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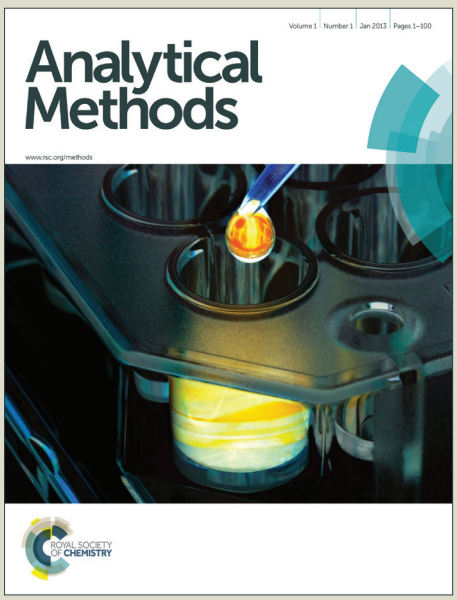

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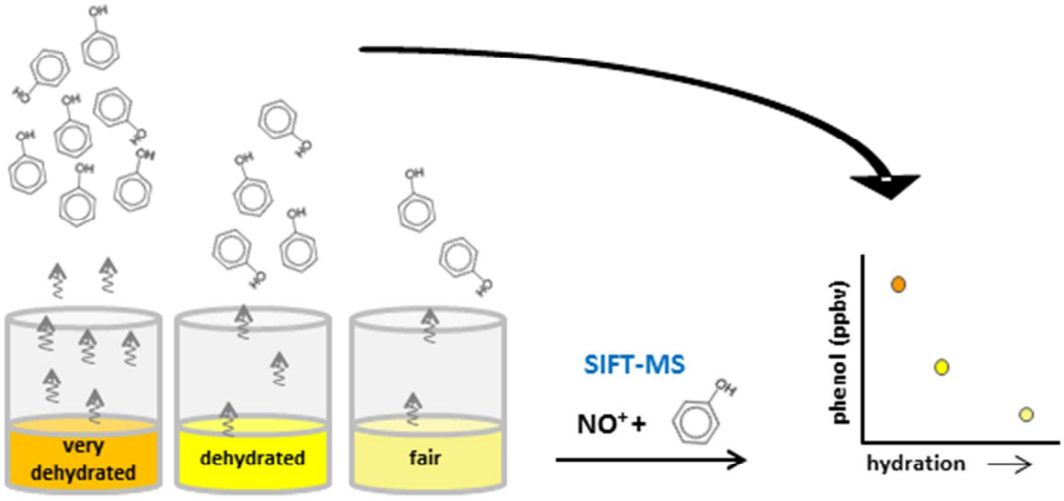

An optimised kinetics library entry has been developed to investigate the effect of urine concentration in the course of (de)hydration on volatile metabolite - phenol.

Quantification of phenol in urine headspace using SIFT-MS and investigation of variability with respect to urinary concentration

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To quantify phenol in human urine or exhaled breath using selected ion flow tube mass spectrometry (SIFT-MS) requires a careful study of its reactions with the appropriate SIFT-MS precursor ions in the presence of water vapour. The reactions of NO^+ precursor ions with the isobaric compounds phenol and dimethyl disulphide (DMDS) have been studied using the SIFT technique to identify the appropriate product ions in order to optimise the SIFT-MS kinetics library entries for these compounds. This allows accurate quantification when these compounds co-exist in humid biofluids, in particular urine headspace and exhaled breath. These optimised kinetics library entries have been used to investigate the effect of hydration status of healthy individuals on the concentration of phenol in their urine. Using these new kinetics, it is seen that hydration status of the donor volunteers (assessed using urinary osmolality and creatinine concentration) affects urinary headspace phenol concentrations measured via SIFT-MS. A strong correlation between headspace phenol concentration and both the urinary osmolality and urinary creatinine concentration has been demonstrated. Thus, to obtain urinary concentrations of phenol by headspace analyses using SIFT-MS it is essential to account for the osmolality or creatinine concentration of the urine.

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1. Introduction

Phenol has been proposed as a potential biomarker of several cancer states and its concentration is altered within the breath and urine of patients diagnosed with gastro-esophageal [1-3], colonic [4-6] and breast cancer [7] compared to healthy controls. The mechanism of phenol production in cancer remains unknown, but may be related to dysfunctional aromatic amino acid metabolism[8-11].

As phenol commonly occurs in urine from healthy volunteers it is necessary to accurately quantify this compound in order to observe subtle differences between cancer and healthy patients.

Analytical methods currently used to study phenol in urine or urinary headspace usually involve chromatographic techniques with solid phase extraction (detection limit 65 ng/ml)[12],liquid extraction [13], or flourometric detection [14]. Solid-phase micro-extraction, SPME, has also been used to extract phenol and cresols directly , avoiding the use of a liquid trap, and concentrations of phenol and cresol determined using internal standards[15]. Due to the nature of SPME extraction there can be difficulties with accurate absolute quantification using this technique [16]. GC/MS methods often require lengthy analysis times, time consuming extraction of analytes and calibration using internal or external standards.

Selected ion flow tube mass spectrometry (SIFT-MS) facilitates real-time quantification of volatile compounds down to ppbv level without the need for time-consuming instrument calibration. To realise accurate quantification of compounds it requires kinetics library entries, which is commonly used terminology describing an equation used to calculate concentration from ion signals. Such as library is constructed from detailed ion chemistry studies of the reactions of the precursor ions (H_3O^+, NO^+ and O_2^+) with the targeted analyte molecules to identify product ions (also called analyte ion) [17, 18]. SIFT-MS has been previously used to quantify volatile organic compounds (VOCs) in the headspace of human urine [19-21], including seminal studies of increased acetone levels in relation to ovulation[22] and increased urinary formaldehyde concentrations in patients suffering from bladder and prostate cancer [23].

Although SIFT-MS is a valuable platform for urinary headspace analysis there are often some difficulties that need to be overcome, principally due to the overlap of product ions of isobaric compounds that co-exist in the biofluid gas/vapour being analysed [24]. This is a problem that has been met and solved in the present study of phenol in urine because it is isobaric with dimethyl disulphide (DMDS) which can co-exist with phenol in the exhaled

breath of smokers and in urine as a metabolite from food rich in onions, garlic or radishes. The basic reactions of the SIFT-MS precursor ions (H_3O^+, NO^+ and O_2^+) with phenol and DMDS has previously been reported by Spanel *et al*. [25, 26] in separate studies.

The aims of the present study are to carry out a careful analysis of the relevant SIFT-MS ion chemistry that will allow accurate quantification of phenol and DMDS in human urine, breath or other biological samples based on previous kinetics data. The important aspects of the study are:

(1). To construct basic kinetics library entries for the analytical reactions of NO^+ precursor ions with phenol and DMDS and to account for the formation of the hydrates of the product ions of these compounds, specifically to determine the so-called A_{eff} coefficient that describes formation rate of monohydrated ions[27].

(2). To optimise the phenol kinetics data entry in order to account for overlaps between the isobaric ions and others such as hydrated protonated acetone ions and DMDS, which are both present in human urine at relatively high concentrations depending on diet and metabolic status.

(3). To establish the effect of hydration status of individuals on urinary phenol concentration in relation to osmolality and urinary creatinine concentration.

2. Experimental section

2.1 Ion chemistry of phenol and DMDS in SIFT-MS

The details of the ion chemistry and other analytical aspects of SIFT-MS (*Profile 3,* Instrument Science Limited, Crewe, U.K.) have been previously presented in several reviews [28, 29] and need not be re-iterated here. Phenol reacts with all three precursor ions of SIFT-MS. The reaction of phenol with H_3O^+ produces a protonated molecule at *m/z* 95 and its monohydrate at *m/z* 113. However, acetone is always present at a relatively high concentration in human breath or urine and so it reacts with H_3O^+ to form protonated acetone, the dehydrate of which, $CH_3COCH_3H^+(H_2O)_2$, at *m/z* 95 overlaps with that of protonated phenol. The reaction of NO^+ with phenol results in a molecular ion due to charge transfer at *m/z* 94 and its monohydrate at *m/z* 112 (ion signal ratio 65% and 35% in dry air, 40% and 60% in humid air respectively), see mass spectrum in Figure 1A. However, it must be noted that the reaction of the isobaric DMDS with NO^+ also proceeds via charge transfer forming molecular isotopologue ions at *m/z* 94 $(CH_3)_2{}^{32}S^{32}S^+$ and 96 $(CH_3)_2{}^{34}S^{32}S^+$, see Figure 1B. Formation of the hydrates of these ions is negligible, typically at the 1% level. The presence of ions of sulphur compounds in MS spectra can be checked by the measurement of the relative signal level ratio of the isotopologues ions knowing that the fractional abundance of $^{32}S/^{34}S$ is 4.4%. Thus, when there are two sulphur atoms in the ions the signal level ratio should be close to 9%. This principle can be used in the SIFT-MS kinetics library optimisations and the contribution of the molecular ions of DMDS to the total signal level at *m/z* 94 ion can be subtracted to provide analysis of the isobaric phenol, as will be shown later. Similarly, the contribution to the signal level at *m/z* 96 due to the ^{18}O isotopologue of the molecular ion of phenol can be accounted for. Due to the high recombination energy of $O_2^{+\bullet}$ (12.02 eV), its reactions with polyatomic molecules often produce several fragment ions that can overlap when analysing complex matrices such as human urine, thus producing SIFT-MS spectra that are too difficult to interpret for analysis.

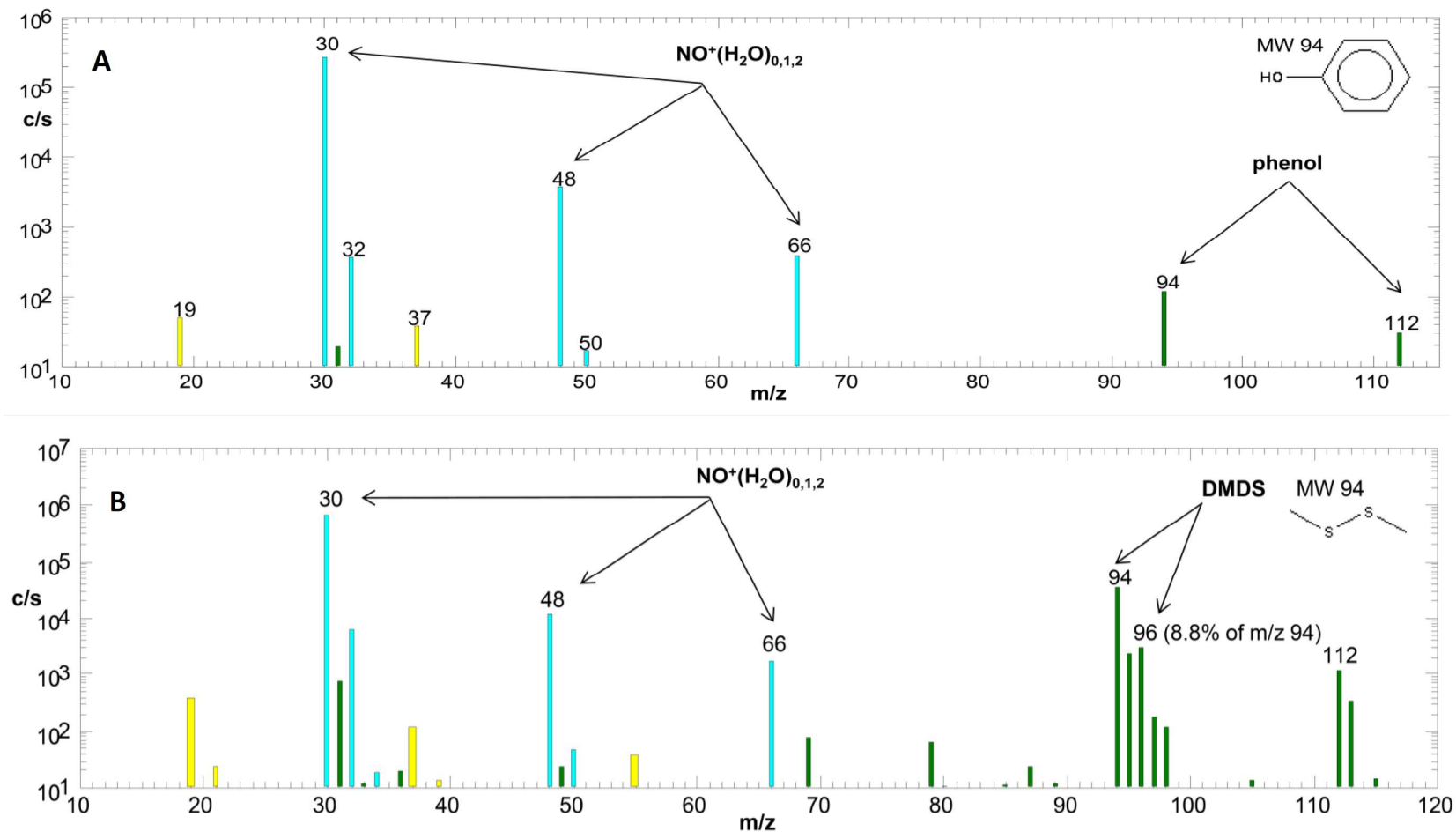

Figure 1 The SIFT-MS spectra obtained as the headspace above A) phenol and B) DMDS was sampled. The arrows indicate the product ions resulting from the reactions with the NO^+ precursor ions. Both analytes react with NO^+ forming the same m/z product ions 94 and 112. DMDS produces another product ion at m/z 96 that indicates presence of sulphur isotope 34S used in optimisation of kinetics library entries.

2.2 Reactions of the primary product ions of NO^+ with water molecules, determination of Ae_{ff}, and k_{M+} for phenol and DMDS

The efficiency coefficient A_{eff} has been used to describe the rate of formation of the hydrates of protonated molecules [30, 31]. When using NO^+ precursor ions a fraction of the product ions can also associate with water molecules in humid samples to produce hydrates [17]. The primary reaction of NO^+ ions with phenol molecules results in the formation of molecular ion $[M]^+$. The three-body rate constant, k_{M+} for the association of $[M]^+$ ions describes the rate of hydration of these ions in gas phase, which for phenol proceeds thus:

$$[C_6H_5OH]^+ + H_2O + He \rightarrow [C_6H_5OH]^+(H_2O) + He \quad (1)$$

A_{eff} describes the relative rate of hydrate ion formation with respect to hydration of H_3O^+, which means the total contribution for formation of the protonated product ion. It can be obtained experimentally by relating the conversion rate of the $[M]^+$ ion to its hydrates to the conversion rate of NO^+ to its hydrates [17]:

$$A_{eff} = \frac{2\ln[M^+]_0/[M^+]}{(k_{H_3O^+}/k_{NO^+})k_{H_3O^+}\ln[NO^+]_0/[NO^+]} \quad (2)$$

The ratio $k_{H_3O^+}/k_{NO^+}$ is used to relate the association reaction of H_3O^+ with H_2O to the slower association reaction of NO^+ with H_2O. The subscript 0 indicates the respective ion count rate in the absence of water vapour in the helium carrier gas.

The value of three-body association rate constant can be calculated as follows:

$$k_{M+} = A_{eff} \cdot \frac{k_{H_3O^+}}{k_{NO^+}} \cdot k_{NO^+} = A_{eff} \cdot k_{H_3O^+} \quad (3)$$

The values of $k_{H_3O^+}$ (6.0×10^{-28} cm^6s^{-1}) and k_{NO^+} (5.0×10^{-29} cm^6s^{-1}) are known as previously determined[27, 31].

2.3 Analysis of phenol and DMDS in combination; optimisation of kinetics library entries and correction for humidity influence

In order to minimise the effect of the overlaps of isobaric product ions of the NO^+ reactions with phenol and DMDS during SIFT-MS analyses, it is necessary to obtain accurate kinetics data for these reactions. Air/vapour mixtures of phenol (10 mg) and DMDS (1μL of neat solution) were separately prepared in 6 L Nalophan bags filled with synthetic air at vapour concentrations of typically 10–20 ppmv. Each mixture was introduced into the SIFT-MS instrument via a heated calibrated capillary and full scan mass spectra in dry and then humid

air were acquired for the H_3O^+, NO^+ and O_2^+ precursor ion as they were alternately injected into the helium carrier gas in the reactor flow tube. The flow rate of the injected gaseous sample was controlled by a needle valve and monitored by a flow meter (manufactured by Voegtlin, Aesch, Switzerland). The ranges of *m/z* over which the spectra were taken were chosen to cover all values of the expected primary product ions and any adduct (hydrated) ions that might form, but was typically 10-200 and spectra were accumulated for 3 sequential scans each with duration of 200 seconds.

The influence of sample humidity on the product ion distributions was investigated by introducing water vapour into the helium carrier gas from a separate source that can be heated to vary the water concentration in the helium carrier gas from an equivalent sample humidity from 0.7% of to 6% appropriate to the absolute humidity of exhaled human breath and that of the headspace above aqueous liquids at body temperature[27, 32].

2.4 Urine sample collection and preparation

Having established an appropriate SIFT-MS kinetics library entry (as described in Section 3.2 below) for the accurate determination of phenol in humid air, the phenol levels in the headspace of urine were investigated with particular focus regarding the hydration status of small cohort of healthy adults.

Seven healthy volunteers (three males and four females, age 26-33) who had fasted for a minimum of four hours, attended in the morning and a first mid-stream urine sample was donated (time zero). Immediately following initial sample collection, a standardised volume of mineral water (500 mL) was consumed by each of these participants. Additional mid-stream urine samples were then collected each hour for up to 4 hours, in order to obtain at least four samples in total from each participant. 5 mL of urine was aliquoted for urinary creatinine and osmolality measurements. Urinary creatinine and osmolality are both readily accessible clinical assays typically used to diagnose and monitor a number of disease processes such as renal failure or diabetes insipidous. For scientific purposes they can be utilised to provide a reflection of urinary concentration. Urinary creatinine measures the concentration of this excreted metabolite (produced from the breakdown of the muscle protein creatine) and all other excreted metabolites are then expressed relative to urinary creatinine. Urinary osmolality provides an absolute measure of urinary concentration for normalisation purposes. Urinary creatinine concentration has been widely used in analytical chemistry to standardise urinary metabolite concentrations [33]. Creatinine adjustment has been

shown to provide improved correlation with blood concentrations of the parent chemical [34, 35], so this method of standardisation was used in these experiments. Urinary osmolality was also recorded here to establish if this also correlated with urinary creatinine concentration and phenol concentration as it actually reflects the concentration of salts in urine.

Urine samples for SIFT-MS analysis were processed as follows: 4 mL of urine and 80uL of concentrated HCl (in order to obtain pH of about 2, measured by pH meter) were added into 20 mL capped glass vials to prevent loss of volatiles. The samples were then placed in to water bath and heated at 90˚C for 90 minutes, a thermometer was used during the course of hydrolisation to ensure that the set temperature does not fluctuate and remains stable. This process of hydrolisation was necessary as it is known that phenol (and other phenolic compounds such as cresols) are excreted in the urine conjugated to sulphate or glucuronic acid[36]. This hydrolyses phenol from these conjugates to allow accurate measurement of total urinary phenol rather than just the un-bound 'free' component.

Samples were then allowed to cool and SIFT-MS analyses of the urine headspace were performed at 37˚C. A heated calibrated capillary with a needle was used to sample the headspace from headspace sample vials and a second needle was used to maintain atmospheric pressure inside the sample vial. The concentration of phenol was measured using the multiple ion monitoring (MIM) mode and the absolute concentration was obtained.

3. Results and discussion

3.1 Reactions of the primary product ions of NO^+ with water molecules, determination of Ae_{ff}, and k_{M+} for phenol and DMDS

The primary reactions of NO^+ with both phenol and DMDS proceed via charge transfer. For phenol, the primary product ions are at *m/z* 94 and then its monohydrate forms at *m/z* 112; for DMDS, the primary product ions are at *m/z* 94 and 96 and only relatively weak signals of their monohydrates are formed. The Ae_{ff}, and k_{M+} values that describe the monohydrates formation were calculated according to Equations (2) and (3) above. The efficiency of formation of the phenol monohydrate was determined as $Ae_{ff} = 0.06$ and that for the DMDS monohydrate as $Ae_{ff} = 0.03$. These efficiencies are some 50 and 100 times smaller than the Ae_{ff} obtained for the hydration of the $C_2H_5O^+$ ion product of the NO^+/ethanol reaction that is reported by Michalcikova *et al.* [17] as 3.5. The values of the three-body rate constant for the association of the primary product ions with H_2O were $k_{M+} = 3.5 \times 10^{-29}$ cm^6s^{-1} for phenol and $k_{M+} = 1.7 \times 10^{-29}$ cm^6s^{-1} for DMDS.

3.2 Analysis of phenol and DMDS in combination, optimisation of kinetics library entries and humidity correction

As reported previously [37, 38], SIFT-MS allows real time, online quantification of any gaseous analyte from the measured precursor ion and product ion count rates. For accurate and immediate quantification it is important to assign to each neutral analyte an appropriate set of precursor ions and a number of product ions together with known reaction rate constant and factors *f* (explained below). The *Profile 3* instrument software stores these data in a kinetics library. This takes the form of a plain text file that consists of number of entries that are labelled by the name of the compound followed by a symbol indicating the precursor ion in parentheses, see Table 1. The precursor ion rows contain *m/z*, rate constant *k* and the precursor ion factor f_i. The product ion rows contain *m/z* and the product ion factor *fp*. The f_i are used to multiply the acquired raw count rates of the ion with its *m/z* given at the beginning of the row according to the equation used to calculate absolute concentrations. Normally, f_i values of 1.0 are used, as indicated in the DMDS and phenol examples in Table 1. The *fp* values are again used to multiply the acquired product ion count rates and also are normally set as 1.0, see Table 1. However, in the case when other ion chemistry reactions occur this simple calculation does not provide valid results. This is the case when product ion overlaps occur between the product ions for DMDS and phenol at *m/z* 94 and their hydrates. Thus, values other than 1.0 account for the influence of humidity and product ion overlaps.

Table 1 Kinetics library entries without optimisation. These kinetics entries were published in separate papers by Spanel *et al* [16,17]and the rate constant were used in the present study.

dimethyl disulphide(NO+)	phenol(NO+)
1 precursor	3 precursors
30 2.4e-9 1.0	30 2.2e-9 1.0
1 products	48 1.6e-9 1.0
94 1.0	66 1.3e-9 1.0
	2 products
	94 1.0
	112 1.0

Analysis of **phenol** in the presence of DMDS can be achieved by adding a third product ion with *m/z* 96 (the ^{34}S isotopologue) to the kinetics entries with negative value of the *fp*

coefficient in order to subtract the contribution of the DMDS product ions. This is achieved by utilising the ideas outlined in experimental section 2.1. Thus, the phenol kinetics library entries are adjusted by multiplying the raw count rates of *m/z* 96 by *fp* = -11.4 (calculated as 1/0.088, which means that the contribution of DMDS is now calculated from the count rate at *m/z* 96), see Table 2.

Table 2 Optimised kinetics library entries. Rate constant for the reaction of DMDS and phenol with NO^+ precursor ions have been adopted from previous studies by Spanel *et al* [16,17], in bold are the *fp* and *fi* coefficient acquired by fitting the experimental data acquired in Section 2.1.

DMDS_94_ corr(NO+)	Phenol_96 _corr(NO+)	Phenol_96_water_corr(NO+)	Phenol_112only(NO+)
1 precursor	3 precursors	3 precursors	3 precursors
30 2.4e-9 1.0	30 2.2e-9 1.0	30 2.2e-9 1.0	30 2.2e-9 1.0
2 products	48 1.6e-9 1.0	48 1.6e-9 1.0	48 1.6e-9 1.0
94 **-0.0024**	66 1.3e-9 1.0	66 1.3e-9 **9.0**	66 1.3e-9 1.0
96 **11.4**	3 products	3 products	1 product
	94 1.0	94 1.0	112 **2.5**
	96 **-11.4**	96 **-11.4**	
	112 1.0	112 1.0	

Equation 4 shows how these parameters are used to calculate analyte concentration [M] with the example of "Phenol_96_water_corr(NO+)" library entries:

$$[M] = \frac{1}{kt_r} \frac{f_{p1}[94]+f_{p2}[112]+f_{p3}\ 11.4[96]}{f_{i1}[30]+fi2[66]} \quad (4)$$

where *k* is the rate constant for the reaction of NO^+ with phenol, t_r is the reaction time, the numbers in square brackets indicate the count rates of ions at the *m/z* (94, 112, 96, 30 and 66), and f_{p1}, f_{p2} = 1.0, , f_{p3} = -11.4, , f_{i1} = 1.0 and f_{i2} =-9.0 calculated by fitting the experimental data as described in the text.

This kinetics library entry can be used for quantification of phenol from human exhaled breath. Unfortunately, urine contains other metabolic products with molecular weight 96 that are not present in exhaled breath but interfere with DMDS in the urine headspace. Examples include 2,5-dimethyl furan and furfural produced by sugars. The ion chemistry study of furfural has been previously described by Mochalski *et al.* [39]. The actual percentage of molecular ion at m/z 96 is thus not 8.8% but higher due to overlaps with product ions relating

to these additional compounds. For the purposes of phenol monitoring in urine headspace at certain humidity, a new kinetics library entry has been developed in this study, where the concentration is calculated only from the monohydrate of the parent phenol ion at *m/z* 112 (see Table 2 and Figure 3C), when the branching ratio of the product ions at *m/z* 94 and 112 are 40% and 60% respectively.

In order to analyse **DMDS** in presence of phenol we have excluded the ions at *m/z* 94 from the calculation of DMDS concentration by adding a negative f_p coefficient -0.0024 that has been determined as a contribution of ^{18}O of the OH functional group of phenol molecule (the fractional abundance of $^{16}O/^{18}O$ is 0.24%). Thus, DMDS is now calculated from the ion at *m/z* 96 multiplied by the f_p value 11.4, see Table 2.

3.3 Influence of absolute humidity on derived phenol concentration

When analysing humid samples such as human breath or urine headspace it is necessary to investigate the influence of water molecules on the ion chemistry of the product ions that are present in such samples. The variation in phenol concentration without humidity correction is 20 % (see Figure 2) over the complete absolute humidity range up to that appropriate for exhaled breath of 6% [40], which is not acceptable for accurate quantification of traces. Thus, the count rates of precursor ion at m/z 66 are multiplied by factor f_i = 9.0 (see Table 2) that was obtained by fitting the experimental data and the humidity influence was compensated for. With this adjustment only 2% of variation in the phenol concentration has been achieved, see Figure 2. Detailed examples of optimisation of the kinetics library entries have been reported in many other publications [24, 31, 40].

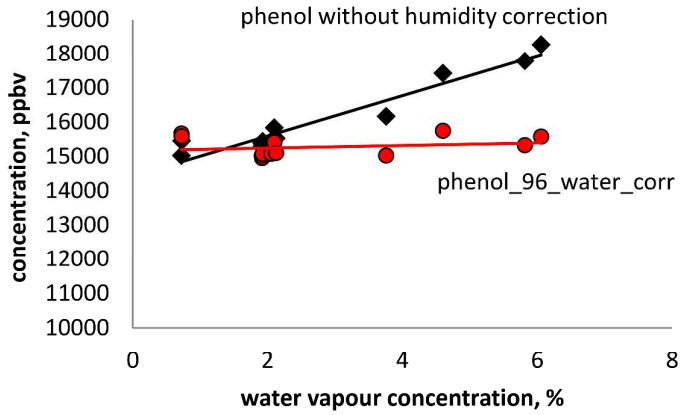

Figure 2 Concentrations of phenol calculated from the m/z 94, m/z 96 and m/z 112 with (red points) and without correction for humidity (black diamonds).

A validation experiment was carried out in order to test the new optimised kinetics library entries (Table 2) that allow minimising the cross-sensitivity between DMDS and phenol. Samples of reference compounds were sequentially introduced into the SIFT-MS. Initially, it has been used the previous 'non-optimised' kinetics library which uses the sum of product ions resulting in reaction with NO^+ multiplied by *f* factors 1.0 given in Table 1. When only DMDS is introduced a false concentration profile of phenol can be also seen in Figure 3 (A). When only the reference mixture of phenol is introduced a false positive signal for DMDS appeared. The same experimental data were evaluated with the optimised kinetics entries given in Table 2. As can be seen in Figure 3 (B) and (C) the overlaps between *m/z* values have been dramatically reduced.

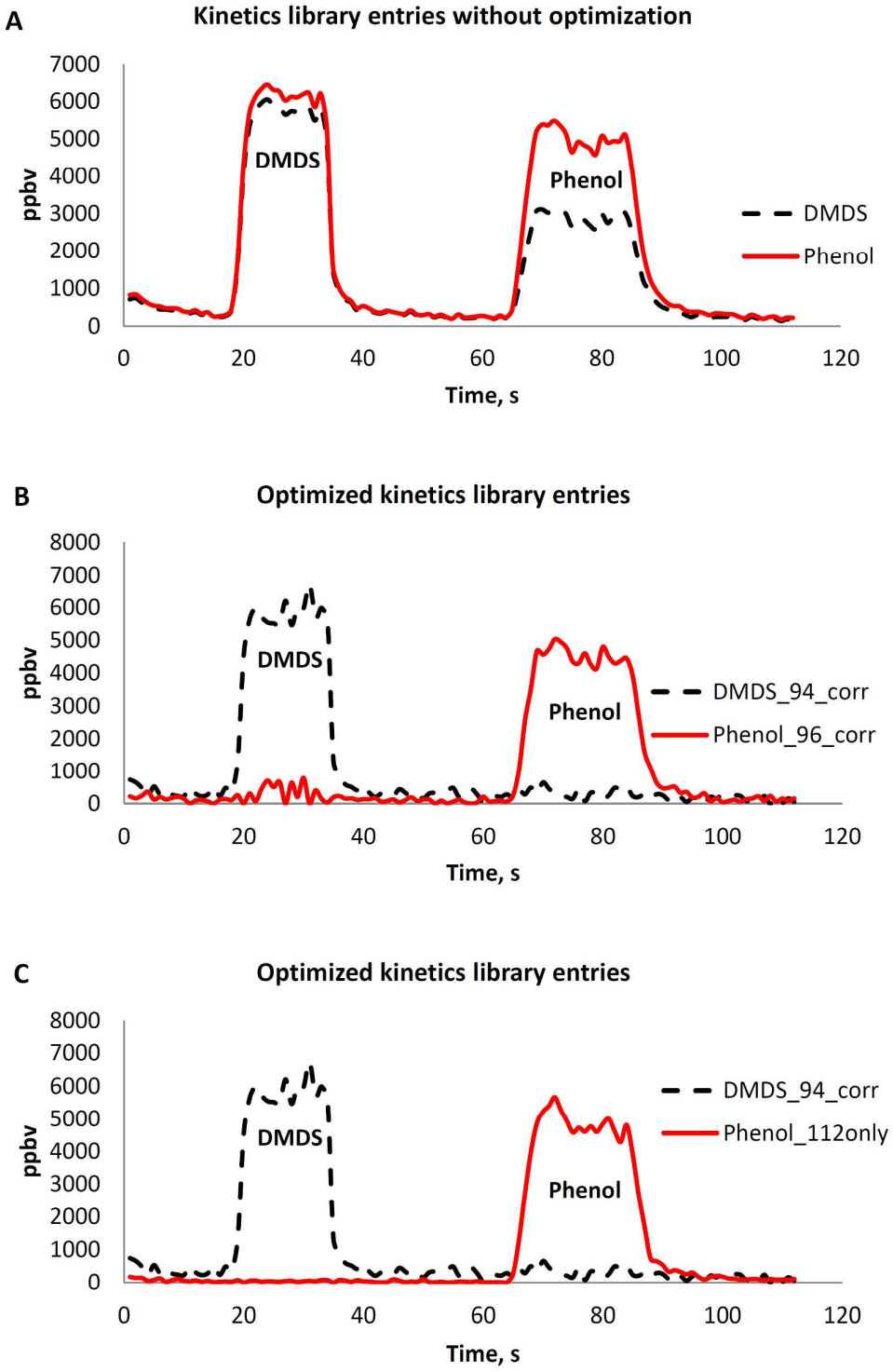

Figure 3 (**A**) Time profile of the concentration of DMDS and phenol calculated (in ppbv) from the sum of the characteristic product ions in a validation experiment when the samples of reference compounds are introduced sequentially, black dashed line indicates DMDS and red line indicates phenol. Note that overlap between m/z 94 causes cross-sensitivity as indicated. Time profiles at (**B**)

and (**C**) are the same raw experimental data evaluated using the optimised kinetics library entries as given in Table 2; note that cross-sensitivity has been dramatically reduced in both cases.

3.4 The influence of hydration status of 7 healthy volunteers on their urine headspace phenol concentration

The baseline urinary phenol levels widely varied between the seven healthy volunteers, ranging from 20 to 114 ppbv (Table 3). Following rehydration of the volunteers by drinking standard volume of water the percentage decrease in phenol levels ranged from 40 to 89%. As starvation continued up to 4 hours the percentage increase in phenol ranged from 59 to 69%. These changes in phenol concentrations were seen to parallel changes in urinary osmolality and creatinine reflecting the hydration status of volunteers, which are shown on semi-logarithmic scales in Figure 4 for each volunteer over the 4 hour dehydration period. The correlation of urinary phenol was somewhat stronger with creatinine (r = 0.93) than with osmolality (r =0.83); see Figure 5. The correlation of osmolality with creatinine was very strong as expected (r =0.95; Figure 5). Therefore, the quantification of VOCs released from urine samples should be normalised to the creatinine level.. A more pragmatic reason to normalise to creatinine rather than osmolality is that creatinine determination is an automated process, allowing high sample throughput, in contrast to osmolality that requires manual determination.

Table 3 Absolute values of phenol (ppbv) in the headspace above the urine samples of each of the seven volunteers given in ppbv during the course of the dehydration experiment from the initial level (time 0) during the subsequent four hours.

Time	*Vol A*	*Vol B*	*Vol C*	*Vol D*	*Vol E*	*Vol F*	*Vol G*
0	40 ± 13	20 ± 4	23 ± 6	43 ± 5	96 ± 26	114 ± 22	91 ± 17
1	15 ± 7	11 ± 7	20 ± 5	42 ± 15	47 ± 18	48 ± 19	22 ± 7
2	9 ± 5	12 ± 3	10 ± 3	26 ± 12	11 ± 4	18 ± 11	22 ± 5
3	10 ± 4	24 ± 9	12 ± 4	74 ± 15	27 ± 7	31 ± 6	28 ± 4
4	28 ± 5	39 ± 13	--*	51 ± 17	--*	63 ± 15	53 ± 14

*Volunteer C and E did not provide a fifth urine sample.

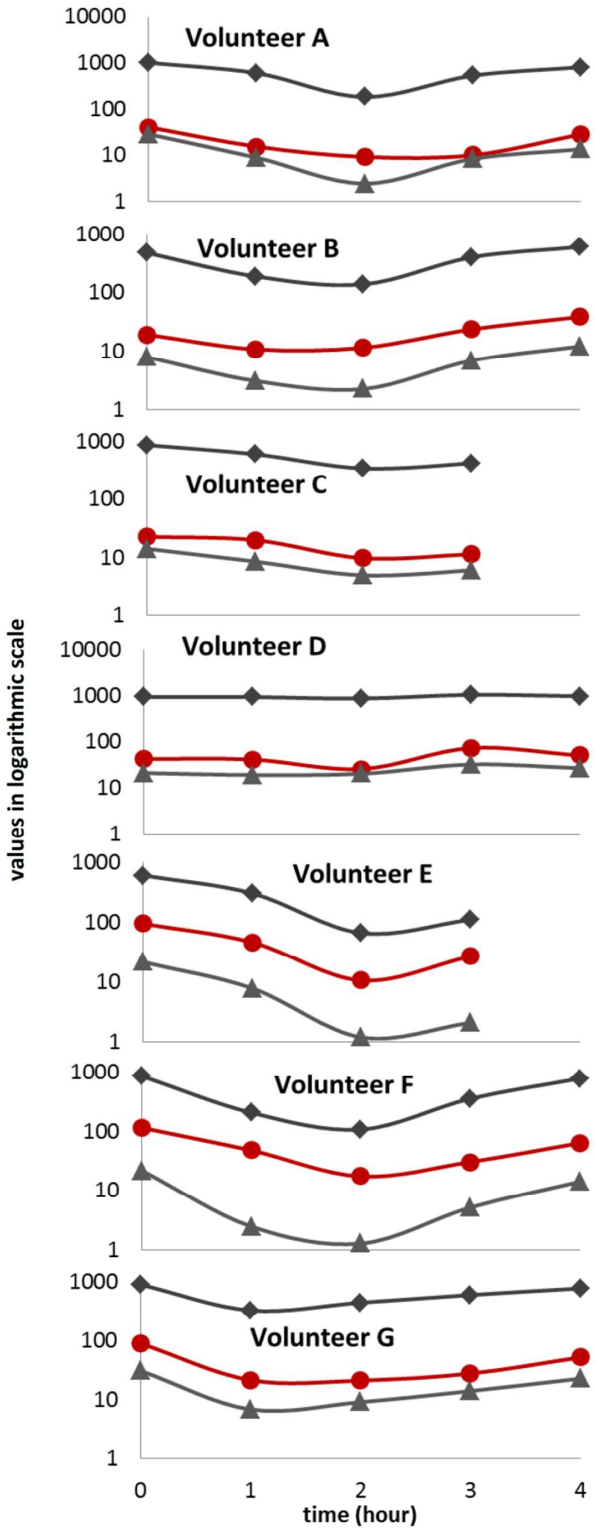

Figure 4 Concentration profile of phenol (ppbv)-red label, osmolality (mosmol/kg)-black label and creatinine (mmol/L)-grey label during the course of dehydration on semi logarithmic scale.

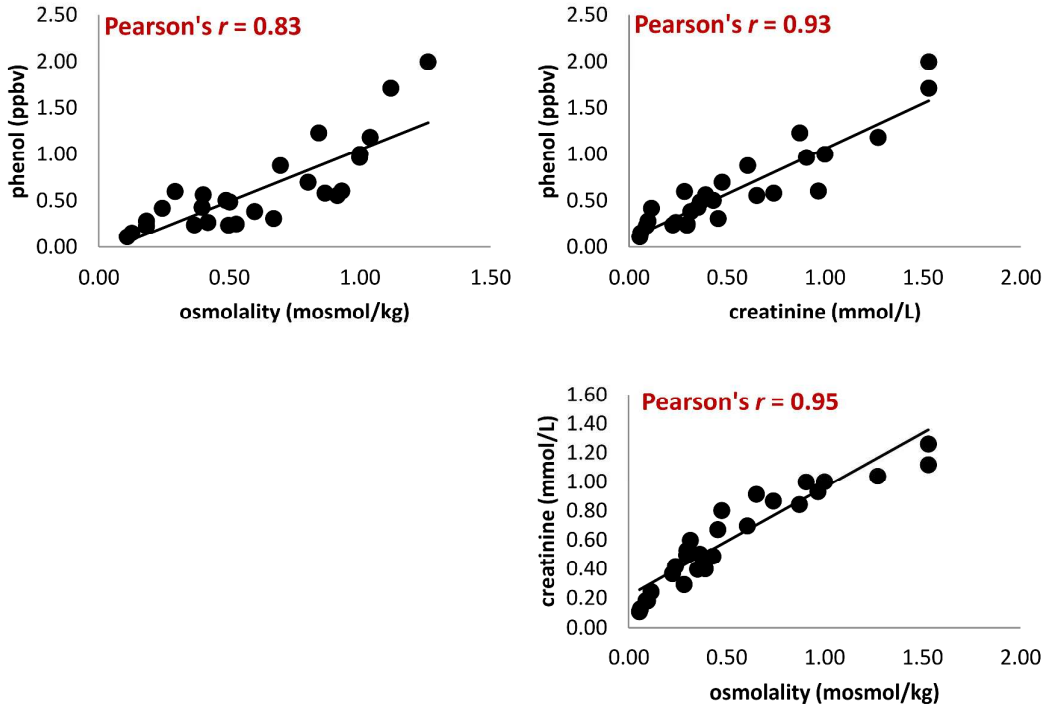

Figure 5 Correlation of urine phenol levels and osmolality (in the left top corner), creatinine (right top corner) and correlation of urinary creatinine (mmol/L) and osmolality levels (mosmol/kg), each taken relative to the initial levels before water consumption.

4. Conclusions

It has been shown that SIFT-MS provides fast and quantitative method for the determiation of urinary phenol without the need of time consuming calibration. Through the methods described in this study, we have expanded the kinetics library entry on SIFT-MS to allow accurate measurement of phenol in humid exhaled breath and urine headspace. Measurements of phenol in humid exhaled breath have been commenced and preliminary results look. This methodological step is essential to avoid overlap with DMDS and other isobaric metabolic products producing ions at *m/z* 96 that have hindered previous studies.

Having established appropriate kinetics library entries for phenol, a pilot study has been carried out of the influence of dehydration status of seven individuals on the headsapace concentration of phenol that has been suggested as a biomarker of tumours in the body. Future studies need to account for urinary creatinine concentration when investigating urinary VOCs, particularly in disease states that may affect hydration status, such as cancer.

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Notes

The authors declare no competing financial interest.

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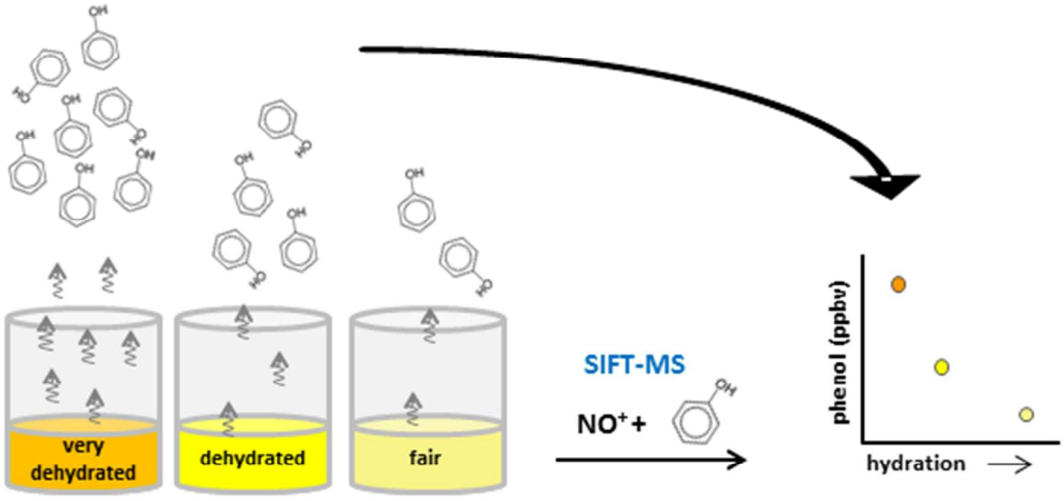
Table of content



An optimised kinetics library entry has been developed to investigate the effect of urine concentration in the course of (de)hydration on volatile metabolite - phenol.