Evaluation for the Characterization of Isomeric Products from Drug Metabolism

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Introduction: During the stages of drug metabolism, numerous byproducts and isomeric species with different characteristics are generated. These compounds are of great interest to the pharmaceutical industry, as studying their safety and how they are eliminated by the body is crucial for the viability of their commercialization. In this work, we propose techniques for the mimicking of metabolites and methods for characterizing these isomeric compounds using paracetamol as a model species.

Methods and Techniques: Previous studies demonstrated how electrosynthesis mimics the metabolites produced during the first phase of metabolism. Furthermore, active sites of enzymes and specific biomolecules were shown to interact with these metabolites simulating phase II metabolic compounds. Analyses performed by Mass Spectrometry, coupled with techniques such as High Field Asymmetric Waveform Ion Mobility Spectrometry (FAIMS) and Multiple Photon Infrared Ionization Spectroscopy (IRMPD), enable the separation of these compounds and the characterization of their structures, presenting an alternative to chromatography.

Results: Paracetamol was used to develop the experimental parameters necessary to simulated phase II metabolism using NAC (N-acylcysteine) as the enzymatic counterpart. These methodologies were used to generate isomeric metabolites. These metabolites were evaluated by IRMPD and IMS so their unambiguous determination could be carried. The combined use of these methods allowed for an easy and rapid identification of drugs metabolites by electrosynthesis without the need of analytical standards.

Conclusion: This work not only proves the feasibility of IRMPD and FAIMS techniques for metabolite identification but also serves as proof of concept for their applicability to various studies related to metabolomics. Providing an innovative approach to metabolite characterization, it significantly contributes to the advancement of pharmaceutical research and the viability of new drugs.

Agradecimentos: