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Rapid Assessment of Metabolism by Electrochemistry/MS -Drugs, Xenobiotics, Plants

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Introduction
The metabolic pathways and the biotransformation of drugs including xenobiotics or plants are crucial for elucidation of degradation routes of the active compounds, especially in the area of possible toxicity. *In vitro* studies are based on incubating drug candidates with, e.g., liver cells (microsomes) and isolating and detecting the metabolic products. With the availability of the ROXY™ Electrochemistry (EC) system oxidative metabolism, which usually occurs by Cytochrome P450 oxidation, can be mimicked successfully within seconds and detected by MS. Combining EC with MS creates a powerful platform for oxidative metabolism and overcomes some of the laborious tasks such as isolating the metabolites form *in vivo*, e.g., urine, plasma, or *in vitro* studies, e.g., microsomes.
Methods
The ROXY™ EC System (Antec Scientific, Boston, USA) includes a potentiostat equipped with a ReactorCell or µ-PrepCell2.0, and an infusion pump. For efficient oxidation, the cells are equipped with a boron-doped diamond (BDD) working electrode and a HyREF reference electrode. The system is controlled by Dialogue Elite software (Antec). The drugs were dissolved in 10 mM ammonium formate buffer (pH 7.4 adjusted with ammonium hydroxide solution) in 25 to 50 % acetonitrile at concentrations of ca. 10 uM and pumped at a constant flow rate through the cell. The outlet of the cell was connected directly (on-line) to the ESI-MS source. Different MS instruments have been employed equipped with ESI to record mass spectra.
Preliminary Data
The on-line coupling of electrochemistry EC with MS (EC/MS) provides a versatile and user-friendly platform for fast screening of target compounds (i.e., drugs, xenobiotics, plants) on oxidative metabolism (phase 1 reactions), thereby mimicking the metabolic pathway of CYP450 reactions. MS voltammograms can be recorded automatically to obtain a metabolic fingerprint of the compound of interest in less than 10 min. Numerous drug compounds have been electrochemically treated and the generated oxidation products showed excellent agreement with the biotransformation products obtained by the CYP450 reactions (enzyme assays or microsomes). In addition, rapid and easy studies of adduct formations can be performed simply by adding Glutathione or other additives after the electrochemical cell (phase II reactions). Electrochemistry/MS as a purely instrumental approach has thereby demonstrated its value as a fast mimicry tool. "*In electro*" as an attractive alternative to *in vivo* and *in vitro* studies in drug, xenobiotic and plant metabolism.
Novel Aspect
Rapid screening of drug, xenobiotic or plant metabolism by electrochemical oxidation and direct MS detection, without biological interference.
Conflict of Interest Disclosure
The authors declare no competing financial interest.

Oral Choice:
Drug Metabolism and Pharmacokinetics

Second Oral Choice:
Metabolomics: Untargeted Profiling
Poster:
Metabolomics: Untargeted Metabolite Profiling

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