Original Article

Protective Efficacy of Cinnamon and Green Tea Against Bisphenol in Rat Kidney

Green Tea Offers More Nephroprotection than Cinnamon against Bisphenol an Induced Tubular Damage in Rat Kidney: A Histological Quantitative Approach

Huma Beenish[1], Hira Cheema[1], Ayesha Yasser[1], Tooba Khurshid[2], Maleeha Bano[3] and Tayyaba Qurashi[1]

ABSTRACT

Objective: To compare protective efficacy of cinnamon extract and green tea against Bisphenol A induced histological changes in rat kidney.

Study Design: Randomized control trial study

Place and Duration of Study: This study was conducted at the Department of Anatomy, Islamic International Medical College, and National Institute of Health, Islamabad from September 2016 to September 2017.

Materials and Methods: Sixty adult male Sprague Dawley rats were divided into four groups with 15 rats in each group. Control group A rats were given distilled water for 30 days subcutaneously. Experimental group B rats were administered Bisphenol A at a dose of 30mg/kg/day subcutaneously for 30 days. Experimental group C rats were given cinnamon at a dose of 200mg/kg/day orally along with subcutaneous Bisphenol A injection. Experimental group D rats were given green tea orally along with subcutaneous Bisphenol A injections. After dissection right kidneys of all rats were examined for histological changes.

Results: The histological parameters of rat kidneys were observed under light microscope. These included height of epithelium of PCT, luminal diameter of PCT, height of epithelium of DCT and luminal diameter of DCT. Worsening of these parameters from control group was maximally seen in group B. However, both groups C and D caused improvement in all measured histological parameters but group D displayed more nephroprotection than group C.

Conclusion: The oxidative stress caused by Bisphenol A has adversely affected kidneys and green tea was found to be more beneficial in ameliorating nephrotoxic effects of Bisphenol A than cinnamon.

Key Words: Bisphenol A, Cinnamon extract, Green tea, Rat kidney, Histology

Citation of article: Beenish H, Cheema H, Yasser A, Khurshid T, Bano M, Qurashi T. Green Tea Offers More Nephroprotection than Cinnamon Against Bisphenol an Induced Tubular Damage in Rat Kidney: A Histological Quantitative Approach. Med Forum 2021;32(11):28-32.

INTRODUCTION

Kidney is the most vital component of urinary system which removes metabolic wastes of human body and conserves fluids and electrolytes.[1] Different disease processes affect histology and function of nephron which lead to renal diseases like glomerulosclerosis and tubulointerstitial fibrosis.[2].

1. Department of Anatomy, Islamic International Medical College, Rawalpindi.
2. Department of Anatomy, Army Medical College, Rawalpindi.
3. Department of Anatomy, Hitec-IMS, Taxila

Correspondence: Dr. Huma Beenish, Assistant Professor of Anatomy, Islamic International Medical College, Rawalpindi.
Contact No: 03334796000
Email: huma.beenish@riphah.edu.pk

Received: January, 2021
Accepted: September, 2021
Printed: November, 2021

Acute renal diseases then progress to chronic kidney disease. The consequences related with chronic kidney disease (CKD) include loss of nephron resulting in end stage renal disease leading to early mortality.[3]

Chronic kidney disease also results from environmental toxins which cause oxidative stress to the renal tubular cells leading to cell death.[4] Bisphenol A (BPA) is one of them. BPA is a plasticizer, a polymer of polycarbonated plastics and epoxy resins.[5] Research shows BPA was greater than 2.2 million metric tonnes has since 2011. BPA is used in formation of food containers, drinking bottles, toys, inner lining of metal cans and water supply pipes.[6]

Numerous studies relate prevalence of BPA in human tissues and body fluids such as urine, serum, plasma, saliva and breast milk. Human exposure to BPA occurs mainly through food and drinking water.[7] BPA can be hydrolyzed under high temperature and acidic or basic conditions to leak into food and drink containers. BPA causes its effects in animal models at doses in range of human exposures.[8]

Natural plant derived antioxidants have been used extensively as compared to synthetic antioxidants due to safety, health benefits and consumer suitability.[9] Herbs are increasingly being investigated as adjunct therapies for CKD. Cinnamomum cassia is a common species of cinnamon widely distributed in Asia. Many studies have indicated antioxidative role of cinnamon against kidney damage caused by various toxins and diabetes.[10] A study on beneficial effects of cinnamon showed that a dose of 0.5g/kg can be used safely for medicinal purpose.[11]

In addition to cinnamon, green tea (Camellia sinensis) also protects kidneys due to its antioxidative potential. It possesses anti-inflammatory and anticarcinogenic properties as well. It is also protective against renal injury.[12] This study was planned to compare the modulatory effect of cinnamon and green tea consumption on daily basis to counteract the nephrotoxic changes caused by BPA.

MATERIALS AND METHODS

Research was carried out on sixty adult male rats of Sprague Dawley breed. They were selected by simple random sampling mechanism with balloting method. Their weight was approximately 250 to 300 grams. Animals were distinguished into four groups such that each group had 15 rats. Control group rats were given 1ml of refined water subcutaneously for 30 days. In group B rats were given 30mg/kg/day BPA, subcutaneously. Group C rats were given 200mg/kg/ day cinnamon aqueous extract via gavage tube 2 hours before daily subcutaneous injection of BPA. Group D rats were given 200mg/kg/day green tea aqueous extract via gavage tube 2 hours before daily subcutaneous injection of BPA. Animals were dissected after 30 days. Kidneys were stripped from disciple structures and were immediately placed in containers. Quantitative parameters measured by using image J software which were height of epithelium of PCT luminal diameter of PCT, height of epithelium of DCT, luminal diameter of DCT.

RESULTS

Group-wise distribution of Mean Height of Epithelium and mean Luminal Diameter in PCT.

Mean of height of epithelium in PCT of group B was found to be significantly less than group A (p=0.00). Both group C and D showed increase in this parameter but it was significantly increased in group D as compared to group C (p=0.000). Mean of luminal diameter in PCT of group B was significantly increased as compared to group A (p=0.00). This diameter was found to be decreased in both group C and D but group D showed significant decrease in this parameter as compared to group C. (p=0.000)

Table No.1: Group-wise distribution of Mean Height of Epithelium and mean Luminal Diameter in PCT

	Height of Epithelium in PCT in µm				Luminal Diameter in PCT in µm			
Groups	A	B	C	D	A	B	C	D
Mean	81.204	24.968	32.109	60.114	121.493	140.695	119.399	100.622
SEM	1.233	.781	.625	2.227	4.788	2.356	2.214	1.505
***P* value**	0.000*				0.000*			

**p<0.05*

Table No.2: Showing multiple comparison of the mean Height of Epithelium in PCT and mean luminal diameter in PCT

	Height of Epithelium		Luminal Diameter	
Groups	**Mean Difference**	**P value**	**Mean Difference**	**P value**
A vs B	56.236	0.000*	19.202	0.000*
A vs C	49.096	0.000*	2.093	0.960
A vs D	21.090	0.000*	20.871	0.000*
B vs C	7.141	0.003*	21.295	0.000*
B vs D	35.147	0.000*	40.073	0.000*
C vs D	28.006	0.000*	18.778	0.000*

*p<0.05

Table No.3: Group-wise distribution of Mean Height of Epithelium and mean Luminal Diameter in DCT

	Height of Epithelium in DCT in µm				Luminal Diameter in DCT in µm			
Groups	A	B	C	D	A	B	C	D
Mean	66.325	20.696	32.024	38.597	134.747	139.293	137.615	116.691
SEM	5.476	1.056	6.125	1.2033	3.566	2.792	4.444	5.941
P value	0.000*				0.002*			

*p<0.05

Group-wise distribution of Mean Height of Epithelium and mean Luminal Diameter in DCT.

Mean of height of epithelium in DCT of group B was found to be significantly less than group A (p=0.00). Both group C and D showed increase in this parameter. Mean difference between group C and D was 6.57 (p=0.685) which was statistically insignificant. Mean of luminal diameter in DCT of group B was significantly increased as compared to group A (p=0.00). This diameter was found to be decreased in both group C and D but group D showed significant decrease in this parameter as compared to group C. (p=0.000). (Table1).

Table No.4: Showing multiple comparison of the mean Height of Epithelium in DCT and mean luminal diameter in DCT.

	Height of Epithelium		Luminal Diameter	
Groups	**Mean Difference**	**P value**	**Mean Difference**	**P value**
A vs B	45.629	0.000*	4.546	0.881
A vs C	34.302	0.000*	2.868	0.966
A vs D	27.728	0.000*	18.056	0.024*
B vs C	11.327	0.234	1.678	0.993
B vs D	17.901	0.019*	22.602	0.003*
C vs D	-6.574	0.685	20.924	0.007*

DISCUSSION

Comparison of protective effect of cinnamon and green tea by measuring height of epithelium and luminal diameter of PCT indicated greater nephroprotection offered by green tea in measured histological parameters. Decrease in height of epithelium in group B was ameliorated both in group C and D but comparison of both showed that green tea increased epithelial height more than cinnamon.

Increase in luminal diameter was caused by BPA in group B. This parameter showed decreased both in group C and D but group D significantly improved this parameter as compared to C. Hence all the observed parameter of PCT indicate that green tea is more nephroprotective than cinnamon against BPA damage.

In present study the histomorphological alterations in group B might be due to vulnerability of the enzymatic systems of tubular membranes to toxins.[10] BPA was the chief event accountable for necrosis of renal tubules. Ahmed noticed similar changes in histology of PCT.[14] The alterations in PCT are in line with those described by Daniela-saveta.[15]

The study done by Morgan displayed amelioration of renal parameters of PCT in group C thus reflected shielding effect of cinnamon against BRA toxicity. Cinnamon leads in reduction of luminal obstruction and cloudy swelling of PCT.[15] Gehad E .Elshopakey in his publication inferred that cinnamon aqueous extract reduced the oxidative stress in kidneys initiated by diclofenac sodium and oxytetracycline.[16] All the above stated studies supported our results in group C which depicted substantial amelioration in PCT histology when compared with group B. In this study green tea upgraded PCT histology more than cinnamon.

Although ameliorative properties of green tea on histologicalmorphological changes due to BPA nephrotoxicity have not been studied but Sardana utilized green tea against nephrotoxicity caused by administration of gentamycin. The catechins inhibited degenerative changes of renal tubules in rat kidney owing to its antioxidative effects.[17] Wala Ahmad inferred in his study that green tea improved oxidative stress related tubular histological changes plus epithelial detachment and cast formation caused by bisphenol A.[18]

Beneficial properties of green tea on PCT were reflected by conclusions of Zhou who noticed same degeneration of PCT, while discovering the protective effect of EGCG (green tea polyphenol (−)-epigallocatechin-3-gallate) on obstructive nephropathy. The electron microscopy revealed that administration of EGCG in nephropathy exhibited intact basement membrane of PCT.[19] Ai Peng reflected that the EGCG ameliorated the tubular damage initiated by immune mediated glomerulonephritis.[20]According to Elzoghby green improved degeneration of epithelial cells of tubules caused by organophosphorus insecticide.[21]

The proximal tubular necrosis of cyclosporine treated rats was ameliorated by green tea as stated by Ryn.[22]

Height of epithelium in DCT showed significant decrease in this study, while luminal diameter showed significant increase in group B as compared to group A. Decrease in height of epithelium was ameliorated significantly both in group C and D. The increase in luminal diameter of DCT caused by BPA was found to be decreased both in group C and D.

Present findings of cellular debris in lumen of DCT and dilatation of DCT lumen in group B are supported by publication of Ahmed who described cellular debris in dilated lumen of DCT in BPA treated rats.[24] Study conducted by Fathy also supported the tubular degeneration with epithelial cells and hyaline casts in tubular lumen in fish kidney exposed to BPA.[25] Diminution of ATP causing oxidative stress leads to the necrosis of epithelium of DCT.[26] Tomza in 2018 reported that pre and postnatal exposure to 50µg/kg body weight of BPA shows enlarged cells lining renal tubules and decreased lumen space.[27]

Muhammad showed ameliorative effect of cinnamon on tubular degenerative changes caused by diabetes, thus supported the improved parameters in group C. Mnati proved that cinnamon is protective against prioxicam induced altered kidney morphology.[28] Amelioration of histomorphological parameters of DCT by use of green tea and cinnamon was due to their antioxidative properties.

CONCLUSION

Co-administration of cinnamon and green tea with BPA reduced the histological damage in proximal and distal convoluted tubules of nephrons in rats. Green tea is more effective than cinnamon to combat oxidative stress induced nephrotoxicity caused by BPA.

Recommendations: In present study we found that BPA causes nephrotoxic effects in rat kidney. Effects of BPA on human kidney should be explored with reference to its accumulation and excretion by human body. Green tea and cinnamon can be co administered against BPA nephrotoxicity to observe whether their nephroprotective effect is additive or not.

Author's Contribution:

Concept & Design of Study:	Huma Beenish
Drafting:	Hira Cheema, Ayesha Yasser
Data Analysis:	Tooba Khurshid, Maleeha Bano, Tayyaba Qurashi
Revisiting Critically:	Huma Beenish, Hira Cheema
Final Approval of version:	Huma Beenish

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Eckardt KU. The noblesse of kidney physiology. Kidney Int 2019;96(6):1250–3.
2. Menon R, Otto EA, Hoover P, Eddy S, Mariani L, Godfrey B, et al. Single cell transcriptomics identifies focal segmental glomerulosclerosis remission endothelial biomarker. JCI insight 2020;5(6).
3. Levin A, Stevens PE, Bilous RW, Coresh J, De Francisco ALM, De Jong PE, et al. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl 2013;3(1):1–150.
4. Daenen K, Andries A, Mekahli D, Van Schepdael A, Jouret F, Bammens B. Oxidative stress in chronic kidney disease. Pediatr Nephrol 2019;34(6):975–91.
5. Priego AR, Parra EG, Mas S, Morgado-Pascual JL, Ruiz-Ortega M, Rayego-Mateos S. Bisphenol A Modulates Autophagy and Exacerbates Chronic Kidney Damage in Mice. Int J Mol Sci 2021;22(13):7189.
6. Subhashini S, Rajapaksha SM, Ranatunga S, Perera S, Wickramarathna ST, Herath S, et al. Development of PP/Recycled-PET Blended Low Speed Wheels to Reduce the Virgin Plastic Usage in the Industry 2021;
7. Aslanturk A, Uzunhisarcikli M. Protective potential of curcumin or taurine on nephrotoxicity caused by bisphenol A. Environ Sci Pollut Res 2020;27(19):23994–4003.
8. Almeida S, Raposo A, Almeida-González M, Carrascosa C. Bisphenol A: Food exposure and impact on human health. Compr Rev Food Sci Food Saf 2018;17(6):1503–17.
9. Yaribeygi H, Simental-Mendía LE, Butler AE, Sahebkar A. Protective effects of plant-derived natural products on renal complications. J Cell Physiol 2019;234(8):12161–72.
10. Vijayakumar K, Rengarajan RL, Suganthi N, Prasanna B, Velayuthaprabhu S, Shenbagam M, et al. Acute toxicity studies and protective effects of Cinnamon cassia bark extract in streptozotocin-induced diabetic rats. Drug Chem Toxicol 2021;1–11.
11. Guldiken B, Catalkaya G, Ozkan G, Ceylan FD, Capanoglu E. Toxicological effects of commonly used herbs and spices. Toxicology. Elsevier; 2021.p.201–13.
12. Parvardeh S, Mohseni Kouchsfahani H, Nebyunii M. The effect of green tea hydroalcohalic extract of camellia sinensis on AQP1 gene expression in proximal tubuls of gentamicin treated rat kidney. Armaghane Danesh 2018;23(2):146–59.
13. Talebi M, Talebi M, Farkhondeh T, Mishra G, İlgün S, Samarghandian S. New insights into the role of the Nrf2 signaling pathway in green tea catechin applications. Phyther Res 2021.
14. Veljković M, Pavlović DR, Stojiljković N, Ilić S, Petrović A, Jovanović I, et al. Morphological and morphometric study of protective effect of green tea in gentamicin-induced nephrotoxicity in rats. Life Sci 2016;147:85–91.
15. Morgan AM, El-Ballal SS, El-Bialy BE, El-Borai NB. Studies on the potential protective effect of cinnamon against bisphenol A-and octylphenol-induced oxidative stress in male albino rats. Toxicol Reports 2014;1:92–101.
16. Elshopakey GE. veterinary sciences Cinnamon Aqueous Extract Attenuates Diclofenac Sodium and Oxytetracycline Mediated Hepato-Renal Toxicity and Modulates Oxidative Stress, Cell Apoptosis , and Inflammation in Male Albino Rats 2021.
17. Veljković M, Ilić S, Stojiljković N, Veličković L, Pavlović D, Radenković M, et al. Beneficial effects of green tea extract in gentamicin-induced acute renal failure in rats. Acta Fac Medicae Naissensis 2015;32(1):51–8.
18. Fadda W, Essawy A, Faried M. Green tea extract protects the renal cortex against bisphenol A-induced nephrotoxicity in the adult male albino rat: a histological andimmunohistochemical study. Eur J Anat 2019;(June):412–20.

19. Kharroubi W, Dhibi M, Haouas Z, Chreif I, Neffati F, Hammami M, et al. Effects of sodium arsenate exposure on liver fatty acid profiles and oxidative stress in rats. Environ Sci Pollut Res 2014; 21(3):1648–57.
20. Peng A, Ye T, Rakheja D, Tu Y, Wang T, Du Y, et al. The green tea polyphenol (−) epigallocatechin-3-gallate ameliorates experimental immune-mediated glomerulonephritis. Kidney Int 2011;80(6):601–11.
21. Elzoghby RR, Ahlam FH, Abdel-Fatah A, Farouk M. Protective role of vitamin C and green tea extract on malathion-induced hepatotoxicity and nephrotoxicity in rats. Am J Pharmacol Toxicol 2014;9(3):177.
22. Ryu HH, Kim HL, Chung JH, Lee BR, Kim TH, Shin BC. Renoprotective effects of green tea extract on renin-angiotensin-aldosterone system in chronic cyclosporine-treated rats. Nephrol Dial Transplant 2011;26(4):1188–93.
23. Ibrahim HM, Moustafa AEGA, Elgebaly HA. Effect of black and green tea on experimental sodium oxalate-induced nephrotoxicity in adult male mice. Egypt J Histol 2019;42(2):358–68.
24. Ahmed WMS, Moselhy WA, Nabil TM. Bisphenol A toxicity in adult male rats: hematological, biochemical and histopathological approach. Glob Vet 2015;14(2):228–38.
25. Elshaer F, Abu-Shaeir W, Bakry S. Histopathological changes in the Kidney of mosquito fish, Gambusia affinis and guppy fish, Poecilia reticulata exposed to Bisphenol A. Egypt J Aquat Biol Fish 2013;17(4):83–93.
26. Rahimi O, Farokhi F, Khojasteh SMB, Ozi SA. The effect of Bisphenol A on serum parameters and morphology of kidney's tissue. In: Biological Forum. Research Trend; 2015.p.86.
27. Tomza-Marciniak A, Stępkowska P, Kuba J, Pilarczyk B. Effect of bisphenol A on reproductive processes: a review of in vitro, in vivo and epidemiological studies. J Appl Toxicol 2018; 38(1):51–80.
28. Mnati IM, Maaroof BO. Histopathological changes induce by piroxicam administration in kidneys of adult male albino mice Mus musculus. J Madenat Alelem Univ Coll 2017;9(1):174–88.