IN SILICO BIOTRANSFORMATION OF BUPRANOLOL

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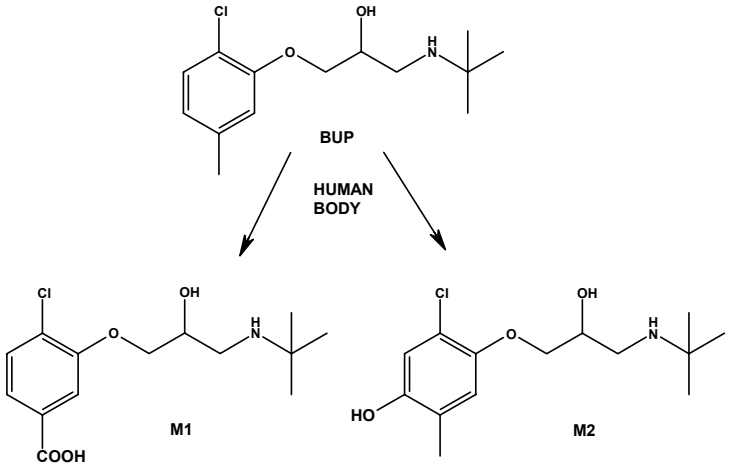
Bupranolol (BUP) is the only registered drug, which demonstrates antagonistic activity against all four known subtypes of β-adrenoceptors. It contains chiral center and its side chain is similar to that of most other β-blockers, except that tertiary butyl group replaces the more common isopropyl group. Because of its high lipophilicity it undergoes extensive metabolism in human liver to more hydrophilic compounds [1,2]. The major pathway of human metabolism is oxidation of the aromatic ring methyl group of bupranolol to carboxyl group (M1) [1]. Another metabolite is formed by hydroxylation of aromatic ring by polymorphic cytochrome P450 CYP2D6 (M2) [2]. Its high affinity to that monooxygenase and rapid metabolism are infrequent combinations in enzymology [2].



The aim of present study was to perform biotransformation of bupranolol *in silico* using available software: Metabol Expert [3], Metasite [4] and Meteor [5]. Additionally biocatalysis/biodegradation on-line database of the University of Minnesota was used to predict microbial biotransformation [6]. The obtained results were compared. Log P values of predicted metabolites were calculated since this factor plays important role as well in distribution and the fate of drugs in the body.

[1] Waller AR, Chasseaud LF, Bonn R, Taylor T, Darragh A, Girkin R, Down WH, Dyle E, 1982, Drug Metab Dispos. 10, 51-54;
[2] Appana G, Tang BK, Müller R, Kalow W; 1996, Drug Metab Dispos., 24, 303-306;
[3] Pallas, Metabol Expert, 2004, CompuDrug Chemistry Ltd.;
[4] Metasite, 2005, Molecular Discovery Ltd.;
[5] Meteor, Version 8.0, 2004, Lhasa Ltd., University of Leeds, UK;
[6]The University of Minnesota Biocatalysis/Biodegradation Database, http://umbbd.ahc.umn.edu/

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