

Development and Optimization of a Time-of-Flight Mass Spectrometer for Non-Targeted Metabolomics

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Introduction

The ecTOF is a new conceptual device developed by TOFWERK AG for target and non-targeted analysis. This instrument combines gas chromatography with simultaneous chemical and electron ionization (CI and EI respectively) and a high-resolution time-of-flight (TOF) mass analyzer [1].

This unique technical combination enables improved understanding of the molecular structure of unknown compounds. For mass spectrometry applications in metabolomics, increased identification confidence of unknown compounds is critical, as identification of unscreened compounds can aid in the diagnosis, prognosis, and treatment of disease [2].

Materials and Methods

In this study a first functioning proof-of-concept (PoC) setup was further developed to the prototype stage in CAD. To evaluate the instrument capabilities for targeted and non-targeted metabolomic analysis, steroid standards and a clinical urine sample was analyzed using the PoC instrument. The learning of this phase was used for the design adaptations. The prototype was not tested due to the restricted time scale of this work.



Fig. 1: CAD Model of the ecTOF prototype

Results

The prototype was designed in CAD (Fig. 1), incorporating the improvements and adjustments from the PoC instrument. In this thesis it was possible to verify that the ecTOF was able to identify known steroids in targeted analyses. In addition, unknown steroids could be identified using the additional information obtained in the same chromatographic run.

Discussion

The resulting design could meet most requirements for the prototype. Special focus was placed on the redesign of the vacuum system and ion optics of the instrument. Required parts are ready for assembly and subsequent testing. Suggestions for further working steps and future developments were made.

In terms of chemical analysis capabilities of the instrument, all 40 targeted standard steroids were detected with the ecTOF PoC. In clinical urine samples, routinely screened steroids could either be detected automatically or tentatively identified manually using the additional information provided by the ecTOF compared to conventional analysis. An additional steroid not targeted in the routine analysis also was tentatively identified (Fig. 2).

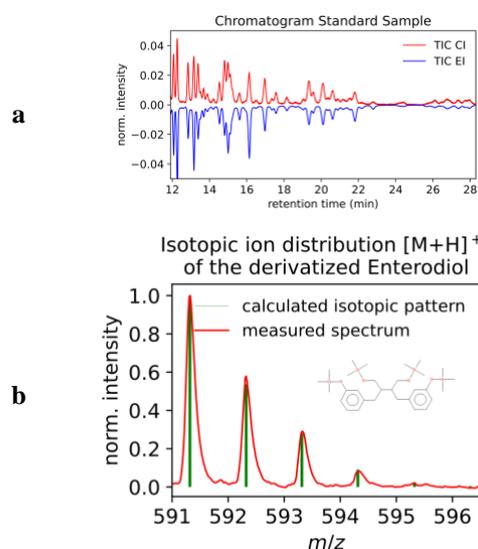


Fig. 2: a) Simultaneous CI (red) and EI (blue) total ion chromatogram of the standard sample. b) Isotopic distribution of the tentatively identified steroid Enterodiol.

References

[1] S. Bräkling et al., "Parallel Operation of Electron Ionization and Chemical Ionization for GC-MS Using a Single TOF Mass Analyzer," *Analytical Chemistry*, p. acs.analchem.2c00933, Apr. 2022, doi: 10.1021/ACS.ANALCHEM.2C00933.

[2] O. Fiehn, "Metabolomics by Gas Chromatography-Mass Spectrometry: Combined Targeted and Untargeted Profiling," *Curr Protoc Mol Biol*, vol. 114, Apr. 2016, doi: 10.1002/0471142727.MB3004S114.

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