

THE EFFECT OF NIGELLA SATIVA OIL ON THE MORPHOLOGICAL STRUCTURE OF RENAL TISSUES IN GENTAMICIN-INDUCED NEPHROTOXICITY

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Abstract: Gentamicin, a widely used aminoglycoside antibiotic, is known to cause nephrotoxicity as a major side effect, limiting its clinical application. This study aimed to evaluate the protective effect of *Nigella sativa* oil on gentamicin-induced nephrotoxicity by assessing the morphological changes in renal tissues in an experimental rat model. Rats were divided into control, gentamicin-treated, and gentamicin plus *Nigella sativa* oil-treated groups. Histopathological examination revealed severe tubular necrosis, glomerular damage, and interstitial inflammation in the gentamicin group. In contrast, co-administration of *Nigella sativa* oil significantly reduced these histological alterations, indicating improved renal morphology. The findings suggest that *Nigella sativa* oil exerts nephroprotective effects, likely through its antioxidant and anti-inflammatory properties, and could be considered a potential therapeutic agent against gentamicin-induced renal injury. Further research is necessary to elucidate the underlying molecular mechanisms and clinical applicability.

Keywords: Gentamicin, Nephrotoxicity, *Nigella sativa* oil, Morphological changes, Tubular necrosis, Glomerular damage, Interstitial inflammation, Histopathological examination.

INTRODUCTION

The kidneys are vital organs responsible for maintaining systemic homeostasis through regulation of fluid balance, electrolyte levels, and waste excretion. However, their high perfusion rate and complex tubular structure make them particularly susceptible to drug-induced injuries[1,2]. Among nephrotoxic agents, gentamicin, an aminoglycoside antibiotic widely used for treating severe Gram-negative infections, is known for its potent bactericidal properties. Despite its clinical effectiveness, gentamicin is associated with dose-dependent nephrotoxicity, primarily targeting the proximal convoluted tubules, leading to tubular necrosis, interstitial inflammation, and glomerular damage. The underlying mechanisms of gentamicin-induced nephrotoxicity involve the generation of reactive oxygen species (ROS), lipid peroxidation, mitochondrial dysfunction, and subsequent apoptotic or necrotic cell death. Due to the absence of specific therapeutic agents to prevent or reverse this toxicity, there is increasing interest in exploring natural antioxidants as potential nephroprotective compounds. *Nigella sativa*, commonly known as black seed, has been traditionally used in various cultures for its medicinal properties. Its volatile oil, rich in thymoquinone, exhibits strong antioxidant, anti-inflammatory, and cytoprotective activities. Thymoquinone has been shown to scavenge free radicals, enhance endogenous antioxidant enzymes, and modulate inflammatory cytokines, thus presenting a potential intervention against renal oxidative injury. This experimental study aims to evaluate the protective effects of *Nigella sativa* oil on the morphological structure of renal tissues in rats subjected to gentamicin-induced nephrotoxicity. Through detailed histological analysis, the study seeks to determine whether *Nigella sativa* oil can mitigate renal tissue damage and preserve cellular integrity, offering insights into its therapeutic potential in nephrotoxic conditions.

MATERIAL AND METHODS

Drug-induced nephrotoxicity remains a major concern in clinical settings, particularly with aminoglycoside antibiotics such as gentamicin. Numerous studies have documented that gentamicin administration leads to acute tubular necrosis, mainly due to oxidative stress, mitochondrial injury, and impaired renal perfusion. Walker and Shah (1988) reported that gentamicin stimulates excessive

production of reactive oxygen species (ROS), especially hydrogen peroxide, contributing to structural and functional deterioration in the renal cortex. In recent years, the role of natural antioxidants in preventing renal damage has attracted significant scientific interest. *Nigella sativa*, widely used in traditional medicine[3,4], has emerged as a promising nephroprotective agent due to its strong antioxidant and anti-inflammatory profile. Thymoquinone, the active compound in *Nigella sativa* oil, has demonstrated potent free radical scavenging ability and capacity to restore endogenous antioxidant defense mechanisms such as superoxide dismutase and glutathione peroxidase (Ali & Blunden, 2003). Several experimental studies support the renoprotective effects of *Nigella sativa* in various nephrotoxic models. Abdel-Daim et al. (2016) observed significant attenuation of gentamicin-induced renal injury in rats following co-treatment with *Nigella sativa* oil. Histopathological evaluations showed decreased tubular necrosis, interstitial edema, and inflammatory infiltration in treated animals compared to those receiving gentamicin alone. These findings suggest that *Nigella sativa* oil may provide a protective effect against drug-induced renal damage. However, further studies focusing on morphological changes in renal architecture are essential to validate these outcomes. This study aims to bridge that gap by evaluating histological alterations in kidney tissues and assessing the nephroprotective potential of *Nigella sativa* oil in an experimental gentamicin-induced toxicity model[5,6].

Nephrotoxicity refers to renal damage caused by exposure to toxic substances, often manifesting in the form of impaired renal function and structural alterations in kidney tissue. Gentamicin, an aminoglycoside antibiotic widely used to treat severe bacterial infections, is well-documented for its nephrotoxic side effects. The pathogenesis involves the accumulation of gentamicin in proximal tubular cells, leading to oxidative stress, mitochondrial dysfunction, and cellular apoptosis. In recent years, interest has grown in the use of natural substances with protective properties to counteract drug-induced organ damage. *Nigella sativa* (commonly known as black seed) oil, with its potent antioxidant and anti-inflammatory properties, is one such candidate. The present study is aimed at evaluating the protective effects of *Nigella sativa* oil on renal morphology in a model of gentamicin-induced nephrotoxicity. This investigation not only provides insight into therapeutic alternatives but also contributes to the understanding of natural agents in nephroprotection.

Gentamicin exerts its nephrotoxic effect primarily through its accumulation in the renal proximal tubules, where it triggers a cascade of cellular events. It disrupts lysosomal integrity, causes the release of cathepsins, and induces oxidative stress by generating reactive oxygen species (ROS). These free radicals initiate lipid peroxidation, damaging the cellular membrane and contributing to the death of renal epithelial cells. Gentamicin also activates pro-inflammatory cytokines, thereby aggravating interstitial inflammation and renal fibrosis. Histopathological studies show acute tubular necrosis, epithelial desquamation, and glomerular alterations in affected kidneys. The severity of nephrotoxicity is dose-dependent and can lead to acute kidney injury (AKI) if left unmitigated. Understanding the detailed molecular mechanism of gentamicin-induced renal injury underscores the importance of investigating effective protective agents, such as *Nigella sativa* oil.

Nigella sativa oil contains a variety of biologically active components, including thymoquinone, nigellone, and various unsaturated fatty acids. Thymoquinone, in particular, is known for its strong antioxidant capabilities, as it scavenges free radicals and enhances the activity of endogenous antioxidant enzymes such as superoxide dismutase and glutathione peroxidase. Additionally, *Nigella sativa* exhibits anti-inflammatory properties by downregulating the expression of pro-inflammatory mediators such as TNF- α and IL-1 β . In nephrology research, *Nigella sativa* oil has shown promise in reducing renal oxidative stress, preserving the integrity of tubular epithelial cells, and preventing the histological progression of kidney damage. Its multifunctional properties suggest a potential therapeutic application in drug-induced nephrotoxicity, particularly in attenuating the harmful effects

of aminoglycosides like gentamicin[7,8]. Thus, exploring *Nigella sativa* oil's protective effect in this context is of significant clinical interest.

The main objective of this study was to evaluate the morphological changes in renal tissue following gentamicin-induced nephrotoxicity and to assess the potential protective effect of *Nigella sativa* oil. Experimental subjects consisted of healthy laboratory rats, which were randomly divided into three groups: a control group receiving no treatment, a nephrotoxic group administered gentamicin alone, and a treatment group receiving both gentamicin and *Nigella sativa* oil. Gentamicin was administered intraperitoneally at nephrotoxic doses for a fixed period, while *Nigella sativa* oil was given orally. Following treatment, animals were sacrificed and their kidneys were harvested for histological examination. Renal tissue sections were stained using Hematoxylin and Eosin (H&E) and examined under light microscopy to assess tubular necrosis, glomerular integrity, inflammatory infiltration, and other morphological parameters. Statistical analyses were employed to determine the significance of observed changes among the groups.

Histopathological analysis of the gentamicin-only group revealed significant renal damage, including marked tubular epithelial degeneration, interstitial inflammation, and vacuolar changes. Extensive necrosis was observed in the proximal tubules, along with cytoplasmic swelling and nuclear pyknosis. The glomeruli showed varying degrees of shrinkage and capillary collapse. Conversely, the group treated with *Nigella sativa* oil demonstrated substantial preservation of renal architecture. Tubular epithelial cells appeared more intact, and signs of inflammation and necrosis were significantly reduced. The glomerular structures retained their normal morphology, and interstitial congestion was minimal. Quantitative assessment showed lower renal injury scores in the *Nigella*-treated group compared to the gentamicin-only group. These results indicate that *Nigella sativa* oil provides a significant degree of protection against gentamicin-induced structural renal damage.

The findings of this study are consistent with previously reported data on the nephroprotective effects of *Nigella sativa*. Several studies have demonstrated that thymoquinone mitigates oxidative stress and inhibits apoptosis in renal cells subjected to toxic insult. The preservation of renal morphology observed in this study aligns with earlier experimental models of nephrotoxicity where *Nigella sativa* reduced histopathological damage and improved renal function biomarkers. Moreover, the anti-inflammatory actions of *Nigella sativa*, as reflected in the suppression of leukocytic infiltration and cytokine expression, support the hypothesis of its multifaceted protective mechanism. This study contributes to the growing body of evidence that natural antioxidants can serve as adjunct therapies in drug-induced renal injury. Further investigation into dosage optimization, treatment duration, and possible interactions with conventional drugs is warranted to confirm the therapeutic potential of *Nigella sativa* oil in clinical settings.

The present study demonstrates that *Nigella sativa* oil exhibits significant protective effects on renal tissues subjected to gentamicin-induced nephrotoxicity. Its ability to preserve morphological integrity, reduce cellular degeneration, and attenuate inflammation highlights its potential as a nephroprotective agent. These results advocate for the inclusion of *Nigella sativa* oil as a supplementary treatment in patients receiving nephrotoxic medications, particularly aminoglycosides. From a clinical standpoint, the use of natural antioxidants like *Nigella sativa* could minimize adverse effects, enhance patient outcomes, and support renal health during antibiotic therapy. However, large-scale studies and clinical trials are essential to validate its efficacy, determine safe dosing regimens, and understand its long-term impact. Until such data become available, *Nigella sativa* oil remains a promising, evidence-backed natural product with considerable potential in nephrotoxicity prevention and renal tissue protection.

DISCUSSION

The findings of this experimental study provide valuable insight into the protective role of *Nigella sativa* oil against gentamicin-induced nephrotoxicity. The histological analysis clearly revealed that gentamicin alone causes extensive renal damage, characterized by tubular necrosis, glomerular atrophy, interstitial inflammation, and cytoplasmic vacuolation. These observations are in line with numerous studies that have documented gentamicin's dose-dependent nephrotoxicity through oxidative stress and mitochondrial dysfunction. However, co-administration of *Nigella sativa* oil significantly alleviated these histopathological changes. Kidney sections from rats receiving both gentamicin and *Nigella sativa* oil demonstrated well-preserved glomerular structures, minimal tubular degeneration, and notably reduced inflammatory infiltration. This suggests that the bioactive components of *Nigella sativa*, particularly thymoquinone, may exert potent antioxidative and anti-inflammatory effects that counteract gentamicin-induced cellular injury.

Previous investigations, such as those by Ali et al. (2012) and Abdel-Daim et al. (2016), have also demonstrated that *Nigella sativa* supplementation reduces lipid peroxidation and improves renal function markers in nephrotoxicity models. These effects are likely due to the enhancement of endogenous antioxidant defense mechanisms such as catalase, superoxide dismutase, and glutathione peroxidase, which neutralize reactive oxygen species (ROS) produced during drug-induced oxidative stress. Moreover, the reduction in histopathological damage in this study supports the hypothesis that *Nigella sativa* oil may help stabilize renal membranes, preserve mitochondrial integrity, and modulate the immune response. The decreased infiltration of leukocytes observed in the [9,10,11]treated group indicates that the oil might suppress pro-inflammatory cytokines like TNF- α and IL-6, which are often elevated in drug-induced nephropathy. While the results are promising, it is essential to acknowledge limitations. The study was conducted on a small sample size and within a short duration. Moreover, although morphological evidence of renal protection was clearly observed, functional biochemical markers (e.g., serum creatinine, urea, electrolyte balance) were not assessed in this particular study, which could provide a more comprehensive picture of nephroprotection.

RESULTS

The histopathological examination of renal tissues revealed significant differences among the experimental groups. In the control group, kidney sections showed normal morphology with intact glomeruli, well-preserved tubular epithelium, and no signs of inflammation or necrosis [12]. The renal architecture appeared regular, with clear Bowman's capsules and healthy interstitial tissue. In contrast, the gentamicin-only group demonstrated severe nephrotoxic damage. The most prominent changes included marked tubular epithelial cell necrosis, cytoplasmic vacuolization, loss of brush borders, and desquamation of tubular cells into the lumen. Additionally, there was evident interstitial inflammatory cell infiltration and congestion. The glomeruli exhibited mild to moderate shrinkage and capillary loop collapse, indicating compromised filtration function. These findings are consistent with acute tubular necrosis, a hallmark of gentamicin-induced renal injury.

Remarkably, rats treated with both gentamicin and *Nigella sativa* oil showed considerable improvement in renal morphology. Tubular epithelial cells appeared largely intact with minimal signs of necrosis or vacuolar degeneration. The glomerular structure was well-preserved, and interstitial inflammation was significantly reduced compared to the gentamicin-only group. The degree of cellular swelling and tubular lumen obstruction was noticeably lower. Quantitative assessment of renal damage scores confirmed a statistically significant reduction in tissue injury in the *Nigella sativa*-treated group ($p < 0.05$). These results suggest that *Nigella sativa* oil exerts a protective effect against gentamicin-induced nephrotoxicity, likely through its antioxidant and anti-inflammatory properties, contributing to the preservation of renal histological integrity.

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