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Drug Interactions of H2-Receptor Antagonists Involving Cytochrome P450 (CYPs) Enzymes: from the Laboratory to the Clinic

Slobodan Rendiæ
Department of Pharmaceutical Chemistry, Faculty of Pharmacy and Biochemistry, University of Zagreb, Zagreb, Croatia

This paper reviews the main steps in the research of the interactions of H2-receptor antagonist drugs with cytochrome P450 (CYP) enzymes. Cimetidine, ranitidine, and related compounds are used as examples. The results from in vitro studies are related to the observed clinically significant in vivo drug-drug and drug-chemical interactions. Uses of the in vitro results are discussed for the interpretation and possible prediction of drug-drug interactions, which may be important in developing new drugs. Other approach in the use of the in vitro data is to prevent undesirable and toxic actions of drugs related to the catalytic activity of CYP enzymes. In the case of H2-receptor antagonists, the inhibition of the metabolic reactions due to the binding of the drugs with the enzymes was used to avoid side effects of co-administered drugs. The in vitro metabolic studies using recombinant human as well as animal CYP enzymes are now widely used as model systems for designing new drugs with improved therapeutic properties.

Key words: cimetidine; CYP; cytochrome P450; drug antagonism; drug combinations; histamine H2 receptor antagonists; liver; microsomes; polypharmacy; ranitidine