# Human Metabolism Prediction: Facts or Fantasy?

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**Abstract**

Xenobiotic metabolism has become of paramount significance in drug research, development, and therapy. Nowadays, medicinal chemists active in the various stages of drug discovery and development are aware that unfavourable metabolic outcomes (e.g., reactive metabolites, enzyme inhibition) may exclude promising candidates from further development due to later toxic effects. Computational evaluation and/or prediction of phase I and II xenobiotic biotransformations may be critical in predicting their pharmacological and toxicological consequences.

The knowledge of metabolism pathways is essential in any drug discovery project in order to stabilise the clearance of compounds, and also to decrease or eliminate the formation of potentially toxic intermediates which can induce Adverse Drug Reactions. Although simulation studies of xenobiotic-enzyme interactions can realistically predict phase I biotransformation, phase II reactions are still very difficult to predict due to high number of false positive results. However, when the generation of metabolites in silico is combined with experimental metabolite identification, the false positive data can be removed.

The paper present an innovative procedure, fast, economic and modular, that merge in silico data with experimental data to produce relevant information in order to address ADR problems and poor PK properties. Numerous real case examples will be reported.