Nephroprotective Effects of Combined Black Cumin (*Nigella sativa* L.), Gotu Kola (*Centella asiatica* (L.) Urb.), and Moringa (*Moringa oleifera* Lam.) Extracts in a Gentamicin- and Piroxicam-Induced Renal Injury Rat Model

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Abstract

Drug-induced nephrotoxicity from aminoglycosides and non-steroidal anti-inflammatory drugs (NSAIDs) remains a significant clinical challenge. This study evaluated the nephroprotective potential of combined ethanolic extracts of Nigella sativa, Centella asiatica, and Moringa oleifera (40:30:30 ratio) against gentamicin- and piroxicam-induced acute renal failure in rats. Thirty male Wistar rats were divided into six groups: Normal Control, Renal Failure (RF), and four treatment groups receiving extract doses of 49.5, 99, 148.5, and 198 mg/kg/day. Acute renal failure was induced using intraperitoneal gentamicin (100–80 mg/kg/day) and oral piroxicam (3.6 mg/kg/day) alongside 28 days of extract administration. On day 28, serum urea, creatinine, urine protein. Induction with gentamicin and piroxicam significantly elevated serum urea, creatinine, urine protein ($p < 0.05$ vs. Normal Control). Co-administration of the herbal extract combination successfully attenuated the elevation of renal function parameters. Among all dosages, Dose 2 (99 mg/kg/day) exhibited the most prominent therapeutic response, bringing serum urea, creatinine, and CAT activity closest to normal baseline values ($p < 0.05$ vs. RF group). In conclusion, the combined ethanolic extract of Nigella sativa, Centella asiatica, and Moringa oleifera, particularly at 99 mg/kg/day, demonstrates significant nephroprotective efficacy by mitigating oxidative stress and preserving glomerular and tubular integrity.

Keyword: *Nephroprotection, Nigella sativa, Centella asiatica, Moringa oleifera, Gentamicin, Piroxicam*

Introduction

The kidneys play some essential roles to maintain homeostasis in the body. They regulate plasma osmolarity, blood pressure, acid-base balance, and also excrete toxins, metabolic waste products, and excess ions. The kidneys also have a role in producing erythropoietin and converting vitamin D to its active form (Ogobuiro & Tuma, 2023).Despite their important physiological function, kidney impairment, including Acute Kidney Injury (AKI) and Chronic Kidney Disease remain as a significant global health concerns. Both conditions are associated with various complications, including cardiovascular disease, progressive loss of kidney function, reduced quality of life, disability, and an increased risk of death (Chawla et al., 2022). AKI affects 3-7% of hospitalized patients and 25-30% of patients in intensive care, mostly in low-and middle-income countries, causing up to 1.4 million deaths. CKD affects 5-15% of adults in developed nations, with several risk factors, including aging, diabetes mellitus, hypertension, obesity, and cardiovascular disease (Afrifa et al., 2026).

Given the high prevalence and severe consequences of kidney impairment, strategies aimed at preserving renal function have become a focus in this study. Current research increasingly explores natural compounds with nephroprotective activities. Plant extracts, such as black cumin (Nigella sativa), moringa (Moringa oleifera), and gotu kola (Centella asiatica) have demonstrated promising therapeutic potential in preserving renal function. Black cumin can preserve kidney function through antioxidants, antiinflammation, and antifibrosis activity (Hannan et al., 2021). Meanwhile, moringa's nephroprotective activities came from its antioxidant and antiinflammation activity (Pareek et al., 2023). Whereas, Gotu kola can show protective activity through its tissue healing and antifibrosis activities (Bansal et al. 2024). This study focuses on researching the nephroprotective effects of the three extracts across various doses using drug-induced kidney injury animal model.

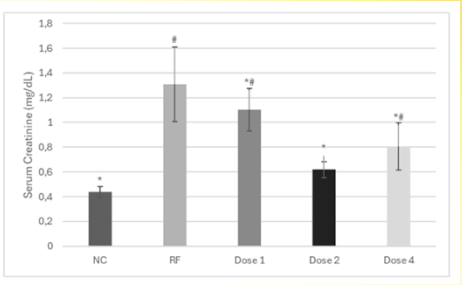
Research Method

Animals were randomly assigned to six groups (n=4 per group) which were the normal control group (NC), renal failure group (RF), and three different doses of Nigella sativa, Centella asiatica, and Moringa oleifera extracts, which were 49,5 mg/kg/day (Dose 1), 99 mg/kg/day (Dose 2), 148,5 mg/kg/day (Dose 3), and 198 mg/kg/day (Dose 4).

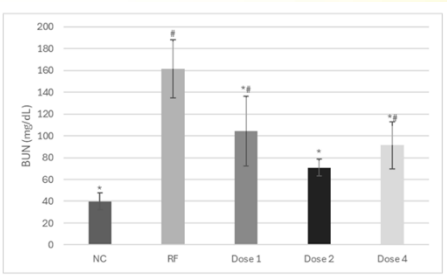
For the first 14 days, all groups only received extracts with the dose according to each group, while NC and RFG received 0,5% CMC-Na. Then, for the 14 days, all groups received the treatment and inducers simultaneously. The inducers used were intraperitoneal injection of gentamicin at 100 mg/kg/day combined with piroxicam suspension at 3,6 mg/kg/day for 7 days, then the gentamicin dose were reduced to 80 mg/kg/day while piroxicam was maintained at the same dose.

Discussion & Result

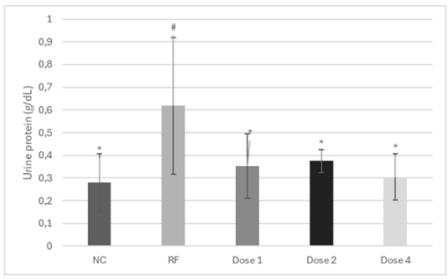
Administration of the plant extracts demonstrated varying degrees of nephroprotection. Specifically, Dose 2 showed the most prominent reduction in both BUN and serum creatinine levels compared to the untreated RF group). This renoprotective efficacy can be attributed to the synergistic antioxidant and anti-inflammatory properties of the active compounds present in the extracts (such as flavonoids, thymoquinone, or saponins) , which mitigate oxidative stress and cellular damage within the proximal tubules (**Figure 1a-b)** (Hannan et al., 2021; Pareek et al., 2023; Bansal et al., 2024).



(A) Blood urea nitrogen (BUN)



(B) serum creatinine



(C) urine protein levels at endpoint

Conclusion

Based on the findings of this study, the induction of acute renal failure using a combination of gentamicin and piroxicam was successfully established, as demonstrated by significant elevations in serum urea, creatinine, and urine protein. The administration of the combined ethanolic extracts of *Nigella sativa*, *Centella asiatica*, and *Moringa oleifera* exhibited notable renoprotective effects across various dosages. The renoprotective efficacy was not strictly dose-dependent, with Dose 2 (99 mg/kg/day) demonstrating the most optimal therapeutic response in mitigating oxidative stress and preserving proximal tubular and glomerular integrity. These findings indicate that the combination of these plant extracts holds promising therapeutic potential as a natural renoprotective agent against drug-induced nephrotoxicity.