

How do metabolites differ from their parent molecules and how are they excreted?

Johannes Kirchmair*, Unilever Centre for Molecular Sciences Informatics, Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge, CB2 1EW, United Kingdom.

*jk528@cam.ac.uk

Metabolism changes the physicochemical properties and bioactivity profile of small organic molecules. Knowing the metabolic fate of molecules hence is of fundamental importance to the successful design and development of drugs, cosmetics, nutritional supplements and agrochemicals.

In the current study we aim to give answer to three important questions pertinent to the design and development of new molecules with favourable ADME properties: (i) How does metabolism alter the physicochemical property space from substrate to metabolic product? (ii) What shifts in physicochemical property space do individual metabolic reactions introduce into molecules? (iii) What are the physicochemical properties of metabolites found in the bile, faeces and urine?

The study is based on the statistical analysis of the Accelrys Metabolite Database, DrugBank, HMDB and TCM Database@Taiwan and covers three different chemical spaces: Approved drugs, human metabolites and molecules related to traditional Chinese medicine. For a better resolution, biotransformations were classified into Phase I and Phase II reactions and analysed individually. The results provide new insights on how metabolism affects molecular structure and physicochemical properties and suggest rules-of-thumb for metabolic reactions and excretion routes.