



# Cinnamon Mitigates Gentamicin-Triggered Lipid Metabolic Disruptions: An Experimental Study in Male Rabbits

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## ABSTRACT

Gentamicin is a potent aminoglycoside antibiotic commonly used in clinical settings, yet it is associated with nephrotoxicity and disturbances in lipid metabolism. Previous studies have reported that gentamicin administration can significantly elevate serum lipid levels, while cinnamon (*Cinnamomum verum*) has been shown to possess lipid-lowering and antioxidant effects in experimental models. This study aimed to evaluate the protective effect of cinnamon on gentamicin-induced alterations in the blood plasma lipid profile in male rabbits. Twenty healthy male rabbits were randomly divided into four groups: control (distilled water), gentamicin (50 mg/kg orally, every other day for 14 days), cinnamon (200 mg/kg orally, every other day for 10 weeks), and a combined treatment group receiving both agents. Blood samples were collected at the end of the treatment period via cardiac puncture. Plasma was separated by centrifugation and analyzed for total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) using enzymatic colorimetric methods. Data were analyzed using one-way ANOVA followed by Tukey's post hoc test ( $p < 0.05$ ). Results showed that gentamicin significantly increased TC ( $124.82 \pm 1.23$  mg/dl), TG ( $65.41 \pm 2.58$  mg/dl), and LDL ( $67.71 \pm 2.48$  mg/dl), while decreasing HDL ( $40.90 \pm 1.66$  mg/dl) compared to the control group. Cinnamon administration alone significantly reduced TC ( $109.07 \pm 4.52$  mg/dl), TG ( $46.26 \pm 1.38$  mg/dl), and LDL ( $59.15 \pm 1.37$  mg/dl), and increased HDL ( $50.08 \pm 1.95$  mg/dl). In the combined group, cinnamon partially mitigated gentamicin-induced lipid abnormalities, with values approaching those of the control group. These findings suggest that cinnamon may offer a protective effect against gentamicin-induced dyslipidemia, likely due to its antioxidant and hypolipidemic properties.

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## INTRODUCTION

Gentamicin, an aminoglycoside antibiotic widely used to treat severe Gram-negative bacterial infections, is known to induce nephrotoxicity and oxidative stress, which may disrupt normal lipid metabolism and lead to dyslipidemia. Lipid profile abnormalities, such as elevated total cholesterol, triglycerides, and low-density lipoprotein (LDL) levels, are frequently associated with drug-induced organ damage and may contribute to cardiovascular complications in experimental animals and humans alike [1]. Understanding the metabolic impact of gentamicin is essential for developing protective strategies against its side effects [2].

Cinnamon (*Cinnamomum verum*), a common medicinal plant and dietary spice, is rich in polyphenolic compounds and possesses potent antioxidant, anti-inflammatory, and lipid-lowering properties [3]. Numerous studies have demonstrated the efficacy of cinnamon in regulating lipid metabolism, improving insulin sensitivity, and scavenging reactive oxygen species, suggesting its potential role as a natural therapeutic agent against drug-induced toxicity [4]. Several experimental studies have demonstrated that gentamicin administration can significantly alter lipid metabolism in animal models [5]. For instance, [6] reported that gentamicin treatment in rats led to increased serum cholesterol and triglyceride levels due to

oxidative stress-induced hepatic and renal dysfunction. These effects may be attributed to increased lipid peroxidation and impaired lipid clearance mechanisms. Cinnamon has been shown to exert hypolipidemic effects in various animal models [7]. In a study by [8], cinnamon supplementation reduced total cholesterol, LDL, and triglycerides while increasing high-density lipoprotein (HDL) in diabetic rats. Similarly, [9] found that cinnamon extract improved lipid profiles and antioxidant status in rats exposed to oxidative stress. Moreover, [10] demonstrated that cinnamon administration alongside nephrotoxic agents like cisplatin or gentamicin significantly mitigated the elevation in lipid markers and oxidative damage in rat tissues. These findings support the hypothesis that cinnamon may play a protective role against gentamicin-induced dyslipidemia. This study aims to investigate the protective effects of cinnamon supplementation on the blood plasma lipid profile in male rabbits treated with gentamicin. The findings may provide biochemical evidence for the use of cinnamon as an adjunct therapy to mitigate gentamicin-induced metabolic disturbances.

## MATERIALS AND METHODS

"In this study, cinnamon and gentamicin were employed as treatment agents. The cinnamon powder was obtained

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from a licensed herbal medicine market in Al-Bayda City, ensuring its suitability for experimental use and in El-Bayda, Libya, gentamicin (Gentafar®, 10% Farvet, Holland) was bought at a pharmacy". We bought twenty mature male rabbits in good health from verified local farms. These rabbits were housed in a room that was appropriate for the trial duration and furnished in accordance with US-EPA 2004. The rabbits were kept in accordance with the US-EPA2004 for animal care and the Libyan Ministry of Agriculture's principles and guidelines. Each rabbit was kept in a suitable steel cage with a temperature between 22 and 26°C, a humidity level between 40 and 70%, and a clean environment with a 12-hour cycle of light.

For the course of the entire trial, a proper diet consisting of cleanwater and balanced feed has been supplied. The animals received the following treatment after being randomly assigned to four groups, each consisting of five rabbits: Group 1: Gentamicin (50 mg/kg body weight) was administered orally to each rabbit on alternate days for 14 days. Group 2: Each rabbit received 200 mg/kg body weight of cinnamon orally every other day for 10 weeks. Group 3: Gentamicin (50 mg/kg body weight) and cinnamon (200 mg/kg body weight) were administered orally to each rabbit every day. Group 4: was administered 8 milliliters of distilled water orally as a control for 14 days.

As soon as possible, the remaining fraction of the separated blood samples was put on ice. To create plasma, samples were centrifuged at 860 xg for 20 minutes. At the end of the treatment period, blood samples were collected via cardiac puncture under anesthesia. Plasma was separated and analyzed for lipid profile parameters, including total cholesterol (TC), triglycerides (TG), LDL, and HDL, using standard enzymatic colorimetric methods.

Minitab software (version 17) or GraphPad Prism 8 was used for statistical analysis as needed. Following the identification of a normal distribution in the data, an "ANOVA" analysis using the Tukey multiple comparison test was performed to obtain a significance threshold of  $P < 0.05$ .

## RESULTS

The data in Table 1 provide an overview of how cinnamon, gentamicin, and their combination affected the male rabbits' blood plasma lipid profile, which includes total cholesterol, triglycerides, "HDL", and "LDL". A thorough examination of the observed values and their statistical significance may be found here: TC, or total cholesterol: The cholesterol levels of the gentamicin-only group "GIN" were the highest at 124.82±1.228 mg/dl, substantially higher than those of the cinnamon "CIN", control "CON", and combination "CIN+GIN" groups ( $p < 0.05$ ).

A cholesterol-lowering impact was suggested by the "CIN" group's lower cholesterol levels (109.07±4.520 mg/dl), which were comparable to the control but substantially lower than those of the "GIN" group. The cholesterol levels in the "CIN+GIN" group were more in line with the control (119.70±1.214 mg/dl). Triglycerides "TG": Once more, the group that received just gentamicin had the highest triglyceride levels (65.41±2.576 mg/dl), which were considerably higher than those of any other group ( $p < 0.05$ ).

Compared to the other groups, the "CIN" group had the lowest triglyceride values (46.26±1.379 mg/dl). Although cinnamon can cut triglycerides even when gentamicin is present, its impact is not as strong as when it is given alone, according to the combined "CIN+GIN" group's intermediate triglyceride levels (56.33±1.354 mg/dl).

High-Density Lipoprotein "HDL": The group that took gentamicin had the lowest "HDL" levels (40.90±1.659 mg/dl), which was much lower than the group that just took cinnamon. "HDL" levels were substantially greater in the "CIN" group (50.08±1.953 mg/dl) than in the "GIN" group. The "CIN+GIN" group's "HDL" levels were 45.60±0.509 mg/dl, which is comparable to control values. Low-Density Lipoprotein "LDL": The "GIN" group had the highest "LDL" values (67.71±2.480 mg/dl), which were noticeably higher than those of the "CIN" group. As seen by the considerably lower "LDL" levels (59.15±1.370 mg/dl) in the "CIN" group compared to the "GIN" group. "LDL" levels (63.13±0.755 mg/dl) in the "CIN+GIN" group were comparable to those in the control group.

**Table 1. Plasma Cholesterol, triglycerides, high density lipoprotein, low density lipoprotein of male rabbits treated with Cinnamon, Gentamicin, and their combination.**

Lipids Profile (mg/dl)	Experimental groups			
	CON	CIN	GIN	CIN+GIN
<b>Cholesterol</b>	118.62±1.7 34 <sup>b</sup>	109.07±4.52 0 <sup>b</sup>	124.82±1.228 <sup>a</sup>	119.70±1.214 <sup>b</sup>
<b>TG</b>	60.48±1.41 5 <sup>b</sup>	46.26±1.379 c	65.41±2.576 <sup>a</sup>	56.33±1.354 <sup>b</sup>
<b>HDL</b>	46.20±0.53 6 <sup>ab</sup>	50.08±1.953 b	40.90±1.659 a	45.60±0.509 b
<b>LDL</b>	63.75±0.75 2 <sup>ab</sup>	59.15±1.370 b	67.71±2.480 <sup>a</sup>	63.13±0.755 5 <sup>ab</sup>

For every treatment group, the values are shown as means ± SE; n = 5. The mean values within a row that did not share a common superscript letter (a, b, or c) showed significant differences ( $p < 0.05$ ).

## DISCUSSION

The present study aimed to investigate the impact of cinnamon (*Cinnamomum verum*), gentamicin, and their combination on plasma lipid profile parameters total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) in male rabbits. The data clearly demonstrate that gentamicin administration resulted in significant dyslipidemia, while cinnamon showed a lipid-lowering and potentially protective effect against gentamicin-induced changes. Gentamicin-treated rabbits (GIN group) exhibited significantly elevated levels of TC, TG, and LDL, along with decreased HDL compared to the control group. These findings are consistent with previous studies that have shown gentamicin's ability to impair renal function and induce oxidative stress, leading to altered lipid metabolism [11]. Gentamicin may increase hepatic lipid synthesis and reduce the clearance of lipids from plasma by damaging the kidneys and affecting lipoprotein lipase activity [12]. The reduction in HDL levels also supports the notion that gentamicin may impair reverse cholesterol transport, thereby elevating cardiovascular risk [13]. In contrast, cinnamon-treated rabbits (CIN group) displayed a significant improvement in lipid profile, with notably reduced TC, TG, and LDL, as well as increased HDL. These hypolipidemic effects of cinnamon have been attributed to its active polyphenolic compounds, such as cinnamaldehyde and procyanidins, which enhance lipid metabolism, inhibit cholesterol biosynthesis, and improve antioxidant status [14]. Additionally, cinnamon has been shown to upregulate peroxisome proliferator-activated receptor alpha (PPAR-α), promoting fatty acid oxidation and reducing lipid accumulation [15]. Interestingly, the group that received both gentamicin and cinnamon (CIN+GIN) demonstrated intermediate values for all lipid parameters. TC, TG, and LDL were lower than those in the gentamicin-only group, while HDL was higher. Although

not fully restored to the level of the cinnamon-only group, these results suggest a partial protective effect of cinnamon against gentamicin-induced dyslipidemia [1]. This supports the hypothesis that cinnamon's antioxidant properties can ameliorate oxidative damage and stabilize lipid metabolism under drug-induced stress conditions [16].

Taken together, the data indicate that gentamicin significantly alters lipid metabolism, promoting atherogenic profiles, while cinnamon exerts a counteracting effect by restoring lipid balance. The partial normalization of lipid markers in the CIN+GIN group further reinforces the therapeutic potential of cinnamon in mitigating drug-induced lipid disorders. These findings may have clinical relevance in preventing or managing cardiovascular risk associated with aminoglycoside antibiotics.

## CONCLUSION

In conclusion, the results imply that gentamicin by itself has a detrimental effect on the lipid profile by markedly increasing "LDL", triglycerides, and total cholesterol while lowering "HDL". However, by increasing "HDL" levels and decreasing "LDL", triglycerides, and total cholesterol, cinnamon seems to enhance lipid profiles. Together, cinnamon seems to lessen some of the effects of gentamicin on lipid levels, suggesting that cinnamon may have a protective impact against lipid abnormalities brought on by gentamicin.

**Conflict of interest.** Nil

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