Application note 34 | GC-MS

Detection of biomarkers in breath

a metabolic study using Gas Chromatography-Mass Spectrometry

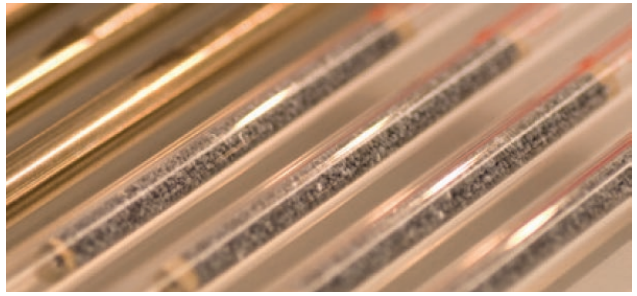
Exhaled breath contains hundreds of volatile organic compounds. The concentration of some of these compounds changes in case of disease. Metabolomics using mass spectrometry is rapidly growing in importance as a non-invasive tool to improve diagnosis and treatment of diseases and speed up drug development processes. It can be applied to many biological problems where a 'good' and 'bad' state can be identified. Comparison of metabolites may lead to better understanding of biochemical differences.

Metabolic profiling

In the human body, many chains of chemical reactions occur within a cell. Since numerous chemicals (known as “metabolites”) may be involved, metabolic pathways can be quite elaborate. The strength of metabolic profiling is the instantaneous snapshot of the physiology of the cell. It involves analysis of the changes in the complete set of metabolites in the cell, tissue or body fluids, between a control group and a test group. Because of the complexity of the samples, a separation technique needs to be coupled to a sensitive detection technique to create both sufficient selectivity and sensitivity. Gas Chromatography followed by Mass Spectrometry (GC-MS) is a well-established combination for this purpose.

Breath analysis

Normal metabolic activity and pathological disorders (such as inflammations) release different amounts of volatile organic compounds (VOCs) within the human organism. These VOCs enter the blood stream and are eventually metabolized or excreted via exhalation, skin emission, urine, etc. Identification and quantification of potential disease biomarkers can be seen as the driving force for the analysis of exhaled breath. The fact that breath sampling is non-invasive makes it a very attractive method.



Chronic Obstructive Pulmonary Disease (COPD)

COPD is a treatable, but slowly progressive lung disease including bronchitis and lung emphysema. Although inhalation of steroids is a known method to treat COPD, responsiveness to these steroids strongly depends on which type of inflammation caused the COPD. Nowadays many different tests are necessary to identify the inflammation type. As an alternative to these tests, it was checked if the inflammation type can be identified by exhaled breath metabolomics. For this purpose exhaled compounds were analyzed using GC-MS and a standard hospital test was performed. Data from mild versus moderate COPD patients were compared.

Results

The airway inflammation in COPD appeared to be of a complex nature: therefore no single, representative biomarker could be found using either of the techniques applied. Figure 1 shows an example of two GC-MS chromatograms obtained from exhaled compounds. The difference between the two chromatograms is characterized by changes in multiple peaks.

By combining quantitative GC-MS with metabolic profiling, both type and activation of inflammation could successfully be identified.

It is increasingly recognized that COPD is not a single disease entity, and that ‘fingerprints’ derived from both clinical and inflammatory markers are needed to predict diseaseprogression and therapeutic responses. Our findings may be used for the clinical implication of exhaled breath profiling in the phenotyping and monitoring of COPD, ultimately leading to personalized medicine and better control of the disease.

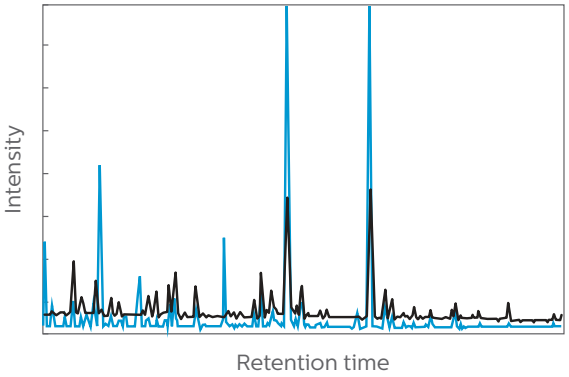


Figure 1: overlay of two GC-MS chromatograms
The blue chromatogram corresponds to a mild and the black one to a moderate COPD patient. The two large peaks (representing N,N-dimethylacetamide and phenol from the sampling bag) are artifacts that were not included in the analyses.

Materials Analysis offers a full range of analytical methods and expertise to support both research and manufacturing, serving customers by taking an integral, solution-oriented approach.

Application note 34
Hugo Knobel
Phone: +31 (0)6 54696323
E-mail: hugo.knobel@philips.com

© 2015 Koninklijke Philips N.V. All rights reserved.
Specifications are subject to change without notice.
Trademarks are the property of Koninklijke Philips N.V.
(Royal Philips) or their respective owners.

www.innovationservices.philips.com/materials-analysis

Issue: April 2015