Rapid Mimicking of Drug Metabolism by Electrochemistry-MS

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1. Objective

Using Electrochemistry-MS (EC-MS) as an alternative tool to enzymatic CYP450 reactions in (drug) metabolism:

- Rapid, enzyme free metabolism
- No microsomes (or test animals), green chemistry
- Phase I and II metabolism
- EC-MS as a "real" biomimetic tool

2. Introduction

The knowledge of the metabolic pathways and the biotransformation of new drugs are crucial for elucidation of degradation routes of the new drug 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 in the liver cells by Cytochrome P450 oxidation, can be mimicked successfully within seconds and detected by mass spectrometry. 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.

For more information, visit our booth #614

3. Instrumentation

3.1. Oxidative Metabolism (Phase I)

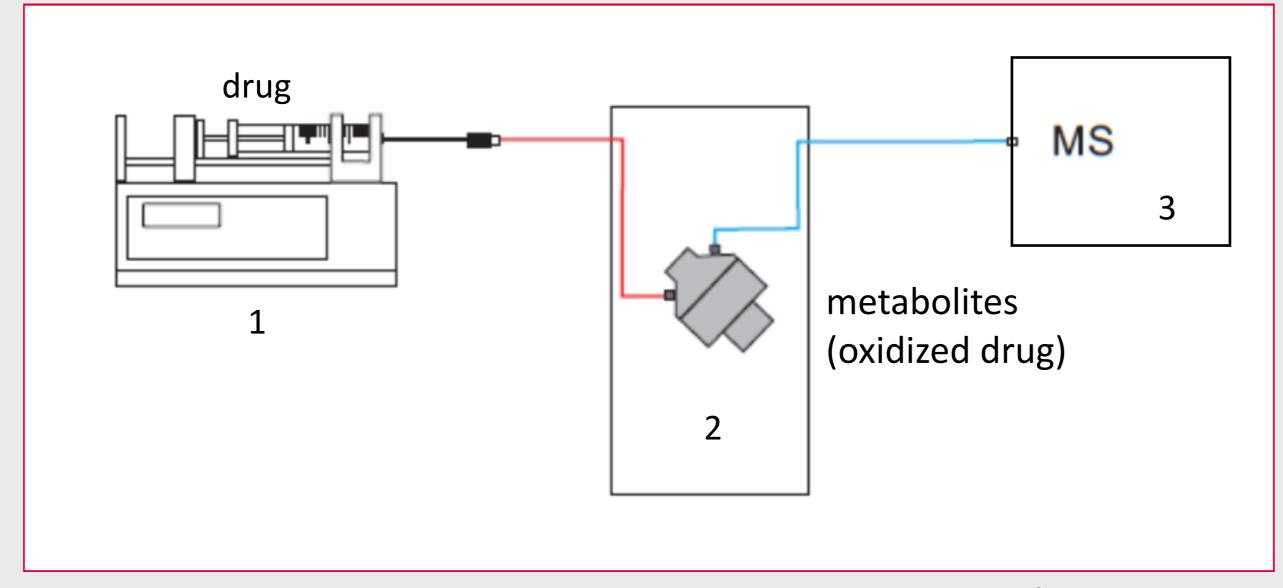


Figure 1: Schematics infusion Electrochemistry/MS system: 1) Infusion pump, 2) ROXY Potentiostat equipped with EC cell, 3) generic MS

3.2. Adduct Formation (Phase II)

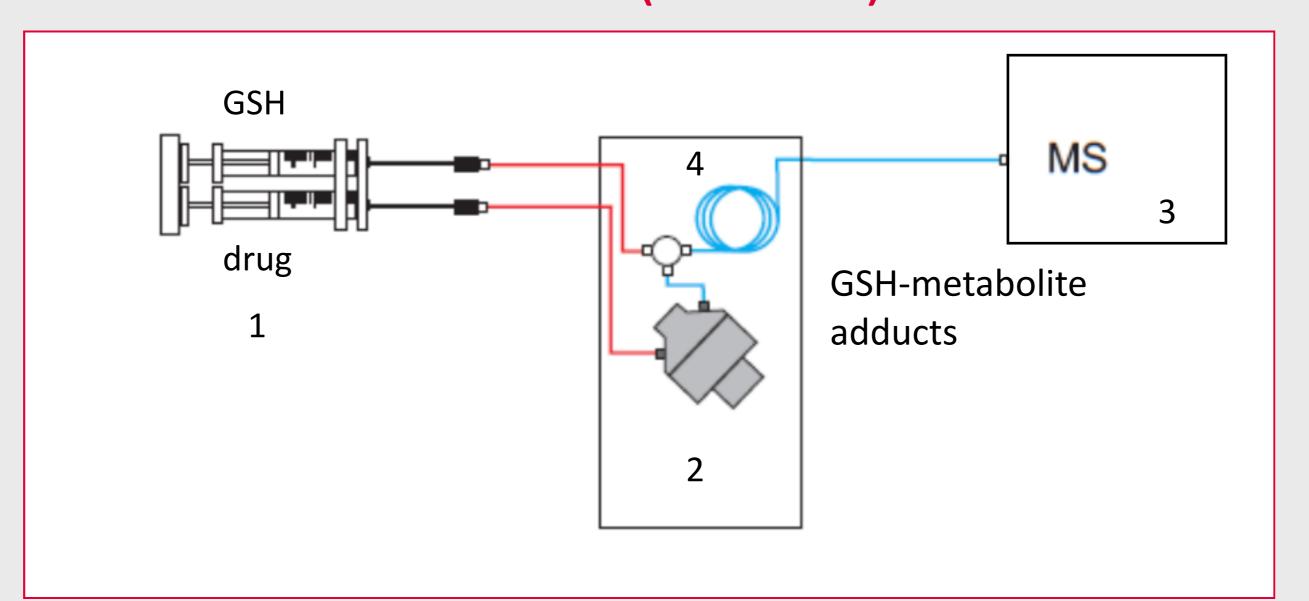


Figure 2: Schematics for adduct formation: same set-up as in Figure 1, except for 1) dual infusion pump and 4) T-piece with mixing coil for GSH addition

4. Results

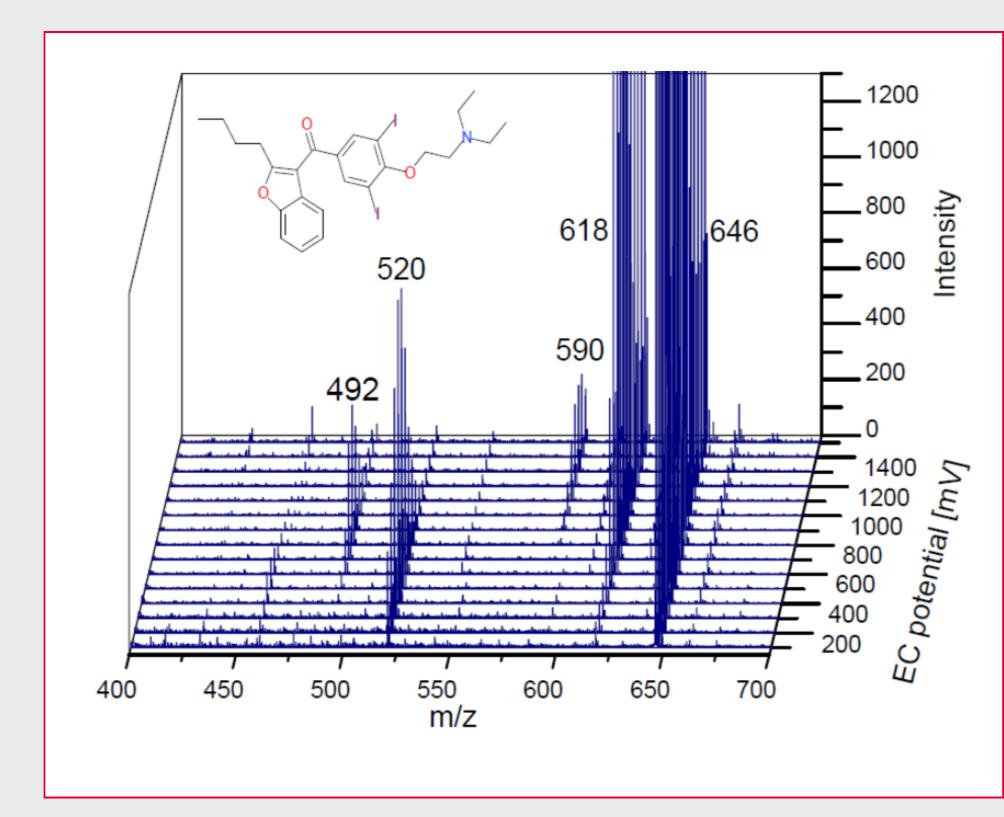


Figure 3: Example of a MS-Voltammogram, oxidative "fingerprint" of the drug compound Amodiarone (m/z 646) with it major metabolites.

Other trade names:

Other trade names: Cordarone, Nexterone. Used in antiarrhythmic medication.

5. Publications using ROXY™ EC to mimic drug metabolism (since 2017)

Mechanism of aromatic hydroxylation of lidocaine at a Pt electrode under acidic conditions

T Gul, R Bischoff, HP Permentier - Electrochimica Acta, 2017 - Elsevier

... 2.2. Electrochemical measurements. Constant potential measurements were performed with an **Antec ROXY** potentiostat (**Antec** Leyden, Zoeterwoude, The Netherlands) controlled by **Antec** Dialogue software. Cyclic voltammetry ...

Electrochemical simulation of biotransformation reactions of citrinin and dihydroergocristine com-

pared to UV irradiation and Fenton-like reaction

J Keller, H Haase, M Koch - Analytical and bioanalytical chemistry, 2017 - Springer

... μm spacers. An electrochemical potentiostat **ROXY** (**Antec** Leyden) was used to apply a potential ramped between 0 and 2000 mV versus Pd/H 2 at a scan rate of 20 mV/s (continuous scan mode). Electrochemical conditions ...

Electrochemical oxidation of phosphatidylethanolamines studied by mass spectrometry

S Colombo, G Coliva, A Kraj, JP Chervet... - Journal of Mass ..., 2018 - Wiley Online Library

... The EC reactions were conducted in the **ROXY** EC system (**Antec** Scientific, Zoeterwoude, NL) consisting of the **ROXY** potentiostat for the control of the flow-through μ-PrepCell 2.0 supplied with a Magic Diamond™ working electrode (borondoped diamond (BDD)) and a Pd/H 2 ...

Structural characterization of electrochemically and in vivo generated potential metabolites of selected cardiovascular drugs by EC-UHPLC/ESI-MS using an ...

M Szultka-Młyńska, S Bajkacz, I Baranowska... - Talanta, 2018 - Elsevier

... The simulation of oxidative metabolism was performed in an electrochemical thin-layer cell equipped with a potentiostat containing an electrochemical cell ReactorCell™, infusion pump and all the necessary HPLC connections (ROXY™ system Antec Leyden, Zoeterwoude ...

<u>Electrochemistry coupled online to liquid chromatography-mass spectrometry for fast simulation of biotransformation reactions of the insecticide chlorpyrifos</u>

TF Mekonnen, U Panne, M Koch - Analytical and bioanalytical chemistry, 2017 - Springer

... Mass voltammograms were generated by **Roxy** ™ potentiostat (**Antec** Leyden, Zoeterwoude, The Netherlands) equipped with µPrepCell ™ and/or SynthesisCell ™ with boron doped diamond (BDD) working electrode (WE), Pd/H 2 reference electrode, and Ti auxiliary electrode ...

<u>Prediction of biotransformation products of the fungicide fluopyram by electrochemistry coupled</u> online to liquid chromatography-mass spectrometry and comparison ...

TF Mekonnen, U Panne, M Koch - Analytical and bioanalytical chemistry, 2018 - Springer

... Mass voltammogram of FLP was recorded (continuous scan, 10 mV/s) using a **Roxy**™ potentiostat (**Antec** Leyden, Zoeter woude, The Netherlands) coupled online to an electrospray ionization (ESI) source of a single quadrupole mass spectrometer (Agilent Technologies GmbH ...

<u>Investigations of the Copper-Catalyzed Oxidative Cross-Coupling of Tetrahydroisoquinolines with</u> <u>Diethylzinc by a Combination of Mass Spectrometric and ...</u>

JA Willms, H Gleich, M Schrempp... - ... A European Journal, 2018 - Wiley Online Library

... Voltage/ion intensity curves were obtained with a commercial electrochemical flow cell [Antec Scientific ROXY potentiostat and thin-layer ReactorCell (cell volume: 0.7 μ L) with a magic diamond (MD) working electrode (Ø: 8 mm), an HyREF reference electrode ...

<u>Hydroxylation and dimerization of zearalenone: comparison of chemical, enzymatic and electrochemical oxidation methods</u>

J Keller, H Haase, M Koch - World Mycotoxin Journal, 2017 - wageningenacademic.com ... Oxidation of zearalenone by EC/MS, Fenton-like reaction and Ce(IV) World Mycotoxin Journal 10 (4) 299 was pumped through the μPrepCell by using a SP2-**ROXY** dual piston syringe pump (**Antec** Leyden) and a flow rate of 80 μl/min ...

<u>Laccase-and electrochemically mediated conversion of triclosan: Metabolite formation and influence on antibacterial activity</u>

E Jahangiri, B Seiwert, T Reemtsma, D Schlosser - Chemosphere, 2017 – Elsevier

... 2.4. Electrochemical (EC) conversion of TCS. TCS conversion was performed on a ROXY Potentiostat electrochemical system (Antec, The Netherlands), which was controlled by the Dialogue software (Antec). A commercially ...

Oxidation of 4-Isopropylphenol in Aqueous Solutions as a Model for Oxidation of Flavonoids to Form Dimers

IG Zenkevich, TI Pushkareva - Chemistry of Natural Compounds, 2018 – Springer

... Electrochemical oxidation of 4-isopropylphenol (1) (c 50–100 Pg/mL) was conducted in a mixture of aqueous NH 4 OAc (pH ~7.4) and MeCN (3:1) in a **ROXY** electrochemical cell (**Antec**, Leyden, Netherlands) using a Magic Diamond boron-doped diamond electrode at 37°C ...

Untargeted screening of phase I metabolism of combretastatin A4 by multi-tool analysis

K Jaroch, PZ Goryńska, <u>K Goryński</u>, T Stefański... - Talanta, 2018 – Elsevier

... 2.3. **ROXY™** system. All electrochemical experiments mimicking metabolism reactions in liver microsomes were conducted via the **ROXY™** EC system (**Antec**) connected on-line to the high resolution mass spectrometer Q-Exactive Focus ..

<u>Analysis of Protein-Phenolic Compound Modifications Using Electrochemistry Coupled to Mass</u> <u>Spectrometry</u>

C Kallinich, S Schefer, S Rohn - Molecules, 2018 - mdpi.com

... Exemplarily, the electrochemical oxidation of chlorogenic acid was optimized by varying the voltage from 0.3 V to 3 V in steps of 0.3 V using a boron-doped diamond electrode and a **Roxy** [®] potentiostat (**Antec** Scientific, Zoeterwoude, The Netherlands) ...

Online Monitoring of Methanol Electro-Oxidation Reactions by Ambient Mass Spectrometry

S Cheng, Q Wu, HD Dewald, H Chen - Journal of The American Society for ..., 2017 – Springer

... oxidation of methanol. A **Roxy** potentiostat (**Antec** BV, Zoeterwoude, Nertherlands) was used to apply potential to the cell for triggering methanol oxidation when the methanol sample flowed through the cell. Sample solutions were ...

Preparing the key metabolite of Z-ligustilide in vivo by a specific electrochemical reaction

F Duan, W Xu, J Liu, Z Jia, K Chen... - Journal of separation ..., 2018 - Wiley Online Library

... working electrode, a Pd/H2 (HyREF™) reference electrode and a titanium auxiliary electrode connected to a **Roxy** potentiostat, a syringe pump and the necessary reaction buffer flow connector controlled by Dialog software, version 2.02 (**Antec**, Zoeterwoude, the Netherlands) ...

<u>Chromato–Mass Spectrometric Identification of Unusual Products of 4-Isopropylphenol Oxidation</u>

in Aqueous Solutions

IG Zenkevich, TI Pushkareva - Russian Journal of General Chemistry, 2018 - Springer... Electrochemical oxidation of a solution of 4- isopropylphenol (50–100 μ g/mL) was performed in mixtures of an aqueous solution of ammonium acetate (pH ~7.4) and acetonitrile (3 : 1 v/v) in a **ROXY** electrochemical cell (**Antec**, Netherlands) equipped with a Magic Diamond ...

Investigation of the oxidative transformation of roxarsone by electrochemistry coupled to hydrop-hilic interaction liquid chromatography/mass spectrometry

LM Frensemeier, L Büter, M Vogel... - Journal of Analytical Atomic ..., 2017 - pubs.rsc.org

... an HPLC system from **Antec** Leyden (Zoeterwoude, The Netherlands) and 0.1% formic acid in water and acetonitrile as mobile phase. The system comprised two LC 100 pumps, an OR 110 degasser, an AC 100 controller, an AS 100 autosampler and a **ROXY™** column oven ...

Electrochemical simulation of triclosan metabolism and toxicological evaluation

<u>L Zhu</u>, Y Shao, H Xiao, B Santiago-Schübel... - Science of The Total ..., 2018 – Elsevier

... 2.2. Online EC-MS. A commercial EC reactor (**Antec** Leyden, The Netherlands) with a built-in platinum counter electrode and **Roxy** potentiostat was set up as reported in previous investigations (Chen et al., 2012; Hoffmann et al., 2011) ...

<u>Electrochemistry-High Resolution Mass Spectrometry to Study Oxidation Products of Trimetho-</u> <u>prim</u>

MA Lecours, <u>E Eysseric</u>, <u>V Yargeau</u>, J Lessard... - Environments, 2018 - mdpi.com

The study of the fate of emerging organic contaminants (EOCs), especially the identification of transformation products, after water treatment or in the aquatic environment, is a topic of growing

interest. The ROXY EC system (Antec Scientfic) coupled to mass spectrometry has been ..

6. Conclusion

With 18 references [1] over the last 1.5 years the successful use of EC-MS to mimic (drug) metabolism has been well proven.

[1] Google scholar, KW: Antec and ROXY