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RESEARCH ARTICLE

Investigation of the Effects of Polydatin on Gentamicin-Induced Renal Toxicity in Rats

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ABSTRACT

Gentamicin (GNT), an aminoglycoside antibiotic, induces nephrotoxicity through mechanisms like tubular apoptosis and inflammation. Polydatin (Poly), a natural polyphenolic compound with antioxidant and anti-inflammatory properties, has shown potential in alleviating renal damage. This study aimed to investigate the protective effects of Poly in rats with GNT-induced kidney injury using biochemical, molecular, and histopathological methods. 35 *Wistar albino* rats were divided into 5 groups (7 rats/group), including control, Poly (100 mg/kg), GNT (100 mg/kg), and two combined treatment groups (GNT+Poly at 50 mg/kg and 100 mg/kg). After 7 days of treatment, kidney tissues and blood were collected for analysis of renal function markers, oxidant-antioxidant parameters, gene expression (NF-ϰB, TNF-α, Caspase-3, Bax, Bcl-2, KIM1, AQP2), and histopathological evaluation. GNT increased serum urea and creatinine levels ($p<0.001$), increased MDA levels ($p<0.001$) and decreased antioxidants ($p<0.001$); also increased the expression of NF-ϰB and TNF-α ($p<0.001$), increased Caspase-3 and Bax ($p<0.001$) and decreased Bcl-2 levels ($p<0.001$). When administered together with GNT, Poly decreased MDA levels ($p<0.001$) and increased GSH levels ($p<0.001$), decreased inflammation markers (NF-ϰB and TNF-α) ($p<0.01$), decreased Caspase-3 and Bax ($p<0.01$) and increased Bcl-2 levels ($p<0.01$), and also improved histological damage and decreased histological score ($p<0.05$). In GNT-induced renal toxicity, Poly 100 treatment provided renal protection by reversing oxidative stress, inflammation, and apoptosis.

Keywords: Apoptosis; Gentamicin; Nephrotoxicity; Oxidative Stress; Polydatin

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Ratlarda Gentamisin Kaynaklı Böbrek Toksisitesi Üzerine Polidatin' in Etkilerinin Araştırılması

ÖZ

Bir aminoglikozid antibiyotik olan gentamisin (GNT), tübüler apoptoz ve inflamasyon gibi mekanizmalar yoluyla nefrotoksisiteye neden olur. Antioksidan ve anti-inflamatuar özelliklere sahip doğal bir polifenolik bileşik olan polidatin (Poly), böbrek hasarını hafifletme potansiyeli göstermiştir. Bu çalışma, biyokimyasal, moleküler ve histopatolojik yöntemler kullanarak GNT kaynaklı böbrek hasarı olan sıçanlarda Poly'nin koruyucu etkilerini araştırmayı amaçlamıştır. 35 *Wistar albino* sıçan, kontrol, Poly (100 mg/kg), GNT (100 mg/kg) ve iki kombine tedavi grubu (GNT+Poly 50 mg/kg ve 100 mg/kg) olmak üzere 5 gruba (grup başına 7 sıçan) ayrıldı. 7 günlük tedaviden sonra böbrek fonksiyon belirteçleri, oksidan-antioksidan parametreler, gen ekspresyonu (NF-ϰB, TNF-α, Kaspaz-3, Bax, Bcl-2, KIM1, AQP2) ve histopatolojik değerlendirme analizi için böbrek dokuları ve kan toplandı. GNT serum üre ve kreatinin düzeylerini ($p<0,001$), MDA düzeylerini ($p<0,001$) arttırdı ve antioksidanları ($p<0,001$) azalttı; ayrıca NF-ϰB ve TNF-α ekspresyonunu artırdı ($p<0,001$), Kaspaz-3 ve Bax'ı artırdı ($p<0,001$) ve Bcl-2 düzeylerini azalttı ($p<0,001$). GNT ile birlikte uygulandığında Poly, MDA düzeylerini düşürdü ($p<0,001$) ve GSH düzeylerini artırdı ($p<0,001$), inflamasyon belirteçlerini (NF-ϰB ve TNF-α) azalttı ($p<0,01$), Kaspaz-3 ve Bax'ı azalttı ($p<0,01$) ve Bcl-2 düzeylerini artırdı ($p<0,01$) ve ayrıca histolojik hasarı iyileştirdi ve histolojik skoru azalttı ($p<0,05$). GNT kaynaklı böbrek toksisitesinde, Poly 100 tedavisi oksidatif stres, inflamasyon ve apoptozu tersine çevirerek böbrek koruması sağlamıştır.

Anahtar kelimeler: Apoptozis; Gentamisin; Nefrotoksisite; Oksidatif Stres; Polidatin

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INTRODUCTION

Ketosis A sudden and usually reversible decrease in renal function is defined as acute renal failure (ARF). Although its pathogenesis is complex, ischemia, toxins, and nephrotoxic drugs cause ARF. Nephrotoxic drugs such as aminoglycoside antibiotics cause approximately 20% of all ARF cases in intensive care units (Saeedavi et al. 2023). Gentamicin (GNT) is an aminoglycoside derivative antibiotic frequently used in urinary tract, eye, and soft tissue infections, especially against gram-negative bacteria. It is known that nephrotoxicity and ototoxicity develop in patients treated with GNT for 7 days or longer. However, the rapid bactericidal effect still allows broad-spectrum GNT to be used in treatment (Pakfetrat et al. 2022).

In GNT kidney injury, tubular apoptosis and necrosis are induced, leukocyte and inflammatory cell infiltration increases, and glomerular congestion develops. However, increased excessive reactive oxygen species (ROS) production and induction of inflammatory and cell death pathways are considered to be the basic mechanisms of GNT-induced renal dysfunction (Abukhalil et al. 2025). Considering all these mechanisms involved in pathogenesis, effective therapeutic approaches are needed to prevent or reduce GNT-induced renal injury. One of these approaches is the use of plant-based antioxidants that are natural and have few side effects (Şimşek et al. 2024; Keleş et al. 2014).

Polydatin (Poly), which is Resveratrol-3-β-mono-D-glucoside and is generally used as a food flavoring agent, is a natural polyphenolic compound with significant nutritional value obtained from Polygonum cuspidatum roots, grapes, peanuts, cocoa products, and hop flowers (Dahran et al. 2025; Highab et al. 2024). Poly, which is widely consumed in Asian populations, has been reported to be frequently used in hepatorenal toxicities and to improve damage due to its antioxidant and anti-inflammatory effects (Abdul-Hamid et al. 2023; Dahran et al. 2025).

The presented study aimed to investigate the possible mechanisms of action of the Poly in rats with GNT-induced kidney damage using biochemical, molecular, and histopathological methods.

MATERIALS and METHODS

Chemicals

This GNT (40 mg/1 ampoule) used in the study was supplied by Deva Drug Company (Istanbul, Turkey), and Poly (98%, Cas No: 65914-17-2) was supplied by Aktin Chemical Company (Chengdu, China).

Experimental Animals

Thirty-five male *Wistar albino* rats (10-12 weeks and 220–250 grams), were used in the experiment. A seven-day adaptation period preceded the experimental phase to ensure acclimatization to the laboratory environment. All animal-related procedures were conducted at the KONUDAM Center (Konya/Türkiye) in compliance with institutional ethical standards.

Ethics Committee Approval

The study received ethical approval from the Necmettin Erbakan University KONÜDAM Experimental Medicine Research and Application Center Directorate, with decision number 2024-63, issued on 11.07.2024.

Experimental Design

Wistar albino rats were randomly divided into 5 groups with 7 rats in each group.

1. **Control group (C):** Animals received oral saline once daily for 7 consecutive days.
2. **Polydatin group (Poly):** Polydatin was administered orally at a dose of 100 mg/kg/day for 7 days, as described by Ali et al. (2022).
3. **Gentamicin group (GNT):** Rats were given intraperitoneal gentamicin at 100 mg/kg/day for 7 days, following the protocol of Hakyemez et al. (2022).
4. **Gentamicin + Polydatin 50 group (GNT+Poly50):** Gentamicin (100 mg/kg/day, i.p.) was administered for 7 days, alongside oral Polydatin at a dose of 50 mg/kg/day for the same period.

Gentamicin + Polydatin 100 group

5. **(GNT+Poly100):** Animals received gentamicin intraperitoneally at 100 mg/kg/day for 7 days, in combination with oral Polydatin at 100 mg/kg/day.

Twenty-four hours after the final dose, the rats were euthanized under light sevoflurane anesthesia, and blood samples from the jugular vein, along with kidney tissues, were collected for further analysis. Blood samples were centrifuged at 1,507 x g for 10 minutes at 4°C and serum was separated.

Serum Renal Function Markers

Quantification of serum urea and creatinine levels was performed using commercially available diagnostic kits (Diasis Diagnostic Systems, Istanbul, Turkey), strictly adhering to the manufacturer's protocol. Creatinine was analysed according to the Jaffe reaction at 492 nm wavelength and 37°C temperature according to the manufacturer's instructions. Urea was analysed at 340 nm wavelength and 37°C according to the manufacturer's instructions.

Analysis of Oxidant-Antioxidant Parameters

Kidney tissue was weighed and homogenized at a ratio of 1/20 with 1.15% potassium chloride in a tissue homogenizer (IKA, T18 digital ultra-turrax, Germany). The supernatant obtained at 10000 rpm was used for the measurement of glutathione peroxidase (GPx) (Matkovics, 1988) activity and glutathione (GSH, Sedlak and Lindsay, 1968) levels, while the supernatant

obtained at 3500 rpm was used for the determination of malondialdehyde (MDA) (Placer et al. 1966), superoxide dismutase (SOD) (Sun et al. 1988), catalase (CAT) (Aebi, 1984) and protein (Lowry et al. 1951).

RT-PCR

At the end of the experiment, mRNA transcription levels of genes listed in Table 1 were analyzed by the RT-PCR method in kidney tissues obtained. RNA isolation was performed using commercially available QIAzol Lysis Reagent (Qiagen, 79306). Isolated total RNA was converted to cDNA with cDNA Synthesis Kit (ABM, G236, Richmond, Canada). Reactions were combined with 4 µL of 5X RT buffer, 1 µL of dNTP mix, 1 µL of primers, 1 µL of OneScript® Plus RTase, 2 µg of RNA, and nuclease-free water to a final volume of 20 µL on ice. These were followed by incubation at 50–55 °C for 15 min and enzyme inactivation at 85 °C for 5 min. Then, the PCR mixture was prepared by adding 2X qPCR MasterMix (ABM, G891, Richmond, Canada) with primer sequences, and the reaction started. The procedures were carried out in appropriate temperature cycles in the Rotor-Gene Q (Qiagen) device according to the protocol specified by the manufacturer. Gene expressions obtained from the analysis were normalized with the β-Actin reference gene and evaluated using the $2^{-\Delta\Delta CT}$ method (Livak and Schmittgen, 2001).

Hematoxylin and Eosin

Rat kidney samples were kept in 10% buffered formalin solution for fixative purposes for 24 hours. After a routine paraffin follow-up procedure, 5 µm thick sections were taken from kidney tissues and stained with hematoxylin and eosin (H&E). The obtained images were evaluated blindly using a light microscope (Olympus Cx43; Japan). In addition, random areas were selected for each animal to score histopathological lesions, and lesions such as glomerular atrophy, inflammatory cell infiltration, vascular congestion, and degeneration of tubular cells were taken as a basis. Scores were as follows: 0: no damage, 1: mild damage, 2: moderate damage, 3: severe damage.

Statistical Analysis

Group comparisons were conducted using one-way analysis of variance (ANOVA), followed by Tukey's post hoc test for multiple pairwise comparisons (SPSS, version 20.0; Chicago, IL, USA). A p-value of less than 0.05 was considered statistically significant. Data are expressed as mean ± standard deviation (SD).

Table 1. Primer sequences

Gene	Sequences (5'-3')
NF-κB	F: AGTCCCGCCCCTTCTAAAAC
	R: CAATGGCCTCTGTGTAGCCC
TNF-α	F: CTCGAGTGACAAGCCCGTAG
	R: ATCTGCTGGTACCACCAGTT
Caspase-3	F: ACTGGAATGTCAGCTCGCAA
	R: GCAGTAGTCGCCTCTGAAGA
Bax	F: TTTCATCCAGGATCGAGCAG
	R: AATCATCCTCTGCAGCTCCA
Bcl-2	F: GACTTTGCAGAGATGTCCAG
	R: TCAGGTACTCAGTCATCCAC
KIM1	F:TGGCACTGTGACATCCTCAGA
	R: GCAACGGACATGCCAACATA
AQP2	F: AGCTGCCTTCTATGTGGCT
	R: GCGTTGTTGTGGAGAGCATT
β-Actin	F: CAGCCTTCCTTCTTGGGTATG
	R: AGCTCAGTAACAGTCCGCCT

RESULTS

Kidney Function Tests

The effects of GNT and Poly applications on serum urea (Figure 1A) and creatinine (Figure 1B) levels of renal function tests were investigated. According to the obtained data, it was determined that there was no difference between the control and Poly groups in both parameters ($p>0.05$), GNT application provided a significant increase in these parameters compared to the control and Poly groups ($p<0.001$), and Poly50 and Poly100 doses administered together with GNT were effective in reducing urea and creatinine levels ($p<0.001$).

Oxidant-Antioxidant Status

The impact of GNT and Poly on oxidative stress markers—MDA (Figure 2) and GSH (Figure 3A)—as well as antioxidant enzymes GPx (Figure 3B), SOD (Figure 3C), and CAT (Figure 3D), was thoroughly examined. No significant differences were observed in MDA and GSH levels between the Control and Poly groups ($p>0.05$). However, GNT administration led to a marked elevation in MDA levels and a significant reduction in GSH levels compared to the Control and Poly groups ($p<0.001$). Co-administration of Poly with GNT, at both 50 and 100 mg/kg doses, significantly decreased MDA levels and restored GSH concentrations relative to the GNT group ($p<0.001$). Furthermore, GNT treatment substantially suppressed the activities of GPx, SOD, and CAT ($p<0.001$), while concurrent administration of Poly50 or Poly100 effectively enhanced the activity of these antioxidant enzymes, thereby reinforcing the antioxidant defense mechanisms ($p<0.001$)

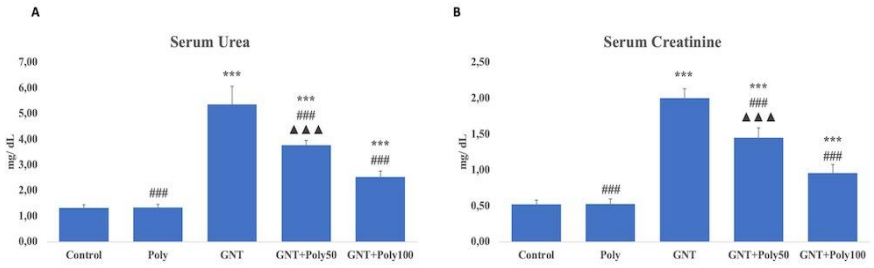

Figure 1: Effects of GNT and Poly on serum urea (A) and serum creatinine (B) levels. Values are given as mean ± SD. Control vs others: *p<0.05, **p<0.01, ***p<0.001, GNT vs others: #p<0.05, ##p<0.01, ###p<0.001, GNT+Poly50 vs GNT+Poly100: ▲p<0.05, ▲▲p<0.01, ▲▲▲p<0.001.

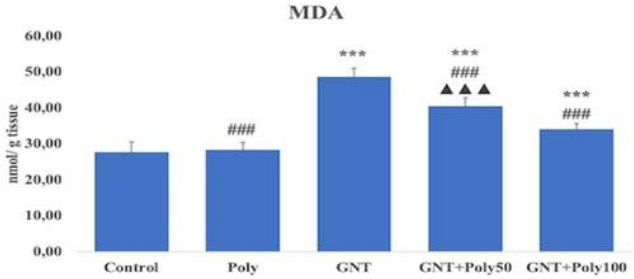

Figure 2: Effects of GNT and Poly on MDA levels in rat kidney tissues. Values are given as mean ± SD. Control vs others: *p<0.05, **p<0.01, ***p<0.001, GNT vs others: #p<0.05, ##p<0.01, ###p<0.001, GNT+Poly50 vs GNT+Poly100: ▲p<0.05, ▲▲p<0.01, ▲▲▲p<0.001.

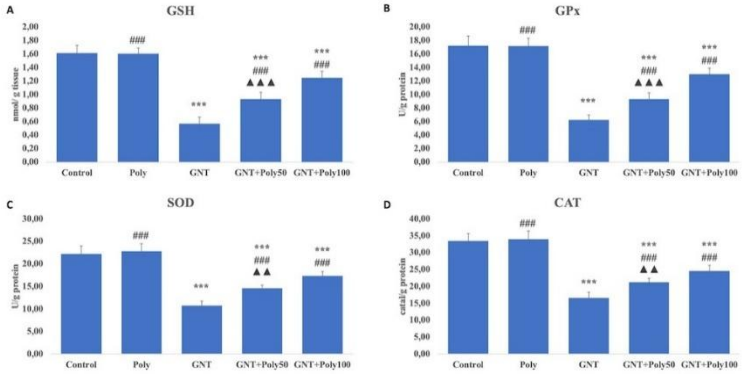

Figure 3. Effects of GNT and Poly on GSH (A) level and GPx (B), SOD (C), and CAT (D) activities and in rat kidney tissues. Values are given as mean ± SD. Control vs others: *p<0.05, **p<0.01, ***p<0.001, GNT vs others: #p<0.05, ##p<0.01, ###p<0.001, GNT+Poly50 vs GNT+Poly100: ▲p<0.05, ▲▲p<0.01, ▲▲▲p<0.001.

Inflammation

The mRNA expression levels of inflammatory markers NF-κB (Figure 4A) and TNF-α (Figure 4B) were analyzed. GNT treatment significantly upregulated the expression of both markers in renal tissue compared to the Control and Poly groups, indicating an inflammatory response (p<0.001). Co-treatment with Poly resulted in a dose-dependent reduction in NF-κB and TNF-α mRNA expression levels, demonstrating its anti-inflammatory potential (p<0.01).

Apoptosis

The impact of GNT and Poly on the expression of apoptotic markers Caspase-3 (Figure 5A) and Bax (Figure 5B), as well as the antiapoptotic marker Bcl-2 mRNA, was evaluated. The results revealed that GNT significantly elevated the mRNA expression of Caspase-3 and Bax (p<0.001) while reducing Bcl-2 expression (p<0.001), indicating the induction of apoptosis. The Poly50 dose administered with GNT had no significant effect on Caspase-3 and Bcl-2 levels (p>0.05). However, the Poly100 dose reduced Caspase-3 and Bax levels and enhanced Bcl-2 expression (p<0.01), suggesting an antiapoptotic role.

Effect of GNT and Poly on KIM-1 and AQP2

The effects of GNT and Poly on the mRNA expression levels of Kidney Injury Molecules-1 (KIM1) and Aquaporin 2 (AQP2), which are indicators of kidney damage, were examined. According to the results, it was determined that GNT administration increased the expression level of KIM1 (Figure 6A) compared to the control and Poly groups, while decreasing the expression level of AQP2 (Figure 6B) (p<0.001). It was determined that the Poly50 dose given together with GNT was not effective in both parameters (p>0.05), while the Poly100 dose decreased the expression level of KIM1 and increased the level of AQP2 (p<0.01).

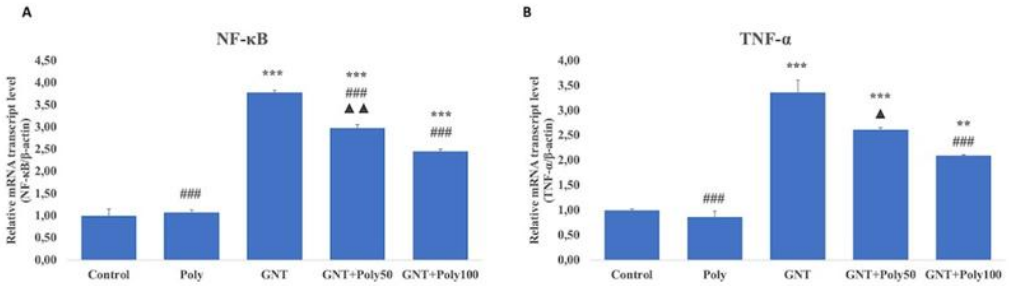

Figure 4: Effects of GNT and Poly on NF-κB (A) and TNF-α (B) mRNA transcription levels in rat kidney tissues. Values are given as mean ± SD. Control vs others: *p<0.05, **p<0.01, ***p<0.001, GNT vs others: #p<0.05, ##p<0.01, ###p<0.001, GNT+Poly50 vs GNT+Poly100: ▲p<0.05, ▲▲p<0.01, ▲▲▲p<0.001.

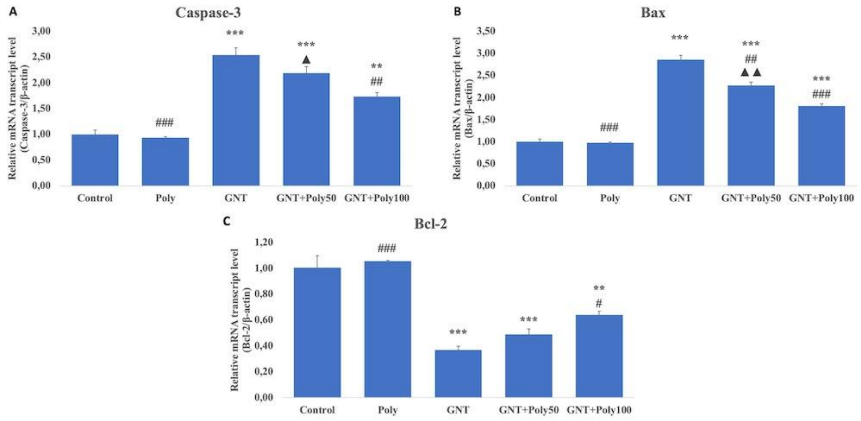

Figure 5: Effects of GNT and Poly on Caspase-3 (A), Bax (B), and Bcl-2 (C) mRNA transcription levels in rat kidney tissues. Values are given as mean ± SD. Control vs others: *p<0.05, **p<0.01, ***p<0.001, GNT vs others: #p<0.05, ##p<0.01, ###p<0.001, GNT+Poly50 vs GNT+Poly100: ▲p<0.05, ▲▲p<0.01, ▲▲▲p<0.001.

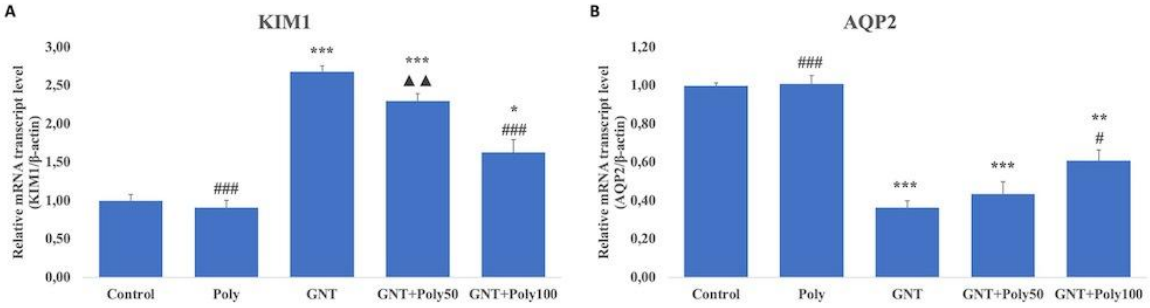

Figure 6: Effects of GNT and Poly on KIM1 (A) and AQP2 (B) mRNA transcription levels in rat kidney tissues. Values are given as mean ± SD. Control vs others: *p<0.05, **p<0.01, ***p<0.001, GNT vs others: #p<0.05, ##p<0.01, ###p<0.001, GNT+Poly50 vs GNT+Poly100: ▲p<0.05, ▲▲p<0.01, ▲▲▲p<0.001.

Effect of GNT and Poly on kidney morphology

H&E staining was performed to explain the histopathological effects of GNT and Poly applications on kidney tissue, and the results are presented in Figure 7. When representative photomicrographs were examined in the control and Poly-only groups, the Malpighian cortex and tubule structures localized in the renal cortex were normal, and there was no morphological difference between these two groups (Figure 7A, 7B). The images in the GNT-applied group included various pathological features such as tubular cell degeneration, inflammatory cell infiltration, vascular congestion, hemorrhage, and atrophic glomeruli (Figure 7C). On the other hand, the combined treatments of GNT and Poly increased the number of Malpighian corpuscles with intact morphology. In addition, there were occasional congested blood vessels and rare degenerative changes in tubular epithelial cells in these groups (Figure 7D, 7E). When the histopathological score results were evaluated, there was a significantly increased damage score in the GNT group, while the histopathological score in the GNT+Poly50 and GNT+Poly100 groups decreased significantly compared to the GNT group (p<0.05) (Figure 7F).

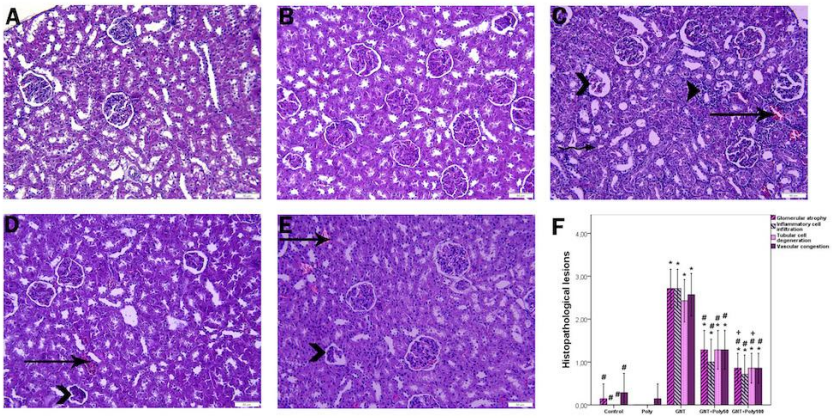

Figure 7: Microscopic images of rat kidney tissues treated with gentamicin and polydatin. Normal histological structure was observed in (A) Control and (B) Poly groups. (C) GNT toxicity caused atrophy of glomeruli (arrowhead), shedding of tubular epithelial cells (curved arrow), an increase in inflammatory cells (arrowhead), and congestion of interstitial blood vessels (arrow). (D) GNT+ Poly 50 and (E) GNT+ Poly 100 groups showed decreased atrophic glomeruli (arrowhead) and occasionally congested interstitial blood vessels (arrow). (F) Histopathological score analysis of H&E staining in five groups. (H&E, ×200; scale bar, 50 μm). Control vs others: *p<0.05, GNT vs others: #p<0.05, GNT+Poly 50 vs GNT+Poly 100: +p<0.05

DISCUSSION

Rapid deterioration of renal function due to exposure to nephrotoxic chemicals and drugs is called nephrotoxicity, and its pathogenesis involves various mechanisms, including ROS release, tubular and glomerular damage, and renal vasoconstriction (Tanyeli et al. 2020). GNT is an antibiotic that causes nephrotoxicity with morphological and biochemical changes in the proximal tubules (Abdel-Fattah et al. 2021). In the presented study, the effects of Poly, a natural antioxidant, were investigated in rats with GNT-induced nephrotoxicity.

Serum urea and creatinine are two important markers that show the structural integrity of the kidney (Akaras et al. 2023a). The first step in evaluating the toxic effects of various compounds is considered to be the increase in serum urea and creatinine levels (Akaras et al. 2023b; Şimşek et al. 2023). It has been revealed in different studies that GNT increases serum urea and creatinine levels (Hakyemez et al. 2022; Pakfetrat et al. 2022). In the presented study, it was determined that serum urea and creatinine levels increased in rats administered GNT, and Poly supportive treatment was effective in reducing these marker levels. Dahran et al. (2025) reported that Poly administration was effective in reducing serum urea and creatinine levels in rats with nephropathy.ROS is a key factor in the pathophysiology of kidney diseases (Kankılıç et al. 2024a; Bal et al. 2023). Both in vivo and in vitro studies demonstrate that GNT enhances ROS production by altering mitochondrial respiration, which subsequently accelerates the peroxidation of polyunsaturated fatty acids (PUFAs) (Aydın et al. 2009; Kandemir et al 2015). Antioxidant enzymes and compounds are essential for maintaining the balance between oxidants and antioxidants in the body (Tuncer et al. 2024). When antioxidant activity declines and antioxidant compounds are depleted, cells become more susceptible to oxidative stress, leading to an increase in oxidants (Aksu et al. 2019; İleritürk et al. 2022). In GNT-induced nephrotoxicity, oxidative stress manifests as elevated lipid peroxidation and reduced antioxidant enzyme activities (Kandemir et al. 2015; Bai et al. 2023). In the present study, GNT treatment resulted in increased MDA levels, reduced GSH levels, and decreased activities of SOD, CAT, and GPx, leading to oxidative stress in the kidneys. Previous studies have shown that Poly supplementation in kidney damage models lowers MDA levels and offers protection against oxidative stress by enhancing antioxidant enzyme activities (Zhou et al. 2022; Demirkapı et al. 2023). Similarly, this study observed that Poly treatment reduced GNT-induced lipid peroxidation and boosted antioxidant enzyme activities, thus mitigating oxidative stress.

The formation of reactive oxygen species causes the activation of pro-inflammatory pathways (Küçükler et al. 2024; Ileriturk et al. 2024). Among these, NF-ϰB signaling has been reported to be the main signal transduction pathway that plays a role in the regulation and activation of the genes of pro-inflammatory cytokines such as TNF-α (Çağlayan et al. 2022; Yeşildağ et al. 2022; Akaras et al. 2023c). Bai et al. (2023) reported that GNT increases the release of pro-inflammatory cytokines and triggers inflammation by activating the NF-ϰB signaling pathway. Hassanein et al. (2021) reported that GNT increases kidney tissue inflammation, which occurs through the activation of NF-ϰB. In the presented study, it was determined that NF-ϰB and TNF-α expression levels increased and inflammation was induced in the kidney tissue of rats

administered GNT, and that Poly, administered together with GNT, was effective in suppressing inflammation by reducing these expression levels. It has been demonstrated in different toxicity models that Poly reduces inflammation and has an anti-inflammatory effect, especially by suppressing NF-κB increases (Chen et al. 2021; Demirkapı et al. 2023).

Apoptosis, or programmed cell death, is a process that removes damaged, surplus, or potentially harmful cells from the body, often leading to cellular stress and/or injury in healthy cells (Yıldız et al. 2022; İleritürk et al. 2023; Akaras et al. 2024). Apoptosis begins with multiple events that lead to the activation of a caspase or protease family (Gür and Kandemir, 2022; Gencer et al., 2024). Caspases are responsible for the morphological and biochemical features of apoptotic cells (Kankılıç et al. 2024b). Caspase-3 has been reported to be one of the most important proteases that initiate both extrinsic and intrinsic apoptosis pathways and is also a marker of the irreversible point of apoptosis (Ekinci-Akdemir et al. 2018, Aksu et al. 2018; Yılmaz et al. 2024). It has been determined in different studies that GNT increases the levels of Caspase-3 and Bax and decreases the levels of Bcl-2 in kidney tissue in rats, and it has been reported that GNT induces apoptosis (Babaeenezhad et al. 2021; Laorodphu et al. 2022). In the presented study, it was determined that with GNT application, caspase-3 and Bax expression levels increased, while the expression of Bcl-2, an antiapoptotic marker, decreased, and apoptosis was induced, and Poly, applied together with GNT, was effective in suppressing apoptosis by regulating these values inversely.

CONCLUSION

As a result, it was determined that oxidative stress, inflammation and apoptosis mechanisms were induced in the kidney tissue of GNT-applied rats, that Poly supportive treatment was effective in protecting the kidney tissue by reversing these mechanisms, and that the use of Poly 100 dose would be more beneficial in GNT-induced kidney toxicities.

Conflict of interest: The authors have no conflicts of interest to report.

Authors' Contributions: ÖK, HŞ and FMK contributed to the experimental design, biochemical analysis. ÖK, drafted and wrote the manuscript. NA, performed histological analysis. All authors have read and approved the finalized manuscript.

Ethical approval: This study was carried out at Necmettin Erbakan University KONUDAM Experimental Medicine Application and Research Center (Konya / Turkey). This research was approved by The Ethics Committee of the Necmettin Erbakan University (dated 11.07.2024 and decision number 2024/63).

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