Advances in Metabolite Identification Using Ion Mobility and Ion Vibrational Spectroscopy

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Introduction: Understanding the intricate processes of drug metabolism is paramount for pharmaceutical advancement and ensuring safety. Reactive metabolites arising from these processes can induce adverse effects, significantly impacting the efficacy and safety profiles of drugs. Hence, there is a pressing need for innovative methodologies that enable precise identification of these metabolites, circumventing the limitations of conventional analytical approaches. Materials and Methods: In this study, we evaluated the utilization of ion mobility and ion vibrational spectroscopy to discern metabolites, without the necessity for preliminary chromatographic steps or analytical standards. Employing flow electrochemical techniques, we emulated Phase I metabolism of diverse compounds like metoprolol, cyclophosphamide, and ifosfamide. Subsequently, we subjected the metabolites generated to mass spectrometric analysis. High Field Asymmetric Waveform Ion Mobility Spectrometry (FAIMS) facilitates the separation of specific isomers replacing chromatograpy, while each population is discerned without the requirement for analytical standards through multiple photon infrared ionization spectroscopy (IRMPD). Results: Our findings underscore the efficacy of this approach in distinguishing isomers and pinpointing reactive metabolites, encompassing drug transformation products. For instance, our evaluation of metoprolol as a proof-of-concept allowed the identification of distinct isomeric metabolites via this approach. Additionally, results pertaining to cyclophosphamide demonstrate the resolution and identification of isomeric transformation products. This methodology affords a comprehensive characterization of species without the need for reference standards, thereby augmenting our understanding of drug metabolism. Conclusions: The outcomes affirm the viability of integrating ion mobility and ion vibrational spectroscopy for metabolite identification. This method shows a promising avenue for elucidating convoluted metabolic transformations and the generated isomeric products. This approach could be also applied for proteomics, specialy when couped to cryogenic infrared strategies and other ion mobility schemes.

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