Potentiation of therapeutic effect of cisplatin and protection against its nephrotoxicity by resveratrol in experimental animals

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Background: Cisplatin (CIS) is one of the most effective anticancer drug used in the treatment of several solid tumors. Its use is limited by its nephrotoxicity. The present study was designed to assess the role of a natural product resveratrol (RSVL) on sensitization of mammary carcinoma (Ehrlich ascites carcinoma) to the action of CIS in mice and the possible protective effect against CIS-induced nephrotoxicity in rats.

Methods: The percent survival of female tumor bearing mice was used for determination the cytotoxic activity of CIS in the presence or the absence of RSVL. Uptake and cell cycle effect, serum creatinine (CREA), blood urea nitrogen (BUN), reduced glutathione (GSH) and histopathological examination of kidney tissues after CIS and/or RSVL therapy were also investigated in mice and rats.

Results: RSVL increased the intracellular level of CIS in EAC cells. CIS at a dose of 5 mg/kg increased the mean survival time of female tumor bearing mice to 25 days compared with 17 days for tumor-bearing control mice. Administration of RSVL at a dose of 25 mg/kg simultaneously with CIS increased the mean survival time to 48 days with 60% survival of the tumor-bearing animals. Cell cycle analysis of tumor cells showed that CIS treatment decreases the proliferation index of tumor cells while in presence of RSVL there were more significant inhibitions. Moreover, There was more increase in the percentage cells in sub-G1 phase 24 and 48 hours after treatment with CIS+RSVL compared with CIS alone (33% and 36% respectively). CIS treatment caused increase in level of creatinine and blood urea with significant decrease in the GSH level in rats. While, in the presence of RSVL, level of creatinine and blood urea restored to control level.

Conclusion: This study suggests that RSVL could increase the cytotoxic activity of CIS and protect against its nephrotoxicity.

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Biography

Zoheir A Damanhouri is currently the Chairman of Pharmacology Department in the Faculty of Medicine at King Abdulaziz University, Jeddah, Saudi Arabia. He obtained his BSc degree in Biochemistry from the University of Lancaster in the United Kingdom, and his MSc and PhD in Pharmaceutical Sciences from the University of Wales. His main research focuses on various areas in pharmacology including natural products on anticancer drugs and their toxicities, implication of herbal medicine co-administration with conventional drugs and therapy also on drug metabolism in particular variability in CYP450 isozymes (and SNP's) and their involvement in drug interactions, adverse drug effects and polymorphism. He has over 40 publications in his specialty in pharmaceutical sciences.

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