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Simulation of drug metabolism

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HIGHLIGHTS

- Investigation of *in-vitro* drug metabolism is possible using several systems
- On-line capillary electrophoresis offers the largest reduction in sample size
- Enzymatic oxidations can be replaced by electrochemistry-assisted approaches
- Electrode-assisted assays obviate the need for expensive cofactors
- Chemical models and light-driven reactions are alternative approaches

ABSTRACT

Searching for more efficient, more economical methods for simulation of drug metabolism using *in-vitro* methodology is one of the most rapidly developing research areas in analytical chemistry. Due to the great progress in recent years, several different approaches are available to mimic the environment of hepatocytes – the site of drug metabolism *in vivo*. These systems can be classified as: biocatalytical, electrochemistry-driven, electrochemical, chemical (free radical), and light-driven, and the computational models known as the *in-silico* approach. This review gives insight into these systems, highlighting the main trends and achievements.

Keywords:
Drug metabolism
Biocatalytical system
Electrochemically-driven enzymatic system (EDES)
Electrochemical-oxidation system
Electrophoretically-mediated microanalysis (EMMA)
Fenton reaction
Immobilized enzyme reactor (IMER)
In-silico model
Light-driven oxidation
Simulation

Abbreviations: CPR, Cytochrome P450 reductase; CYP, Cytochrome P450; DME, Drug metabolizing enzyme; EC, Electrochemical cell; EDES, Electrochemically-driven enzymatic system; EMMA, Electrophoretically-mediated microanalysis; FMO, Flavin-containing monooxygenase; HLM, Human-liver microsome; IMER, Immobilized enzyme reactor; NCE, New chemical entity; PSI, Photosystem I; QSAR, Quantitative structure−activity relationship; RLM, Rat-liver microsome; ROS, Reactive oxygen species

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1. Introduction

Searching for novel methods to ensure reliable metabolic studies on new potential drugs, screening for new enzymatic inhibitors, and predicting hypothetical drug-drug interactions –