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Involvement of Multi-Drug Resistance Protein (Mrp) 3 in Resveratrol Protection against Methotrexate-Induced Testicular Damage

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Abstract : The aim of the present study is to investigate the effect of resveratrol (RES) on methotrexate (MTX)-induced testicular damage. RES (10 mg/kg/day) was given for 8 days orally and MTX (20 mg/kg i.p.) was given at day 4 of experiment, with or without RES in rats. MTX decreased serum testosterone, induced histopathological testicular damage, increased testicular tumor necrosis factor-α level and expression of nuclear factor-κB and cyclooxygenase-2. In MTX/RES group, significant reversal of these parameters was noticed, compared to MTX group. Testicular expression of multidrug resistance protein (Mrp) 3 was three- and five-folds higher in RES- and MTX/RES-treated groups, respectively. In vitro, using prostate cancer cells, each of MTX and RES alone induced cytotoxicity with IC50 0.18 ± 0.08 and 20.5 ± 3.6 μM, respectively. RES also significantly enhanced cytotoxicity of MTX. In conclusion, RES appears to have dual beneficial effect, as it promotes MTX tumor cytotoxicity, while protecting the testes, probably via up-regulation of testicular Mrp3 as a novel mechanism.

Keywords : resveratrol, methotrexate, multidrug resistance protein 3, tumor necrosis factor-α, nuclear factor-κB, cyclooxygenase-2
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