



Negative Response of Phytoestrogens of Pomegranate Flower Extract against Cisplatin-induced Nephrotoxicity in Female Rats

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DEAR EDITOR,

I read with interest the recently published letter,^[1] which was commented on my letter previously published in the “International Journal Prevention Medicine” entitled “Comment on: Pomegranate flower extract doesn't prevent cisplatin-induced nephrotoxicity in female rats.”^[2] The authors of the commentary letter have indicated to the results of Jilanchi *et al.* and concluded that the lack of protective effect of pomegranate flower extract (PFE) in cisplatin (CP)-induced nephrotoxicity seems to be the pro-oxidant activity of pomegranate extract or low dose of this plant extract. Here, I would like to discuss the conclusions of commentary letter^[1] and provide more evidence to support my conclusion about phytoestrogens are the cause of negative response of PFE on CP-induced nephrotoxicity in female rats.^[2]

The experiment was done by Jilanchi *et al.* selected two doses of PFE used as an antioxidant on CP-induced nephrotoxicity in female rats. They observed that PFE not only did not ameliorate the induced nephrotoxicity but also aggravated renal tissue damage in the two selected doses.^[3] On the other hand, the study was done by Motamedi *et al.* demonstrated the same doses and regimen of PFE as an antioxidant on CP-induced nephrotoxicity in male rats. The low dose of PFE plays a protective role against CP-induced renal toxicity in male rats. Conversely, the high dose of PFE was showed no significant role against CP-induced nephrotoxicity in male rats.^[4] Therefore, the lack of protective effect of PFE is not related to the pro-oxidant activity of PFE or low dose of PFE due to the low dose has protective role in male rats and has not protective effect in female rats in spite of male rats more susceptible to CP toxicity rather than female rats due to high gene expression of OCT2 in

male rats which responsible for CP uptake.^[5] However, estrogen abolishes protective effects of erythropoietin against CP-induced nephrotoxicity in ovariectomized rats and increases oxidative stress in the kidney.^[6,7] It also abolishes protective effects of Vitamin E against CP-induced nephrotoxicity.^[8] Finally, I support my first conclusion as PEF contains phytoestrogens, which have estrogenic activity which accountable for increase CP potency and kidney damage to a higher extent. Hence, PEF does not prevent CP-induced nephrotoxicity in female rats.

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Conflicts of interest

There are no conflicts of interest.

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