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Investigating the Serum Creatinine Levels in Wister Albino Male Rats to Examine the Impact of Cinnamon on Gentamicin-Induced Nephrotoxicity

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Abstract **Original Research Article**

Background: The kidneys are two vital excretory organs. It can be harmed by the toxic effects of chemicals, poisons, or the extended and uncontrolled use of medications. Cinnamon is used to flavor pastries and dishes. This plant is one of the oldest medicinal plants used in traditional medicine as a potent medication that may have nephroprotective properties. ***Aim of the study:*** The purpose of our study was to investigate the serum creatinine levels in Wister Albino male rats to examine the impact of cinnamon on gentamicin-induced nephrotoxicity. ***Methods:*** This experimental study was conducted in the department of Physiology, Sir Salimullah Medical College (SSMC), Dhaka from 1st January 2021 to 31st December 2021. A total number of thirty (30) apparently healthy Wister albino male rats, 90-120 days old, weighing between 150-200 gm were taken for the study. All acquired data was entered into a Microsoft Excel Work Sheet and analyzed using descriptive statistics in SPSS 22.0. ***Results:*** The mean (±SD) initial body weight of rats on day-1 were 177.10 ± 5.92, 183.80 ± 9.31 and 178.60 ± 8.19 gm, the final body weight on day- 29 were 208.40 ± 7.52, 207.0 ± 10.30 and 215.80 ± 9.26 gm. The percent (%) change of body weight from final to initial were 17.67 ± 0.98, 12.65 ± 1.23 and 20.85 ± 0.76 % and the kidney weight of rats were 0.86 ± 0.08, 1.25 ± 0.19 and 1.10 ± 0.18 gm in group A1, group A2 and group B respectively. the mean (±SD) kidney weight was significantly ($p<0.001$) higher in group A2 and group B ($p< 0.01$) in comparison to that of group A1. Whereas this levels were significantly ($p<0.05$) lower in group B in comparison to that of group A2. The mean (±SD) initial serum creatinine levels were 0.66 ± 0.08, 0.73 ± 0.05 and 0.74 ± 0.12 mg/dl, mean final serum creatinine level were 0.67 ± 0.07, 2.86 ± 0.07 and 1.60 ± 0.33 mg/dl, in group A1, group A2 and group B respectively. ***Conclusion:*** This study found that the gentamicin induced kidney damage was observed in Wister Albino male rats as evidenced by their measured higher serum levels of creatinine in kidney. From this study it may be concluded that cinnamon has nephroprotective effect on gentamicin induced kidney damage in Wister Albino male rats.

Keywords: Nephrotoxicity, Cinnamon, Gentamicin, Wister albino male rat.

INTRODUCTION

The kidneys are the most important organs in our bodies. One key function of the kidneys is to remove waste items from the body that are consumed or created by metabolism. Another critical function is to regulate the volume and electrolyte composition of bodily fluid. The kidneys' most significant role is to filter the plasma and remove chemicals from the filtrate at varying rates, depending on the body's demands. The kidneys also regulate extracellular volume and acid-base balance, which help to keep blood pressure stable. The renal vascular bed receives a high rate of blood flow, around 22% of cardiac output [1]. As a result, the renal vasculature, glomerulus, tubules, and interstitium are exposed to a large amount of blood-borne toxicants [2]. Patients are exposed to several prescribed and over-the-counter drugs. Unfortunately, medications are the most common cause of acute renal impairment in critically unwell patients after sepsis and hypotension. Acute kidney damage (AKI) is a serious illness with high morbidity and fatality rates [3]. One of the most essential aspects of drug-induced nephrotoxicity is the offending drugs' inherent kidney toxicity. Certain nephrotoxic medicines are more likely to cause kidney harm when

taken at high doses and for lengthy periods of time. Aminoglycoside antibiotics, amphotericin B, anesthetic drugs, and NSAIDs are among the most prevalent therapeutic medicines that cause nephrotoxicity. Gentamicin is commonly used in clinical practice to treat potentially fatal gram-negative aerobic and gram-positive bacterial infections [4]. Gentamicin's treatment efficacy is limited by the danger of significant adverse effects such as nephrotoicity [5]. According to some studies, gentamicin-induced nephrotoxicity occurs by increasing serum creatinine, blood urea nitrogen, and uric acid while decreasing glutathione, superoxide dismutase, catalase, and increasing malondialdehyde levels (oxidative stress biomarker) [6, 7]. Gentamicin also increases reactive oxygen species (ROS) in kidney damage, including superoxide anions and hydroxyl radicals [8]. An imbalance in the formation and removal of reactive oxygen species (RNS) results in increased lipid peroxidation, which eventually leads to inflammation, tissue damage, cell death, and kidney injury progression [9]. Based on these findings, there has been an increase in interest in using alternative medications to treat renal illness. Natural products have gained a lot of interest because they have the potential to be antioxidants while still being harmless. Some research demonstrate success in the medical system by applying various herbal treatments in experimental animals, such as Nigella sativa [10], Alovera [11], and Curcumin [12]. Herbal therapies are generally gentle and harmless [13]. Cinnamon is a botanical medication. Cinnamon is an evergreen tree that belongs to the Lauraceae family and is commonly used as a spice. There are numerous varieties of cinnamon. Cinnamomum zeylanicum (often known as Dalchini) is a type of cinnamon or Ceylon cinnamon native to Sri Lanka and southwestern India. Cinnamaldehyde, eugenol, cinnamic acid, cinnamate, and essential oils are the primary chemical elements of cinnamon [14]. Cinnamon also contains proteins, carbohydrates, vitamins (A, C, K, and B3), and minerals such as calcium, iron, magnesium, manganese, phosphorus, salt, zinc, and choline [13]. Cinnamon has been shown to have anti-inflammatory, antibacterial, and anticarcinogenic properties [15], as well as antidiabetic and memory-enhancing properties [16]. It also has a lipid and cholesterol-lowering impact, which reduces cardiovascular disease [17]. Many investigations have found cinnamon extract to be safe for clinical usage [18, 19]. Furthermore, histological analysis of the kidney revealed less renal tubular injury in cinnamon pretreatment and gentamicin treated rats than in gentamicin treated rats [7].

METHODOLOGY

This experimental study was conducted in the department of Physiology, Sir Salimullah Medical College (SSMC), Dhaka from 1st January 2021 to 31st December 2021. A total number of thirty (30) apparently healthy Wister albino male rats, 90-120 days old, weighing between 150-200 gm were taken for the study. After 14 days of acclimatization, the rats will be separated into two groups: control (group A) and experimental (group B). The control group will be separated into two groups: A1 (baseline control) and A2 (gentamicin-treated control). All rats will be fed a baseline diet for 28 days. In addition, group A1 will be given normal saline (1ml/kg/day) orally for 28 days. In addition to the basal diet, group A2 will receive an intraperitoneal injection of gentamicin (80mg/kg/day) over the last three days. In addition to the basal diet, the experimental group will receive cinnamon extract orally (200mg/kg/day) by gastric gavage for 28 days and gentamicin intraperitoneally (80mg/kg/day) for the final three days (26th to 28th). All rats will be sacrificed on the 29th day. Following sacrifice, blood and kidney samples will be obtained. Blood samples will be taken from the heart. Creatinine levels in the serum will be tested using standard laboratory methods. All acquired data was entered into a Microsoft Excel Work Sheet and analyzed using descriptive statistics in SPSS 22.0.

RESULT

The mean (±SD) initial body weight of rats on day-1 were 177.10 ± 5.92, 183.80 ± 9.31 and 178.60 ± 8.19 gm, the final body weight on day- 29 were 208.40 ± 7.52, 207.0 ± 10.30 and 215.80 ± 9.26 gm. The percent (%) change of body weight from final to initial were 17.67 ± 0.98, 12.65 ± 1.23 and 20.85 ± 0.76 % and the kidney weight of rats were 0.86 ± 0.08, 1.25 ± 0.19 and 1.10 ± 0.18 gm in group A1, group A2 and group B respectively. The mean (±SD) initial body weight of group A1, group A2 and group B were almost similar and the differences were not statistically significant. Final body weight were lower in group A2 and higher in group B than that of group A1, although the differences were not statistically significant. The mean (± SD) percent (%) change of body weight was significantly ($p<0.001$) lower in group A2 in comparison to that of group A1. Whereas, this change was significantly ($p<0.001$) higher in group B than that of group A1 and group A2 [Table-1]. [Table-2] reveals that the mean (±SD) kidney weight was significantly ($p<0.001$) higher in group A2 and group B ($p< 0.01$) in comparison to that of group A1. Whereas this levels were significantly ($p<0.05$) lower in group B in comparison to that of group A2. The mean (±SD) initial serum creatinine levels were 0.66 ± 0.08, 0.73 ± 0.05 and 0.74 ± 0.12 mg/dl, mean final serum creatinine level were 0.67 ± 0.07, 2.86 ± 0.07 and 1.60 ± 0.33 mg/dl, in group A1, group A2 and group B respectively. The mean (±SD) initial and final serum creatinine levels were almost similar in group A1 and the differences were not statistically significant. The mean (±SD) final serum creatinine levels were significantly ($p<0.001$) higher in group A2 and group B in comparison to that of group A1 [Table-3].

Table -1: Body weight in different groups of rats (N=30)

Group	Body weight (gm)		% change in body weight from final (F) to initial (I) [(F-I)/Ix100]
	Initial (I)	Final (f)	
Group A_1 (n=10)	177.10 ± 5.92 (169 - 187)	208.40 ± 7.52 (198 - 222)	17.67 ± 0.98 (16.4 - 19.3)
Group A_2 (n=10)	183.80 ± 9.31 (170 - 200)	207.00 ± 10.30 (193 - 221)	12.65 ± 1.23 (10.5 - 14.1)
Group B (n=10)	178.60 ± 8.19 (167 - 190)	215.80 ± 9.26 (201 - 228)	20.85 ± 0.76 (19.6 - 22.2)
Multiple comparison			
Group	**Initial body weight**	**Final body weight**	**% change of body weight**
	p-value	p-value	p-value
A_1 vs A_2 vs B	0.160 ^{ns}	0.085 ^{ns}	<0.001***
A_1 vs A_2	0.209 ^{ns}	1.000 ^{ns}	<0.001***
A_1 vs B	1.000 ^{ns}	0.240 ^{ns}	<0.001***
A_2 vs B	0.463 ^{ns}	0.119 ^{ns}	<0.001***

Table-2: Kidney weight in different groups of rats (N=30)

Group	Kidney weight (gm)
Group A_1 (n=10)	0.86 ± 0.08 (0.73 - 0.97)
Group A_2 (n=10)	1.25 ± 0.19 (0.96 - 1.53)
Group B (n=10)	1.10 ± 0.18 (0.82 - 1.30)
Multiple comparison	
Group	**Kidney weight**
	p-value
A_1 vs A_2 vs B	<0.001***
A_1 vs A_2	<0.001***
A_1 vs B	0.006**
A_2 vs B	0.034 *

Table-3: Mean initial & final serum creatinine levels in different groups of rats (N=30)

Group	Serum creatinine (mg/dl)		p-value
	Initial (I)	Final (f)	
Group A_1 (n=10)	0.66 ± 0.08 (0.56 - 0.78)	0.67 ± 0.07 (0.58 - 0.78)	0.052^{ns}
Group A_2 (n=10)	0.73 ± 0.05 (0.65 - 0.80)	2.86 ± 0.07 (2.75 - 2.98)	<0.001***
Group B (n=10)	0.74 ± 0.12 (0.57 - 0.89)	1.60 ± 0.33 (1.26 - 2.06)	<0.001***

DISCUSSION

The current investigation was conducted to assess the nephroprotective impact of cinnamon on gentamicin-induced nephrotoxic rats. The study used serum creatinine levels in kidney tissue homogenate to determine renal function. In the current investigation, the end body weight was lower in the gentamicin treated control group and higher in the cinnamon pretreatment and gentamicin treated groups compared to the baseline control group, however the changes were not statistically significant. Atsamo *et al.*, 2021 and Jannat, Sultana, and Islam, 2017 reported very identical results [20, 21]. Morgan *et al.*, (2014) found that oral administration of Bisphenol A (BPA) or Octylphenol (OP) increased final body weight more than the control group, however the difference was not statistically significant [22]. The researchers also detected a reduction in body weight in the cinnamon aqueous extract (CAE) pretreatment group compared to the control group, but it was not statistically significant. This disparity could be attributed to the prolonged duration of the administration of cinnamon extract. Again, Noor and Mahboob (2014) found that cinnamon treated rats had a lower mean body weight than the control group [23]. This variation could be attributed to the decreased dosage of cinnamon extract administered. The study found that kidney weight was considerably higher ($p<0.001$) in the gentamicin-treated control group, as well as in the cinnamon-pretreated and gentamicin-treated groups ($p<0.01$), than the baseline control group. Atsamo *et al.*, 2021; Said, 2010 reported

comparable findings [20, 16]. Jannat, Sultana, and Islam (2017) found a substantial ($p<0.05$) reduction in kidney weight in the gentamicin-treated group compared to the control group [21]. Morgan *et al.*, (2014) observed that oral administration of Bisphenol (BPA) or Octylphenol (OP) resulted in a significant ($p<0.05$) reduction of kidney weight compared to the control group [22]. The researchers also noticed a drop in kidney weight in the cinnamon aqueous extract (CAE) pretreatment group compared to the control group, although the difference was not statistically significant. This disparity could be attributed to the prolonged duration of the administration of cinnamon extract. In this investigation, serum creatinine levels were considerably ($p<0.001$) higher in the gentamicin-treated control group, as well as the cinnamon-pretreated and gentamicin-treated groups, compared to the baseline control group. Several researchers reported comparable findings [7, 16, 17, 20, 21]. Serum creatinine levels were significantly lower ($p<0.001$) in cinnamon-pretreated and gentamicin-treated groups compared to the gentamicin-treated control group. Several researchers reported similar findings [6, 16, 20, 23]. On the contrary, Noor and Mahboob (2014) found that cinnamon treated rats had higher plasma creatinine levels than the control group, but the difference was not statistically significant [23].

Limitation of the study:

This study was a single-center study with a small sample size and a short duration of follow-up, so these findings may not reflect the actual scenario.

CONCLUSION & RECOMMENDATION

This study found that the gentamicin induced kidney damage was observed in Wister Albino male rats as evidenced by their measured higher serum levels of creatinine in kidney. These changes may be due to increased production of free radicals which initiate lipid peroxidation and subsequent cellular damage. Again, serum levels of creatinine in kidney were lower in cinnamon pretreated and gentamicin treated rats than those of gentamicin treated control group suggested the possibility of the cinnamon extract having nephroprotective effect against gentamicin induced kidney injury. From this study it may be concluded that cinnamon has nephroprotective effect on gentamicin induced kidney damage in Wister Albino male rats.

REFERENCES

1. Hannon, M. J., & Thompson, C. J. (2010). The syndrome of inappropriate antidiuretic hormone: prevalence, causes and consequences. *European journal of endocrinology*, *162*(Supplement_1), S5-S12.
2. Harvey, R. A., & Ferrier, D. R. (2017). *Lippincott's illustrated reviews: biochemistry*. Lippincott Williams & Wilkins.
3. Kane-Gill, S. L., & Goldstein, S. L. (2015). Drug-induced acute kidney injury: a focus on risk assessment for prevention. *Critical care clinics*, *31*(4), 675-684.
4. Kumar, V., Abbas, A. K., & Aster, A. J. (2015). The Cellular Responses to Stress and Toxic Insults: Adaptation, Injury, and Death, Robbins and Cotran Pathologic Basis of Disease Ninth Edition (p. 60-61).
5. Deck, D. H., & Winston, L. G. (2012). Aminoglycoside & spectomicin. *Katzung BG, Masters SB, Trevor AJ, edtior. Basic & clinical pharmacology. 12th edition. New Delhi: Mcgraw Hill Education (india) private limited*, *825*.
6. Tanomand, S., & Najafian, M. (2013). Inhibitory effects of cinnamon extract on gentamicin-induced nephrotoxicity in mail adult Wistar rats. *Advances in Environmental Biology*, 2100-2105.
7. Elkomy, A., Aboubakr, M., Medhat, Y., Abugomaa, A., & Elbadawy, M. (2020). Nephroprotective effects of cinnamon and/or parsley oils against gentamicin-induced nephrotoxicity in rats. *J. Anim. Vet. Adv*, *19*(1), 8-14.
8. Yang, C. L., Du, X. H., & Han, Y. X. (1995). Renal cortical mitochondria are the source of oxygen free radicals enhanced by gentamicin. *Renal Failure*, *17*(1), 21-26.
9. Birben, E., Sahiner, U. M., Sackesen, C., Erzurum, S., & Kalayci, O. (2012). Oxidative stress and antioxidant defense. *World allergy organization journal*, *5*, 9-19.
10. Begum, N. A., Dewan, Z. F., Nahar, N., & Mamun, M. R. (2006). Effect of n-hexane extract of Nigella sativa on gentamicin-induced nephrotoxicity in rats. ||| *Bangladesh Journal of Pharmacology*|||, *1*(1), 16-20.
11. Virani, S., Bhatt, S., Saini, M. A. N. I. S. H., & Saxena, K. (2016). Aloe vera attenuates gentamicin-induced nephrotoxicity in wistar albino rats: histopathological and biochemical changes. *Asian J Pharm Clin Res*, *9*(1), 113-117.
12. Bayomoy, M.F.F., Hasab, S.E., Salem, T.E & Salem, G.M., (2011). Protective role of curcumin on gentamicin induced renal toxicity in male Albino rat. *The Egyptian society of experimental biology*. 7(1), pp.63-69.
13. Meena Vangalapati, M. V., Satya, N. S., Prakash, D. S., & Sumanjali Avanigadda, S. A. (2012). A review on pharmacological activities and clinical effects of cinnamon species.
14. Peter, K. V., & Shylaja, M. R. (2012). Introduction to herbs and spices: Definitions, trade and applications. In *Handbook of herbs and spices* (pp. 1-24). Woodhead Publishing.
15. Unlu, M., Ergene, E., Unlu, G. V., Zeytinoglu, H. S., & Vural, N. (2010). Composition, antimicrobial activity and in vitro cytotoxicity of essential oil from Cinnamomum zeylanicum Blume (Lauraceae). *Food and chemical toxicology*, *48*(11), 3274-3280.
16. Said, M. M. (2011). The protective effect of eugenol against gentamicin-induced nephrotoxicity and

oxidative damage in rat kidney. *Fundamental & clinical pharmacology*, *25*(6), 708-716.

17. Cuzzocrea, S., Mazzon, E., Dugo, L., Serraino, I., Di Paola, R., Britti, D., ... & Salvemini, D. (2002). A role for superoxide in gentamicin-mediated nephropathy in rats. *European journal of pharmacology*, *450*(1), 67-76.
18. Sakr, S. A., & Albarakai, A. Y. (2014). Effect of cinnamon on cypermethrin-induced nephrotoxicity in albino rats. *Int. J. Adv. Res*, *2*(7), 578-586.
19. Alshahrani, S., Ashafaq, M., Hussain, S., Mohammed, M., Sultan, M., Jali, A. M., ... & Islam, F. (2021). Renoprotective effects of cinnamon oil against APAP-Induced nephrotoxicity by ameliorating oxidative stress, apoptosis and inflammation in rats. *Saudi Pharmaceutical Journal*, *29*(2), 194-200.
20. Atsamo, A. D., Lontsie Songmene, A., Metchi Donfack, M. F., Ngouateu, O. B., Nguelefack, T. B., & Dimo, T. (2021). Aqueous Extract from Cinnamomum zeylanicum (Lauraceae) Stem Bark Ameliorates Gentamicin-Induced Nephrotoxicity in Rats by Modulating Oxidative Stress and Inflammatory Markers. *Evidence-Based Complementary and Alternative Medicine*, *2021*(1), 5543889.
21. Jannat, N., Sultana, N., & Islam, M. R. (2017). Administration of gentamicin-induced hematobiochemical and renal morphological alterations in Swiss albino mice. *African Journal of Pharmacy and Pharmacology*, *11*(34), 426-432.
22. Morgan, A. M., El-Ballal, S. S., El-Bialy, B. E., & El-Borai, N. B. (2014). Studies on the potential protective effect of cinnamon against bisphenol A-and octylphenol-induced oxidative stress in male albino rats. *Toxicology reports*, *1*, 92-101.
23. Noori, S., Azmat, M., & Mahboob, T. (2012). Study on antioxidant effects of cinnamon and garlic extract in liver, kidney and heart tissue of rat. *Biosci Res*, *9*(1), 17-22.