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Potential Nephrotoxic Sequel of the Kidney Following Exposure to Turmeric Extract in Adult Wistar Rats

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ABSTRACT

Introduction

Turmeric (*Curcuma Longa*) is a rhizomatous, perennial plant, flowering in nature, belonging to the ginger family. It's potential therapeutic benefits, has led to an increase in its consumption globally. Despite severe studies on turmeric there is still existing literature gap on the effect of turmeric on the kidney. This study espoused the potential nephrotoxic sequel of the kidney following exposure to turmeric extract in adult wistar rats.

Methods

Ethical approval for the study was obtained from the Ethics and Research Committee in the Faculty of Basic Medical Sciences of the Delta State University, Abraka. 24 adult female Wistar rats, weighing between 180g - 200g were used as experimental model. They were grouped into 4 groups (A, B, C and D), and were euthanized at the end of the experimental days and effect of tumeric extract were studied.

Results

We found that tumeric extract effect on the kidney histology was unremarkable in all groups with varying doses. Also observed was moderate significant increase in creatinine and urea level in treated groups when compared with control group.

Conclusions

Obtained upshot suggests that oral administration of turmeric with graded doses and time dependent showed no microscopic or cytoarchitectural changes, but with a negative functional report.

Keywords: histologic; homeostatic; non-remarkable; turmeric.

INTRODUCTION

Turmeric (*Curcuma Longa*) is a rhizomatous, perennial plant, flowering in nature, belonging to the ginger family. Its phytochemical constituents include 1, 7-bis (4-hydroxy-3-methoxyphenol-1, 6-eptadiene-3, 5-Dione, and commonly used for traditional[1] and medicinal purposes due to its antioxidant, anti-inflammatory, antimicrobial, anti-angiogenic and anti-cancer properties.[2-8] Turmeric (curcumin) exist as a pure crystalline powder which is soluble in organic solutions such as ether, alcohol, and olive oil.[9] The

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potential therapeutic benefits of turmeric has led to an increase in its consumption globally,[10,11] with several studies showing also the beneficial nephroprotective effect of turmeric,[12-15] despite this, there is still a noticeable increase in the number of individuals affected by kidney related diseases, most especially chronic kidney disease.[16,17] Chronic kidney disease is characterized by progressive loss in kidney function which affects the excretion of metabolic byproducts[18]. Despite studies on the turmeric, [13,19-20] there is still existing literature gaps on the upshot of turmeric on the histology of the kidneys, thus this study sought to investigates the potential nephrotoxic sequel of the kidney following exposure to turmeric extract in adult wistar rats.

METHODS

Twenty - four (24) adult Wistar rats (female), with weight ranging from 180g - 200g were used as experimental model and were obtained from the animal holding facility of the College of Health Science in Delta State University of Abraka. Delta State, Nigeria. The animals were acclimated for two weeks, [21] and were fed twice daily with unrestricted access to food and water under standard conditions (12 hours of light and dark cycle and temperature of about 28 - 31°C) [22]. The experiment lasted for a period of 3 weeks (21 days). Turmeric (curcuma longa) rhizome seed used for the study was obtained and pulverized into fine powder using a blender. Fifty grams (50g) of the powdered seed was cold macerated with 0.5L of 80% methanol in water for 72 hours at ambient temperature (26 - 28ºC). The resultant mixture was filtered using Whatman filter paper (No. 1), the filtrate was concentrated to dryness in vacuo at 40ºC using water bath to give 9g (18% weight) of a semi-solid extract which was then stored in a refrigerator at 4ºC until use. [23,24] Ethical clearance was sought and obtained from the Ethics and Research Committee in the Faculty of Basic Medical Sciences of the Delta State University prior to the inception of this research. This was determined using the resource equation E = Total number of animals - Total number of groups, Where E is the degree of freedom for the analysis of variance A total number of 24 female adult Wistar rats were used for this study. [25] This study adopted an experimental study design, which entails twenty - four (24) female Wistar rats were grouped into 4 groups (group; A, B, C and D). A served as control consisting of 6 rats and B, C and D served as treated group consisting of 6 rats. This groups the animals also into 3 sections, with each section having 8 rats. Sections were labeled accordingly into 7th, 14th and 21st days respectively for easy identification and treatment or administration.

Group A: Six (6) Wistar rats received food and distilled water only (Control)
Group B: Six (6) Wistar rats received 500mg/kg of turmeric extract, food and water only
Group C: Six (6) Wistar rats received 1000mg/kg of turmeric extract, food and water only
Group D: Six (6) Wistar rats received 1500mg/kg of turmeric extract, food and water only.

Table 1. Grouping of rats.

Administration days	Group A (Control)	Group B	Group C	Group D
7th day	2 rats	2 rats	2 rats	2 rats
14th day	2 rats	2 rats	2 rats	2 rats
21st day	2 rats	2 rats	2 rats	2 rats

The doses of turmeric used for this study were 500mg/kg, 1000mg/kg and 1500mg/kg respectively; this was selected based on the knowledge that the LD_{50} of turmeric has been evaluated to be 5000mg/kg body weight in albino rats.[26] Termination of experimental period stipulated for 7, 21 and 42 days, animals were weighed and euthanized by cervical dislocation. Kidney tissues were grossly examined, placed in tissue cassette and processed manually under standard histological procedures which

entails several stages, from fixation using 10% formal saline, tissue processing comprises four sections: dehydration (series changes of the tissue in alcohol with time dependency), clearing (series changes of the tissue in xylene also with time dependent), infiltration (series changes of the tissue in paraffin wax also with time dependency) and embedding (preparation of tissue block, using a mold), sectioning (using a microtome at 5 to 7um), staining (using H and E and special stains), mounting (using DPX) and photomicrography. [27, 28] Prepared Slides were viewed and tissue images were captured using digital microscope "CARL ZEISS (Primo Star)" of about 8.3 mega pixel camera, connected to computer. Obtained micrographs were interpreted to know the histological and cytological effects of turmeric on the kidneys.

RESULTS

Sections of the kidney showed the cortex and medulla. Glomeruli are present in the cortex while tubule extends from the cortex to the medulla. The connective tissue of the glomeruli capillary epithelium and tubular cell all show intact features also seen are stroma blood vessel. Result obtained at various days respectively (7, 14 and 21) depicts features of normal kidney tissue in all groups with varying doses.

Key: G - Glomerulus, BCS - Bowman capsule space, PCT - Proximal convulated tubule, DCT - Distal convulated tubules, N - Nephrocyte,

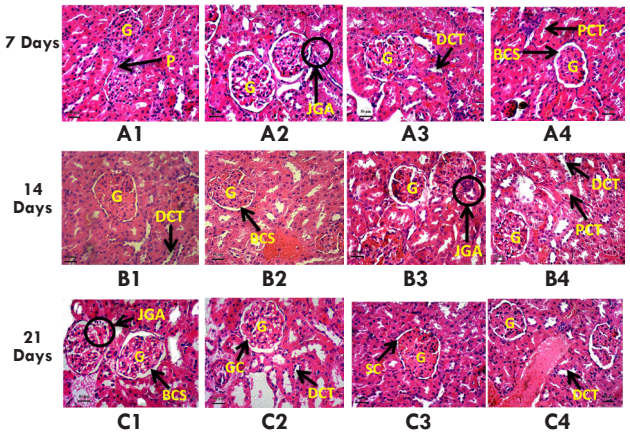

Figure 1. A1–C1: Sections of the kidney for H and E (x400) for group 1 (control), A2 – C2: Sections of the kidney for H and E (x400) for Group 2 (500mg/kg body weight of tumeric extract), A3 - C3: Sections of the kidney for H and E (x400) for Group 3 (1000mg/kg body weight of tumeric extract) and A4 – C4: Sections of the kidney for H and E (x400) for Group 4 (1500mg/kg body weight of tumeric extract)

P – Podpcyte, SC – Squamous cell of bowman's capsule, GC – Glomerular capillary, JGA – Juxtaglomerular apparatus (Table 2).

Table 2. Effect of turmeric on the Urea and Creatinine level in female Wistar rats.

Group	DAY 7		DAY 14		DAY 21	
	Urea (mg/dl)	Creatinine (mg/dl)	Urea (mg/dl)	Creatinine (mg/dl)	Urea (mg/dl)	Creatinine (mg/dl)
A (Control)	15.80±1.28	0.62±0.04	18.69±1.32	0.78±0.05	22.34±1.56	0.84±0.06
B (500mg/kg)	20.70±1.47	1.13±0.09	23.40±0.87	1.55±0.08	27.78±0.34	1.94±0.07
C (1000mg/kg)	24.80±0.96	1.28±0.16	24.70±0.36	1.76±0.06	27.12±0.56	2.08±0.13
D (1500mg/kg)	26.40±0.74	2.07±0.23	27.70±1.28	2.69±0.14	29.59±1.69	2.89±0.09

DISCUSSION

The kidney as an organ for excretion, plays a vital role in term of excretion of biological waste products. [29,30] This study demonstrated that oral administration of graded doses of turmeric extract, showed non remarkable histological effect on the kidneys, this may be due to short term exposure and the probable therapeutic property possessed by turmeric and then undergoing through first pass effect thereby reducing its

potency by intestinal enzymes in the gut wall similar to a treatise conducted by Ahama et al., 2023. [31-33] Antolioli et al., 2012 recorded similar findings,[34] where turmeric decreases adenosine deaminase with resultant modulation of inflammatory cascade which protects the kidneys from renal injuries. Homeostatic distortion in cellular function without anatomical manifestation may show physiological alterations, findings obtained from the serum parameters of urea and creatinine showed a significant rise in urea and creatinine level in the experimental groups as compared with the control this is in keeping with a treatise of Ayodele et al., 2018.[35] Noticeably, this physiologic disturbance occurred in a dosage related manner, with greater disturbance noticed across the group with higher dosage and longer duration of exposure to turmeric extract. These findings are in contrast to the several studies conducted by several authors of [20,32,36] in which turmeric provided ameliorative and kidney restorative properties possibly through anti-inflammatory mediatization.

CONCLUSIONS

This study which has detailed the anatomic architecture and potential nephrotoxicity following exposure to turmeric in adult wistar rats, suggest that oral administration of turmeric with graded dose and time dependent showed no microscopic or cytoarchitectural changes, but with a negative physiologic outcome. However, a long term study is needful to explicate the effects of turmeric on the histology of the kidney and to verify an appropriate dose duration of tumeric intake in consideration with its efficacy and safety use.

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REFERENCES

1. Singh KS, Bhanu B. People of India: Maharashtra. Popular Prakashan 2004; 1(487). https://search.worldcat.org/title/58037479
2. Yadav, R., and Tarun, G. (2017) Versatility of turmeric: a review the golden spice of life. Journal of Pharmacognosy and Phytochemistry. 6(1):41-46. http://www.phytojournal.com/archives/2017/vol6issue1/PartA/6-1-17-211.pdf
3. Dosoky NS, Setzer WN. Chemical composition and biological activities of essential oils of curcuma species. Nutrients. 2018; 10: 1196. doi.org/10.3390/nu10091196
4. Fan X, Zhang C, Liu DB, Yan J, Liang HP. The clinical applications of curcumin: current state and the future. Curr Pharm Des. 2013; 19: 2011-2031. doi.org/10.2174/138161213805289255
5. Kunnumakkara AB, Bordoloi D, Padmavathi G, Monisha J, Roy NK, Prasad S, Aggarwal BB. Curcumin, the golden nutraceutical: multi targeting for multiple chronic diseases. Br J Pharmacol. 2017; 174(11): 1325 - 1348. doi.org/10.1111/bph.13621
6. Stanic Z. Curcumin, a compound from natural sources, a true scientific challenge: a review. Plant Foods Hum Nutr. 2017; 72: 1 - 12. doi.org/10.1007/s11130-016-0590-1
7. Ahmad RS, Hussain MB, Sultan MT, Arshad MS, Waheed M, Shariati MA, Plygun S, Hashempur MH. Biochemistry, Safety, pharmacological activities and clinical application of turmeric: A mechanistic review. Evid Based Complementary Altern Med. 2020: 7656919. Doi:10.1155/2020/7656919
8. Sirotkin AV, Kadasi A, Stochmalova A, Balazi A, Foldesiova M, Makovicky P, Chrenek P, Harrath AH. Effect of turmeric

on the viability, ovarian folliculogenesis, fecundity, ovarian hormones and reaction to luteinizing hormone of rabbits. Animal 2018; 12(6): 1242-1249. DOI: 10.1017/S175173111700235X

9. Jayaprakasha GK, Rao LJM, Sakariah KK. Antioxidant activities of curcumin, demethoxycurcumin and bisdemethoxylcurcumin. Food Chem. 2006; 98(4): 720-724. doi:10.1016/j.foodchem.2005.06.037
10. Akram M, Afzal A, Khan U, Abdul H. Curcuma longa and curcumin. Plant Biol. 2010; 55(2): 65 - 70. https://www.researchgate.net/profile/Muhammad-Akram-88/publication/284415430
11. Jeber ZK, Tawfeek FK. Effect of turmeric oil in reproduction efficiency of immature female rats exposed to oxidative stress induced by potassium dichromate. J Pharmacy Bioall Sci 2012; 9-13. Doi: 10.9790/3008-0440913.
12. Akinyemi AJ, Faboya OL, Paul AA, Olayide I, Faboya OA, Oluwasola TA. Nephroprotective effect of essential oil from ginger and turmeric rhizomes against cadmium induced neprotoxicity in rats. J Oleo Sci. 2018; 67(10): 1339 – 1345. DOI: 10.5650/jos.ess18115
13. Alvarenga LD, Leal VD, Borges NA, Aguiar AS, Faxen-Irving G, Stenvinkel P, Lindholm B, Mafra D. Curcumin - A promising nutritional strategy for chronic kidney disease patients. J funct foods. 2018; 40: 715 - 721. Doi: 10.1016/j.jff.2017.12.015
14. Damiano S, Andretta E, Longobardi C, Prisco F, Paciello O, Squillacioti C, Mirabella N, Florio SF, Ciarcia R. Effects of Curcumin on the Renal Toxicity Induced by Ochratoxin A in Rats. Antioxidants. 2020; 9(4): 332. doi.org/10.3390/antiox9040332
15. Charles IJ, Okayo OD. Prevention of doxorubicin-induce renal function abnormalities by turmeric in Wistar rats. GSC Biological and Pharmaceutical Sciences. 2021; 14: 143-156. doi: 10.30574/gscbps.2021.14.3.0070.
16. Garcia-Garcia G, Jha V. World Kidney Day Steering C. Chronic kidney disease in disadvantaged populations. Curr Opin Nephrol Hypertens. 2015; 24: 203 – 207. doi: 10.1093/ckj/sfu124
17. Forni Ogna V, Ogna A, Ponte B, Gabutti L, Binet I, Conen D, Erne P, Galino A, Guessous I, Hayoz D, Muggli F, Paccaud F, Pechere-Bertschi A, Suter PM, Bochud M, Burnier M. Prevalence and determinants of chronic kidney disease in the Swiss populaitons. Swiss Med Wkly. 2016; 146: w1433. doi:10.1186/s12916-015-0275-x
18. Moradi H, Sica DA, Kalantar-Zadeh K. Cadiovascular Burden Associated with Uremic Toxins in Patients with Chronic Kidney Disease. Am. J. Nephrol. 2013; 38: 136 – 148. DOI: 10.1159/000351758
19. Ali BH, Al-Suhali S, Al-Suleiman Y, Al-Kalbani J, Al-Bahlani J, Al-Bahlani S, Ashque M, Manoj P, Al-Dhahli B, Al-Abri N, Naser HT, Yasin J, Nemmar A, Al-Za'abi M, Hartmann C, Schupp N. Curcumin Ameliorates Kidney Function and Oxidative Stress in Experimental Chronic Kidney Disease. Basic Clin Pharmacol Toxicol. 2018; 122(1): 65 – 73. DOI: 10.1111/bcpt.12817
20. Zahmatkesh M, Tamadon MR. Administration of turmeric (curcumin) in chronic renal failure; a narrative review on current knowledge. J Ren Endocrinol. 2016; 2;e06. file:///C:/Users/MAN%20OF%20FAITH/Desktop/jre-2-e06.pdf
21. Horinzy C. Acclimating research animal through effective nurturing. Taconic: Model for life. 2019; https://tconic.com/taconic-insights/
22. Bailoo et al. Effects of cage enrichment on

behaviour, welfare and outcome variability in female mice. Front Behav Neurosci. 2018; 12: 232. DOI: 10.3389/fnbeh.2018.00232

23. Thakur S, Bawara B, Dubey A, Nandini D, Chauhan NS, Saraf DK. Effect of Carum carvi and Curcuma longa on hormonal and reproductive parameter of female rats. Int J Phytomedicine. 2009; 1: 31 - 38. Doi: 10. 5138/ijpm.2009.0975.0185.05791
24. Ibraheem BO, Oluwagbenga OI, Tawa OO, Jacob OO, Babatunde A. Effects of organic turmeric on liver integrity and oxidative stress of the brain in rabbits exposed to ultraviolet radiation. Int J environ agric biotech. 2018; 3(3): 838 – 845. DOI: 10.22161/ ijeab/3.3.19
25. Festing MFW. How to Reduce the Number of Animals Used in Research by Improving Experimental Design and Statistics, ANZCCART Human Science Fact Sheet 2020; T10. https://materiais. dbio.uevora.pt/MA/Modulo1/Artigos/T10_ HowtoReducetheNumberFactSheet.pdf
26. Ahama EE, Onyilo PO, Agbamu E, Odokuma EI, Ossai FI, Ogorugba CO, Histologic sequelae following exposure to turmeric extract on wistar rats ovary and uterus. Int. J. Biomol. and Biomed. 2023; 16(1): 13 – 20. https://innspub.net/ histologic-sequelae-following-exposure-to-turmeric-extract-on-wistar-rats-ovary-and-uterus/
27. Ahama EE, Odokuma EI. Histomorphological Effects of Oral Nicotine administration on the testes of adult wistar rats. J. Chem. Heal. Ris. 2023; 13(2): 291 – 298. DOI: 10,22034/ jchr.2022.1949064.1488
28. Ahama EE, Odokuma EI, Ehebha SE, Enakpoya PO. Histological Sequel Following Exposure to Levonorgestrel on Wistar Rat Ovary. J. Chem. Heal. Ris. 2023; DOI: 10.22034/jchr.2023.1964971.1600
29. Prozialeck WC, Edward JR. Cell adhension molecules in shemically induced renal injury. Pharmacol Ther. 2007; 114: 74 - 93. doi: 10.1016/j.pharmthera.2007.01.001
30. Boroushaki MT, Mollazadeh H, Rajabian A, Dolati K, Hoseini A, Paseban M, Farzadnia M. Protective effect of pomegranate seed oil against mercuric chloride induced mephrotoxicity in rat. Ren Fail. 2014; 36: 1581 – 1586. DOI: 10.3109/0886022X.2014.949770
31. Labban L. Medicinal and pharmacological properties of turmeric (Curcuma longa): A review. Int J Pharm Biomed Sci. 2014; 5(1): 17 - 23. https://www.researchgate.net/ publication/262005934
32. Weir MA, Walsh M, Cuerden MS, Sontrop JM, Chambers LC, Garg AX. Micro-Particle Curcumin for the Treatment of Chronic Kidney Disease-1: Study Protocol for a Multicenter Clinical Trial, Can J Kidney Health Dis. 2018; 5: 1 – 9. DOI: 10.1177/2054358118813088
33. Ahama EE, Onyilo PO, Agbamu E, Odokuman EI, Ossai IF, Ogorugba OC. Histologic sequelae following exposure to turmeric extract on wistar rats ovary and uterus, Int. J. Biomol. Biomed. 2023; 16(1): 13 – 20. . https://innspub.net/histologic-sequelae-following-exposure-to-turmeric-extract-on-wistar-rats-ovary-and-uterus/
34. Antolioli L, Colucci R, la Motta C, Tuccori M, Awwad O, da Settimo F, Blandizzi C, Fornia M. Adenosine deaminase in the modulation of immune system and its potential as a novel target for treatment of inflammatory disorder. Curr Drug Targets. 2012; 13: 842 – 862. DOI: 10.2174/138945012800564095
35. Ayodele JA, Oluwabamise LF, Awonegan AP, Olayide I, Opeyemi AF, Ademola OT. Nephro-protective Effect of Essential Oils from Ginger (Zingiberofficinale) and Turmeric (Curcuma longa) Rhizomes against Cadmium-induced Nephrotoxicity in Rats, J Oleo Sci. 2018; 6(10): 1339 - 1345.

DOI: 10.5650/jos.ess18115

36. Trujilllo J, Chirino YI, Molina Jijon E, Anderica-Romero AC, Tapia E, Pedraza-Chaverri J. Renoprotective effect of the antioxidant curcumin: recent findings. Redox Biol. 2013; 1: 448 – 456. DOI: 10.1016/j.redox.2013.09.003

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