Journal of Experimental and Clinical Medicine
https://dergipark.org.tr/omujecm

Research Article

J Exp Clin Med
2022; 39(4): 1150-1156
doi: 10.52142/omujecm.39.4.39

The effects of methanolic plant extract on the cardiovascular system of induced preeclamptic Wistar rats

Kenneth ATOE[1,2,3,*], Macdonald IDU[1]

[1]Phytomedicine and Drug Discovery Research Group, Department of Plant Biology and Biotechnology, University of Benin, Benin City, Nigeria
[2]Department of Chemical Pathology, Edo State University Uzairue, Edo State, Nigeria
[3]Applied Environmental Biosciences and Public Health Research Group, Department of Microbiology, University of Benin, Benin City, Nigeria

Received: 18.09.2021 • **Accepted/Published Online:** 15.10.2021 • **Final Version:** 29.10.2022

Abstract

This work investigated the effects of methanolic plant extract on the cardiovascular system of induced preeclampticWistar rats. Preeclampsia is associated with increase in high blood pressure and proteinuria. Studies have shown the only medically acceptable treatment is the removal of the fetus from the mother, however there is considerable lack of studies done to show the use of herbal medicine in the treatment and management of preeclampsia. This study reveals the use of plant extract and its effect on cardiovascular system. Three plants extract; *Jatropha curcas, Alchornea cordifolia and Secamone afzelii* were used for the study. Results showed that there were no observable lesion or abnormally in the cardiovascular system and the use of all three plant extracts significantly reduced blood pressure and proteinuria, thus indicating a reduction of preeclampsia from severe to mild.

Keywords: preeclampsia, highblood pressure, proteinuria, herbal medicine, *Jatropha curcas, Alchornea cordifolia and Secamone afzelii*

1. Introduction

Preeclampsia is a condition that causes an unexpected rise in blood pressure and edema, particularly in the face, hands, and feet, during pregnancy (1). The exact causes of preeclampsia are unknown, however blood vessels in the placenta are thought to be involved. Although preeclampsia may not cause any symptoms, early warning signs include protein in the urine (proteinuria) and increased blood pressure (hypertension). Some pregnant women have elevated blood pressure, but this does not necessarily indicate preeclampsia; the presence of protein in the urine is the most noticeable indication (1). The most prevalent pregnancy-related illness is preeclampsia. It commonly appears in the second trimester and affects one out of every twenty pregnancies.

Preeclampsia causes the heart to become overworked and inefficient in pumping blood because it is unable to relax between contractions. Preeclampsia has been linked to an increased risk of heart failure, heart attack, and stroke among mothers who have recovered from it. It can lead to blood clotting issues, pulmonary edema, seizures, and, in severe cases or if left untreated, death of the mother and newborn (2-6).

The most likely method of treatment for this condition is delivery. Women with this condition are at a higher risk of seizures, placental abruption, stroke, and possibly major bleeding until their blood pressure lowers. If high blood pressure or hypertension occurs too early in pregnancy, delivery may not be the best decision for the baby (3).

Aspirin is now the only medication having strong evidence to support its use in reducing the risk of heart attack and stroke (2, 6). Nutritional supplements and pharmacological therapies are examples of other interventions medicines, as well as dietary and lifestyle modifications, have been studied for their ability to protect against preeclampsia, with varied degrees of success. Vitamin D insufficiency has been linked to an increased risk of preeclampsia (4, 5, 7-10). Vitamin D supplementation has been shown to help reduce preeclampsia risk (11, 5). While supplementation is frequently advised in clinical practice, strong randomized controlled trial (RCT) data is still needed to prove its effectiveness (8, 12). High-dose folic acid does not appear to be useful in preventing repeated preeclampsia (13), while some evidence suggests that supplementing with 5-methyl-tetrahydrofolate, a more accessible form of folic acid, may be effective in preventing recurrent preeclampsia (14).

*Correspondence: atoe.kenneth@edouniversity.edu.ng

Herbal medications are commonly perceived as a safe, natural alternative to conventional drugs, and are frequently used to improve the welfare of many pregnant women, or treat non-life-threatening diseases. Herbal medicine has become increasingly popular over time. Ginger, cranberry, valerian, raspberry leaf, chamomile, peppermint, thyme, fenugreek, green tea, sage, anise, garlic, and bitter kola are the most widely utilized herbs. The usage of herbal medication during pregnancy is linked to a woman's educational status, household economic level, and age. Herbal medications were used to relieve nausea and vomiting, lower the risk of preeclampsia, speed up labor, and treat the common cold and urinary tract infection during pregnancy (15). Though studies have shown that the use of herbal medicine goes a long way in reducing the chances of infections, however, it is best to consult a doctor and a pharmacist before using any herbal therapy during pregnancy to ensure that the herbs are appropriate and safe to use (15,16, 17, 18). The usage of herbal medicine during pregnancy varies a lot depending ethnicity, cultural customs, and socioeconomic level (18). Herbal medication use during pregnancy is quite frequent in Sub-Saharan Africa, according to previous study (16, 17). Study by Gharoro and Igbafe (19) in Benin City, Edo State showed that the use of native medication during pregnancies. Many these patients believed in herbal treatments' efficacy and had found them to be a cost-effective and accessible alternative treatment.

In the present study, extracts from 3 commonly used plants in Benin City are used in the management of preeclampsia in animal models. These are *Jatropha curcas, Alchornea cordifolia and Secamone afzelii.* These plants have been previously reported to have a number of therapeutic properties, including antibacterial, anti-cancer, with capacities to treat coughs, infertility, bacterial infections, inflammation, fever, and bronchial problems. Ugbogu and Chukwuma (20) reported the use of some of these herbs in the management of high blood pressure; but no study has reported use of any herbal preparation in the management of preeclampsia. The aim of the study therefore for to investigate the use of these plant extracts in the management of preeclampsia and associated cardiovascular complications.

2. Materials and Methods

2.1. Collection and preparation of plant samples

Plant samples (leaves) were collected from First Generation Farms Ltd in Iguosula, Uhunmwonde Local Government Area, Edo State. They were identified and verified at the University of Benin's Department of Plant Biology and Biotechnology's Phytomedicine Unit in Benin City. The plant samples were cleaned many times with distilled water, air-dried for two weeks, then processed into powder with a Panasonic® medium kitchen blender, model MX-GX1021WTZ. After soaking 100g of each powder sample in 200ml of methanol for 12 hours, the extracts were filtered using Whatman Filter Paper No 42. (125mm).

2.2. Study design

Females Wistar rats of comparable age (3 days) weighing 237 g (mean) were utilized in the study. The animals were housed in well-ventilated metabolic cages. The animals were given unrestricted access to a standard diet (0.35 g NaCl, 20 g protein, and 1.17 g arginine per 100 g food) as well as ad libitum tap water (pH range 6.8 – 7.2). They were given a one-week acclimation period before the trial began.

In this experiment, the Wistar rats were randomly divided into 15 groups, each with 10 rats. Whereas Group 1 served as the positive control, Groups 2, 3, and 4 served as the negative controls. Other groups are as presented below (Table 1).

Table 1. Designation of experimental groups

Group	Description
Group 1	Control
Group 2	Administered with Ext-JC (No induced Preeclampsia)
Group 3	Administered with Ext-AC (No induced Preeclampsia)
Group 4	Administered with Ext-SA (No induced Preeclampsia)
Group 5	Induced Preeclampsia, no treatment provided
Group 6	Induced Preeclampsia + 100 mg/kg Standard drug
Group 7	Induced Preeclampsia + 50 mg/kg Ext-JC
Group 8	Induced Preeclampsia + 100 mg/kg Ext-JC
Group 9	Induced Preeclampsia + 200 mg/kg Ext-JC
Group 10	Induced Preeclampsia + 50 mg/kg Ext-AC
Group 11	Induced Preeclampsia + 100 mg/kg Ext-AC
Group 12	Induced Preeclampsia + 200 mg/kg Ext-AC
Group 13	Induced Preeclampsia + 50 mg/kg Ext-SA
Group 14	Induced Preeclampsia + 100 mg/kg Ext-SA
Group 15	Induced Preeclampsia + 200 mg/kg Ext-SA

Ext-JC, Metholic leaf extract of Jatrophacacus; Ext-AC, Metholic leaf extract of Alchonneacordifolia; Ext-SA, Metholic leaf extract of Secamone afzelii.Standard drug was methyl DOPA (Aldomet®)

2.3. Induction of preeclampsia

In this work, the Adriamycin Model developed by Podjarny et al (21) was utilized to induce preeclampsia. Adriamycin (Adriablastina, Abic) was delivered into rats under light ether anesthesia at 3.5 mg/kg IV through a superficial caudal vein. Two weeks later, the rats were mated for four days with a fertile male.

2.4. Management of experimental animals

The animals were cared for and used in compliance with international guidelines for laboratory animal care and use (22).

2.5. Determination of blood pressure

Determination of blood pressure of the Wistar rat were by the non-invasive methods described by Feng and DiPetrillo (23), using the CODA® High Throughput System with 2 Activated Channels (CODA-HT2) by Kent Scientific Corporation, USA.

2.6. Determination of ECG

Determination of ECG was according to the methods of Pereira-Junior et al. (24). Prior to ECG recordings, the animals were conditioned for 7 days in a Plexi glass restrainer for 20 minutes each day. All subsequent recordings were made in the morning in a controlled environment (0700-0900h). The animal was restrained in a Plexi glass restrainer with

ventilation holes on the front and other surfaces, and electrodes were connected to a differential A/C amplifier (A-M Systems, USA), with signals digitized by a 16 bit A/D interface converser (Axon 1322-A, USA), and sampled at 10 KHz by software Axoscope 9.0. (USA: Axon Instruments). The ECG recording began 10 minutes after the animal was placed into the Plexi glass restrainer and lasted 5 minutes. The steadiest 180s continuous section from each record was chosen for HRV analysis.

2.7. Determination of proteinuria

This was carried out using the dipstick (combi2) method (25).

2.8. Sacrifice of experimental animal

The animals were anaesthetized with chloroform and humanely slaughtered twenty-four (24) hours after the last dosage of the standard medicine and various treatment extracts were administered to the relevant groups (26). Following that, the hearts were histologically examined using the procedure of Molh et al. (27).

2.9. Statistical analysis

Data collected were analyzed using SPSS version 20 and GraphPad Prism 5. Results were presented in Tables and Quantitative variables were expressed as mean $\pm$ standard deviation

2.10. Ethical issues

The Research and Ethics Committee of the Faculty of Life Sciences, University of Benin, Benin City, granted ethical permission with reference LS19017, dated March 7, 2019.

3. Results

When the methanolic extracts of the test plants were administered to the Wistar rats for the first 15 days, no mortalility was recorded (Fig. 1.) for the highest concentration (5000 mg/kg) for this reason, the extracts were used.

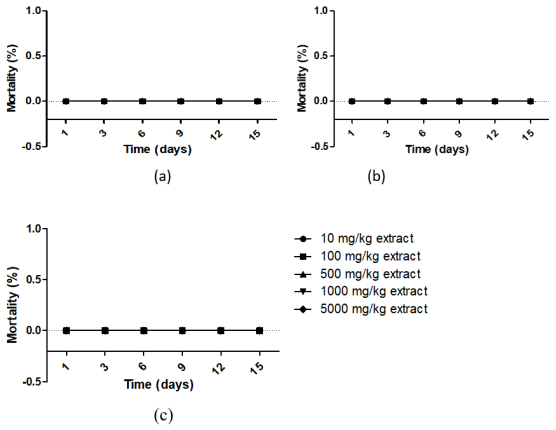


Fig. 1. Percentage mortality of rats used during acute toxicity study for 15 days (a) *Jatropha curcas*(b) *Alchornea cordifolia and* (c) *Secamone afzelii*

Table 2 shows the blood pressure of preeclampsia in rats. In the control, blood pressure during 3rd trimester was 124/98 mmHg. However, when plant extracts were administered, without the inducement of preeclampsia, bp was119/85 for administration of methanolic extracts of *Jatropha curcas*. Blood pressure of the preeclamptic group was 177/121 mmHg during the 3rd trimester. However, upon administration of extracts (100 mg/kg) of *Jatropha curcas*, blood pressure significantly dropped to 118/86 mmHg. Blood pressure in Wistar rats administered with 200 mg/kg of extract of *Alchornea cordifolia* was 127/87 mg/kg during the third trimester. Similarly, although at post-partum, for control group, blood pressure was 121/96 mmHg; however blood pressure of the preeclamptic group was 160/125 mmHg. Blood pressure in Wistar rats administered with 100mg/kg of extract of Secamone afzelii was 141/101 at third trimester and 116/86 at post-partum. Significant reductions in blood pressure were achieved upon administration of methanolic extracts of the testy plants (Table 2).

Table 2. Blood pressure measurement of preeclamptic and control groups after administration of extracts of test plants

Treatments	(n)	Systolic	Diastolic	(n)	Systolic	Diastolic
	3rd trimester			**Post-partum**		
Control	14	124	98	8	121	96
Only Ext-A (No induced PreEc) (200 mg/kg)	15	119	85	12	110	85*
Only Ext-B (No induced PreEc) (200 mg/kg)	19	132	101	13	122	94
Only Ext-C (No induced PreEc) (200 mg/kg)	19	131	95	12	123	91
Induced PreEc, no treatment	26	177*	121*	12	160*	125*
Induced PreEc + 100 mg/kg StdD	36	141	103	10	135	104
Induced PreEc + 50 mg/kg Ext-A	16	143	99	7	117	93
Induced PreEc + 100 mg/kg Ext-A	12	118	86	4	129	101
Induced PreEc + 200 mg/kg Ext-A	12	145	100	3	119	99
Induced PreEc + 50 mg/kg Ext-B	14	143	97	4	113	90
Induced PreEc + 100 mg/kg Ext-B	10	136	96	5	113	87
Induced PreEc + 200 mg/kg Ext-B	19	127	87	10	127	94
Induced PreEc + 50 mg/kg Ext-C	11	140	98	6	136	102
Induced PreEc + 100 mg/kg Ext-C	16	141	101	6	116	86
Induced PreEc + 200 mg/kg Ext-C	13	150*	92	8	121	106
LSD(0.05)		22	14		16	11
F-test		5.913	7.795		4.332	4.241
p-value		<0.001	<0.001		<0.001	<0.001

* Means are significantly different from the Control ($p<0.05$). Values presented are to the nearest integer

Proteinuria was negative in the control group as expected. Similarly, as evidence that the extracts did not cause any damage, proteinuria was also negative in upon administration of 200 mg/kg of the extracts (Table 3). During 3rd trimester, proteinuria was 3+ in the preeclamptic group but reduced to 1+ at postpartum. During the 3rd trimester also, there was at least 33% reduction in level of proteinuria upon administration of plant extracts. Administration of 50mg/kg of methanolic extracts of *Jatropha curcas* reduced proteinuria by over 60% (i.e 1+) compared to 3+ in the preeclamptic group. At postpartum, significant reduction in proteinuria was also recorded upon administration of plant extracts.

Table 3. Level of proteinuria in both preeclamptic groups after administration of extracts of test plants

Group	Baseline	At Third trimester	At post-partum
Control	Negative	Negative	Negative
Only Ext-A (No induced PreEc) (200 mg/kg)	Negative	Negative	Negative
Only Ext-B (No induced PreEc) (200 mg/kg)	Negative	Negative	Negative
Only Ext-C (No induced PreEc) (200 mg/kg)	Negative	Negative	Negative
Induced PreEc, no treatment provided	+++	+++	+
Induced PreEc + 100 mg/kg StdD	NA	+	trace
Induced PreEc + 50 mg/kg Ext-A	NA	+	trace
Induced PreEc + 100 mg/kg Ext-A	NA	++	+
Induced PreEc + 200 mg/kg Ext-A	NA	++	trace
Induced PreEc + 50 mg/kg Ext-B	NA	++	trace
Induced PreEc + 100 mg/kg Ext-B	NA	++	trace
Induced PreEc + 200 mg/kg Ext-B	NA	++	trace
Induced PreEc + 50 mg/kg Ext-C	NA	++	+
Induced PreEc + 100 mg/kg Ext-C	NA	++	+
Induced PreEc + 200 mg/kg Ext-C	NA	++	trace

Present + (The number of "+" indicates level of severity); NA not applicable

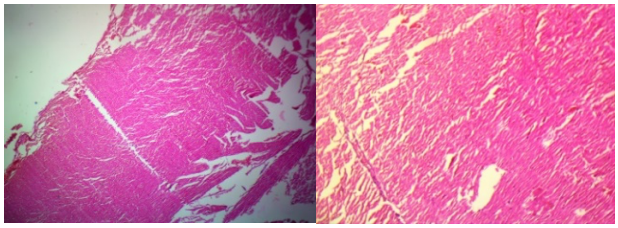
The severity of preeclampsia is shown in Table 4 above. In the third trimester, the percentage increase in blood pressure relative to the control group was 42.7 percent for systolic blood pressure and 23.5 percent for diastolic blood pressure, respectively. Significant decreases in these increases were observed when plant extracts were used in the third trimester and afterward. Similarly, the severity of preeclampsia in the untreated preeclamptic group decreased to mild in the third trimester and postpartum.

Table 4. Severity of preeclampsia in the Wistar rats before and after administration of plant extracts

Group	3rd trimester				Post-partum			
	Percentage rise (%)				Percentage rise (%)			
	Systolic BP	Diastolic BP	Proteinuria	Preeclampsia	Systolic BP	Diastolic BP	Proteinuria	Preeclampsia
Induced PreEc, no treatment provided	42.7	23.5	+++	Severe	32.2	30.2	+	Severe
Induced PreEc + 100 mg/kg StdD	13.7	5.1	+	Mild	11.6	8.3	trace	Mild
Induced PreEc + 50 mg/kg Ext-A	15.3	1	+	Mild	-3.3	-3.1	trace	Mild
Induced PreEc + 100 mg/kg Ext-A	-4.8	-12.2	++	Mild	6.6	5.2	+	Mild
Induced PreEc + 200 mg/kg Ext-A	16.9	2	++	Severe	-1.7	3.1	trace	Mild
Induced PreEc + 50 mg/kg Ext-B	17.7	-1	++	Severe	-6.6	-6.3	trace	Mild
Induced PreEc + 100 mg/kg Ext-B	9.7	-2	++	Mild	-6.6	-9.4	trace	Mild
Induced PreEc + 200 mg/kg Ext-B	2.4	-11.2	++	Mild	5	-2.1	trace	Mild
Induced PreEc + 50 mg/kg Ext-C	12.9	0	++	Mild	12.4	6.3	+	Mild
Induced PreEc + 100 mg/kg Ext-C	13.7	3.1	++	Mild	-4.1	-10.4	+	Mild
Induced PreEc + 200 mg/kg Ext-C	21	-6.1	++	Severe	0	11.5	trace	Mild

1 - 15% rise in BP (compared to control) plus significant Proteinuria – Mild preeclampsia
> 15% rise in BP (compared to control) plus significant Proteinuria – Severe preeclampsia
*Incidences herein reported in the Table above are modal presentation of symptoms by the model animals

There were no significant changes in heart rates and other ECG parameters measured during both 3rd trimester and postpartum (Table 5). Perhaps this insignificant impact on the heart parameters as presented in Table 5 mayhave resulted especially because the increase in blood pressure was acute.This was also evident in the histological findings (Table 6, Fig. 2.).



(a) Normal Heart muscle x4 (b) Normal Heart muscle x10

Fig. 2. Histological slide of a normal heart

Table 5. ECG in both preeclamptic groups after administration of extracts of test plants

Treatments	Heart Rate (/min)	Pdur (ms)	PR-Interval (ms)	QRS (ms)	QT (ms)	QTc (ms)	R amplitude (mV)
Basal reading	203.0	22.3	52.3	18.7	101.0	185.0	0.5
3rd trimester							
Control	276.7	20.7	53.0	11.0	82.3	155.3	0.5
Only Ext-A (No induced PreEc)	275.0	24.7	48.3	13.0	101.0	207.0	0.6
Only Ext-B (No induced PreEc)	272.3	22.0	43.0	13.0	116.0	211.3	0.4
Only Ext-C (No induced PreEc)	260.0	23.0	41.0	15.3	102.7	218.7	0.7
Induced PreEc, no treatment provided	238.3	26.3	41.3	14.7	119.7	225.3	0.9
Induced PreEc + 100 mg/kg StdD	251.7	25.0	51.0	14.7	95.0	189.3	0.6
Induced PreEc + 50 mg/kg Ext-A	274.8	21.8	50.4	22.8	105.2	224.6	0.6
Induced PreEc + 100 mg/kg Ext-A	276.8	31.8	52.0	15.8	83.2	177.2	0.4
Induced PreEc + 200 mg/kg Ext-A	294.6	20.2	47.8	12.8	84.6	187.2	0.5
Induced PreEc + 50 mg/kg Ext-B	275.0	20.0	45.5	15.3	92.5	197.3	0.4
Induced PreEc + 100 mg/kg Ext-B	276.2	27.2	50.4	11.6	107.8	230.6	0.4
Induced PreEc + 200 mg/kg Ext-B	294.8	24.0	44.5	15.3	99.8	219.8	0.6
Induced PreEc + 50 mg/kg Ext-C	291.2	23.6	45.8	15.2	84.6	185.4	0.7
Induced PreEc + 100 mg/kg Ext-C	266.0	24.5	48.5	16.5	93.8	197.3	0.5
Induced PreEc + 200 mg/kg Ext-C	241.0	25.3	48.0	20.0	95.7	190.7	0.4
F-test	4.762	0.859	1.106	1.793	1.993	1.529	2.465
LSD (0.05)	52.4	12.7	24.7	21.7	21.7	43.4	0.3
p-value	<0.001	0.611	0.379	0.066	0.038	0.135	0.010
Post-partum							
Control	262.3	18.7	49.0	10.3	76.0	153.0	0.5
Only Ext-A (No induced PreEc)	254.0	23.3	44.3	13.0	93.3	209.3	0.6
Only Ext-B (No induced PreEc)	258.0	20.0	41.0	13.0	114.0	195.3	0.4
Only Ext-C (No induced PreEc)	246.0	21.0	39.7	14.3	100.7	202.0	0.7
Induced PreEc, no treatment provided	220.0	24.3	41.0	13.7	110.3	208.0	0.9
Induced PreEc + 100 mg/kg StdD	249.0	23.0	47.0	13.7	87.7	175.0	0.6
Induced PreEc + 50 mg/kg Ext-A	221.3	28.0	54.7	19.3	94.0	182.0	0.6
Induced PreEc + 100 mg/kg Ext-A	219.3	23.3	56.3	18.7	96.0	172.0	0.5
Induced PreEc + 200 mg/kg Ext-A	217.3	29.7	57.7	14.3	104.3	192.0	0.5
Induced PreEc + 50 mg/kg Ext-B	209.7	21.3	43.3	15.3	106.3	198.7	0.4
Induced PreEc + 100 mg/kg Ext-B	227.7	24.0	53.3	13.0	87.0	168.7	0.4
Induced PreEc + 200 mg/kg Ext-B	223.0	23.8	55.8	14.3	106.3	204.5	0.5
Induced PreEc + 50 mg/kg Ext-C	268.0	23.9	47.6	15.0	90.4	189.0	0.6
Induced PreEc + 100 mg/kg Ext-C	250.0	23.9	50.1	16.4	92.6	188.4	0.5
Induced PreEc + 200 mg/kg Ext-C	215.2	24.5	49.8	17.3	96.8	182.2	0.4
LSD (0.05)	26.8	12.1	11.9	2.3	23.1	43.2	0.3
F-test	2.209	0.981	1.949	2.947	2.557	1.178	2.188
p-value	0.021	0.490	0.043	0.003	0.008	0.323	0.022

4. Discussion

Preeclampsia is associated with high blood pressure and proteinuria. According to research, the only medically acknowledged treatment for preeclampsia is the removal of the fetus from the mother. However, there are just a few researches that suggest herbal medicine can be used to treat and manage preeclampsia. This study looked at the effects of methanolic plant extract on the cardiovascular system of induced preeclamptic Wistar rats. When 50mg/kg of methanolic extracts of *Jatropha curcas* were given, proteinuria was reduced by roughly 60% (i.e., 1+).

Although all plant extracts caused significant reductions in blood pressure; this was more significant with the use of extracts of *Jatropha curcas*. *Jatropha curcas* L. (Euphorbiaceae) has been previously used to treat a variety of disorders, including skin, cancer, digestive, respiratory, and infectious infections and has also been shown to have anti-inflammatory, antioxidant, antimicrobial, antiviral, anticancer, antidiabetic, anticoagulant, hepatoprotective, analgesic, and abortifacient capacities. This plant has been reported to have Angiotensin I-converting enzyme (ACE)-inhibiting activity (28). Angiotensin I-converting enzyme (ACE) plays an important role in regulating blood pressure and hypertension.

Jatropha curcas contains lignans, which have a steroid-like

chemical structure and are classified as phytoestrogens. Traditionally, lignans have been associated with reduced risk of heart disease, menopausal symptoms, osteoporosis, and breast cancer as Consumption of lignan-rich foods could help to avoid chronic illnesses including cancer and cardiovascular disease (29). *Jatropha curcas* also contains coumaris. Coumarin (2H-1-benzopyran-2-one) is an anti-inflammatory, anticoagulant, antibacterial, antifungal, antiviral, anticancer, antihypertensive, antitubercular, anticonvulsant, antiadipogenic, antihyperglycemic, antioxidant, and neuroprotective plant-derived natural substance.

Table 6. Histological findings of the heart in both preeclamptic groups after administration of extracts of test plants

Groups	Hearth	
	3rd trimester	post-partum
Control	There is no observable lesion	Normal cardiac muscles, no observable lesion seen
Only Ext-A (No induced PreEc)		
Only Ext-B (No induced PreEc)		
Only Ext-C (No induced PreEc)		
Induced PreEc, no treatment		
Induced PreEc + 100 mg/kg StdD		
Induced PreEc + 50 mg/kg Ext-A		
Induced PreEc + 100 mg/kg Ext-A		
Induced PreEc + 200 mg/kg Ext-A		
Induced PreEc + 50 mg/kg Ext-B		
Induced PreEc + 100 mg/kg Ext-B		
Induced PreEc + 200 mg/kg Ext-B		
Induced PreEc + 50 mg/kg Ext-C		
Induced PreEc + 100 mg/kg Ext-C		
Induced PreEc + 200 mg/kg Ext-C		

Results showed from the study, *Alchornea cordifolia* was able to reduce the blood pressure in preeclamptic Wister rats. The history of the use of herbs in the management of diseases dates back to the time of the early man (30, 31). In herbal medicine, herbs/plants are being used in their unaltered form for the treatment of disease. *Alchornea cordifolia* is a plant widely used in Africa alone or in association with other plants to solve many health problems (32). *A. cordifolia* has been very valuable locally in some ethnic groups in Nigeria for the management of haemorrhoids and high blood pressure. It has been found to have anti-inflammatory, antibacterial and analgesic properties (32, 33). Study by Eliakim-Ikechukwu and Riman (34) revealed that *A. corifolia* is capable of inducing elastogensis in the aorta; this attribute of the herb may be beneficial in increasing elastic recoil of the aortic wall and may reduce blood pressure. The phytochemical includes alchorneine, anthranilic acid, gentisinic acid, isoalchorneine, yohimbine and alkaloids (35).

Results from this study also revealed that *Secamone afzelii* had the ability to reduce blood pressure and proteinuria in preeclamtic Wister rats. *Secamone afzelii* is used in traditional medicine for stomach problems, diabetes, colic, dysentery and also for kidney problems. *Secamone afzelii* have also been reported to have anti-inflammatory and antioxidant properties due to flavonoids, triterpenoids, diterpenoids and caffeic acid derivatives (36, 37, 38).

The findings of this study revealed that the administration of *Jatropha curcas* was found to be responsible for lowering severe preeclampsia to mild. There has been no prior research to back this up, but this study has shown that *Jatropha curcas, Alchornea cordifolia and Secamone afzelii* can reduce blood pressure and proteinuria, both of which are symptoms of preeclampsia in the Wistar rats.The incidence of preeclampsia had no significant effect on the heart presentations as shown in the ECG and histology reports. Moreover, the administration of the plant extract did not cause any observable lesion or abnormally in the heart.

Conflict of interest
None to declare.
Funding
None to declare.

Acknowledgments
None to declare.

Authors' contributions
Concept: K.A., M.I., Design: K.A., M.I., Data Collection or Processing: K.A., Analysis or Interpretation: K.A., M.I., Literature Search: K.A., Writing: K.A.

References

1. Felman A. Everything you need to know about preeclampsia. Medical news. 2017.
2. Asuk AA, Willie AJ. The phytochemical proximate mineral compositions of the leaf stem bark root of Jatropha curcas. 2015; https: //doiorg/101016/japjtb
3. Adinma ED. Maternal perinatal outcome of eclampsia in tertiary health institution in Southeast Nigeria. J Matern Fetal. 2013; 26(2): 211-4 doi: 103109/147670582012722708
4. Wei S-Q, Qi H-P, Luo Z-C, Fraser WD. Maternal Vitamin D Status Adverse Pregnancy Outcomes: A Systematic Review Meta-Analysis. J Matern Fetal Neonatal Med. 2013; 26: 889–899
5. Arain N, Mirza WA, Aslam M. Review-Vitamin D the Prevention of Preeclampsia: A Systematic Review. Pak J Pharm Sci. 2015; 28:1015–1021

6. Mol BWJ, Roberts CT, Thangaratinam S, Magee LA, de Groot CJM, Hofmeyr GJ. Pre-Eclampsia. Lancet 2016; 387: 999–1011.

7. Mirzakhani H, Litonjua AA, McElrath TF, O'Connor G, Lee-Parritz A, Iverson R et al. Early Pregnancy Vitamin D Status Risk of Preeclampsia. J Clin Investig. 2016; 126: 4702–4715

8. Purswani JM, Gala P, Dwarkanath P, Larkin HM, Kurpad A, Mehta S 2017The Role of Vitamin D in Pre-Eclampsia: A Systematic Review. BMC Pregnancy Childbirth 2010; 17: 231

9. Akbari S, Khodadadi B, Ahmadi SAY, Abbaszadeh S, Shahsavar F. Association of Vitamin D Level and Vitamin D Deficiency with Risk of Preeclampsia: A Systematic Review Updated Meta-Analysis. Taiwan J Obstet Gynecol. 2018; 57: 241–247

10. Ali AM, Alobaid A, Malhis TN, Khattab AF. Effect of Vitamin D3 Supplementation in Pregnancy on Risk of Pre-Eclampsia—Randomized Controlled Trial. Clin Nutr. 2019; 38: 557–563

11. Nassar N, Halligan GH, Roberts CL, Morris JM, Ashton AW Systematic Review of First-Trimester Vitamin D Normative Levels and Outcomes of Pregnancy. Am J Obstet Gynecol 2011; 205e1–e7

12. Roth DE, Leung M, Mesfin E, Qamar H, Watterworth J, Papp E. Vitamin D Supplementation during Pregnancy: State of the Evidence from a Systematic Review of Randomised Trials. BMJ 2017; 35 j5237

13. Wen SW, White RR, Rybak N, Gaudet LM, Robson S, Hague W et al. Effect of High Dose Folic Acid Supplementation in Pregnancy on Pre-Eclampsia (FACT): Double Blind Phase III Randomised Controlled International Multicentre Trial. BMJ. 2018; 362 k3478

14. Saccone G, Sarno L, Roman A, Donadono V, Maruotti GM, Martinelli P. 5-Methyl-Tetrahydrofolate in Prevention of Recurrent Preeclampsia. J Matern Neonatal Med. 2016; 29: 916–920

15. Laelago T. Herbal Medicine Use during Pregnancy: Benefits Untoward Effects, in Herbal Medicine. Ed. P. Builders. London: Intech Open. 2018.

16. Ahmed M, Hwang JH, Hasan MA, Han D. Herbal medicine use by pregnant women in Bangladesh: a cross-sectional study. BMC Complement Altern Med. 2018a; 18 (1): 333 doi: 101186/s12906-018-2399-y

17. Ahmed SM, Nordeng H, Sundby J, Aragaw Y A, de Boer HJ. The use of medicinal plants by pregnant women in Africa: A systematic review. J Ethnopharmacol. 2018b; 224: 297–313 doi: 101016/jjep201805032

18. Illamola SM, Amaeze OU, Krepkova LV, Birnbaum AK, Karanam A, Job KM, et al. Use of Herbal Medicine by Pregnant Women: WhatPhysicians Need to Know. Front Pharmacol. 2020; 10: 483–1483 doi: 103389/fphar201901483

19. Gharoro EP, Igbafe AA. Pattern of drug useamong antenatal patients in Benin City, Nigeria. Med Sci Monit. 2000; 6(1): 84 - 87

20. Ugbogu OA Chukwuma EC. Ethnobotany of Okomu Forest Reserve Edo State Nigeria. J Appl Sci Environ Manage. 2019; 23 (7): 1391-1401

21. Podjarny E, Bernheim JL, Rathaus M, Pomeranz A, Tobvin D, Shapira J, Bernheim J. Adriamycin nephropathy: a model to study the effects of pregnancy on renal disease in rat. Am J Physiol. 1992; 263 (4 Pt 2):F711-715.

22. National Research Council (NRC) Guide for the care and use of laboratory animals (8th Edition). The National Academic Press, Washington, D.C., 2011; 1-246

23. Feng M, DiPetrillo K. Non-invasive Blood Pressure Measurement in Mice. Methods Mol Biol. 2009; 573: 45 – 55 doi: 101007/978-1-60761-247-6_3

24. Pereira-Junior PP, Marocolo M, Rodrigues FP, Medei M Nascimento JHM. Noninvasive method for electrocardiogram recording in conscious rats: feasibility for heart rate variability analysis. Anais da Academia Brasileira de Ciências 2010; 82(2): 431-437

25. Stefańska K, Zieliński M, Zamkowska D, Adamski P, Jassem-Bobowicz J, Piekarska K et al. Comparisons of Dipstick Test Urine Protein-to-Creatine Ratio Total Protein Measurement for the Diagnosis of Preeclampsia. International Journal of Environmental Research Public Health 2020; 17(12): 4195 https: //doiorg/103390/ijerph17124195

26. Rowell TE. Reproductive cycle of the talapoin monkey (Miopithecus talapoin) Folia Primatol. 1977; 28:188-202.

27. Molh AK, Ting LC, Khan J, Al-Jashamy K, Jaafar H, Islam MN. Histopathological studies of cardiac lesions after an acute high dose administration of methamphetamine The Malaysian journal of medical sciences (MJMS). 2008; 15(1): 23–30

28. Segura-Campos MR, Peralta-González F, Castellanos-Ruelas A, Chel-Guerrero LA, Betancur-Ancona DA. Effect of Jatropha curcas peptide fractions on the angiotensin I-converting enzyme inhibitory activity. BioMed Research International 2013; ID 541947 https: //doiorg/101155/2013/541947

29. Rodríguez-García C, Sánchez-Quesada C, Toledo E, Delgado-Rodríguez M, Gaforio JJ. Naturally Lignan-Rich Foods: A Dietary Tool for Health Promotion? Molecules. 2019 Mar 6;24(5):917. doi: 10.3390/molecules24050917. PMID: 30845651; PMCID: PMC6429205.

30. Sofowora EA. Medicinal plants traditional medicine in Africa. John Wiley sons Ltd, Hoboken. 1982; 64p

31. Kafaru E. Immense help from nature's workshop Nigeria. Elikat Health Services Limited. 1994; P32.

32. Olaleye MT, Adegboye OO Akindahunsi AA. Alchorne acordifoli extract protects Wistar albino rats against acetaminophen-induced liver damage. Afr J Biotech. 2006; 5: 2439-2445

33. Cesario A. Screening of plants used in Argentine folk medicine for antimicrobial activity. Journal of Ethnopharamacology 1993; 139: 119-128

34. Eliakim-Ikechukwu C F Riman E B. The effect of aqueous ethanolic extract of Alchornea cordifolia leaf on the histology of the aorta of Wister rats. Niger J Physiol Sci. 2009; 24(2):149-151

35. Duke J Vasquez R 1994 Amazonian Ethnobotanical Dictionary, Florida, CRC Press Incorporated. 122: 101-102

36. Mensah AY, Houghton PJ, Akyirem GNA et al. Evaluation of the antioxidant free radical scavenging properties of Secamone afzelii Rhoem. Phytotherapy Research 2004; 18(12): 1031-1032 2004

37. Houghton PJ, Hylands PJ, Mensah AY, Hensel A, Deters AM. In vitro tests ethnopharmacological investigations: wound healing as an example. Journal of Ethnopharmacology 2005; 100(1-2): 100–107

38. Zabri HKodjo C, Benie A, Bekro JM, Bekro YA. Phytochemical screening determination of flavonoids in Secamone afzelii (Asclepiadaceae): extracts. African Journal of Pure Applied Chemistry 2008; 2(8): 80–82