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**Review**

# Introduction to early *in vitro* identification of metabolites of new chemical entities in drug discovery and development

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**Abstract:**

The introduction of combinatorial chemistry and robotics for high throughput screening has changed the way drugs are discovered today compared with 10–15 years ago when fewer compounds were tested in animal or organ models. The introduction of new analytical techniques, especially liquid chromatography/mass spectrometry (LC/MS) has made it possible to characterize the chemical properties, permeability, metabolic stability and metabolic fate of a large number of screening hits for further development in a funnel-like manner. The purpose of this contribution is to discuss principles and recent strategies for metabolite identification and to give an introduction to biotransformation studies. Metabolites are experimentally generated with the use of animal and human recombinant expressed enzymes, and different liver and other tissue fractions like microsomes and slices. For separation and identification of structurally diverse metabolites, LC/MS and tandem mass spectrometry (LC/MS/MS) techniques are commonly used. The LC/MS and LC/MS/MS techniques are rapid, sensitive, easy to automate and robust, and therefore, they are the methods of choice for these studies. The outcome of the metabolite identification studies is detection of metabolites that could be pharmacologically active and contribute to the efficacy of a new chemical entity (NCE), and elimination of compounds that form reactive intermediates and/or toxic metabolites that could cause adverse effects of NCE. If such information is available at an early stage during the drug discovery process, the chemical structure of the compound may be modified to reduce the risk of idiosyncratic and/or adverse drug reactions during clinical development.

**Key words:**

metabolite identification, reactive metabolite, liquid chromatography, mass spectrometry, Q-Tof

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