Distribution study of paracetamol and its metabolites in rat by MALDI imaging after on-tissue derivatization

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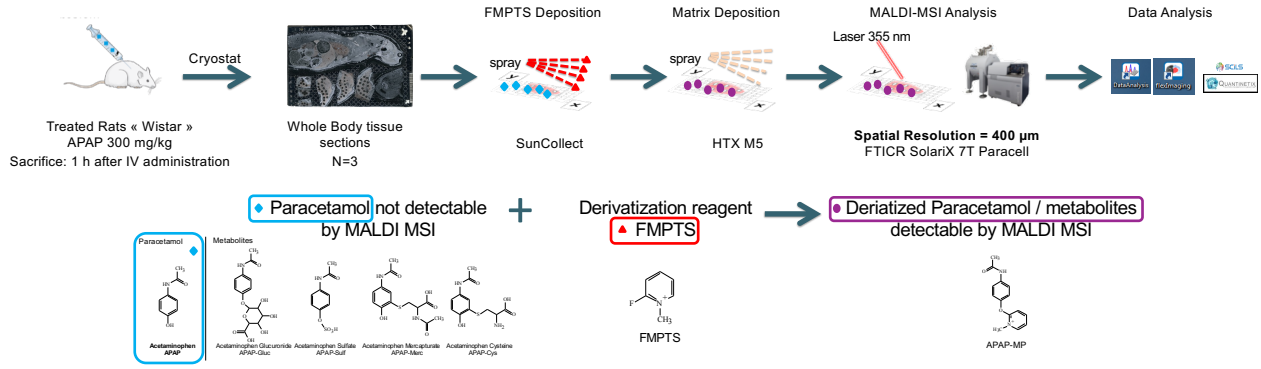
Introduction

Matrix-Assisted Laser Desorption/Ionization (MALDI) Mass Spectrometry Imaging (MSI)[1] is recognized as a promising technique for distribution studies of small exogenous molecules such as drugs[2] and their metabolites. Despite the numerous advantages presented by MALDI MSI, the lack of sensitivity encountered in some cases remains a strong limitation. Therefore, novel procedures could be developed in order to enhance the sensitivity such as adding an on-tissue chemical derivatization (OTCD)[3] step during the sample preparation. OTCD consists in modifying the chemical structure of analytes in order to improve their ionization yields. Thus, we employed the 2-fluoro-1-Methylpyridinium *p*-tolunesolfonate (FMPTS) as derivatization reagent in order to provide a distribution study of paracetamol and its metabolites in treated rats.

Methods



Results

- **The use of the deriatization reagent FMPTs permits the detection of paracetamol and two of its metabolites**

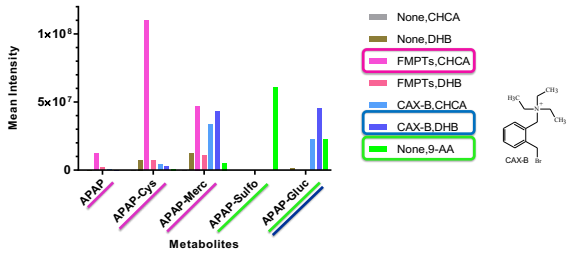


Fig. 1 : Mean intensity of each analytes obtained under the different conditions. CAX-B is a second derivatization reagent tested.

- **The structure of derivatized paracetamol is confirmed**

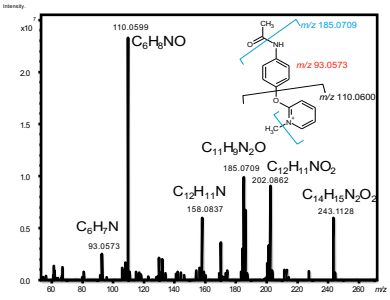
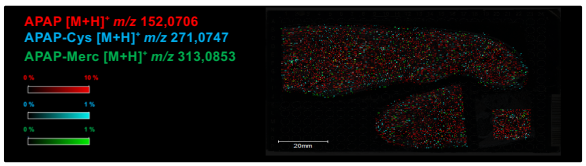


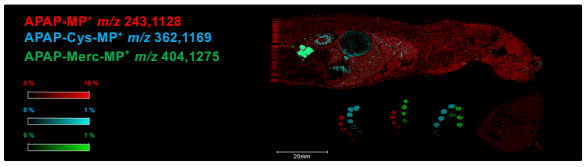
Fig. 2 : MS/MS spectra of derivatized paracetamol with FMPTS.

- **Derivatization allows the distribution study of paracetamol and its metabolites cysteine and mercapturate**

Positive ionization mode without derivatization



Positive ionization mode with FMPTS derivatization



- **Sulfate and glucuronide metabolites are detected in negative ionization mode without derivatization**

Negative ionization mode without derivatization

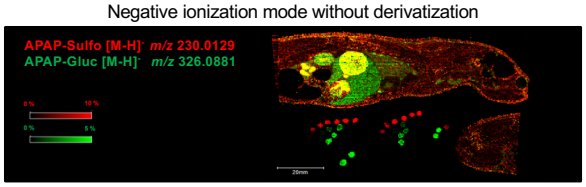


Fig. 3 : MALDI MSI of treated rat tissue sections with and without derivatization.

Conclusion & Perspectives

- OTCD improves the detection sensitivity of paracetamol and some of its metabolites.
- Distribution studies provided by MALDI MSI could help in understanding the impact of paracetamol on reproductive health.
- The development of new derivatization reagents is essential to overcome the problem of low sensitivity encountered in some cases of MALDI MSI analysis.

References :
[1] Caprioli et *al.*, J. *Analytical chemistry*, **1997**, 69 (23), 4751–4760
[2] Schulz et *al.*, *Current opinion in biotechnology*. **2019**, 55, 51-59
[3] Chacon et *al.*, *Journal of mass spectrometry*. **2011**, 46 (8), 840-846