

GC-MS/MS CENTER OF EXCELLENCE

inVentiv Health Clinical's GC-MS/MS center of excellence is ready to leverage its expertise to solve your bioanalytical challenges. With the industry's largest number of GC-MS/MS systems and experienced scientists, inVentiv Health Clinical can help you overcome these.

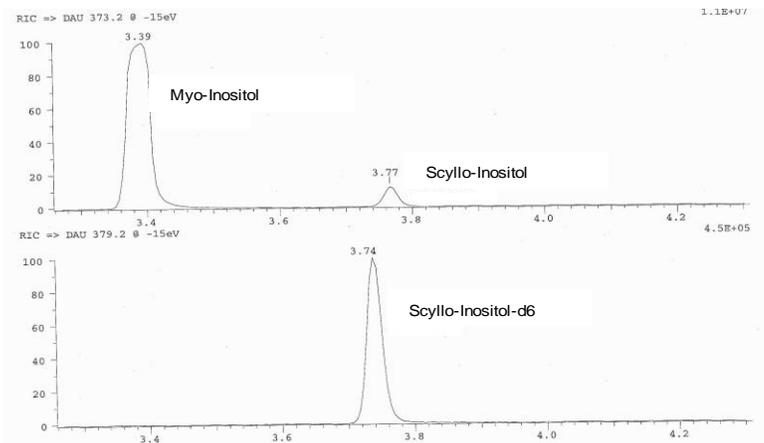
Liquid chromatography with tandem mass spectrometry (LC-MS/MS) is widely used for small molecule bioanalysis. However, as drugs and their metabolites become more polar, LC-MS/MS effectiveness diminishes and will be outperformed by gas chromatography with tandem mass spectrometry (GC-MS/MS). For this reason, inVentiv Health Clinical GC-MS/MS provides a number of advantages for biomarkers analysis:

- Combined assays for metabolites
- More easily identified pathway of interaction
- GC columns allow enantiomers to be easily separated
- More cost effective than LC approaches

BIOMARKERS

Changes in biomarker concentrations can indicate both therapeutic intervention and the pathway of interaction. Unlike LC-MS/MS, GC-MS/MS allows the wide range of biomarker metabolites to be assayed together. By maintaining the integrity of the polar metabolites, GC-MS/MS allows the pathway of interaction to be more easily identified.

Inositols (1,2,3,4,5,6-cyclohexanols) function as the basis for a number of signaling and secondary messenger molecules. As such, inositol therapies are being pursued for many psychiatric therapies ranging from depression to obsessive-compulsive disorder. There are nine naturally occurring forms of inositols, thus effective separation of them is critical for monitoring changes of each with treatment. With peak widths of a few seconds, the major inositols are easily separated (see Figure 1 and Table 1).



BENEFITS OF INVENTIV HEALTH CLINICAL GC-MS/MS

- inVentiv Health Clinical has the largest number of operational GC-MS/MS systems
- More than 100 years of collective experience in GC-MS/MS method development
- inVentiv Health Clinical has analyzed 210,000+ samples over the past five years by GC-MS/MS
- inVentiv Health Clinical knows how to leverage GC-MS/MS to solve problems where LC-MS/MS has been ineffective

BENEFITS OF GC-MS/MS

- Advantageous for molecules which do not ionize well by LC-MS/MS (e.g., pro-drugs, biomarkers, RNA-type molecules).
- Improved signal to noise ratio and lower detection limits. These compounds are derivatized which increases their molecular weight and pulls them away from the high background noise observed in the low mass range.
- Highly efficient and effective separation and sharp, intense peaks (helps lower detection limit)
- Unlike LC-MS/MS, does not encounter matrix effects (e.g., ion suppression/enhancement).



Figure 1. Observed inositols from mouse brain homogenate.

Inositol	Retention Time (min)
Myo	3.65
Allo	3.72
Muco	3.85
Scyllo	4.05

Table 1. Expected retention times for the most prominent inositols

Neurotransmitters and prostaglandins are other classes of biomarkers that have been successfully monitored by inVentiv Health Clinical by using GC-MS/MS.

CHIRALSEPARATION

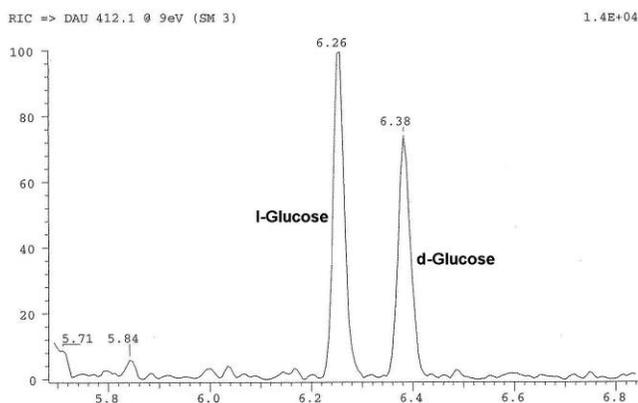


Figure 2. Observed separation between d- and –glucose as physiological levels.

Changes in the ratio of d/l-glucose acted as a physiological endpoint for a recent treatment. The use of inexpensive chiral reagents and the resolving power of the GC column allowed the enantiomers to be easily separated. This approach is more cost effective than more commonly used chiral LC approaches.

REFERENCES

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2. Thakur, R.A., Williard, C., Rajasekaran, A. Chromatography Today (2010) 3, 22.



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