International Journal of Preventive Medicine

Letter to Editor Open Access

Comment on: Effect of Pomegranate Flower Extract on Cisplatin-induced Nephrotoxicity in Male Rats

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How to cite this article: El-Arabey AA. Comment on: Effect of pomegranate flower extract on cisplatin-induced nephrotoxicity in male rats. Int J Prev Med 2016;7:9.

DEAR EDITOR,

I read with interest a recently published article in the "Journal of Nephropathology" by Motamedi *et al*., entitled "Effect of pomegranate flower extract on cisplatin-induced nephrotoxicity in male rats."[1] The authors have concluded that low dose of pomegranate flower extract (PFE) (25 mg/kg) showed protective effects against cisplatin (CP)-induced nephrotoxicity through its antioxidant effects. On the other hand, they did not observed the protective role of a higher dose of PFE (50 mg/kg) versus CP-induced nephrotoxicity in the same animal model. They attributed these effects to the antioxidant dose, because high doses of some antioxidants do not have a protective effect, and can exacerbate tissue damage.[2,3] Here, I would like to explain the potential mechanism may be related to this difference. The CP-induced nephrotoxicity is a gender dependent; the greater intensity of damage in male than female.[4] Gender differences of CP-induced nephrotoxicity may be related to CP uptake by *OCT2*; which has been demonstrated to be higher expressed in male than in female rats.[5] Thus, CP uptake was increased by *OCT2* overexpression in male rats and associated with increased cellular sensitivity to CP toxicity.[6] A study demonstrated that *OCT2* level was significantly reduced in mice after castration.[7] Moreover, a recent study concluded that CP therapy should be avoided when the serum testosterone (TS) level is high because TS in high concentrations (the selected doses: 50 mg/kg and 100 mg/kg) promote CP-induced nephrotoxicity in surgical castrated rats.[8] Furthermore, a recent study showed that the low dose of TS (10 mg/kg) protects kidneys against CP-induced nephrotoxicity in surgical castrated rats.[8] Subsequently, It seems the protective effect of TS on CP-induced nephrotoxicity depend on its dose. In addition, several studies concluded that the consumption of PFE increases significantly TS level in male rats.[9] Finally, I suggest the low dose of PFE (25 mg/kg) increase TS level closed to physiological normal level; however, the high dose of PFE (50 mg/kg) increase TS level in manner leads to increase gene expression of *OCT2*. Therefore, low dose of PFE showed protective effects; in contrast, the high dose of PFE exacerbate tissue damage resulting from increased CP uptake by *OCT2* overexpression in male rats and associated with increased cellular sensitivity to CP toxicity.

Received: 25 Apr 15 **Accepted:** 30 Jul 15
Published: 13 Jan 16

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DOI:
10.4103/2008-7802.173905