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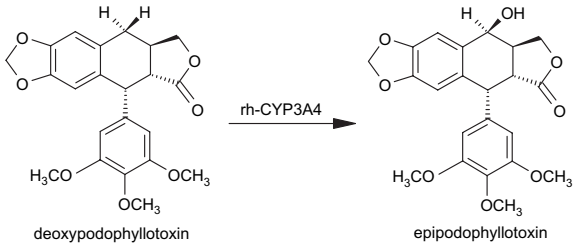
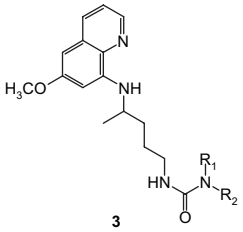
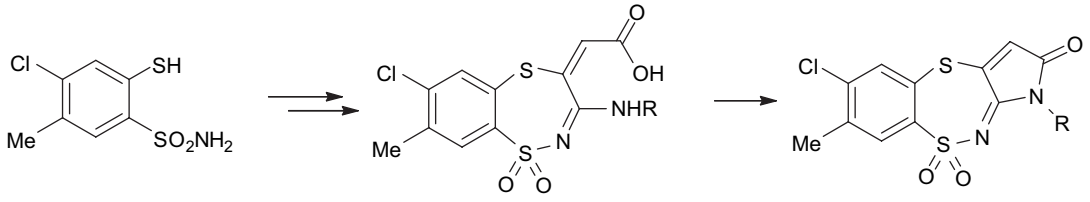
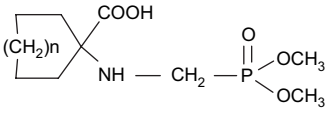
Contents

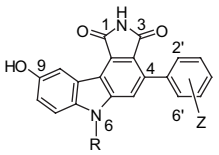
ORIGINAL ARTICLES



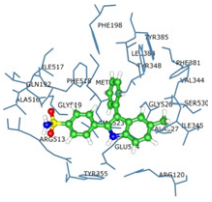




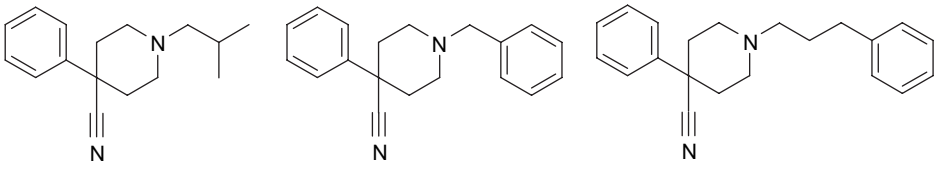


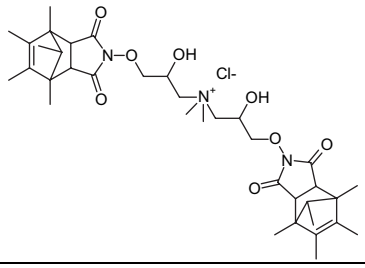


In the present work, modelling study has been performed to explore the physicochemical requirements of 2-sulfonyl-phenyl-3-phenyl-indole analogs as COX-2 enzyme inhibitors. QSAR analysis describes significance of descriptors like atomic van der Waals volume and atomic masses for COX-2 inhibition. Docking study suggested that phenyl sulfonamide moiety positioned in secondary pocket of enzyme which consists of amino acid residues Phe_{518}, Gln_{192}, Arg_{513}, Leu_{352}, Ser_{353} and Val_{523} is responsible for the selectivity. The unsubstituted phenyl ring positions in a hydrophobic cavity are lined by Tyr_{385}, Trp_{387}, Tyr_{348}, Leu_{384} and Met_{522}. Interestingly, the indole C-5 CH_3-substituent is located in a hydrophobic region formed by Ile_{345}, Val_{349}, Ala_{527}, Leu_{531} and Leu_{534}. The hydrophobic interactions of methyl group might be crucial for the potency of 2-sulfonyl-phenyl-3-phenyl-indole analogs. Distinguished descriptor might be helpful in identification of more potent analogs from the virtual library.



SHORT COMMUNICATIONS





PRELIMINARY COMMUNICATIONS

COVER

Overlay of the experimental and docked conformations of the ligand fluorescein in complex with an antifluorescein 4-4-20 Fab fragment (PDB code 1flr, 1.85 Å). The top-scoring conformation (purple) selected by the HINT force field, among the 255 poses generated by AutoDock, nearly overlays the crystallographic structure (yellow), while the conformation selected by the AutoDock scoring function (green) reverses the positions of the carbonyl and hydroxyl groups.
Image provided by Francesca Spyrakis, Alessio Amadasi, Micaela Fornabaio, Donald J. Abraham, Andrea Mozzarelli, Glen E. Kellogg, Pietro Cozzini.

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