Stereoselective inhibition of human CYP2C19 activity by lansoprazole and omeprazole

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Lansoprazole and omeprazole are proton pump inhibitors that contain a chiral benzimidazole sulfoxide structure and are used as a racemic mixture of S- and R-form. This study was addressed to evaluate the stereoselective inhibitory potential of lansoprazole and omeprazole on human CYP isoforms using human liver microsomes in vitro. For the CYP2C19-catalyzed (S)-mephenytoin 4'-hydroxylation, CYP2C9-catalyzed tolbutamide 4-methylhydroxylation, and CYP3A4-catalyzed midazolam 1-hydroxylation, racemic lansoprazole and its enantiomers showed stereoselective inhibitions. Among CYP isoforms tested, CYP2C19 was most strongly inhibited by lansoprazole and omeprazole. And the inhibitory potential was in order of; (S)-lansoprazole > racemic lansoprazole > (R)-lansoprazole. The estimated Kis were 1.3±0.13 (M, 06±0.06 (M and 6.1±2.6 (M for racemic-, (S)-lansoprazole and (R)-lansoprazole, respectively. Racemic, (R)-, and (S)-omeprazole also strongly inhibited CYP2C19 activity. The estimated Kis were 3.5±0.4 (M, 3.4±0.5 (M, and 5.7±0.5 (M for racemic-, (S)- and (R)-omeprazole, respectively.

These results suggest that the lansoprazole and omeprazole inhibit the CYP2C19 catalyzed S-mephenytoin 4-hydroxlyation in a stereoselective manner and enantioselectivity of lansoprazole on CYP2C19 inhibition appears to be more prominent compared to that of omeprazole.