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Evaluation of Nephroprotective Activity of Aqueous and Hydroethanolic Extracts of *Trema guineensis* Leaves (Ulmaceae) against Gentamicin-Induced Nephrotoxicity in Rats

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Authors' contributions

This work was carried out in collaboration between all authors. Author DGC designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors KSL and KYKF managed the analyses of the study. Author BA managed the literature searches. Author YHF supervised the work. Author OAT provided technical support. All authors read and approved the final manuscript.

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ABSTRACT

Aims: The present study investigated the potential nephroprotective activity of aqueous and hydroethanolic extracts of *Trema guineensis* leaves (Ulmaceae) and determined the most active extract in rat.

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Study Design: *Trema guineensis* leaves were collected from Abobo in the district of Abidjan (Côte d'Ivoire). The plant was identified and authenticated by the Department of Botany, Felix Houphouet Boigny University of Abidjan (Côte d'Ivoire).
Place and Duration of Study: Analysis of the plant samples was done in pharmacodynamics Biochemistry Laboratory, Felix Houphouet Boigny University, the Laboratory of Organic Chemistry and Natural Substances, Felix Houphouet Boigny University and the Laboratory of Pharmacology, clinical and therapeutic pharmacy, UFR Pharmaceutical and Biologic Sciences, Felix Houphouet Boigny University between September and October 2016.
Methodology: The extracts obtained starting from 100 g of plant powder on the one hand by decoction in 1 Liter of distilled water and on the other hand by maceration in 1 Liter of ethanol-water mixture 70% (70:30, v/v). The aqueous and hydroethanolic extracts at doses 100 and 200 mg/kg body weight were studied in comparison with vitamin E (250 mg/kg body weight) against gentamicin-induced renal toxicity (80 mg/kg/day). In assessing nephroprotective effect, rats were pretreated by oral gavage daily with vitamin E and extracts at different doses (100 and 200 mg/kg body weight) one hour before gentamicin intraperitoneal injection for seven days.
Results: The administration of gentamicin through intraperitoneal route to rats for seven days, resulted in an increase in urea and creatinine concentrations as well as decrease of total protein concentration in the serum. The values of total protein and albumin concentrations increased in urine after administration of gentamicin. *Trema guineensis* aqueous and hydroethanolic extracts used to treat animals suffering from nephrotoxicity would have significantly reduced ($P < 0.001$ and $P < 0.01$) biochemical parameters considered as markers of nephrotoxicity. Moreover, the aqueous extract (200 mg/kg body weight) and vitamin E restored the toxic effect of gentamicin into equal significance.
Conclusion: The results of this study showed that the aqueous extract possesses a nephroprotective activity against gentamicin-induced kidney damage in rats. So aqueous extract can be utilized for preventives purposes.

Keywords: Nephroprotective; gentamicin; Trema guineensis; rat; vitamin E.

1. INTRODUCTION

The kidney is an organ that possesses several biological roles of which the most important is homeostatic balance of body fluids by cleaning and secreting metabolites like urea, uric acid creatinine and minerals from blood and excreting the nitrogenous wastes along with water, as urine [1]. They are often subjected to high concentrations of potentially toxic agents such as chemicals and drugs by accumulating and producing broad spectrum morphological and functional effects on the kidney [2]. Some reports suggest that between 5 to 20% of cases of acute renal failure can be directly attributed to drugs and chemicals, although minor damage may pass undetected [3].

Gentamicin is one of the aminoglycosides; it is a very important agent for the treatment of Gram-negative bacterial infections. However; its clinical use is limited by its nephrotoxicity [4,5]. It has been estimated that up to 30% of patients treated with aminoglycosides for more than seven days show some signs of nephrotoxicity [6].

Plants are important source of drugs. Many of the modern drugs that are currently available have also been derived directly or indirectly from herbal sources. Herbal medicines have been proved to be highly effective, economic and safe alternative tools for treatment and prevention of various human diseases in Africa and in developing countries [7,8,9].

Trema guineensis (Ulmaceae) is a plant distributed in the west central part of Côte d'Ivoire. The leaves of this plant are locally used for the treatment of various diseases including cardiac failure, constipation, pains, fever, cough, hypertension [10,11,12,13]. Phytochemical study for *Trema guineensis* revealed the presence of sterol, terpen, polyphenol, flavonoid, tannin, saponosid and alkaloid which conferred antimicrobial, cholinergic, analgesic, antioxidant and anti-inflammatory properties on the plant leaves [14,15,16,17,18].

In view of *Trema guineensis* therapeutic advantages, the present study was carried out to evaluate the protective effect of its leaves aqueous and hydroethanolic extracts against gentamicin-induced nephrotoxicity.

2. MATERIALS AND METHODS

2.1 Samples Collection and Extraction

The fresh leaves of *Trema guineensis* were collected from Abobo (Abidjan). The plant species was later identified and authenticated by the Department of Botany, Felix Houphouet Boigny University of Abidjan.

It was dried at room temperature during two weeks and pulverized using an electric grinder (IKA-type MAG®). The powder of leaves served as our sample to be analyzed.

2.1.1 Hydroethanolic extract

100 g of powder of *Trema guineensis* leaves were macerated for 24 hours in 1 Liter of ethanol-water mixture 70% (70:30, v/v). The obtained macerate was then filtered twice on white cotton and once on Whatman filter paper N°3. The filtrate was evaporated and dried at temperature of 40°C using a rotary evaporator type BUCHI 161 Water Bath [19].

2.1.2 Aqueous extract

100 g of *Trema guineensis* leaves powder were added to 1 Liter of boiling distilled water for twenty minutes. The decoction was filtered twice on white cotton and once on Whatman filter paper N°3. The filtrate was dried under reduced pressure using a rotary flash evaporator and stored at a temperature of -4°C until use [20].

2.2 Experimental Animals

Healthy adult Wistar albino rats (*Rattus norvegicus*) weighing between 150-200 g were used for the study. The rats were provided and kept in the laboratory animal house of the Training and Research Unit of Pharmaceutical and Biologic Sciences, Felix Houphouet Boigny University, Côte d'Ivoire. The animal house was according to environmental standard temperature of 26±1°C and relative humidity 50±5% with 12 h light-dark cycle. The animals were housed in large spacious, hygienic plastic cages during the course of the experimental period. The rats fed with FACI® (Fabrication d'Aliments de Cote d'Ivoire) pellets and drank tap water.

2.3 Evaluation of Nephroprotective Activity in Gentamicin Induced Nephrotoxicity

The evaluation of the nephroprotective activity of *Trema guineensis* aqueous and hydroethanolic extracts was conducted using the method described by Paoulomi [21] with some modifications [22]. The animals were divided according to weight in seven groups each of six rats:

Group I (Normal): Normal control treated daily with distilled water and 0.9 % NaCl for 7 days.
Group II (Genta): Negative control treated daily with distilled water and gentamicin (80 mg/kg) for 7 days.
Group III (Vit E): Positive control treated daily with vitamin E (250 mg/kg) and gentamicin (80 mg/kg) for 7 days.
Group IV (EA 100): Rats treated daily with aqueous extract of *Trema guineensis* (100 mg/kg) and gentamicin (80 mg / kg) for 7 days.
Group V (EA 200): Rats treated daily with aqueous extract of *Trema guineensis* (200 mg/kg) and gentamicin (80 mg/kg) for 7 days.
Group VI (EE 100): Rats treated daily with hydroethanolic extract of *Trema guineensis* (100 mg/kg) and gentamicin (80 mg / kg) for 7 days.
Group VII (EE 200): Rats treated daily with hydroethanolic extract of *Trema guineensis* (200 mg/kg) and gentamicin (80 mg / kg) for 7 days.

The test drug (*Trema guineensis*) and the control groups were given by oral gavage 60 minutes prior to the gentamicin intraperitoneal injection in the different groups.

After the last treatment, animals were placed in metabolic cages to collect their urine for 24 hours.

2.4 Collection and Storage of Blood and Organs

After 7th day of last dose, animals were sacrificed after blood collection under ether anesthesia. The both kidneys were removed, rinsed with normal saline, weighed and then fixed in aqueous Bouin. The blood of each animal was collected (tail vein) in a tube without anticoagulant before and after experiment. The blood was centrifuged at 3000 rpm for 10 minutes (Centrifuge B4i) to separate serum. Serum was kept at -20°C until the analysis. The collected urines were quantified and a sample of each urine was stored in eppendorf tubes for the determination of certain biochemical parameters [23].

2.5 Biochemical Assays

The serum samples were used to assay the biochemical parameters such as: creatinine, total

proteins and urea. The collected urine was used to assess the levels of albumin and total proteins in animals using an automatic analyzer (Cobas C 311, Hitachi Rock).

2.6 Statistical Analysis

The values expressed as Mean ± standard deviation (SD) from 6 animals. The statistical analysis was carried out using one way analysis of variance (ANOVA) followed by Dunnett's test. The value of $P < 0.05$ was considered significant.

3. RESULTS AND DISCUSSION

3.1 Results

Before treatment, the biochemical parameters in serum were evaluated statistically equal by comparing each group with every other groups.

After 7 days of treatment, it was observed that the gentamicin produced significant changes in serum urea, serum creatinine, serum total protein, urinary total protein and urinary albumin when compared with normal saline treated animals indicating gentamicin induced toxicity.

Serum urea was increased in rats treated with only gentamicin but treatment with hydroethanolic and aqueous extracts of *Trema guineensis* at doses 100 mg/kg and 200 mg/kg and vitamin E (positive control) significantly ($P < 0.001$) reversed the effect of gentamicin indicating nephroprotective activity (Fig. 1).

The aqueous extract at dose 200 mg/kg and vitamin E significantly ($P < 0.01$) decreased serum creatinine levels in animals (Fig. 2) compared to negative control group.

In all groups, serum total protein levels was elevated with ($P < 0.001$ and $P < 0.01$) significance compared with negative control group (Fig. 3).

Concerning the urine total protein, the Fig. 4 showed significant ($P < 0.001$) increase in total protein levels in negative control group and hydroethanolic-treated groups compared to normal group.

Urinary albumin concentration was also significantly increased ($P < 0.001$) in hydroethanolic-treated groups and negative control group compared to normal group (Fig. 5).

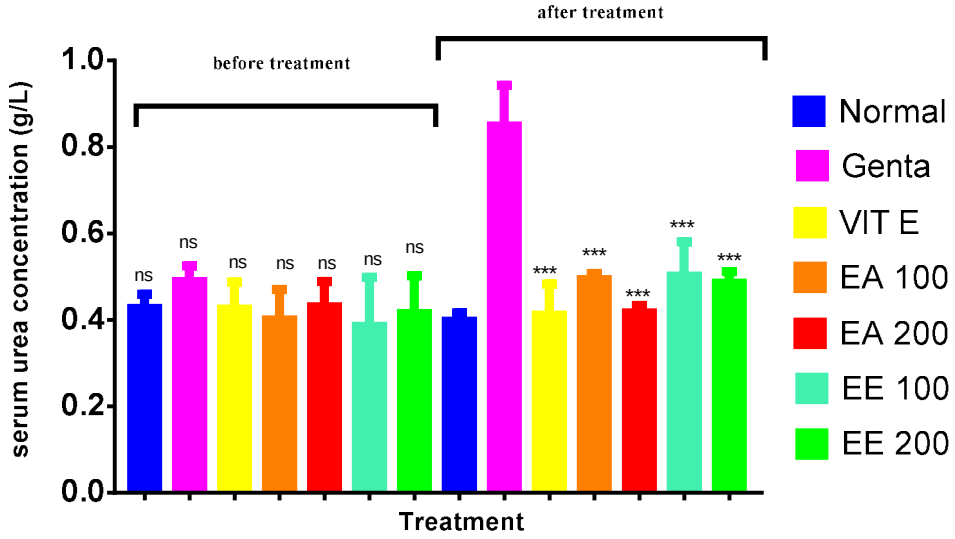

Fig. 1. Effect of *Trema guineensis* extracts (aqueous and hydroethanolic) and vitamin E on serum urea in gentamicin-treated rats compared to negative control group

Values are expressed as mean ± SD (standard deviation) with n = 6 in each group

*ns: No significant difference between the different groups before treatment. Significance ***P<0.001 compared to negative control group (Genta). Normal group: NaCl; Genta: gentamicin; VIT E: vitamin E + gentamicin; EA 100: aqueous extract (100 mg/kg) + gentamicin; EA 200: aqueous extract (200 mg/kg) + gentamicin; EE 100: hydroethanolic extract (100 mg/kg) + gentamicin; EE 200: hydroethanolic extract (200 mg/kg) + gentamicin*

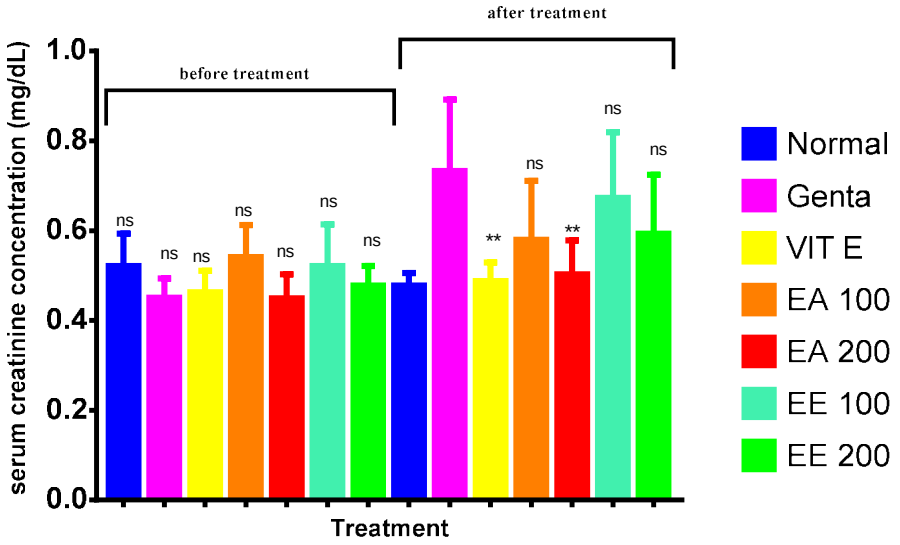

Fig. 2. Effect of *Trema guineensis* extracts (aqueous and hydroethanolic) and vitamin E on serum creatinine in gentamicin-treated rats compared to negative control group

Values are expressed as mean ± SD (standard deviation) with n = 6 in each group
*ns: No significant difference between the different groups before treatment. Significance: **P<0.01, ns: no significance compared to negative control group. Normal: NaCl; Genta: gentamicin; VIT E: vitamin E + gentamicin; EA 100: aqueous extract (100 mg/kg) + gentamicin; EA 200: aqueous extract (200 mg/kg) + gentamicin; EE 100: hydroethanolic extract (100 mg/kg) + gentamicin; EE 200: hydroethanolic extract (200 mg/kg) + gentamicin*

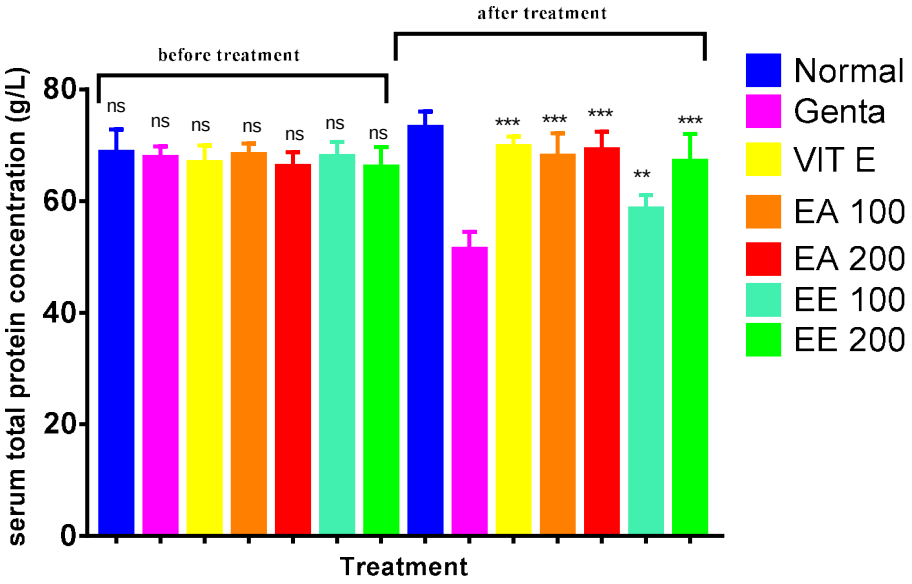

Fig. 3. Effect of *Trema guineensis* extracts (aqueous and hydroethanolic) and vitamin E on serum total protein in gentamicin-treated rats compared to negative control group

Values are expressed as mean ± SD (standard deviation) with n = 6 in each group
*ns: No significant difference between the different groups before treatment. Significance **P<0.01 and ***P<0.001 compared to negative control group (Genta). Normal: NaCl; Genta: gentamicin; VIT E: vitamin E + gentamicin; EA 100: aqueous extract (100 mg/kg) + gentamicin; EA 200: aqueous extract (200 mg/kg) + gentamicin; EE 100: hydroethanolic extract (100 mg/kg) + gentamicin; EE 200: hydroethanolic extract (200 mg/kg) + gentamicin*

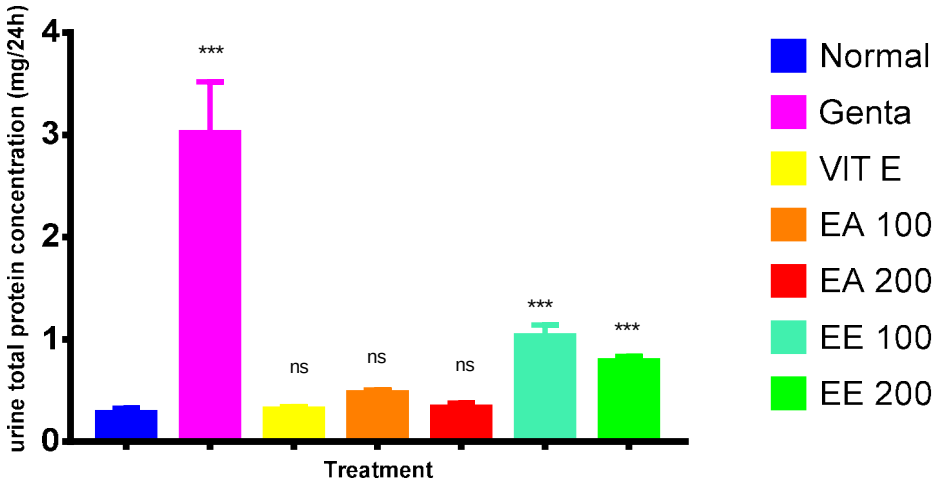

Fig. 4. Effect of *Trema guineensis* extracts (aqueous and hydroethanolic) and vitamin E on urinary total protein in gentamicin-treated rats compared to normal control group

Values are expressed as mean ± SD (standard deviation) with n = 6 in each group
*Significance ***P<0.001 and ns: no significance compared to normal group. Normal group: NaCl; Genta: gentamicin; VIT E: vitamin E + gentamicin; EA 100: aqueous extract (100 mg/kg) + gentamicin; EA 200: aqueous extract (200 mg/kg) + gentamicin; EE 100: hydroethanolic extract (100 mg/kg) + gentamicin; EE 200: hydroethanolic extract (200 mg/kg) + gentamicin*

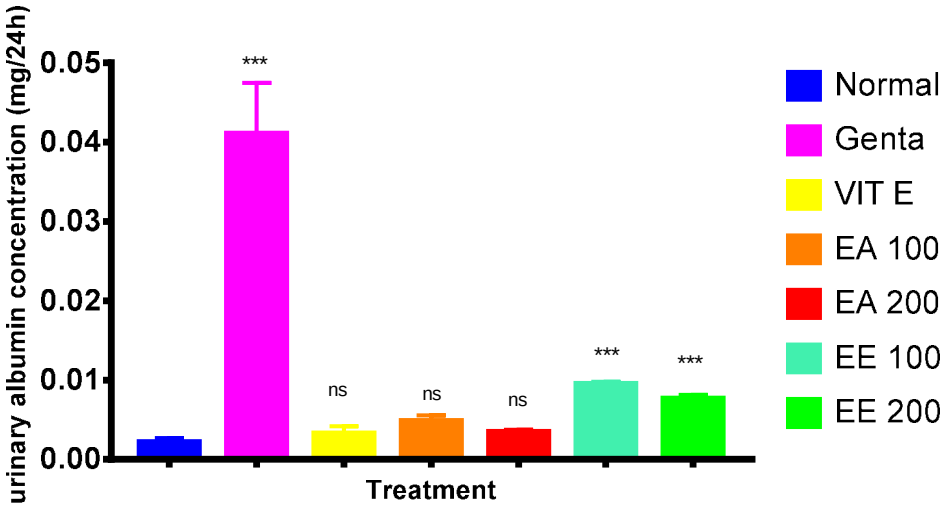

Fig. 5. Effect of *Trema guineensis* extracts (aqueous and hydroethanolic) and vitamin E on albumin in gentamicin-treated rats compared to normal group

Values are expressed as mean ± SD (standard deviation) with n = 6 in each group
*Significance ***P<0.001 and ns: no significance compared to normal group. Normal: NaCl; Genta: gentamicin; VIT E: vitamin E + gentamicin; EA 100: aqueous extract (100 mg/kg) + gentamicin; EA 200: aqueous extract (200 mg/kg) + gentamicin; EE 100: hydroethanolic extract (100 mg/kg) + gentamicin; EE 200: hydroethanolic extract (200 mg/kg) + gentamicin*

3.2 Discussion

The kidney is an essential organ that plays a dominant role in homeostasis by excreting the metabolic waste products. It conserves necessary products depending on body needs. Medicinal plants are commonly used in treating or preventing specific diseases and they are considered to play a beneficial role in health care [24,25]. The present study was carried out to

evaluate the protective effects of the aqueous and hydroethanolic extracts of *Trema guineensis* leaves on gentamicin-induced nephrotoxic in rats.

Nephrotoxicity is a poisonous effect of some substances, as chemicals and some drugs, causing damage to the kidneys [26]. Gentamicin is a commonly used aminoglycoside. Routine therapeutic use of gentamicin (80 mg/kg/day) for more than seven days has been a common cause of nephrotoxicity [27]. It has been shown that nephrotoxicity caused by gentamicin treatment is associated with increased of the release of the oxidants compounds, which might be the major contributing factor towards renal damage [28]. Gentamicin usually accumulates in renal proximal tubules and enhances hydrogen peroxide and oxygen free radicals generation [7,29,30]. Abnormal production of reactive oxygen species may result in cellular injury and necrosis through peroxidation of membrane lipids, protein denaturation and DNA damage [31]. Hydrogen peroxide generated during the gentamicin induced oxidative stress in mitochondrial membranes releases iron from the mitochondria. The released iron makes a complex with gentamicin and accelerates the oxidative stress [32].

Nephrotoxic effect is identified by estimating the biomarkers like serum creatinine and serum urea which are considered reliable markers [33]. Urea is the main product of protein catabolism. It is completely filtered by the glomerulus and passively excreted at high concentrations in the urine. The serum level of urea is used as an index of renal function [34]. Creatinine is an end product of muscle catabolism, which is removed at a constant rate by the kidneys. The serum creatinine concentration is an index of the renal function. The level of serum creatinine increases if the kidney does not work properly [34]. Thus, increases in serum levels of these markers are indicative of renal injury [33]. Therefore, in this study, the nephroprotective activity of our extracts was evaluated by the determination of certain biochemical parameters in both serum (urea, creatinine, total protein) and in the urine (total proteins and albumin) in animals.

Gentamicin-administered rats (negative control group) had encountered acute kidney dysfunction as evidenced by elevation of serum urea and creatinine with low total protein in serum. The results of our investigation is in conformity with previous reports attributing these changes to nephrotoxicity induced by gentamicin [22,35,36]. Treatment with aqueous and hydroethanolic extracts of *Trema guineensis* at dose of 100 mg / kg body weight and 200 mg / kg body weight daily for seven days restored significantly ($P < 0.001$ and $P < 0.01$) creatinine and urea levels (Figs. 1 and 2) compared to the negative group. This result is supported by Paoulomi et al. [21] who indicated that supplementation of *Aloe barbadensis* restored the increased levels of urea and creatinine in gentamicin-induced rats. However, treatment with these extracts resulted in increased serum total protein levels significantly ($P < 0.001$) in comparison with negative control (Fig. 3); this suggests that *Trema guineensis* contents protected the kidney tissue integrity. This result is reinforced by Bamba et al. [22] studies.

Proteins are filtered by the glomerulus, but totally reabsorbed by the proximal tubule. They are not detectable in urine or present in very small quantities [37]. Proteinuria, usually reflecting the loss of normal glomerular filtration impermeability to plasma proteins is an early sign of kidney disease [38]. Thus, detection of proteinuria is necessary for the recognition of most kidney disease [34].

The parameters evaluated in urine of rats were total protein and albumin. These parameters were found to be increased significantly ($P < 0.001$) in gentamicin induced rats and extracts hydroethanolic-treated groups (EE 100; EE 200) when compared to normal rats (Figs. 4 and 5).

The increased concentration of urinary total protein and albumin observed in gentamicin treated in rats only (negative control) could be due to toxicity of free radical generated from gentamicin damaging effect.

There was no statistical difference between the animals groups treated with aqueous extracts (100 and 200 mg/kg body weight) and the group treated with the normal saline; that proves these aqueous extracts would have reduced the nephrotoxicity induced by gentamicin in rats, so that the urinary total protein and albumin concentrations would be close to those of untreated rats. Treatment by *Trema guineensis* normalized the levels of urinary total protein and albumin in gentamicin treated rats. This result is similar to Bamba et al. [22] work. They showed that aqueous and ethanol extracts of *G. celosioides*, *C. nitida*, and *E. angolense* effectively mitigated the effects of gentamicin on proteinuria and albuminuria.

Natural antioxidants have a variety of biochemical actions such as inhibition of reactive oxygen species production, scavenging of free radicals [39]. Many studies showed that the presence of antioxidant compounds in plants conferred them a nephroprotective activity [40,41,42]. The phytochemical investigation of *Trema guineensis* revealed the presence of antioxidant compounds such as phenols, flavonoids, flavonols and sterols [16,17]. The investigation revealed that *Trema guineensis* possessed protective effect against gentamicin induced nephrotoxicity.

4. CONCLUSION

The nephroprotective effect of *Trema guineensis* leaves extracts was evaluated. The present study indicated that the aqueous and hydroethanolic extracts of *Trema guineensis* leaves restored significant gentamicin-induced perturbation rates on biochemical parameters such as urea, creatinine and total protein in serum thus that total protein and albuminin urine. The aqueous extract at dose 200 mg/kg body weight possessed profound nephroprotective activity and also revealed that the nephroprotective activity of this extract was comparable to that of vitamin E.

ETHICAL APPROVAL

The experimental procedures were conducted after the approval of the Ethical Guidelines of University (Côte d'Ivoire) Committee on Animal Resources. All these procedures used, were in strict accordance with the guidelines for Care and Use of Laboratory Animals and the statements of the European Union regarding the handling of experimental animals (86/609/EEC).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Javaid R, Aslam M, Nizami Q, Javaid R. Role of antioxidant herbal drugs in renal disorders: An overview. Free Radicals and Antioxidants. 2012;2(1):1-6.
2. Gaddam SR, Lalitha PR, Gaddam RR, Dyaga VC. Evaluation of nephroprotective activity of the methanolic extract of *Phyllanthus niruri* (Family Euphorbiaceae). Int. J. Pharm. Phytopharmacol. Res. 2015; 4(5):276-280.
3. Mohana LS, Usha KRT, Sandhya RKS. A review on medicinal plants for nephroprotective activity. Asian J. Pharm. Clin. Res. 2012;5(4):8-14.
4. Sahar K. Nephroprotection of lacidipine against gentamycin-induced nephrotoxicity in albino rats. Journal of Experimental Pharmacology. 2010;2:59–63.
5. Maldonado PD, Barrera D, Medina-Campos O, Hernandez-Pando Ribarra-Rubio M, Pedraza-Chaverri J. Aged garlic extract attenuates gentamycin induced renal damage and oxidative stress in rats. Life Sci. 2003;73(20):2543–2556.
6. Pani SR, Mishra S, Sahoo S, Panda PK. Protective effect of herbal drug in cisplatin induced nephrotoxicity. Indian Journal of Pharmacology. 2011;43(2):200-202.
7. Islam R, Alam AHMK, Rahman BM, Salam KA, Hossain A, Baki A, Sadik G. Toxicological studies of two compounds isolated from *Loranthus globosus* Roxb. Pak. J. Biol. Sci. 2007;10:2073-2077.
8. Suji J. JA, Vimalastalin R. Nephroprotective activity of *Aristolochia indica* leaf extract against gentamicin induced renal dysfunction. International Journal of Research in Biochemistry and Biophysics. 2014;4(2):13-18.
9. Sangita S, Swarn L, Kavindra NT. Protective role of *Phyllanthus fraternus* against cyclophosphamide induced nephrotoxicity in mice. Journal of Scientific Research. 2014;58:75-85.
10. Aké Assi L. Quelques plantes utilisées dans le traitement des maladies cardiaques en Côte d'Ivoire. Bull. Méd. Trad. Pharm. ACCT. Paris 2. 1988;(1):96-100.
11. N'Guessan K. Contribution à l'étude ethnobotanique en pays Krobou (République de Côte D'ivoire). Thèse 3eme cycle, Faculté sciences et Techniques de l'Université Nationale. 1995;557.
12. Kerharo J, Bouquet A. Plantes médicinales et toxiques, de la Côte d'Ivoire-HauteVolta. Mission d'Etude de la Pharmacopée Indigène en A.O.F. Ed. Vigot Frère. 1950;1011.
13. Guédé-Guina F. Docteur « plantes mes amies ». Editeurs. Educi. 2003;37-40.
14. Akinyemi KO, Oluwa OK, Omomigbehin EO. Antimicrobial activity of crude extracts of three medicinal plants used in South-West Nigerian folk medicine on some food borne bacterial pathogens. African Journal

of Traditional, Complementary and Alternative Medicines. 2006;3(4):13-22.

15. Gnahoué G, N'guessan JD, Koffi E, Traoré F, Guédé-Guina F. *In vitro* anti-cholinesterase and cholinergic effect of the aqueous extract of *Trema guineensis* on rabbit duodenum. Trop. J. Pharm. Res. 2009;8(1):11-17.
16. Kouakou YKF, Gnahoue G, Yapi HF, Ayebe EA, N'guessan JD, Djaman AJ. Toxicological and phytochemical screening study of *Trema guineensis* (Ulmaceae), plant of Côte d'Ivoire (West Africa). World Journal of Pharmaceutical Research. 2014;3(8):12-23.
17. Kouakou YKF, Yapi HF, Gnahoue G, Bahi GA, Djaman AJ. Anti-inflammatory and antioxidant activities of ethanol and aqueous leaves extract of *Trema guineensis*. Asian J. Biochem. 2015;10(4): 145-155.
18. Kouakou YKF, Yapi HF, Bahi GA, Gnahoue G, Djaman AJ. Evaluation of antalgic activity and trace elements analysis of *Trema guineensis* extracts in acetic acid induced in rats. Open Access Library Journal. 2016;3:1-7.
19. Guede-guina F, Vangah-manda M, Harouna D, Bahi C. Potencies of Misca, a plant source concentrate against fungi. Journal of Ethnopharmacology. 1993;14: 45-53.
20. De Moua RMX, Pereira PS, Januàrio AH, França S de C, Dias DA. Antimicrobial screening and quantitative determination of benzoic acid derivative of *Gomphrena celosioides* by TLC-densitometry. Chem. Pharm. Bull. 2004;52(11):1342-1344.
21. Paoulomi C, Aniruddha M, Subhangkar N. Protective effects of the aqueous leaf extract of *Aloe barbadensis* on gentamicin and cisplatin-induced nephrotoxicity rats. Asian Pacific Journal of Topical Biomedicine. 2012;S1754-S1763.
22. Bamba A, Yapi HF, Aka KAE, Djyh BN. Evaluation of nephroprotective properties of aqueous and ethanolic extracts of *Gomphrena celosioides*, *Cola nitida* and *Entendrophragma angolense* against gentamicin induced renal dysfunction in the albino rats. European Journal of Pharmaceutical and Medical Research. 2016;3(11):62-69.
23. OVF. Informations sur la Protection des Animaux. Prélèvement de sang chez les rongeurs de Laboratoire et les lapins à des fins expérimentales. Office Veterinaire Federal. 1981;No. 800.116-1.04.
24. Hall JE. Text Book of medical physiology. 12th Ed. Saunders Elsevier. Philadelphia, USA. 2011;307-326.
25. Arunachalam K, Suchetha KN, D'Souza P, Divya B. Evaluation of renal protective activity of *Adhatoda zeylanica* (medic) leaves extract in wistar rats. Nitte Univ. J. of Hea. Sci. 2013;3(4):55-66.
26. Saxena R, Masood M, Khan f, Qureshi Z, Rathore M. Effect of *Dalbergia sissoo* leaves on aminoglycosides induced nephrotoxicity in experimental rats. International Journal of Pharmacology and Pharmaceutical Sciences. 2016;3(2):5-14.
27. Balakumar P, Rohilla A, Thangathirupathi A. 2010. Gentamicin induced nephro-toxicity: Do we have a promising therapeutic approach to blunt it? Pharmacol. Res. 2010;62(3):179-186.
28. Kang C, Lee H, Hah DY, Heo JH, Kim CH, Kim E, Kim JS. Protective effects of *Houttuynia cordata* Thunb. on gentamicin-induced oxidative stress and nephrotoxicity in rats. Toxicol Res. 2014;29(1):61-67.
29. Tavafi M, Ahmadvand H, Toolabi P. Inhibitory effect of olive leaf extract on gentamicin-induced nephrotoxicity in rats. Iran. J. Kidney Dis. 2012;6(1):25-32.
30. Yukawa O, Nakazawa T. Radiation induced lipid peroxidation and membrane bound enzymes in liver microsomes. Int. J. Radiat Biol. 1980;37:621-631.
31. Parlakpinar H, Tasdemir S, Polat A, Bay-Karabulut A, Vardi N, Ucar M, Acet A. Protective role of caffeic acid phenethyl ester (cape) on gentamicin-induced acute renal toxicity in rats. Toxicology. 2005; 207(2):169-177.
32. Afeefa T, Uzma S, Saeed M, Furqan KH, Khalid H, Nadeem IB, Bashir A. Evaluation of protective and curative role of α-lipoic acid and selenium in gentamicin-induced nephrotoxicity in rabbits. Pakistan Journal of Pharmaceutical Sciences. 2012;25(1): 103-10.
33. Adelman RD, Spangler WL, Beasom F, Ishizaki G, Conzelman GM. Frusemide enhancement of neltimicin nephrotoxicity in dogs. J. Antimicrob. Chemother. 1981;7(4): 431–440.
34. Lesely AS, Levey AS. Measurements of Kidney function. Medical Clinics of North America. 2005;89:457-473.
35. Javed S, Khan JA, Khaliq T, Javed I, Abbas RZ. Experimental evaluation of

nephroprotective potential of *Calotropis procera* (Ait) flowers against gentamicin-induced toxicity in albino rabbits. Pak. Vet. J. 2015;35(2):222-226.
36. Reddy VC, Amulya V, Lakshmi CHA, Reddy DBPK, Praveen DB, Pratima D, Thirupathi AT, Kumar KP, Sengottuvelu S. Effect of simvastatin in gentamicin induced nephrotoxicity in albino rats. Asian J. Pharm. Clin. Res. 2011;5(1):36-40.
37. Trolliet P. Explorations fonctionnelles tubulaires. Revue française des laboratoires. 1994;268:29-34.
38. Cohen EP, Lemann J. The role of the laboratory in evaluation of kidney function. Clinical Chemistry. 1991;37(6):785-796.
39. Abdollahi M, Larijani B, Rahimi R, Salari P. Role of oxidative stress in osteoporosis. Therapy. 2005;2(5):787-796.
40. Nandave M, Ojha SK, Joshi S, Kumari S, Arya DS. *Moringa oleifera* leaf extract prevents isoproterenol-induced myocardial damage in rats: Evidence for an antioxidant, antiperoxidative, and cardioprotective intervention. Journal of Medicinal Food. 2009;12(1):47-55.
41. Adeneye AA, Benebo AS. Protective effect of the aqueous leaf and seed extract of *Phyllanthus amarus* on gentamicin- and acetaminophen-induced nephrotoxic rats. J. Ethnopharmacol. 2008;118(2):318-323.
42. Miller NJ, Rice-Evans CA. The relative contribution of ascorbic acid and phenolic antioxidants to the total antioxidant activity of orange and apple fruit juices and blackcurrant drink. Food Chem. 1997; 60(3):331-337.

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