# The Protective Role of Silymarin and Aerobic Exercise on Gentamicin-induced Nephrotoxicity

Dear Editor,

Gentamicin (GM) is commonly used against Gram-negative microorganisms, but the compound's therapeutic use is mainly limited by nephrotoxicity which is observed in 10%–20% of patients treated with GM.[1] Silymarin (SM) as an antioxidant agent has anti-inflammatory actions, and it improves structural and enzymatic changes induced by GM.[2] On the other hand, lifelong physical activity has been recommended to improve antioxidant content.[3] Thirty-seven adult male Wistar rats (175.56 ± 2.24 g) were used in five groups as follows:

Group 1 ($n$ = 6, control group) that received vehicle dimethyl sulfoxide (DMSO) for 3 days a week during the 6 week study period and then saline was injected for 10 days. Group 2 ($n$ = 6, GM group) that received the same regimen as Group 1 but GM (100 mg/kg/day) for 10 days instead of saline. Group 3 ($n$ = 7, GM + SM group) that received SM (200 mg/kg/day) dissolved in DMSO for 3 days a week during the 6 week study period and then GM was injected for 10 days. Group 4 ($n$ = 9, GM + exercise [EX]) that received DMSO for 3 days a week and treadmill EX (5 days in week) during the 6 week study period and then GM was injected for 10 days. Group 5 ($n$ = 9, GM + SM + EX) that received SM dissolved in DMSO for 3 days a week and EX during the 6 week study period and then GM was injected for 10 days.

The rats were exposed to treadmill EX 5 sessions a week for a period of 6 weeks as described before.[4,5]

The levels of serum creatinine (Cr), blood urea nitrogen (BUN), nitrite (by Griess reaction), and malondialdehyde (MDA)[5,6] were determined.

The removed kidney was weighted and subjected to hematoxylin and eosin staining. Kidney tissue damage score (KTDS) was graded from 0 to 4. Independent Student's $t$-test, Mann–Whitney test for comparison between control and GM groups, and ANOVA analysis followed by least significant difference, and Kruskal–Wallis tests were employed to compare the parameters between all GM-treated groups.

The serum levels of BUN (19.2 ± 1.0, 66.4 ± 11.6 mg/dl, $P < 0.05$) and Cr (0.48 ± 0.02, 1.16 ± 0.18 mg/dl, $P < 0.05$),

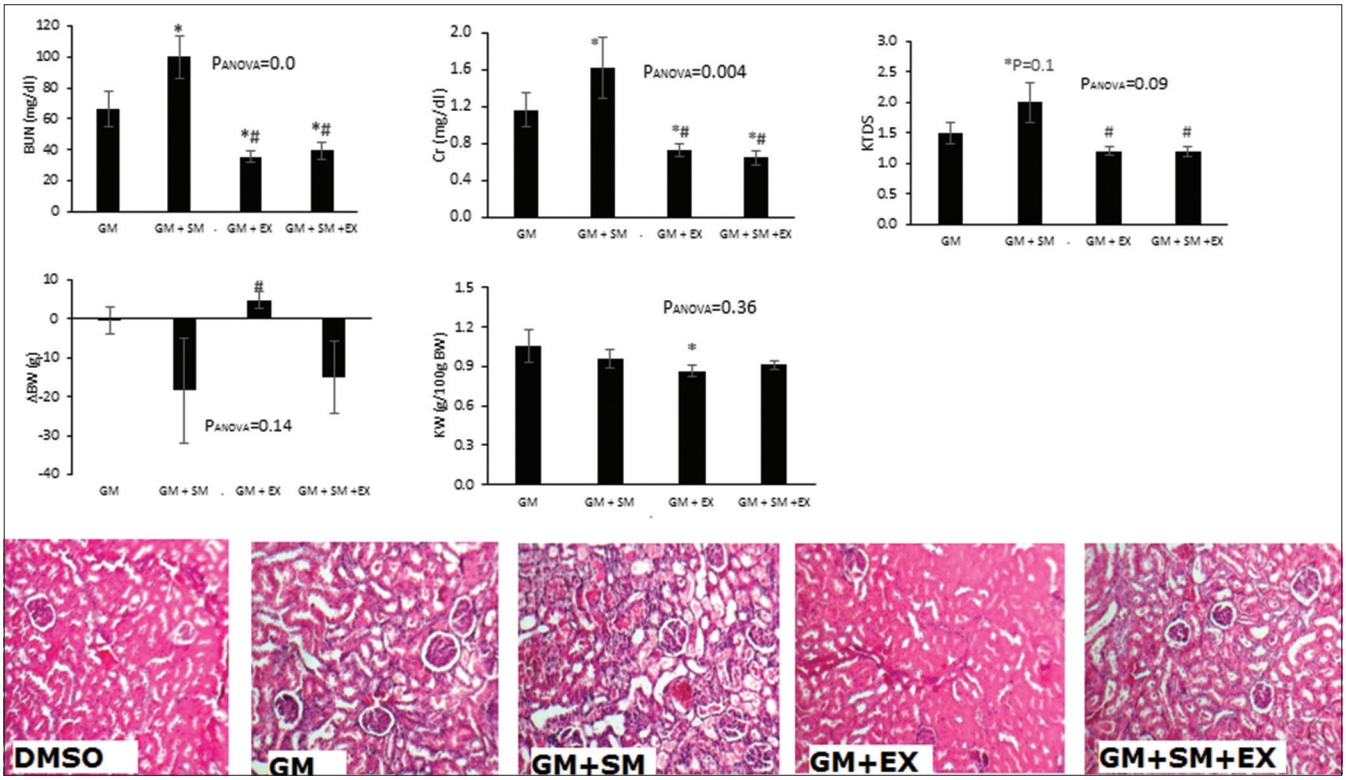


**Figure 1: The serum levels of blood urea nitrogen, creatinine, and kidney tissue damage score, kidney weight and change of body weight between the gentamicin-treated groups (see text for group information). * and # symbols indicate significant difference from gentamicin or gentamicin + silymarin groups, respectively ($P < 0.05$)**

KTDS (0.25 ± 0.25, 1.5 ± 0.22, $P < 0.05$), kidney weight (0.64 ± 0.01, 1.05 ± 0.12 g, $P < 0.05$), and body weight change (19.25 ± 2.92, −0.33 ± 3.46 g, $P < 0.05$) between control and GM alone treated groups were significant, while the serum level of MDA (4.37 ± 1.42, 4.72 ± 0.46 μmol/l) and nitrite (13.06 ± 1.01, 12.02 ± 0.51 μmol/l) were insignificant. In GM-treated groups, SM alone increased the serum levels of BUN and Cr as well as KTDS significantly ($P < 0.05$), but when SM was accompanied with EX or EX alone, decreased these parameters significantly ($P < 0.05$) [Figure 1]. The serum nitrite and MDA levels were 12.02 ± 0.51 and 4.72 ± 0.46, 15.67 ± 0.97 and 5.96 ± 0.62, 11.24 ± 0.85 and 6.77 ± 0.80, and 20.61 ± 5.03 μmol/l and 8.91 ± 1.88 μmol/l in Groups 2–5, respectively, with no significant difference between the groups.

SM exerts positive effects in patients with renal insufficiency.[6] Conversely, SM administration also resulted in persistence of oxidative stress and inflammatory processes, tubular necrosis, and apoptosis in rats with glycerol-induced acute kidney injury.[7] In our results, however, SM alone did not protect the kidney against GM, but aerobic EX either alone or accompanied with SM provides the protective effect against GM-induced nephrotoxicity. EX increased renal drug metabolism, and in agreement with our study, moderate EXs improve metabolic parameters, renal function, and structure on GM-induced acute kidney injury in rats.[8] As conclusion, aerobic EX alone or accompanied with SM may be recommended to attenuate GM-induced nephrotoxicity while SM as an antioxidant may not act such mission.

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## Conflicts of interest

There are no conflicts of interest.

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