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

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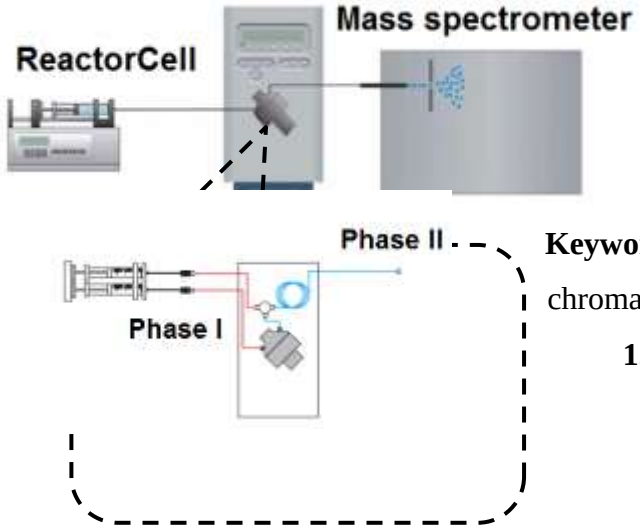
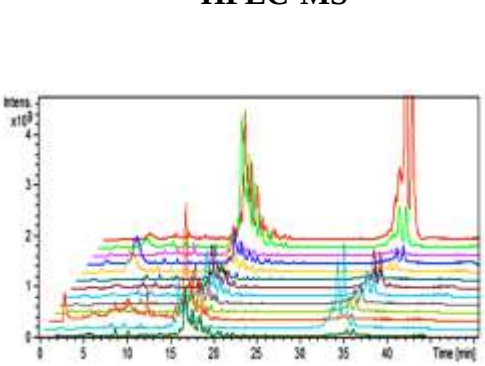
Abstract

In the last few years, a number of studies were conducted which aimed at understanding the mechanisms of cardiovascular drug, metabolism, and there is still the need to determine the metabolites of cardiac drugs for the purpose of metabolism control. In this study, we employ a direct combination of electrochemical oxidation and mass spectrometric (EC-MS) identification for monitoring the oxidation pathway of ten cardiovascular drugs (metoprolol, propranolol, propafenone, mexiletine, oxprenolol, pirbuterol, pindolol, cicloprolol, acebutolol and atenolol). Oxidation was accomplished in an electrochemical thin-layer cell coupled *on-line* to electrospray ionization mass spectrometry (EC/ESI-MS). For further characterization of electrochemical products, the approach involving liquid chromatography linked to tandem mass spectrometry was used. Appropriate conditions for oxidation and identification processes with such parameters as the potential value, mobile phase (type and pH) and working electrode were optimized. Optimization was performed with the use of central composite design (CCD). Besides electrochemical oxidation of analytes (phase I of metabolic transformation), addition of glutathione (GSH) for follow-up reactions (phase II conjunction) was also investigated. The electrochemical results were compared to *in-vivo* experiments by analyzing plasma and urine samples from patients who had been administered selected cardiovascular drugs. These results show that electrochemistry coupled to mass spectrometry turned out to be an analytical tool suitable to procure a feasible analytical base for the envisioned *in vivo* experiments.





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1. Introduc