PRELIMINARY COMMUNICATION

PERAZINE AS A POTENT INHIBITOR OF HUMAN CYP1A2 BUT NOT CYP3A4

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The effects of perazine on the activities of CYP1A2 and CYP3A4 in a primary culture of human hepatocytes of one patient were studied in vitro. The CYPs activities were assessed by measuring the rate of acetanilide 4-hydroxylation (CYP1A2) and cyclosporine A oxidation (CYP3A4) after treatment with TCDD (a CYP1A subfamily inducer) or rifampicin (mainly a CYP3A4 inducer). The amounts of the metabolites formed in hepatocytes were assayed in the extracellular medium using the HPLC method. TCDD and rifampicin induced the formation of 4-hydroxyacetanilide and cyclosporine A metabolites (monohydroxycyclosporine A, dihydroxycyclosporine A, N-desmethylcyclosporine A), respectively. The formation of 4-hydroxyacetanilide was strongly inhibited by three different concentrations of perazine (10, 25 and 50 μM) reaching 8, 3 and 2% of the control value, respectively. In the case of CYP3A4 activity, no such an effect of perazine was observed. Perazine showed only a week inhibition of the activity of cyclosporine A oxidase (to 96–86% of the control value). The obtained results suggest a strong inhibitory effect of perazine on human CYP1A2 activity with predicted Ki value similar to those of the known for CYP1A2 inhibitors, such as furafylline and fluvoxamine.

Key words: perazine, inhibitor, human cytochrome P-450, CYP1A2, CYP3A4, hepatocytes

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