5000 mg/kg (Figure 1). This finding suggests that these plant extracts may be safe for use in the tested animal model at the concentrations investigated. Table 2 shows the levels of liver transaminase enzymes and total proteins in the third trimester and postpartum. Aspartate transaminase levels increased significantly during PE, rising from 37.0 U/l to 54.8 U/l when compared to controls. However, using plant extracts at low-to-moderate concentrations reduced AST concentrations to 35.1 U/l and 34,5 U/L when 50 mg/kg *J. curcas* and *A. cordifolia* were administered throughout the third trimester, respectively. Similarly, post-partum AST levels decreased from 60.7 U/l during PE to 25.3 - 39.2 U/l. A significant reduction in ALT levels (from 37.0 U/l to 54.8 U/l during PE to 35.1 U/l and 34.5 U/l after therapy) suggests improved liver function. However, total protein levels remained stable, indicating no significant disruption in overall protein balance. ALT serves as a sensitive indicator of liver damage since it is primarily located in the cytoplasm of hepatocytes, providing a more quantitative assessment of liver damage than AST.[21] PE induced in Wistar rats resulted in elevated levels of liver enzymes, including aspartate transaminase (AST) and alanine transaminase (ALT), which are markers of liver damage. This is consistent with the known hepatic involvement in PE. However, treatment with low-to-moderate concentrations (50-200 mg/kg) of plant extracts significantly reduced AST and ALT levels, suggesting an improvement in liver function.

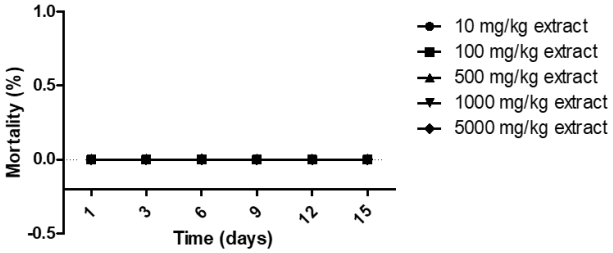
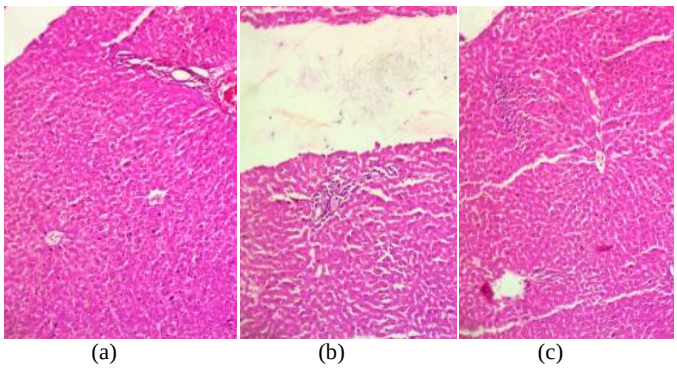
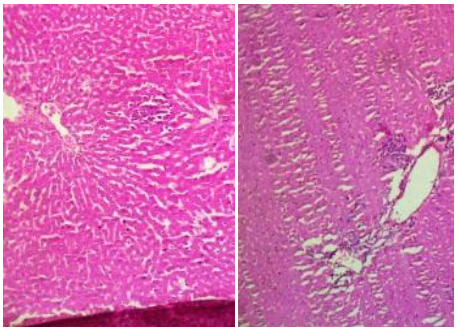


Figure 1: Results of acute toxicity study**.** *The graph shows that all points are superimposed on the other, an indication of zero mortality irrespective of the extract concentration during the 1st to the 15th day.*

Liver histology in preeclamptic rats treated with the plant extracts revealed normal liver sections, while untreated preeclamptic rats exhibited congested sinusoids. These findings indicate that the plant extracts may have hepato-protective effects, potentially ameliorating liver damage caused by PE. These findings align with Ngueguim*et al*.[24], who observed a similar reduction in transaminase levels in rats given an aqueous extract of *Dichrocephala integrifolia* alongside ethanol, suggesting the protective role of bioactive compounds such as tannins and saponins.[24,25]Although liver histology in preeclamptic Wistar rats revealed congested sinusoids during the third trimester, liver sections were normal when preeclamptic rats were given low-to-medium dosages of methnolic extracts of *Jatropha curcas*, *Alchonnea cordifolia*, and *Secamone afzelii* (Plate 1).



(a) (b) (c)



(d) (e) Mag. x10

Plate 1: Histological slides of preeclampticwistar rats treated with with methanolic plant extracts of *Jatropha curcas*, *Alchonnea cordifolia*, and *Secamone afzelii.*

The results show (a) normal liver, (b) liver with expansion of portal tract by lymphocytes, (c) liver with lymphocytic infiltration of sinusoid, (d) liver with portal tract expansion and inflammation; and (e) and liver with severe inflammation, periportal, hepatic necrosis.

The histopathological evaluation of preeclamptic Wistar rats treated with methanolic plant extracts of *Secamone afzelii*, *Alchonnea cordifolia*, and *Jatropha curcas* revealed periportal inflammation (mixed population) in preclampsia treated with *Secamone afzelii* and *Jatropha curcas*, congested hepatic veins primarily in rats administered *Secamone afzelii*, and also the central veins in rats treated with *Jatropha curcas* and *Secamone afzelii* (Table 3). Nevertheless, rats receiving *Secamone afzelii* treatment and those with induced PE were shown to have clogged sinusoids. These results imply that the liver health of PE patients may be affected by treatment with these plant extracts.

Preeclamptic wistar rats treated with methanolic plant extracts of *Jatropha curcas*, *Alchonnea cordifolia*, and *Secamone afzelii* had higher packed cell volume and platelet counts (Table 4). During PE, Packed cell volume increased by at least 24% in both the third trimester and afterwards when low doses (50-100 mg/kg). Similarly, despite the fact that PE produced a 50% decrease in platelet counts, administration of low-to-medium doses of test plant extracts significantly improved the outcomes. The administration of 50 mg/kg of *S. afzelii* to preeclamptic Wistar rats increased platelet counts from 349.1 $x10^3$ to 720.4 $x10^3$.

It was critical to assess the induced prognosis of PE based on HELLP Syndrome, where positive analyte differential values were compared to the control animal (Table 5). Using outcome of symptoms to determine, results showed that when all extracts were used, there was an improvement in prognosis. However, when 100 mg/kg *J. curcas* and 200 mg/kg *S. afzelii* were administered, the best results were seen at post-partum. In general, the prognosis of the disease following treatment with the plant extracts, was better after postpartum than throughout the third trimester.

Table 2: Liver transaminase enzymes and total proteins at 3rd trimester and postpartum

Treatments	3rd trimester			Post-partum		
	Aspartate trans-aminase (U/l)	Alanine transaminase (U/l)	Total protein (g/dl)	Aspartate transaminase (U/l)	Alanine transaminase (U/l)	Total protein (g/dl)
Control	37.0	20.0	11.6	39.6	21.4	11.8
Normotensive, administered *J. curcas*	39.5	19.1	10.4	40.0	21.3	10.1
Normotensive, administered *A. cordifolia*	39.4	17.4	9.6	31.7	21.3	11.2
Normotensive, administered *S. afzelii*	46.2	19.1	10.4	37.9	15.6	12.2
Preeclamptic, only	54.8	41.2	9.6	60.7	47.3	11.9
Preeclamptic, administered methyl DOPA (at 10 mg/kg)	31.1*	13.7*	10.7	34.7*	21.3*	13.6
Preeclamptic, administered *J. curcas* (50 mg/kg)	35.1*	15.1*	12.7	34.7*	11.3*	11.0
Preeclamptic, administered *J. curcas* (100 mg/kg)	39.9	15.6*	12.9	26.4*	10.7*	11.4
Preeclamptic, administered *J. curcas* (200 mg/kg)	38.8	15.1*	11.9	39.2*	17.7*	11.1
Preeclamptic, administered *A. cordifolia (*50 mg/kg)	34.5*	14.1*	12.2	28.7*	9.4*	11.5
Preeclamptic, administered *A. cordifolia (*100 mg/kg)	40.5	15.3*	11.4	30.4*	11.1*	11.1
Preeclamptic, administered *A. cordifolia (*200 mg/kg)	38.6	15.6*	11.1	27.9*	13.0*	10.5
Preeclamptic, administered *S. afzelii* (50 mg/kg)	47.3	16.4*	12.9	25.3*	16.2*	11.9
Preeclamptic, administered *S. afzelii* (100 mg/kg)	39.3	14.4*	12.5	29.6*	14.8*	10.1
Preeclamptic, administered *S. afzelii* (200 mg/kg)	31.5*	12.6*	12.3	27.1*	7.4*	11.8
LSD (0.05)	11.3	19.1	4.6	21.3	11.5	3.2
F-test	1.353	9.537	1.875	2.411	5.247	0.949
p-value	0.236	0	0.073	0.021	0.000	0.523

In-PreEc – Induced preeclampsia;

**Preeclampsia means with asterisks superscript significantly from the negative control (Induced PreEc, no treatment provided) (p<0.05).*

Preeclampsia (PE) caused a decrease in packed cell volume (PCV) and platelet counts, consistent with the hematological alterations seen in the condition. However, administration of the plant extracts, particularly *Secamone afzelii*, improved both PCV and platelet counts significantly. This improvement suggests that these extracts may help mitigate the hematological complications associated with PE despite a 50% reduction in platelet counts. This is consistent with Yücel and Ustun,[26] who reported higher platelet counts in patients with severe PE compared to controls. The increase in packed cell volume and platelet counts indicates that the plant extracts could enhance the

hematological profile of preeclamptic patients.[26,27,28] The study also assessed PE prognosis

using HELLP syndrome indicators. Prognosis was evaluated based on positive differential values of analytes compared to control animals. Treatments with the plant extracts led to improved prognostic indices during both the third trimester and postpartum. In particular, the extracts were effective at improving prognosis at higher doses, such as 100 mg/kg *Jatropha curcas* and 200 mg/kg *Secamone afzelii*. These results suggest that plant extracts may provide therapeutic benefits in managing PE and its associated complications. This study is pioneering in its investigation of *J. curcas* and *S. afzelii* extracts on PE prognosis. Further research is required to confirm these results and to understand the underlying mechanisms at play, as well as to establish optimal dosing regimens for potential clinical applications.[28,29]

Table 3: Histological assessment of preeclamptic wistar rats treated with with methanolic plant extracts of *Jatropha curcas*, *Alchonnea cordifolia*, and *Secamone afzelii*

Groups	Liver	
	3rd trimester	**post-partum**
Control	Section shows normal hexagonal units of hepatocyte sheets disposed in cords, separated by sinusoidal channels which connects the peripheral portal tracts to the central vein.	Normal
Normotensive, administered *J. curcas*	Normal	Normal, but with congested central veins
Normotensive, administered *A. cordifolia*	Normal	Normal, but with congested central veins
Normotensive, administered *S. afzelii*	Normal	Normal
Preeclamptic, only	Section of the liver tissue show congested sinusoids	Normal but markedly distended central veins with congestion
Preeclamptic, administered methyl DOPA (at 10 mg/kg)	Few foci of hepatocellular necrosis (piece meal necrosis, dilated hepatic arteries) and areas of regeneration	Normal
Preeclamptic, administered *J. curcas* (50 mg/kg)	Section of liver tissue shows periportal inflammation (Lymphocytes around the portal traids) extending to surrounding sinusoids	Section of the liver shows mild periportal tract inflammation
Preeclamptic, administered *J. curcas* (100 mg/kg)	Section of the liver tissue shows periportal necrosis and expansion of portal tract by lymphocytic infiltrates. Also present are prominent congested distended central veins	Normal
Preeclamptic, administered *J. curcas* (200 mg/kg)	Marked periportal inflammation with lymphocytes extension into the sinusoid, with porto-central involvement.	Normal, but with few markedly distended congested central vessels
Preeclamptic, administered *A. cordifolia (*50 mg/kg)	Periportal inflammation (Periportal hepatitis) interphase hepatitis, porto-central inflammation and piece meal necrosis	Normal
Preeclamptic, administered *A. cordifolia (*100 mg/kg)	Periportal inflammation with interface hepatitis.	Normal
Preeclamptic, administered *A. cordifolia (*200 mg/kg)	Sections of the liver tissue show hepatic necrosis with Periportal inflammation, bridging fibrosis, interphase hepatitis	Normal but with prominent distended and congested central vessels
Preeclamptic, administered *S. afzelii* (50 mg/kg)	Mild hepatocellular necrosis	Normal
Preeclamptic, administered *S. afzelii* (100 mg/kg)	Section shows hepatocellular necrosis, periportal inflammation (mixed population), congested hepatic veins majorly, along with the central veins	Normal hepatic plate with mild periportal inflammation and necrosis
Preeclamptic, administered *S. afzelii*	Hepatocellular necrosis, periportalinflammation (mixed	Sections of the liver shows normal hepatic plate

(200 mg/kg)	population), congested hepatic veins predominantly, and also the central veins. The sinusoids are also congested	with mild pericentral inflammation and fibrosis

In-PreEc – Induced preeclampsia

Table 4: Packed cell volume and platelet counts of preeclamptic wistar rats treated with with methanolic plant extracts of *Jatropha curcas*, *Alchonnea cordifolia*, and *Secamone afzelii*

Group	Packed cell volume (%)		Platelet counts ($x10^3$)	
	3rd trimester	Post-partum	3rd trimester	Post-partum
Control	45.79	41.46	600.7	549.5
Only Ext-A (No induced PreEc)	36.58	36.85	445.6	600.1
Only Ext-B (No induced PreEc)	41.19	40.1	743	354.8
Only Ext-C (No induced PreEc)	43.46	41.46	397.9	644.6
Induced PreEc, no treatment provided	30.23	33.33	349.1	361.2
In-PreEc + 100 mg/kg Methyldopa	44.00*	38.75	455.3*	498.2*
In-PreEc + 50 mg/kg J. curcas	40.22*	36.58	523.2*	530.3*
In-PreEc + 100 mg/kg J. curcas	39.95*	42.81*	551.1*	572.5*
In-PreEc + 200 mg/kg J. curcas	38.06*	41.19*	464.4*	560.4*
In-PreEc + 50 mg/kg A. cordifolia	38.21*	39.83	543.8*	445.2
In-PreEc + 100 mg/kg A. cordifolia	39.56*	39.29	561.5*	660.5*
In-PreEc + 200 mg/kg A. cordifolia	35.77	40.91*	659.6*	754.3*
In-PreEc + 50 mg/kg S. afzelii	37.12*	38.48	720.4*	514.0*
In-PreEc + 100 mg/kg S. afzelii	39.29*	41.73*	491.0*	446.7
In-PreEc + 200 mg/kg S. afzelii	37.66*	44.44*	563.6*	546.1*
F-test	0.624	0.659	1.225	0.803
LSD (0.05)	6.23	7.31	112.9	125.3
p-value	0.824	0.794	0.031	0.022

In-PreEc – Induced preeclampsia
Means on the same column with asterisks significantly differ from mean value obtained in the preeclamptic (untreated) group.

Table 5: Prognosis of preeclampsia based on HELLP Syndrome using positive differential values of the analytes compared to the control animal.

Group (3rd trimester)	PCV	PLT	AST	ALT		Prognosis index
Preeclamptic, only	**-15.56**	-251.6	17.8	21.2		1
Preeclamptic, administered methyl DOPA (at 10 mg/kg)	**-1.79**	-145.4	-5.9	-6.3		3
Preeclamptic, administered *J. curcas* (50 mg/kg)	**-5.57**	-77.5	-1.9	-4.9		3
Preeclamptic, administered *J. curcas* (100 mg/kg)	**-5.84**	-49.6	2.9	-4.4		2
Preeclamptic, administered *J. curcas* (200 mg/kg)	**-7.73**	-136.3	1.8	-4.9		3
Preeclamptic, administered *A. cordifolia (*50 mg/kg)	**-7.58**	-56.9	-2.5	-5.9		3
Preeclamptic, administered *A. cordifolia (*100 mg/kg)	**-6.23**	-39.2	3.5	-4.7		2
Preeclamptic, administered *A. cordifolia (*200 mg/kg)	**-10.02**	58.9	1.6	-4.4		3
Preeclamptic, administered *S. afzelii* (50 mg/kg)	**-8.67**	119.7	10.3	-3.6		3
Preeclamptic, administered *S. afzelii* (100 mg/kg)	**-6.5**	-109.7	2.3	-5.6		2
Preeclamptic, administered *S. afzelii* (200 mg/kg)	**-8.13**	-37.1	-5.5	-7.4		3

(post-partum)						
Preeclamptic, only	-8.13	-188.3	21.1	25.9		1
Preeclamptic, administered methyl DOPA (at 10 mg/kg)	-2.71	-51.3	-4.9	-0.1		3
Preeclamptic, administered *J. curcas* (50 mg/kg)	-4.88	-19.2	-4.9	-10.1		3
Preeclamptic, administered *J. curcas* (100 mg/kg)	1.35	23	-13.2	-10.7		5
Preeclamptic, administered *J. curcas* (200 mg/kg)	-0.27	10.9	-0.4	-3.7		4
Preeclamptic, administered *A. cordifolia (*50 mg/kg)	-1.63	-104.3	-10.9	-12		3
Preeclamptic, administered *A. cordifolia (*100 mg/kg)	-2.17	111	-9.2	-10.3		4
Preeclamptic, administered *A. cordifolia (*200 mg/kg)	-0.55	204.8	-11.7	-8.4		4
Preeclamptic, administered *S. afzelii* (50 mg/kg)	-2.98	-35.5	-14.3	-5.2		3
Preeclamptic, administered *S. afzelii* (100 mg/kg)	0.27	-102.8	-10	-6.6		4
Preeclamptic, administered *S. afzelii* (200 mg/kg)	2.98	-3.4	-12.5	-14		5

Prognostic index scale; 5 excellent, 4 very good, 3 good, 2 fair, 1 poor
**occurrence of low PCV, elevated liver enzymes and low platelet counts imply a poorly status of preeclampsia upon management of the disease condition with the experimental treatments.*

Conclusion

In the treatment of PE in Wistar rats, this study highlights the potential medicinal effects of methanolic plant extracts from *Jatropha curcas, Alchornea cordifolia, and Secamone afzelii*. In preeclamptic rats, the extracts enhanced liver histology and shown potential hepatoprotective benefits by reducing levels of liver enzymes such as ALT and AST. They demonstrated improvements in hematological indicators like as platelet counts and packed cell volume, indicating that they may be able to lessen the hematological problems related to PE. Interestingly, the extracts showed better results for HELLP syndrome, especially at larger doses.Plant extracts could offer a secure and practical method of treating PE and its side effects. To verify these results and comprehend the mechanisms of action, more study is necessary. To transform these plant extracts into effective PE therapies, it will be crucial to establish the best dosage schedules and investigate clinical uses.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article are original and that any liability for claims relating to the content of this article will be borne by them.

References

1 Gizachew A, Abebe T, Tadesse A. Preeclampsia and associated factors among pregnant women attending antenatal care in Dessie referral hospital, Northeast Ethiopia. BMC Pregnancy Child birth, 2015; 15 (73):1-11.
2 Han Y, Yang Z, Ding X, Yu H. Differences in Liver Injury and Trophoblastic Mitochondrial Damage in Different Preeclampsia-like Mouse Models. Chin. Med. J.. 2015;1 (1):1-2.
3 Atoe K, Idu M. Effects of methanol leaf extracts of selected plants on the plasma electrolytes levels in preeclamptic-induced wistar rats. Trop. J. Nat. Prod. Res. 2021; 5(10): 1863–1867
4 Elcuk NY, Odabas AR, Cetinkaya R, Tonbul HZ, San A. Outcomes of pregnancies with HELLP syndrome complicated by acute renal failure. Ren. Fail. 2000,22 (3), 319–327.
5 Rana S, Lemoine E, Granger JP, Karumanchi SA. Preeclampsia: pathophysiology, challenges, and perspectives. Circ. Res.2019;124:1094–112.
6 Sibai BM, Ramadan MK, Usta I, Salama M, Mercer BM, Friedman SA. Maternal morbidity and mortality in 442 pregnancies with hemolysis elevated liver enzymes, and low platelets (HELLP syndrome). Am. J. Obstet.Gynecol.1993,169, 1000–1006.
7 Schroeder BM. American College Of, O. and Gynecologists. ACOG practice bulletin on diagnosing and managing preeclampsia and eclampsia. American College of Obstetricians and Gynecologists. Am. Fam. Physician. 2002;66:330–331.
8 Barton JR, SibaiBM. Diagnosis and management of hemolysis, elevated liver enzymes, and low platelets syndrome. Clin.Perinatol. 2004, 31:807-33.
9 Martin JN Jr, Rose CH, Briery CM. Understanding and managing HELLP syndrome: the integral role of aggressive glucocorticoids for mother and child. Am J Obstet. Gynecol. 2006, 195:914-934.
10 Atoe K, Idu M, Ikhajiagbe B, Bakre AG. The influence of methanol extracts of some plant species used in the management of pregnancy-related symptoms on the reproductive parameters of pregnant wistarrats. Trop. J. Nat. Prod. Res. 2023; 7(12): 5658–5663.
11 Ertan AK, Wagner S, Hendrik HJ, Tanriverdi HA, Schmidt W. Clinical and biophysical aspects of HELLP-syndrome. J. Perinat. Med. 2002, 30:483-489.
12 Szabo S, Mody M, Romero R, Xu Y, Karaszi K, Mihalik N, Xu Z, Bhatti G, Fule T, Hupuczi P, Krenacs T, Rigo J Jr, Tarca AL, Hassan SS, Chaiworapongsa T, Kovalszky I, Papp Z, Than NG. Activation of villous trophoblastic p38 and ERK1/2 signaling pathways in preterm pre-eclampsia and HELLP syndrome. Pathol. Oncol. Res. 2015;21 (3):659-668.
13 Kathleen A, Pennington M, Schlitt L, Jackson C, Danny J. Pre-eclampsia: multiple approaches for a multifactorial disease. Dis. Model. Mech. 2012;5 (1):9–18.
14 McCarthy FP, Ryan RM, Chappell LC. Pro spective biomarkers in preterm preeclampsia: a review. Pregnancy Hypertens. 2018;14:72–8.
15 Phipps EA, Thadhani R, Benzing T, Karumanchi SA. Pre-eclampsia: pathogenesis, novel diagnostics and therapies. Nat. Rev. Nephrol.2019;15:275–89.
17 Abeer A, Alkredes Z. The significance of blood parameters in women with preeclampsia. Int. J. Sci. Eng. Res. 2018;9 (1):714-719.
16 Lekva T, Sugulle M, Moe K, Redman C, Dechend R, Staff AC. Multiplex analysis of circulating maternal cardiovascular biomarkers comparing preeclampsia subtypes. Hypertens. 2020;75:1513–22.
18 Muneera A, AlSheeha R, Alaboudi M, Alghasham J, Ishag A. Platelet count and platelet indices in women with preeclampsia. Vasc. Health Risk Manag. 2016; 12 (1):477–480.
19 Houghton PJ, Hylands PJ, Mensah AY, Hensel A, Deters AM. In vitro tests and ethnopharmacological investigations: wound healing

as an example. J. Ethnopharmacol. 2005;100 (1-2):100–107.
20 Saad B, Azaizeh H, Abu-Hijleh G. Said O. Safety of traditional Arab herbal medicine. Evid Based Complement Alternat. Med. 2006 3:433-439.
21 Al-Hashem, F. Camel's milk protects against aluminum chloride-induced toxicity in the liver and kidney of white albino rats. Am.J.Biochem.Biotechnol. 2009;5 (3): 98–109.
22 Podjarny E, Bernheim J, Rathaus M, Pomeranz A; Tovbin, D, Shapira J, Bernheim J. driamycin nephropathy: a model to study effects of pregnancy on renal disease in rats. Am. J. Physiol. 1992; 263 (4 Pt 2): 711 - 715.
23 National Research Council (NRC). Guide for the care and use of laboratory animals (8th Edition). The National Academic Press; Washington; D.C;. 2011; 246p.
24 Ngueguim TF, Mbatchou A, Donfack JH, Dzeufie DDP, Gounoue KR. *Dichrocephala integrifolia* (Linn. f.) O. kuntze (Asteraceae) leaves aqueous extract prevents ethanol-induced liver damage in rats. Pharmacologia2016;7 (6-7): 337–343.
25 Atoe K, Idu M, Ikhajiagbe B, Bakre AG. Lipid ratios in adriamycin-induced pre-eclamptic wistar rats exposed to methanolic plant extracts. J. Appl. Sci. Environ. Manage. 2021;25 (9):1617- 1623.
26 Yücel B, Ustun B. Neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, mean platelet volume, red cell distribution width and plateletcrit in preeclampsia. Pregnancy hypertens. 2017;7, 29–32. https://doi.org/10.1016/j.preghy.2016.12.002
27 Sibai BM. The HELLP syndrome: much ado about nothing? Am. J. Obstet.Gynecol.1990,162, 311–316
28 Dillasamola D, Almahdy A, Putri BO, Kurniawan H, Sari AN. Teratogenic effect of ethanol extract of yellow root stem (Cosciniumfenestratum (Gaertn.) Colebr) on Mice. *Trop. J. Nat. Prod. Res. 2024; 8*(1): 5770–5773.
29 Adebisi MI,Bello SO,Shehu CE,Abdullahi MI,Ugwah-Oguejiofor CJ, Ndodo N, Umar M. Dioscoreaprehensilis Ameliorates the features of preeclampsia in l-ng -nitroarginine methyl ester (L-NAME) preeclamptic model. Trop. J. of Nat. Prod. Res. 2018; 2(9):422-428.

