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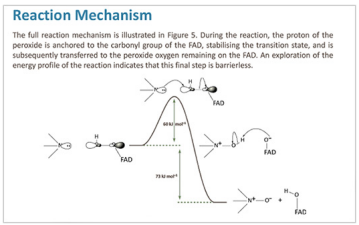
Existing computational models of drug metabolism are heavily focused on predicting oxidation by cytochrome P450 (CYP) enzymes, because of their importance in phase I drug metabolism, reactive metabolite formation, and drug-drug interactions. Due, in part, to the success of these models, new drug candidates are typically well-optimised with respect to CYP metabolism However, novel metabolites are observed due to other, less-studied, enzyme families such as the flavin containing monooxygenases (FMOs) are found in multiple tissues, including the liver, and have five active isoforms (FMO 1-5). In common with CYPs, FMOs are responsible for phase I, oxidative metabolism and catalyse a variety of reaction types, including N- and S-oxidation, demethylation, desulphuration and Bayer-Villiger oxidation.

The objective of this study was to elucidate the reaction mechanism of FMO-mediated oxidation to inform the development of models to predict the metabolism of novel substrates.



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