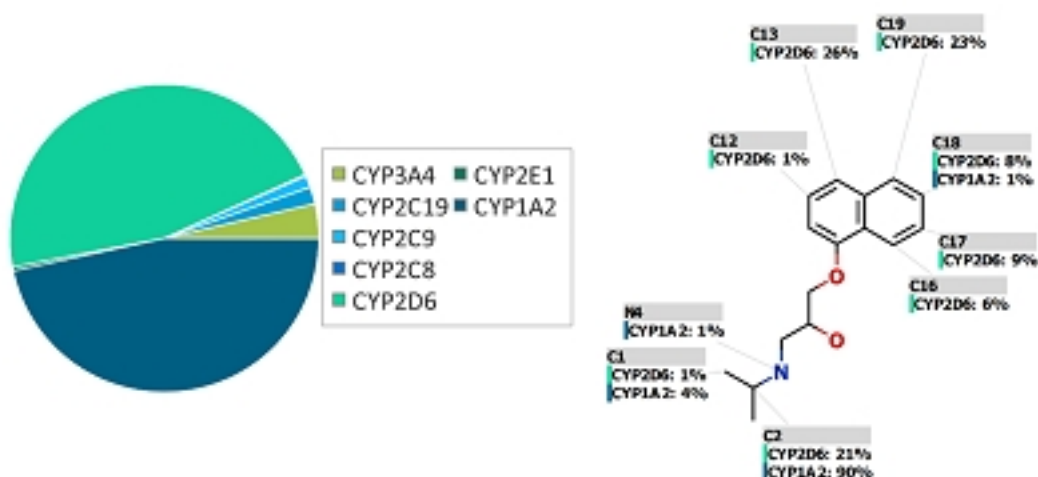


This paper appears in J. Comput.-Aided Mol. Des. and describes the underlying methods and validation of the new model predicting the most likely Cytochrome P450 isoforms responsible for metabolism of a compound in StarDrop's [P450 module](#).



Abstract

In the development of novel pharmaceuticals, the knowledge of how many, and which, Cytochrome P450 isoforms are involved in the phase I metabolism of a compound is important. Potential problems can arise if a compound is metabolised predominantly by a single isoform in terms of drug-drug interactions or genetic polymorphisms that would lead to variations in exposure in the general population. Combined with models of regioselectivities of metabolism by each isoform, such a model would also aid in the prediction of the metabolites likely to be formed by P450-mediated metabolism. We describe the generation of a multi-class random forest model to predict which, out of a list of the 7 leading Cytochrome P450 isoforms, would be the major metabolising isoforms for a novel compound. The model has a 76% success rate with a top-1 criterion and an 88% success rate for a top-2 criterion and shows significant enrichment over randomised models.

Preprint: WhichP450

Written by Peter Hunt

Tuesday, 13 February 2018 16:26 - Last Updated Friday, 20 April 2018 13:45

You can download a copy of this article as a [PDF](#).