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Monitoring hydrogen sulfide in simulated breath of anesthetized subjects

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Dedicated to Detlef Schröder, a superb ion chemist and friend.

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ABSTRACT

Human breath can be a complex mixture of trace gases in humid air, with the addition of various anesthetizing agents it becomes even more complex and can present a challenge for the accurate quantification of components. The purpose of this paper was to investigate the quantification of H_2S as a function of several potential matrix/interference compounds using negative-ion atmospheric pressure chemical ionization with mass spectrometric detection. Analysis was performed by humidifying zero-air and adding various compounds that would be encountered in a perioperative situation. Nitrous oxide, carbon dioxide and to a lesser extent humidity have significant effects on the instrument response to hydrogen sulfide concentration, while halogenated species were found to have little if any complicating effect. It was found that H_2S can be accurately quantified by using either $[SO_3]^-$ or $[SO_2]^-/[SO_3]^-$, both of which eliminate the response variability due to interferences.

1. Introduction

Hydrogen sulfide, although traditionally known as a toxic gas, is an important component of biological systems. It is now known that its function varies widely; generally it is produced in the metabolism of cysteine [1] and can serve, for example, as a neuromodulator in the brain [2], a vasodilator in the cardiovascular system [3], or as an indicator of inflammatory processes [4]. Hydrogen sulfide is present in the breath of healthy individuals in concentrations in the range from 1 ppb to 70 ppb [5].

Mass spectrometry has long been available for breath analysis and has been used for breath monitoring and cardio-pulmonary function testing, in high-performance athletics, for example [6]; but H_2S has not been an analytical target probably because isobaric interference prevents the detection of H_2S in breath (SH^+/O_2H^+) using an electron impact single-quadrupole system. Instead, solid state detectors have been applied for H_2S analysis, but these suffer from complications due to non-resolvable interferences in complex samples and environments [7]. Quantitative mass spectrometric studies of H_2S, both in breath and as a pure gas, are few. Proton Transfer Mass Spectrometry (PTR-MS) of H_2S in humid air in a Selected Ion Flow Tube (SIFT) has shown good quantification with H_3O^+ only if the influence of secondary reactions of the H_3S^+ ion are taken into account, while NO^+ and $O_2{}^+$ were found unsuitable for H_2S analysis [8]. To the best of our knowledge, the only quantitative mass spectrometric study of H_2S in exhaled breath was performed by the same method [9], with H_2S concentrations from 1 ppb to 3 ppb in nose exhaled breath and up to 50 ppb in the static mouth cavity. Atmospheric pressure chemical ionization (APCI) has been used to quantify H_2S in dry air in the positive ion mode with a detection limit of 1 ppbv [10]. Similar negative ion APCI studies in dry air, directed at the detection of toxic industrial compounds and chemical warfare agents, have shown good quantitative response of the $m/z = 33$ anion, HS^-, for ppm level concentrations of H_2S [11]. Very low levels of ambient water and other possible interferences, such as CO_2 or N_2O, in these studies make them of limited value for breath analysis.

The goal of this study was to test the application of atmospheric pressure chemical ionization (APCI) mass spectrometry for the quantitative detection of H_2S in simulated breath in real time. Negative ion APCI was the ionization method of choice, since protonated H_2S, H_3S^+, suffers from isobaric interferences and poor production efficiency since H_3S^+ can be deprotonated by water clusters [8,9]. In order to more fully evaluate the viability of the method, we included the effects of common chemical interferences with molecules such as nitrous oxide, carbon monoxide and halocarbons associated with the breath of anesthetized subjects [12].

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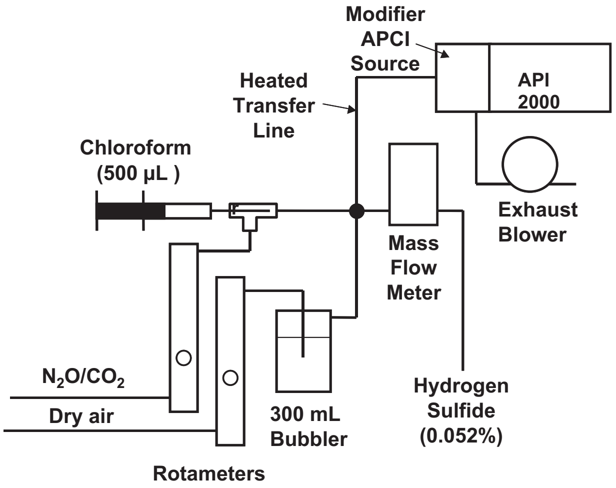
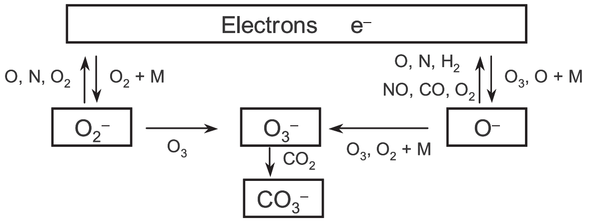


Fig. 1. Schematic of experiment showing flow path and metering devices.

2. Experimental

Experiments were performed with a Sciex API 2000 tandem quadrupole mass spectrometer using a modified Atmospheric Pressure Chemical Ionization (APCI) ion source. The standard APCI ion source is equipped with a heated nebulizer (HN) inlet for vaporization of liquid-phase samples prior to entering the ionization region of the source. In these experiments the HN nebulizer was removed and replaced with a Pyrex tube 30 cm in length and of identical diameter to the HN inlet. The input end of the tube was reduced to 9 mm to match the heated transfer line used to transport the gas mixture from the mixing manifold to the ion source. The mixing manifold is illustrated in Fig. 1. Provision was made for the metered introduction of nitrous oxide, chloroform, carbon dioxide and hydrogen sulfide into a humidified stream of ‘zero-air’ flowing nominally at 10 L min^{-1}.

The mass spectrometer was operated in the negative ion mode in which anions of H_2S and oxidized products of H_2S were observed. The declustering potential was set at −20 V in all experiments, producing spectra with very few ion clusters [13]. The curtain gas flow was approximately 1.5 L min^{-1} of nitrogen and the corona discharge current was 5 mA. The principal reagent ions for the production of observed sulfur containing anions were O_2^- and O_3^-. O_3^- ions originate from ozone created in the corona discharge of the APCI source where the neutral ozone concentration can be on the order of parts per thousand [14]. The presence of CO_2 in the sample air, even in trace quantities, produced CO_3^- as the most intense peak in the mass spectrum. The response of the instrument to H_2S was studied as a function of the concentration of different breath components: nitrous oxide (0–5% by volume), chloroform (0% and 1%) or CO_2 concentration (trace concentration to 2.5%) to determine the routes of production of the various sulfur-containing anions with these molecules. The response of H_2S also was studied with several combinations of components to explore the effects of combined chemistries. Zero-air, carbon dioxide (99.98%) and nitrogen (99.98%) were purchased from Linde. Nitrous oxide (99.97%) and hydrogen sulfide (99.7%) were purchased from Matheson Gas Company. Chloroform (99.9%) was purchased from Sigma–Aldrich.



Scheme 1. Possible paths for the generation of the primary chemical reagents, O_2^- and O_3^-, in the APCI discharge.

3. Results and discussion

In the negative ion mode, the principal reagent ions in APCI are O_2^- and O_3^-, produced in the discharge as illustrated in Scheme 1. Ionization of analyte ions entrained in the inlet air stream is achieved via chemical reactions with these primary reagent ions.

Spectra of the pure air negative-mode APCI are dominated by the O_2^- ($m/z = 32$), O_3^- ($m/z = 48$), and CO_3^- ($m/z = 60$) anions (see Fig. 2a and b). Also present are the NO_2^- ($m/z = 46$), NO_3^- ($m/z = 62$) and CO_3^- (H_2O) ($m/z = 78$). Oxygen adducts of O_2^- and O_3^-, O_2^- (O_2) and O_3^- (O_2), possible isobaric interferences with sulfur oxide anions, are not observed in humid air mass spectra. When hydrogen sulfide is added to the analyte air stream ions with masses corresponding to HS^- ($m/z = 33$), SO_2^- ($m/z = 64$), SO_3^- ($m/z = 80$), SO_4^- ($m/z = 96$) and SO_5^- ($m/z = 112$) can be observed in the mass spectrum (Fig. 2c). While the HS^- ion is observed, it is less intense in our humid air experiments than in previous dry air experiments [11]. Depending on the concentration of H_2S, the HS^- ion intensity is 10–30 times less than that of SO_2^- and is further reduced by the addition of N_2O or CO_2. In the presence of 1% or more of CO_2, HS^- formed with 10 ppm H_2S is barely above the background level and is more than 100 times less intense than SO_2^-. For this reason,

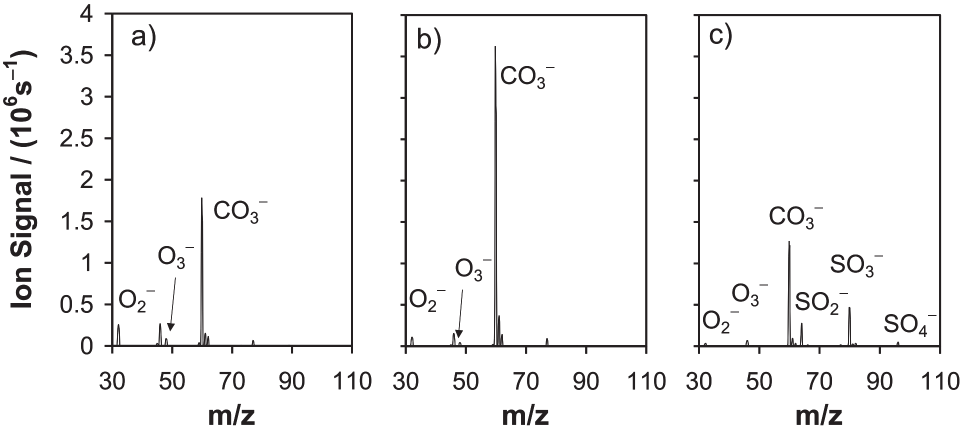


Fig. 2. Typical negative ion mass spectra collected: (a) from humid air, (b) from humid air with nitrous oxide present, and (c) from humid air with nitrous oxide and hydrogen sulfide present.