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STEREOSELECTIVE METABOLISM AND INHIBITION OF LANSOPRAZOLE ENANTIOMERS ON HUMAN LIVER CYPs.

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Stereoselective metabolism and inhibitory potential of lansoprazole enantiomers were evaluated from the incubational studies of human liver microsomes and cDNA-expressed CYP isoforms *in vitro*. The formation of lansoprazole sulfone from both enantiomers appeared to be catalyzed by single and low affinity enzyme. Lansoprazole 5-hydroxylation, however, appeared to be mediated by two kinetically distinct CYP enzymes. The intrinsic clearance of sulfone metabolite and 5-hydroxylansoprazole formation from *S*-enantiomer were 3-fold and 8-fold greater than those from R-enantiomer in the microsomal incubations, respectively. The formation rate of 5-hydroxy-lansoprazole from *S*-enantiomer by cDNA-expressed CYP2C19 was three fold less than that from R-form, but cDNA-expressed CYP2C9 produced 5-hydroxy metabolite at 3.3-fold greater formation rate at 50 μM of *S*-enantiomer than of *R*-form. The estimated IC_{50} of S-lansoprazole on the inhibition of CYP2C19- catalyzed *S*-mephenytoin (50 μM) hydroxylation was 22-fold lower than that of *R*-enatiomer (0.5 ± 0.3 μM vs 11.6 ± 2.5 mM). These results suggest that CYP2C9, CYP2C19, and CYP3A4 involve in the stereoselective metabolism of lansoprazole, and lansoprazole inhibits CYP2C19 isoform in a stereoselective manner.