Pharmacological Reports
2012, 64, 1411–1418
ISSN 1734-1140

Effect of classic and atypical neuroleptics on cytochrome P450 3A (CYP3A) in rat liver

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Abstract:
Background: Cytochrome P450 3A (CYP3A) subfamily is involved in the metabolism of xenobiotics (e.g., drugs) and endogenous substances (e.g., steroids). The aim of the present study was to investigate the influence of classic and atypical neuroleptics on the level and activity of CYP3A in rat liver, measured as a rate of testosterone 2β- and 6β-hydroxylation.
Methods: The reactions were studied in control liver microsomes in the presence of neuroleptics, as well as in the microsomes of rats treated intraperitoneally (*ip*) with pharmacological doses of the drugs (promazine and thioridazine 10 mg/kg; chlorpromazine 3 mg/kg; haloperidol 0.3 mg/kg; risperidone 0.1 mg/kg; sertindole 0.05 mg/kg) for one day or two weeks (twice a day), in the absence of the neuroleptics *in vitro*.
Results: The investigated neuroleptics added *in vitro* to control liver microsomes produced a moderate or week inhibitory effects on CYP3A activity. After one-day exposure of rats to neuroleptics, only chlorpromazine significantly increased the activity of CYP3A. Chronic treatment of rats with thioridazine diminished the protein level and activity of CYP3A, while risperidone induced this enzyme.
Conclusion: The observed changes in the CYP3A expression after prolonged exposition to neuroleptics suggest their influence on the enzyme regulation.

Key words:
neuroleptics, rat, CYP3A, direct effect, one-day treatment, chronic treatment