REAL-TIME HIGH-RESOLUTION TANDEM MASS SPECTROMETRY IDENTIFIES FURAN DERIVATIVES IN EXHALED BREATH

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ETH Zürich
ANALYSIS OF EXHALED BREATH

Adapted from *Metabolites* 2015, 5(1), 3
ANALYSIS OF EXHALED BREATH

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<table>
<thead>
<tr>
<th>Exhaled Breath</th>
<th>Sampling</th>
<th>Analysis</th>
<th>Data processing</th>
<th>Final Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atm. gases (O₂, N₂, H₂O, CO₂, etc)</td>
<td>MEPS, SPME, NTs</td>
<td>Comprehensive off-line</td>
<td>Statistical treatment (MVA, PCA, PLS, etc)</td>
<td>VOCs fingerprints as diseases biomarkers</td>
</tr>
<tr>
<td>VOCs</td>
<td></td>
<td>GC-MS, PTR-MS, PTR-TOF-MS, SIFT-MS</td>
<td></td>
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<tr>
<td>Exogenous</td>
<td>Laser Spectroscopy, Chemical Sensors</td>
<td>Real-time</td>
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<td>Endogenous</td>
<td></td>
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ANALYSIS OF EXHALED BREATH

Advantages
- Separation
- Identification

Disadvantages
- Off-line
- High volatility

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**Advantages**
- On-line
- Quantification

**Disadvantages**
- Identification
- m/z range
ANALYSIS OF EXHALED BREATH

**Ambient MS**

- Ions are formed in an ion source outside the mass spectrometer without sample preparation or separation

- **Desorption ESI (DESI)**

- **Extractive ESI (EESI)**
ANALYSIS OF EXHALED BREATH

Ambient MS: Secondary ESI (SESI)

FP7-2013-IAPP
"Analytical Chemistry Instrumentation Development"
ANALYSIS OF EXHALED BREATH

Ambient MS: Secondary ESI (SESI)

Exhaled breath

e-cigs

Plants
ANALYSIS OF EXHALED BREATH

Ambient MS: Secondary ESI (SESI)

- On-line
- Low volatility
- m/z range
- Identification
- Real-time HRMS/MS

Disadvantages
- Quantification
ANALYSIS OF EXHALED BREATH

Furan derivatives in Breath

- Presence in breath has been suggested
- Related to smoking or fungal infection
- Source is still unclear

Proper identification of the whole family of furan derivatives in the exhalome would be useful for a better understanding of the origin and function.
ANALYSIS OF EXHALED BREATH

Furan derivatives in Breath

LTQ Orbitrap
- Mass Acc. < 1 ppm
- Resolution ≅ 250 000
- Repeatability < 10%
ANALYSIS OF EXHALED BREATH

Furan derivatives in Breath

TripleTOF
- High Sensitivity
ANALYSIS OF EXHALED BREATH

Confirmation by real-time HRMS/MS

MS$^2$ Standard

$\text{C}_2\text{H}_4$ $\text{C}_2\text{H}_6$

$\text{C}_2\text{H}_5\text{O} \text{ 139.1110}$

$\text{C}_6\text{H}_{13} \text{ 121.1007}$

$\text{C}_7\text{H}_{15} \text{O} \text{ 111.0802}$

$\text{C}_4\text{H}_9 \text{ 93.0695}$

$\text{C}_6\text{H}_{11} \text{ 95.0851}$

$\text{C}_5\text{H}_7 \text{ 79.0538}$

$\text{C}_6\text{H}_9 \text{ 81.0695}$

$\text{C}_4\text{H}_5\text{O} \text{ 83.0489}$

$\text{C}_2\text{H}_2$ $\text{C}_2\text{H}_4$ $\text{C}_3\text{H}_6$ $\text{C}_3\text{H}_4$

$\text{C}_4\text{H}_9 \text{ 67.0540}$

$\text{C}_5\text{H}_7 \text{ 55.0539}$
ANALYSIS OF EXHALED BREATH

Confirmation by real-time HRMS/MS

MS² Standard

Isolation window

MS² Breath
ANALYSIS OF EXHALED BREATH CONDENSATE

Confirmation by UHPLC-HRMS

Cold trap
-78.5 °C

Collection of EBC
ANALYSIS OF EXHALED BREATH CONDENSATE

Quantification by UHPLC-HRMS

Cold trap
-78.5 °C

EBC
Exhaled Breath
≈ 30 ppb
≈ 100 pptv

EBC
Exhaled Breath
≈ 5 ppb
≈ 10 pptv

15 min ≈ 119±25 L breath ≈ 1.8±0.5 mL EBC

C1-C5 Furans
100-1000 pptv

C6-C12 Furans
5-50 pptv
ANALYSIS OF EXHALED BREATH CONDENSATE

Furan Derivatives in Breath

Real-time HRMS

UHPLC-HRMS

MS/MS confirmation

Quantification

pptv range
EXHALED BREATH: ONGOING PROJECTS

Targeted analysis

- Aldehydes

- Benzothiazoles
Untargeted analysis

Clinical studies
- Sleep Apnea
- Chronic obstructive pulmonary disease
- Cystic Fibrosis
- Pulmonary fibrosis
- Lung cancer
ZENOBI’s group
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