DIFFERENTIATION OF BUSPIRONE HYDROXY METABOLITES WITH CYCLIC ION MOBILITY SPECTROMETRY

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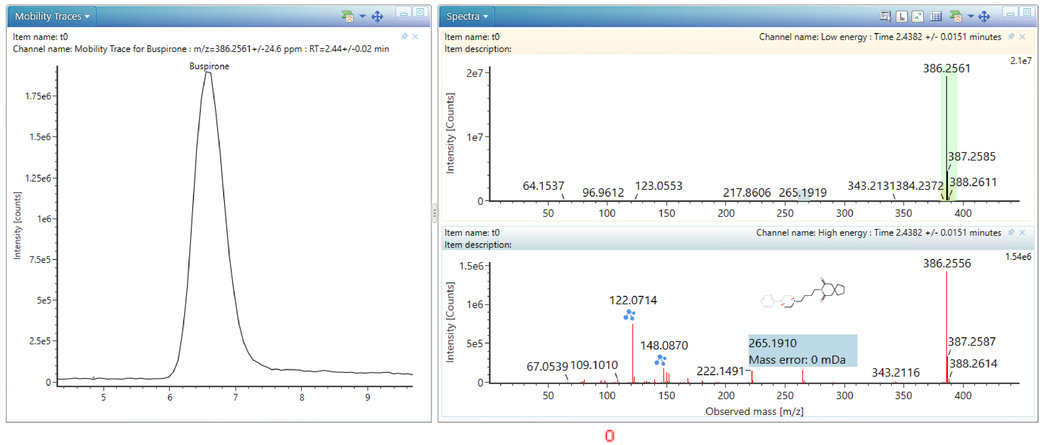
INTRODUCTION

- **Buspirone is an anxiolytic pharmaceutical which undergoes multiple hydroxylation reactions during metabolism.**
- **These metabolites can in part be differentiated by liquid chromatography, ion mobility and CID fragmentation.**
- **Here, we demonstrate the use of cyclic ion mobility (cIMS) to increase the gas-phase resolution between isobaric metabolites.**

Buspirone IMS and fragmentation description.



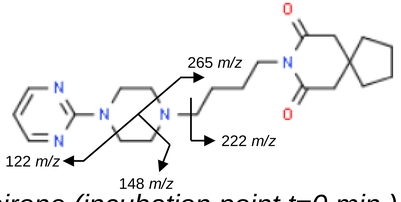
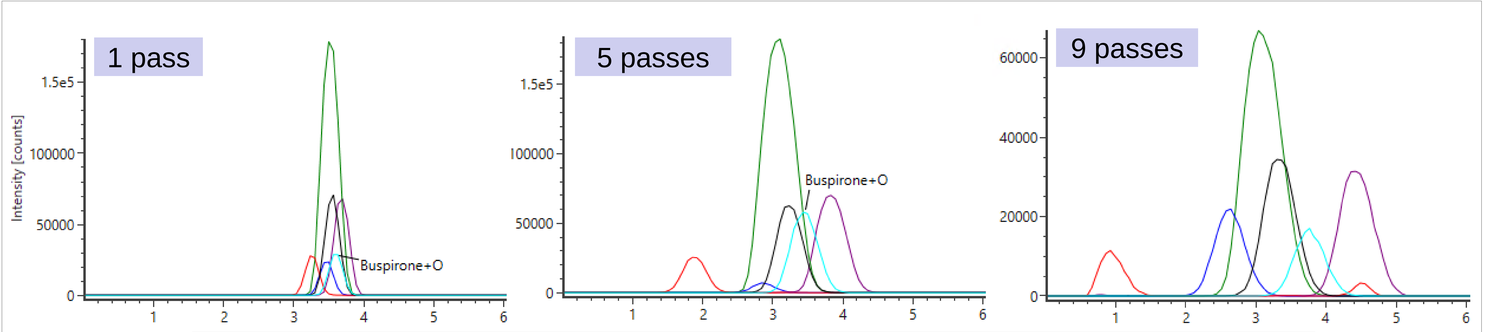


Figure 1: Display of Buspirone (incubation point t=0 min.) ion mobility arrival time distribution (ATD) and precursor/fragment ion spectra as obtained on a LC TW-IMS QTof instrument. The fragment ion pathway is also described.

Increasing the number of passes in the cIMS mobility cell improves +O separation for the oxidized metabolites. Further localization information can be obtained from fragment ion shifts.



Trace	RT (min.)	+16 m/z (+O) fragment shifts for metabolite localization	
black	4.38	222 ⇨ 238 *m/z*	265 ⇨ 281 *m/z*
red	4.62	265 ⇨ 281 *m/z*	222 ⇨ 238 *m/z*
blue	5.33	222 ⇨ 238 *m/z*	265 ⇨ 281 *m/z*
green	5.83	265 ⇨ 281 *m/z*	222 ⇨ 238 *m/z*
purple	6.48	148 ⇨ 166 *m/z*	122 ⇨ 138 *m/z*
teal	7.25	no shifts observed	no shifts observed

Figure 2: ATD plots, retention time (RT), drift time (DT) and fragment ion mass shifts for the 6 observed buspirone+O metabolites in the t=120 min. incubation sample.

Observation of additional +2x(+O) metabolite using cIMS improved resolution.

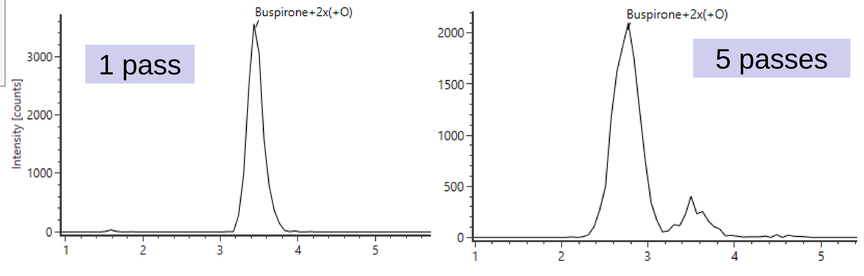


Figure 3: Appearance of an additional drift "peak" at RT of 4.35 min. and 418.2449 m/z after 5 cIMS passes.

CONCLUSIONS

- **cIMS provides exceptional gas-phase separation of isobaric buspirone hydroxy metabolites.**
- **Fragment ion mass shifts describe metabolite localization information.**
- **Increases in IMS resolution afforded by cIMS reveal a possible additional hydroxy metabolite, warranting further investigation.**