Effects of methanolic leaf extracts of *Jatropha curcas, Alchonnea cordifolia, Secamone afzelii* in Doxorubicin-induced hypertensive nephropathy in pregnant Wistar rats

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Abstract

This study assessed the Effects of methanolic leaf extracts of *Jatropha curcas*, *Alchonnea cordifolia, Secamone afzelii* inDoxorubicin-induced hypertensive nephropathy in pregnant Wistar rats. Plant samples (leaves) were washed severally with distilled water, air-dried, and crushed to powder and were filtered, then soaked in 200mL of methanol for 12 hours. The LD50 was determined to ascertain the safety of the plant extracts for use. Female Wistar rats, aged 3 days apart, used in the study, were acclimatized for one week. Doxorubicin nephropathy was induced with 3.5mg dose intravenously through the caudal vein. Urea levels were found to have increased significantly in the third trimester (9.3 mmol/L) in the hypertensive nephropathic group. Hypertensive nephropathy also caused an increase in plasma Creatinine levels (333.64 µmol/L) and (172.73 µmol/L) in the third trimester and postpartum, respectively. The administration of plant extracts resulted in a significant decrease in urine creatinine (845.45–481.82 µmol/L) and a significant increase in Protein-Creatinine Ratio (PCR, 3.0–7.3 mg/dL) in the nephropathic group, but a contrary report in the post-partum group, with significant increases in micro-protein (17.1–21.9 mg/dL). Plasma urea and plasma creatinine had a significant relationship in the third trimester (r=0.853 and 0.810, p=0.01). Plasma urea, on the other hand, had no significant association with plasma creatinine throughout the postpartum period. This study's findings suggested that *Jatropha curcas, Alchonnea cordifolia,* and *Secamone afzelii* extracts could be useful in the treatment of chronic renal disease.

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Introduction

Doxorubicin-induced hypertensive nephropathy is a well-known rat model of chronic kidney failure.[1] Reduced glomerular filtration and recurrent large proteinuria are symptoms of chronic kidney disease. Chronic kidney disease has become an important research area due to its rising morbidity and death.[2] Damage to the glomerular filtration barrier, which includes fenestrated endothelium, Glomerular Basement Membrane (GBM), and Slit Diaphragm (SD), is a key factor in proteinuria in chronic kidney illness.[3,4] Slit diaphragm is the most significant component of the glomerular filtration barrier in particular.

Almost every physiological system in the mother undergoes changes as a result of pregnancy, but the renal system is perhaps the most affected.[5] Many changes in renal function occur during normal pregnancy, and without a thorough understanding of these changes, routine clinical investigations such as plasma uric acid, urea, and creatinine could be misinterpreted.[6] Changes in other systems, notably those in hemodynamic regulation, have an impact on renal function.[7] Pregnancy's systemic hemodynamic profile is marked by an increase in intravascular volume, cardiac output, and heart rate, as well as a marked decrease in vascular resistance and a tendency toward a decrease in mean blood pressure, in addition to an increase in Renal Plasma Flow (RPF) and Glomerular Filtration Rate (GFR).[8,9] GFR increases have major clinical consequences during pregnancy, such as uric acid, urea, and creatinine levels in the blood.[10]

Apart from conventional methods for management of diseases, the reliance on herbal remedies has increased tremendously recently. The utilization of medicinal plants as a foundational component of African traditional healthcare is one of the oldest and most diverse therapeutic systems in the world. It is common in the developing world, especially among the poor. Their use in the developed world has also increased in recent years. The source and composition of these medicines varied across the globe, but herbs and other botanicals are basis for their preparations. Because herbal medications are mainly outside the purview of governmental monitoring, they are manufactured by semi-trained herbalists and are not tested for safety. When a plant with unknown toxicity is swallowed, an innocuous herb is mistaken for a poisonous one due to incorrect identification, preparations are contaminated with toxic non-herbal compounds, or a herb amplifies the nephrotoxic action of a conventional drug, poisoning might ensue.

A number of plants, including *Jatropha curcas*, *Alchonnea cordifolia, and Secamone afzelii* have been previously used in management of hypertension generally, but no report of their use in management of the nephropathy especially during pregnancy has been reported.[11,12] This is even more predicated because poorly controlled hypertension can lead to nephropathy. The purpose of this study therefore was to assess the effects of methanolic leaf extracts of *Jatropha curcas*, *Alchonnea cordifolia, Secamone afzelii* in Doxorubicin-induced nephropathy in pregnant Wistar rats.

Materials and Methods

Collection and preparation of plant samples

Plant samples (leaves) were obtained from First Generation Farms in Iguosula, Uhunmwonde Local Government Area of Edo State, Nigeria. They were identified and verified at the University of Benin's Department of Plant Biology and Biotechnology's Phytomedicine section in Benin City. The specimen numbers UBH-J404, UBH-A560 and UBHS566 were issued for *Jatropha curcas, Alchorneacordifolia* and *Secamone afzelii,* respectively. The plant samples were cleaned multiple times with distilled water, air-dried for two weeks, then crushed 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). To eliminate methanolic residues just before the extract was dry, water was added, and the set-up was run in a rotavapor (model: IKA Rotary evaporator RV 3 V).

Study design

The study adopted a randomized controlled trial. The study used age-matched (±3 days) female Wistar rats weighing 220 to 256 g (mean, 237 g). The animals were maintained in a well-ventilated Animal House, Department of Biochemistry, University of Benin, Benin City, Nigeria with daily light and darkness variations during the month of May, 2019. The animals were given unrestricted access to a regular 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 begun.

In this study, the Wistar rats were randomly divided into fifteen (15) groups consisting of ten (10) rats each in a group. Whereas the first group served as the positive control, the second, third, and forth served as the negative controls respectively. The remaining groups are as presented in Table 1.

Induction of pregnancy-related nephropathy using the Doxorubicin Model

Doxorubicin was administered into rats under mild ether anesthesia at a dose of 3.5 mg/kg IV into a superficial femoral vein. The rats were mated with a fertile male for four days after two weeks. The presence of spermatozoa in the vaginal smear on the first day of pregnancy was documented.[13]

Individual metabolic cages were used to collect spot urine samples for urinalysis, which was used to check for proteinuria. Tail-cuff manometry with an automated sphygmomanometer was used to monitor blood pressure in awake rats (NarcoBiosystems). Rats were placed in the Plexiglas restraint cages on at least two occasions before each blood pressure measurement to ensure that they slept peacefully during the procedure. Each rat had his or her blood pressure taken fifteen times. The first three recordings were eliminated, and the average of the remaining twelve was used as the final result.

Confirmation of nephropathy

Nephropathy was confirmed by elevated blood pressure (177/121 mmHg) and significant proteinuria (+++) when compared to the control animals (Table 2), as well as elevated plasma creatinine and urine protein creatinine ratio as renal markers. Elevated blood pressure and increased proteinuria, as well as ele-

Table 1. Designation of experimental groups.

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

Ext-JC: Methanolic leaf extract of *Jatropha curcas*; Ext-AC: Methanolic leaf extract of *Alchonnea cordifolia*; Ext-SA: Methanolic leaf extract of *Secamone afzelii*. The standard drug used was Methyldopa. Induced Hyp. Nephropathy: Induced hypertensive nephropathy.

Table 2. Blood pressure and proteinuria measurements.

Treatments Blood pressure	Parameter	Control	Induced
Third trimester	Systolic (mmHg)	124	177
	Diastolic (mmHg)	98	121
Post-partum	Systolic (mmHg)	121	160
	Diastolic (mmHg)	96	125
Proteinuria			
Third trimester	Proteinuria	Negative	+++
Post-partum	Proteinuria	Negative	+

vated renal indicators, were used to confirm nephropathy (Table 1). All rats used in the study spilled proteins, excepting the control which were not administered Doxorubicin. The CODA® High Throughput System with 2 Activated Channels (CODA-HT2) from Kent Scientific Corporation, USA, was used to measure the Wistar rat's blood pressure utilizing the non-invasive methods described by Feng and DiPetrillo.[14] The rats were placed gently in the CODA System restrainer, and the back hatch was replaced to keep the rat within. Before beginning the blood pressure measurement routine, all of the Wistar rats to be tested on the same CODA system were allowed 5 minutes to adjust to their restrainers. This period allows the Wistar rats to relax and warm up, which allows blood to flow more freely. Determination of proteinuria was carried out using the dipstick (Combi- 2) method.

Management of experimental animals

The animals were cared for and used in compliance with international guidelines for laboratory animal care and use.[15]

Sacrifice of experimental animal

The animals were anaesthetized with chloroform and humanely killed 24 hours after the last dosage of the standard medication and various treatment extracts were administered to the appropriate groups. There were no ethical concerns.

Processing blood for plasma

A blood sample was taken through heart puncture and placed in a heparin container. After that, the sample was centrifuged for 5 minutes at 3000rpm to yield clear slightly yellow supernatant plasma.

Urine collection

Prior to the sacrifice of the experimental animals they were kept in the metabolic cage and their urine collected over night into a clean bottle for estimation of protein creatinine ratio.

Determination of renal markers

Estimation of plasma and urine creatinine levels

Both were estimated using the colorimetric method and standard Randox Diagnostics kits. The estimating principle was based on the Jaffe's reaction, in which creatinine in plasma or urine creates a quantifiable orange color in an alkaline media when combined with Picric acid. The color is measured at 520 nm after a 15-minute incubation period at room temperature for color development.[16,17]

Estimation of urea levels

Urea was estimated using the colorimeter with standard kits from Randox Diagnostics. The principle for estimation was based on the Urease-Berthelot method. In this method, urea in plasma is hydrolyzed to ammonia in the presence of urease. The ammonia is then measured photometrically by Berthelot's reaction.[18]

Determination of protein creatinine ratio

Total Protein in the urine was determined quantitatively following the procedure developed by Fujita *et al.*,[19] a sensitive dye binding colorimetric method employing pyrogallol red. Pyrogallol red is combined with molybdenum acid at a low pH. When the complex is combined with protein, a blue- purple color is formed. The increase in absorbance at 600nm is directly proportional to the protein concentration in the urine. Urine protein creatinine ratios was determined as the ratio of the total urine protein to urine creatinine.

Statistical analysis

SPSS version 20 was used to analyze the data at a 95% statistical significance level. Tables were used to present the findings, with quantitative variables reported as mean ± standard deviation. After determining analyses of variance (one–factor), means were separated using the Least Significant Difference (LSD, $p<0.05$). In addition, bivariate correlation was used to determine the relationship between early and late renal indicators in pregnant Wistar rats during the third trimester and postpartum period in response to the administration of methanolic leaf extracts from test plants.

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 7th, 2019.

Results

The LD_{50} of the extract given to Wistar rats is shown in Figure 1. There was no mortality after administration of the various plant extracts (at varied concentrations), indicating that they were safe to use.

Table 3 shows the impact of plant extract treatment on proteinuria incidence in rat models. Proteinuria was not found in either the control or the plant extract-treated mice. On the other hand, the incidence of hypertensive nephropathy revealed that the test animals exhibited positive proteinuria cases. Proteinuria levels in the third trimester were three times greater than after delivery. When plant extracts were given during the third trimester, proteinuria was reduced by around one-third. However, postpartum treatment of test animals with plant extracts at 100 mg/kg of Jatropha curcas and *Secamone afzelii re*duced proteinuria by two-thirds. When *Alchonnea cordifolia* was used, proteinuria was decreased to trace levels.

Urea levels rose in the third trimester (9.3 mmol/L) and decreased in the postpartum period (6.43 mmol/L), respectively (Table 4). Creatinine levels were 333.64 µmol/L and 172.73 µmol/L in the third trimester and postpartum, respectively. Except for 50 mg/kg *Secamone afzelii* (3.67 mmol/L) and 200 mg/kg *Alchonnea cordifolia* (99.09 µmol/L), there were no significant variations in Urea and creatinine among the Nephropathic groups treated with the plant extracts at the third trimester. However, creatinine levels were found to be the same (81.82 µmol/L) in both 50 mg/kg *Alchonnea cordifolia* and 100 mg/kg *Alchonnea cordifolia.*

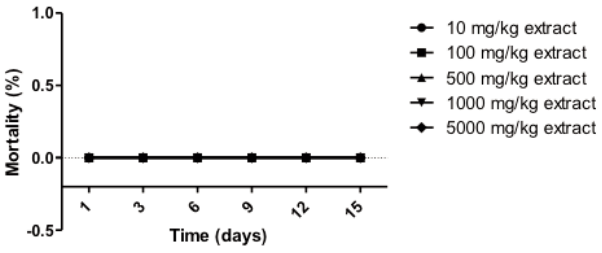

Figure 1. Presentation of LD50.

Micro protein levels in the nephropathic group with extract were higher (28.6 mg/dL) than in the control group at the third trimester, although there was a little decrease (18.7 mg/dL) in the 50 mg/kg *Secamone afzelii* and 50 mg/kg *Alchonnea cordifolia* groups (Table 5). During the third trimester, the nephropathic group had a considerable decrease in urine creatinine (481.82–845.45 µmol/L) and a significant increase in PCR (2.6–7.3). Table 6 presents the bivariate correlation between early and late renal markers in pregnant Wistar rats during 3rd trimester and postpartum period in response to administration of methanolic leaf extracts of test plants. Results revealed that throughout the third trimester, there was a strong significant association (r=0.853** and 0.810**, p0.01) between plasma Urea and Creatinine. However, at post-partum, there was a mild connection with plasma creatinine (r=0.387) and a negative correlation with plasma urea (-0.073).

High doses (200 mg/kg) of the extract supplied to the nephropathic rats showed significant tubulo-interstitial necrosis in the third trimester (Table 7). 100 mg/kg *Jatropha curcas* caused mod-

Table 3. Proteinuria levels in pregnant Wistar rats during 3rd trimester and postpartum.

Group	Baseline	At Third trimester	At post-partum
Control	Negative	Negative	Negative
Only Ext-A (No Induced H. Nep.)	Negative	Negative	Negative
Only Ext-B (No Induced H. Nep.)	Negative	Negative	Negative
Only Ext-C (No Induced H. Nep.)	Negative	Negative	Negative
Induced H. Nep., no treatment provided	+++	+++	+
Induced H. Nep. + 100 mg/kg StdD	NA	+	Trace
Induced H. Nep. + 50 mg/kg Ext-JC	NA	+	Trace
Induced H. Nep. + 100 mg/kg Ext-JC	NA	++	+
Induced H. Nep. + 200 mg/kg Ext-JC	NA	++	Trace
Induced H. Nep. + 50 mg/kg Ext-AC	NA	++	Trace
Induced H. Nep. + 100 mg/kg Ext-AC	NA	++	Trace
Induced H. Nep. + 200 mg/kg Ext-AC	NA	++	Trace
Induced H. Nep. + 50 mg/kg Ext-SA	NA	++	+
Induced H. Nep. + 100 mg/kg Ext-SA	NA	++	+
Induced H. Nep. + 200 mg/kg Ext-SA	NA	++	Trace

H. Nep.: Hypertensive nephropathy; Ext-JC: Methanolic leaf extract of *Jatropha curcas;* Ext-AC: Methanolic leaf extract of *Alchonnea cordifolia*; Ext-SA: Methanolic leaf extract of *Secamone afzelii.* The standard drug used was Methyldopa ; Present + (The number of "+" indicates level of severity); NA: not applicable.

Table 4. Late renal markers in pregnant Wistar rats during 3rd trimester and postpartum period in response to administration of methanolic leaf extracts of test plants.

Treatments	3rd trimester		Post-partum	
	Urea (mmol/L)	Creatinine (µmol/L)	Urea (mmol/L)	Creatinine (µmol/L)
Control	5.75	127.27	3.70	90.91
Only Ext-A (No Induced H. Nep.)	5.33	125.45	5.68	145.45
Only Ext-B (No Induced H. Nep.)	5.40	113.64	6.22	172.73
Only Ext-C (No Induced H. Nep.)	7.78	129.09	5.60	109.09
Induced H. Nep., no treatment provided	9.30	333.64	4.43	172.73
Induced H. Nep. + 100 mg/kg StdD	5.43*	188.18*	6.43*	154.55
Induced H. Nep. + 50 mg/kg Ext-JC	2.80*	181.82*	3.45	163.64
Induced H. Nep. + 100 mg/kg Ext-JC	3.40*	130.91*	3.87	127.27
Induced H. Nep. + 200 mg/kg Ext-JC	3.37*	172.73*	5.62	172.73
Induced H. Nep. + 50 mg/kg Ext-AC	4.50*	126.36*	4.47	81.82*
Induced H. Nep. + 100 mg/kg Ext-AC	5.38*	125.45*	3.80	81.82*
Induced H. Nep. + 200 mg/kg Ext-AC	4.05*	99.09*	4.52	100.00*
Induced H. Nep. + 50 mg/kg Ext-SA	2.83*	135.45*	5.87*	127.27
Induced H. Nep. + 100 mg/kg Ext-SA	4.50*	134.55*	5.52	154.55
Induced H. Nep. + 200 mg/kg Ext-SA	4.68*	137.27*	3.65	109.09*
F-test	3.235	2.81	1.096	1.480
LSD (0.05)	1.90	53.64	1.38	54.55
p-value	0.004	0.009	0.399	0.181

H. Nep.: Hypertensive nephropathy; Ext-JC: Methanolic leaf extract of *Jatropha curcas*; Ext-AC: Methanolic leaf extract of *Alchonnea cordifolia*; Ext-SA: Methanolic leaf extract of *Secamone afzeli*. The standard drug used was Methyldopa. *Means of values in the nephropathic group significantly differed when administered plant extracts

erate to severe interstitial necrosis, while 100 mg/kg *Alchonnea* and 50 mg/kg *Secamone* exposed rats developed moderate tubulointerstitial necrosis with fibrinoid exudates. After the administration of plant extracts, 100 and 200 mg/kg *Alchonnea cordifolia,* and 200 mg/kg *Secamone afzelii* showed normal renal tissue in hypertensive nephropathy, but there was mild tubular necrosis in the 100 mg/kg *Secamone afzelii* and 100 mg/kg *Jatropha curcas* due to the low concentration of plant extracts.

Microscopic sections of renal histology of different treatment groups are shown in Figure 2. Histopathological investigations revealed: i) normal kidney with glomeruli and tubules in the group administered with plant extracts only both in the 3rd trimester and post-partum; ii) extensive renal tubular necrosis with congestion was reported in 50 mg/kg *Jatropha curcas* and 50 mg/kg *Alchonnea cordifolia* group owing to low concentration of plant extract in the hypertensive nephropathy rats; iii) kidney with moderate tubulointerstitial necrosis was observed in 50 mg/kg *Secamone afzelii* and 100 mg/kg *Secamone afzelii in* hypertensive nephropathy and it was mild in the post-partum group; iv) kidney with interstitial inflammation generally observed in the nephropathic group in the 3rd trimester.

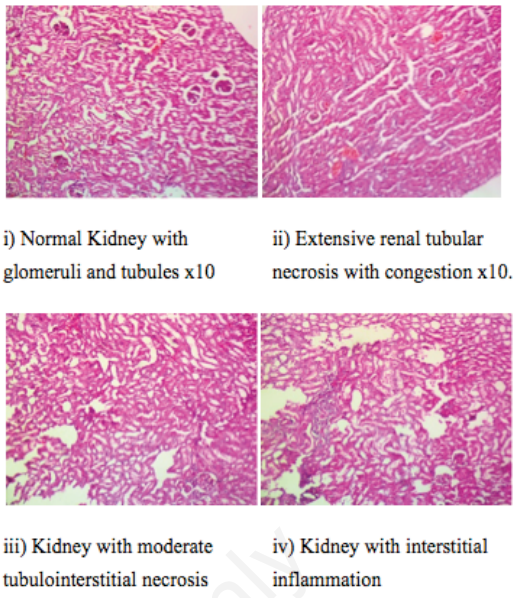

Figure 2. Histopathology slides showing different levels of nephropathies.

Table 5. Early renal markers in pregnant Wistar rats during 3rd trimester and postpartum period in response to administration of methanolic leaf extracts of test plants.

Treatments	3rd trimester			Post-partum		
	Micro P	Urine creatinine	PCR	Micro Protein	Urine creatinine	PCR
Control	22.9	18.7	1.4	12.7	15.8	0.9
Only Ext-A (No Induced H. Nep.)	20.0	14.2	1.3	15.4	13.7	0.8
Only Ext-B (No Induced H. Nep.)	24.3	17.4	1.2	14.7	13.1	0.9
Only Ext-C (No Induced H. Nep.)	20.3	13.2	1.3	13.9	8.8	1.1
Induced H. Nep., no treatment provided	16.2	5.3	7.3	20.2	8.1	5.7
Induced H. Nep. + 100 mg/kg StdD	28.6	7.5	4.1	19.8	13.5	1.5
Induced H. Nep. + 50 mg/kg Ext-JC	26.4	8.4	3.9	21.8	12.3	1.6
Induced H. Nep. + 100 mg/kg Ext-JC	21.8	6.9	3.9	13.4	10.4	1.1
Induced H. Nep. + 200 mg/kg Ext-JC	26.5	9.3	3.2	17.1	11.1	1.4
Induced H. Nep. + 50 mg/kg Ext-AC	18.7	8.6	2.6	20.6	12.7	1.7
Induced H. Nep. + 100 mg/kg Ext-AC	23.5	6.6	4.1	19.4	15.0	1.3
Induced H. Nep. + 200 mg/kg Ext-AC	25.4	7.4	3.8	23.2	14.6	1.5
Induced H. Nep. + 50 mg/kg Ext-SA	18.6	6.7	3	21.9	13.6	1.5
Induced H. Nep. + 100 mg/kg Ext-SA	21.3	9.3	2.9	21.3	12.9	1.5
Induced H. Nep. + 200 mg/kg Ext-SA	27.5	7.6	3.1	18.4	12.2	1.6
F-test	5.23	3.205	3.742	1.202	1.395	1.020
LSD (0.05)	9.3	2.5	3.1	5.2	6.3	0.7
p-value	<0.001	0.004	0.001	0.324	0.215	0.460

H. Nep.: Hypertensive nephropathy; Ext-JC: Methanolic leaf extract of *Jatropha curcas*; Ext-AC: Methanolic leaf extract of *Alchonnea cordifolia*; Ext-SA: Methanolic leaf extract of *Secamone afzelii.* The standard drug used was Methyldopa.

Table 6. Bivariate correlation between early and late renal markers in pregnant Wistar rats during 3rd trimester and postpartum period in response to administration of methanolic leaf extracts of test plants.

Parameters	PCR: 3rd trimester		PCR: Post-partum	
	R	p-value	R	p-value
Plasma Urea	**0.810****	0.003	-0.073	0.832
Plasma Creatinine	**0.853****	0.001	0.387	0.240

**Correlation is significant at the 0.01 level (2-tailed).

Discussion

The physiological state of pregnancy causes several changes that influence the metabolism of various biochemical markers. These alterations are considered to create a favorable environment for the developing fetus, but they may have an impact on the maternal health and may result in difficulties with metabolism and excretion of biochemical indicators of renal impairment. Moreover, with the increase in Glomerular Filtration Rates (GFR) during pregnancy and the increase in renal blood flow, creatinine clearance is increased and would require further examination for potential renal assault in pregnant patients with plasma creatinine level closer to the upper references for the 'normal' population.[20]

In this study, the hypertensive nephropathy group administered 200 mg/kg *Alchonnea cordifolia* in the third trimester significantly decreased creatinine levels (Table 3). This was in line with the findings of Okonkwo *et al.*[21] In the cases, the creatinine levels were significantly lower than those of control. Some reports show that the glomerular filtration rate during pregnancy increased by approximately 50%,[22] leading to an increased excretion of creatinine. Creatinine is filtered easily, and its levels drop during normal pregnancy, partly because the GFR increases as a result of pregnancy and partly because of plasma expansion hemodilution, which culminates in the drop in plasma creatinine levels.[23] Therefore, plasma creatinine reductions are complementary to plasma expansion, renal vasodilatation, hyperfiltration and enhanced permeability of the glomerular membrane basement. The small increase in the level of creatinine recorded during pregnancy might suggest the development of renal disease.[23]

The concentration of plasma urea was significantly decreased. This is comparable to that described by Okonkwo *et al.*,[21] who observed that hydration, GFR growth, anabolic rates and a higher fetal need for maternal protein might lead to the fall. The increase of glomerular filtration, usually in a pregnancy, leads to decreased urea concentrations.[24] With GFR increasing without significantly increasing urea production, its plasma concentration drops. During late embryo, protein metabolism changes imply that amino acids are conserved for synthesis of tissue and data shows an improved metabolic rate and higher placental absorption which subsequently reduces urea plasma concentration.

In the nephropathic rats in the third and post-partum, the Protein Creatinine Ratio (PCR) increased considerably in hypertensive nephropathy rats, temporarily with conditions such as stress, pregnancies, food, cold and hard activity. Persistent urine protein implies probable renal injury or another disease that

Table 7. Histology of the kidneys of pregnant Wistar rats during 3rd trimester and postpartum period in response to administration of methanolic leaf extracts of test plants.

Groups	Kidney 3rd trimester	Post-partum
Control	Section shows essentially normal cortical parenchyma with well distributed glomerular structures. The medulla also appears normal with relatively normal sized neurons. No observable lesion	Normal kidney and attached adrenal. No observable lesion
Only Ext-A (No Induced H. Nep.)	Normal	Normal kidney tissues
Only Ext-B (No Induced H. Nep.)	Normal	Normal kidney tissues
Only Ext-C (No Induced H. Nep.)	Normal	Normal kidney tissue
Induced H. Nep., no treatment	Section of the renal tissue shows extensive tubulo-interstitial necrosis with some lumen filled by fibrinoid exudates. Some of the glomeruli appeared congested	Normal renal tissue with very mild tubular necrosis
Induced H. Nep. + 100 mg/kg StdD	Section of the kidney shows mild interstitial necrosis, foci of thyroidisation of some tubules, and hypercellularity of glomeruli mesangial cells.	Normal renal tissue with, though a focus of mild tubular necrosis seen
Induced H. Nep. + 50 mg/kg Ext-JC	Mild to moderate tubulo-interstitial necrosis	Normal renal tissue with congested vessel
Induced H. Nep. + 100 mg/kg Ext-JC	Moderate to severe interstitial necrosis.	Mild tubular necrosis though more wide spread
Induced H. Nep. + 200 mg/kg Ext-JC	Severe tubulo-interstitial necrosis with marked fibrinoid exudates. Peritubular haemorrhage, interstitial inflammation, congested glomeruli, thyroidisation of some tubules are also present.	Very mild perivascular and tubulointerstitial inflammation
Induced H. Nep. + 50 mg/kg Ext-AC	Severe tubulo-interstitial necrosis, fibrinoid exudates within tubules. Mild to moderate glomerular haemorrhage	Normal renal tissue with congested glomeruli
Induced H. Nep. + 100 mg/kg Ext-AC	Moderate to severe tubulo-interstitial necrosis with fibrinoid exudates, haemorrhagic glomeruli, and thyroidisation of some tubules.	Normal renal tissue
Induced H. Nep. + 200 mg/kg Ext-AC	Severe tubulo-interstitial necrosis, interstitial haemorrhage, severe interstitial neutrophilic inflammation	Normal renal tissue
Induced H. Nep. + 50 mg/kg Ext-SA	Moderate tubulointerstitial necrosis, Mild glomerular haemorrhage, interstitial neutrophilic inflammation and haemorrhage	Normal renal tissue with some foci areas of tubular necrosis
Induced H. Nep. + 100 mg/kg Ext-SA	Moderate tubulointerstitial necrosis, glomerular haemorrhage, mesangial hypercellularity	Mild tubular necrosis with perivascular inflammation, congested glomeruli and interstitial haemorrhage
Induced H. Nep. + 200 mg/kg Ext-SA	Severe tubulointerstitial necrosis, glomerular haemorrhage and mesangialhypercellularity	Normal renal tissue

H. Nep.: Hypertensive nephropathy; Ext-J: Methanolic leaf extract of *Jatropha curcas*; Ext-AC: Methanolic leaf extract of *Alchonnea cordifolia*; Ext-SA: Methanolic leaf extract of *Secamone afzelii*. The standard drug used was Methyldopa.

requires further testing to identify the reason. The urine protein-creatinine ratio for proteinuria prediction has been regarded as essential. It compares the protein excretion in the urine to the creatinine excretion in the urine, therefore adjusting protein excretion to the glomerular filtration rate.[25]

Conclusion

This study showed that *Jatropha curcas*, *Alchonnea cordifolia* and *Secamone afzelii* methanolic plant extracts have potentials in the management of chronic hypertensive kidney disease.

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