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CYTOTOXIC AND CYTOPROTECTIVE ACTIVITIES OF CURCUMIN. A MOLECULAR TOXICOLOGICAL APPROACH.

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Curcumin, which is a widely used constituent of *Curcuma longa,* has been widely and for a long time used in the treatment of sprain and inflammation in indigenous medicine. Apart from anti-inflammatory activities, curcumin also has been shown to possess various other biological activities, such antioxidant., antimutagenic and anti-carcinogenic activities. As yet, however, little is known about the cytotoxicity of the compound as well as about its cytoprotective properties against drug-induced toxicities.

In the present study we therefore investigated the cytotoxicity as well as the cytoprotective activities of curcumin. Rat liver hepatocytes were chosen as in vitro test system for this purpose. Paracetamol was chosen as a model-toxin to test the cutoprotective activities of curcumin, because several molecular mechanisms of cell injury due to paracetamol are known to operate more or less simultaneously (1).

At relatively low concentrations curcumin was found to protect significantly against paracetamol-induced lipid peroxidation (LPO), but without protection against paracetamol-induced lactate dehydrogenese (LDH)-leakage and glutathione (GSH)-depletion. At high concentrations of curcumin, however, the observed protective effect against paracetamol-induced LPO was accompanied by a tendency to increase cellular GSH-depletion and LDH-leakage. From these and some other experiments it is concluded that the cytoprotective activities of curcumin are most likely the result of a strong antioxidant capacity of curcumin and, moreover, that the cytotoxic potential of the drug is most likely caused by its capability to conjugate covalently to GSH (2). In another study, curcumin was also found to be a potent inhibitor of rat liver P450 1A1/1A2 measured as ethoxyresorufin deethylation (EROD) activity, in ß-napthoflavone (ßNF)-induced microsomes, a less potent inhibitor of P450 2B1/2B2, measured as pentoxyresorufin depentylation (PROD) activity, in phenobarbital (PB) induced microsomes and a weak inhibitor of P450 2E1, measured as P-nitrophenol (PNP) hydroxylation activity, in pyrazol-induced microsomes. K values were 0.14 and 76.02 μM for the EROD-and PROD-activities, respectively, while 30 µM of curcumin inhibited only 9% of PNP-hydroxylation activity. In ethoxyresorufin deethylation (EROD) and pentoxyresorufin depentylation (PROD) experiments, curcumin showed a competitive type of inhibition (2).