Molecular modelling and quantitative structure-activity relationship studies on the interaction of omeprazole with cytochrome P450 isozymes

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Abstract

Molecular modelling of the anti-ulcerative agent, omeprazole, with the putative active sites of cytochromes P4503A4 and P4502Cl9, enzymes which are the major catalysts of omeprazole metabolism in man, are reported. Interactive docking of omeprazole in both CYP3A4 and CYP2C 19 gives rise to binding orientations which are consistent with both the known sites of metabolism reported for these isoforms and with evidence from site-directed mutagenesis experiments on CYP2C19, a P450 associated with genetic polymorphism in human drug metabolism. The potential P450 enzymic interactions, inhibition and induction of omeprazole are discussed in the light of molecular modelling and QSAR (quantitative structure-activity relationship) studies on related compounds.
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