

## Sex-related Difference in Protective Role of Aerobic Exercise against Cisplatin-induced Hepatotoxicity

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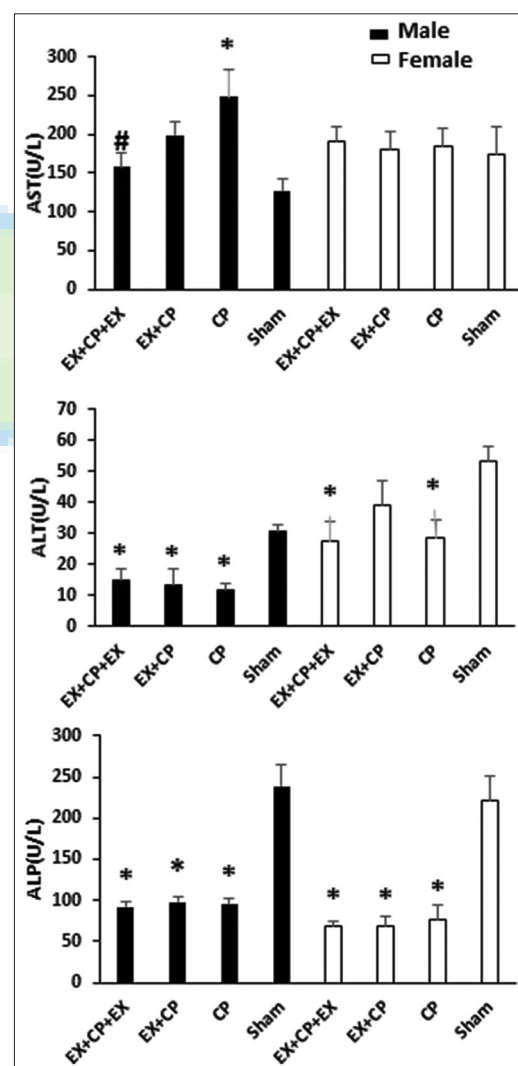
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### DEAR EDITOR,

Cisplatin (CP) as a potential chemotherapeutic drug is accompanied with nephrotoxicity<sup>[1]</sup> and hepatotoxicity.<sup>[2]</sup> Aerobic exercise could attenuate CP-induced nephrotoxicity gender dependently.<sup>[3,4]</sup> The experimental design was described before<sup>[3,4]</sup> briefly, sixty Wistar rats were divided into eight groups. The male animals in Group I (named EX + CP + EX) had aerobic exercise on a treadmill 1 h/day and five days/week for 8 weeks. Then, the exercise protocol was continued for another week which was accompanied with reducing the intensity of training, and during this week, the animals also received CP (2.5 mg/kg/day). Groups II (named EX + CP) had the same protocol as Group I without exercise in the last week during CP therapy. Groups III (named CP) and IV (named sham) received CP and saline respectively during the last week of the study without exercise. The female rats in Groups V–VIII had the same protocol as the male rats in Groups' I–IV. The animals were exposed to moderate exercise with the 65% oxygen consumption.<sup>[5]</sup> Blood samples were obtained 1 week after CP administration.

CP increased the serum levels of aspartate aminotransferase (AST) in male ( $P < 0.05$ ) not in female rats. The serum levels of AST decreased significantly in EX + CP + EX group compared to CP group ( $P < 0.05$ ). The serum levels of alkaline phosphatase (ALP) decreased in all CP treated male and female groups compared to sham group ( $P < 0.05$ ). The serum levels of alanine aminotransferase decreased in all male groups and EX + CP + EX and CP in female groups when compared with sham group [ $P < 0.05$ , Figure 1].

AST increased in male positive control (Group III) compared to sham group as reported before.<sup>[6]</sup> CP increases toxicity via reduces antioxidant enzymes



**Figure 1:** The serum levels of alkaline phosphatase, alanine aminotransferase, and aspartate aminotransferase. \*Indicates significant difference from negative control group (sham) and #indicates significant difference from positive control group (cisplatin) ( $P < 0.05$ ) one-way ANOVA followed by the least-squares deconvolution posttest

and increases malondialdehyde level,<sup>[6,7]</sup> and appropriate exercise increases antioxidant enzymes.<sup>[8,9]</sup> Administration of CP induces magnesium deficiency<sup>[10]</sup> whereas ALP activity was reduced due to magnesium depletion.<sup>[11]</sup> Therefore, aerobic exercise may reduce CP-induced hepatotoxicity by increasing activation of antioxidant system in male rats.

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### Conflicts of interest

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