Biochem Pharmacol. 2002 Aug 15;64(4):573-82.

Modulation of P-glycoprotein expression and function by curcumin in multidrug-resistant human KB cells.

Anuchapreeda S[1], Leechanachai P, Smith MM, Ambudkar SV, Limtrakul PN.

Author information

Abstract

Multidrug resistance (MDR) is a phenomenon that is often associated with decreased intracellular drug accumulation in the tumor cells of a patient, resulting from enhanced drug efflux. It is often related to the overexpression of P-glycoprotein (Pgp) on the surface of tumor cells, thereby reducing drug cytotoxicity. In this study, curcumin was tested for its potential ability to modulate the expression and function of Pgp in the multidrug-resistant human cervical carcinoma cell line KB-V1. Western blot analysis and reverse transcription-polymerase chain reaction (RT-PCR) showed that treatment with 1, 5, and 10 microM curcumin for up to 72hr was able to significantly lower Pgp expression in KB-V1 cells. Curcumin (1-10 microM) decreased Pgp expression in a concentration-dependent manner and was also found to have the same effect on MDR1 mRNA levels. The effect of curcumin on Pgp function was demonstrated by rhodamine 123 (Rh123) accumulation and efflux in Pgp-expressing KB-V1 cells. Curcumin increased Rh123 accumulation in a concentration-dependent manner (1-55 microM) and inhibited the efflux of Rh123 from these cells, but did not affect the efflux of Rh123 from the wild-type drug-sensitive KB-3-1 cells. Treatment of drug-resistant KB-V1 cells with curcumin increased their sensitivity to vinblastine, which was consistent with an increased intracellular accumulation of Rh123. In addition, curcumin inhibited verapamil-stimulated ATPase activity and the photoaffinity labeling of Pgp with the prazosin analog [125I]iodoarylazidoprazosin in a concentration-dependent manner, demonstrating that curcumin interacts directly with the transporter. Thus, curcumin seems to be able to modulate the in vitro expression and function of Pgp in multidrug-resistant human KB-V1 cells. In summary, this study describes the duel modulation of MDR1 expression and Pgp function by the phytochemical curcumin, which may be an attractive new agent for the chemosensitization of cancer cells.

PMID: 12167476

[PubMed - indexed for MEDLINE]