Please Exhale: Quick and Easy Breath Analysis

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When we drink alcohol, its “flag” precedes us, and enjoyment of large amounts of garlic or onion can often be detected by others the next morning. However, our breath does not only betray what we have consumed; some diseases also produce telltale breath odors. Breath analysis has some interesting advantages for clinical diagnosis, for example, unlike drawing blood, it requires no puncture. However, it has proven to be difficult.

The complexity of the equipment is considerable, the samples require complex preparation before the actual analysis can take place, and until now only small, volatile compounds have been reliably detected. Swiss researchers have now developed a mass-spectrometric method to quickly and easily obtain a proper fingerprint of breath, including the quantitative detection of large, nonvolatile compounds.

Renato Zenobi and his team at the ETH in Zurich have based their new method on quadrupole time-of-flight mass spectrometry (QTOF). In this method, molecules are electrically charged and then separated and identified according to their molecular weight. In a QTOF machine, molecules are accelerated in an electrical field. The time-of-flight component separates the molecules according to their mass-to-charge ratio. The time it takes the fragments to fly to the detector depends on their masses. The quadrupole may be used to fragment the molecules before they enter the TOF part. The instrument generates a spectrum of fragments that is characteristic of the original molecule and identifies it.

The crucial new twist to Zenobi's method is the way the sample is inserted into the mass spectrometer. Usually, samples are first extracted and the resulting liquid is atomized with an electric field. Instead, Zenobi's team carries out a direct droplet-droplet extraction: the breath sample is led into the electrospray array, where it crosses a stream of charged reagent drops that absorb and charge the molecules of interest.

During their journey into the mass spectrometer, the droplets lose their solvent and continuously fragment until nothing is left but the charged molecules, which then proceed into the QTOF mass spectrometer. This allows the analysis to be carried out continuously over longer periods of time so that larger samples can be examined. The samples do not need to be prepared, which reduces loss.

Most importantly, in contrast to current methods, the droplet components of the breath samples, which contain the larger, nonvolatile substances, are also included. This allows traces of these compounds to be detected and quantified.

The urea content of breath samples after different meals can, for example, lead to conclusions about the metabolic processes involved. Likewise, information about smokers' metabolism of nicotine is also accessible.

Citation: Renato Zenobi, Rapid In Vivo Fingerprinting of Nonvolatile Compounds in Breath by Extractive Electrospray Ionization Quadrupole Time-of-Flight Mass Spectrometry, *Angewandte Chemie International Edition*, doi: 10.1002/anie.200602942

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