Improved sensitivity and higher lipid annotation ID capabilities using a new vacuum insulated heated ESI source

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Introduction

Abundance of lipids in typical samples such as plasma extracts can vary drastically. Therefore, analytical equipment with a high sensitivity and dynamic range is required in lipidomics research. Here we present results of a new vacuum insulated heated ion source (VIP-HESI) coupled with a timsTOF Pro ion mobility mass spectrometer including trapped ion mobility separation and CCS values.

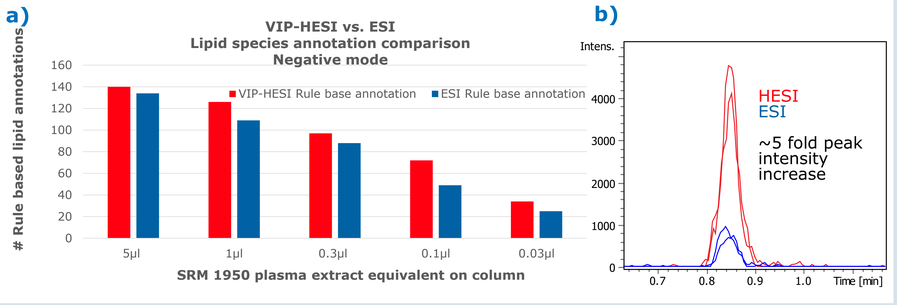
As part of the evaluation process dilution series of a lipid standard with and without matrix were acquired to asses the limit of detection (LOD) and the dynamic range. In a second experiment the lipid ID annotation capability was examined using a commercially available serum standard.

All experiments were compared to data which was acquired with the standard Bruker Apollo II source.

Methods

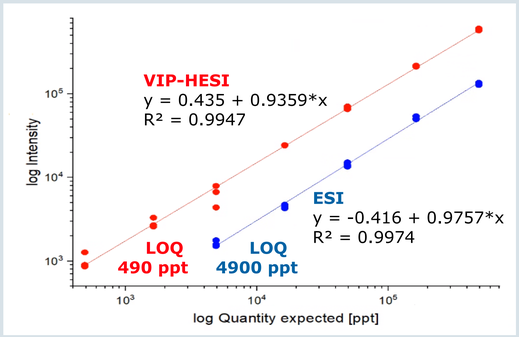
- LC: Elute UHPLC, YMC-Triart C18, 100 x 2.1 mm ID, S-1.9 um.
- 5-minute gradient program
- Injection volume: 5 µL
- MS: timsTOF Pro (Bruker)
- Acquisition: PASEF neg mode
- Software: MetaboScape 2021b (Bruker) for the untargeted ID part via a rule-based lipid annotation. TASQ 2021b (Bruker) for the quantitative analysis.
- Chemicals: Reference serum SRM1950 (Sigma); deuterated SPLASH mix lipid standard (Avanti Lipids)

A higher Lipid ID annotation capability



Lipid ID annotation capability on different dilution levels of the reference serum SRM1950
The VIP-HESI reveals on all concentration levels a higher number of rule-based lipid annotations like shown in figure **a)**. The lower the concentration level the higher this effect can be observed. The higher performance can be explained with the better ionization capability of the VIP-HESI like shown in figure **b)** in which an unprecedented lipid shows an intensity increased by a factor of five.

A better dynamic range



Dilution series of the Lyso PE 18:1(d7) with logarithmic scaling

The improved LODs result also in a higher dynamic range. For the shown lipid the limit of quantification (LOQ) is one order of magnitude lower by maintaining the linearity of the calibration function.

Improved levels of detection (LOD)

	Without matrix			With matrix		
	HESI neg [ppt]	ESI neg [ppt]	LOD ESI/ HESI	HESI neg [ppt]	ESI neg [ppt]	LOD ESI/ HESI
Lyso PC 18:1(d7)	238	793.3	**3.3**	238	2380	**10**
Lyso PE 18:1(d7)	163.3	1633.3	**10.0**	490	1633.3	**3.3**
PA 15:0-18:1(d7)	690	2300	**3.3**	6900	23000	**3.3**
PC 15:0-18:1(d7)	502	5020	**10**	1506	1506	**1**
PE 15:0-18:1(d7)	176.7	1766.7	**10**	1766.7	5300	**3.0**
PG 15:0-18:1(d7)	267	8900	**33.3**	890	8900	**10**
PI 15:0-18:1(d7)	85	8500	**100**	28333*	8500*	**0.3***
PS 15:0-18:1(d7)	130	3900	**30**	1300	13000	**10**
SM d18:1-18:1(d9)	296	2960	**10**	986.7	2960	**3.0**
Average gain			**23.3**			**4.89**

LOD's were visually determined by S/N of 3.

The next lowest concentration was checked to exclude artefacts.

Legend LOD ratio ESI/HESI: **<1** | **1-10** | **>10**

*Interference from plasma matrix reduces the LOD

LOD comparison between the VIP-HESI and the standard Bruker Apollo II source
For the evaluation a dilutions series of SPLASH mix was prepared without matrix in methanol and with matrix in SRM1950 (30 µL SRM1950 plasma extract equivalent in 1 mL Methanol)shows the results for negative.

Technical drawing of the VIP-HESI source

Conclusions

The novel VIP-HESI source in combination with mobility offset mass aligned data acquisition offers a deeper and broader analysis by CCS-enabled lipidomics workflows based on:

- Better LODs and an improved linear dynamic range in positive and particularly in negative mode.
- A higher number of lipid ID annotations for untargeted workflows.

Lipids: ID and Structural Analysis