

Protective Effect of Caffeine Apoptosis Induced by Anthracyclines

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SUMMARY

We studied the effects of the xanthine derivative, caffeine (CAF), on cell killing by anthracycline antibiotics *in vitro* and *in vivo*. CAF reduced the cytotoxicity of epirubicin (EPI) in cultured P388 leukemia cells. The treatment with CAF diminished G₂ blocking effects induced by anthracyclines in cells. CAF also weakened the inhibition of anthracycline-induced nucleic acid synthesis in cells. When CAF was added to the growth medium before EPI exposure, a modification in intracellular EPI accumulation was observed. The treatment with CAF significantly diminished the lethality of anthracyclines in mice. Thus, CAF inhibited cell death induced by EPI *in vitro* and *in vivo*. CAF, however, did not affect the antitumor activity of EPI of mice bearing P388 leukemia. These results suggest the antagonistic effect of CAF on the toxicological actions of anthracyclines in cells and mice. From these data, this protection by CAF may be important in reducing side effects of the antitumor drug.