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OPTIMIZATION OF THERMOSPRAY CONDITIONS

EFFECT OF REPELLER POTENTIAL AND VAPORIZER TEMPERATURE

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SUMMARY

Vaporizer temperature and repeller potential were optimized for five test compounds analysed by liquid chromatography–thermospray mass spectrometry. Optimum values were about the same for most compounds. The MH^+ ion intensity of one thermally labile compound was maximal at a lower vaporizer temperature than those of the more stable compounds. The repeller potential affected the abundance of ammonium adduct ions relative to the MH^+ ions. The solvent-buffer ions could be used to optimize the vaporizer temperature but not the repeller potential for the test compounds.

INTRODUCTION

Thermospray (TSP) equipment has been commercially available for only a few years but in many laboratories it has today replaced other means of interfacing liquid chromatography (LC) with mass spectrometry (MS). The increasing popularity of this new technique is a good index of its versatility and reliability. Although the TSP interface is easy to use, it is not always a simple matter to achieve high sensitivity and reproducibility.

Several parameters affect the performance of the TSP interface, *e.g.*, mobile phase composition and flow-rate, temperature settings and, on Finnigan interfaces, repeller potential. In the direct ionization (filament-off) mode, 0.1 *M* ammonium acetate in water as the mobile phase affords the best sensitivity[1,2]. If, for chromatographic reasons, it is necessary to add an organic modifier, methanol will impair the TSP performance to the least extent[2]. A correct setting of the vaporizer temperature is fundamental for the TSP ionization process[3], whereas the jet (source block) temperature seems to be less critical. The effect of the repeller potential has not previously been studied in a systematic manner.

The aim of this work was to investigate if optimum values of repeller potential and vaporizer temperature are the same for different compounds, at a given mobile phase composition and flow-rate. We also wanted to study whether acceptable conditions for the analyte can be obtained by optimizing the TSP ionization of the solvent–buffer molecules.

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EXPERIMENTAL

Chemicals

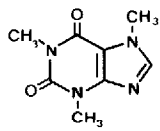
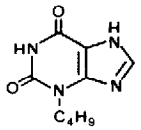
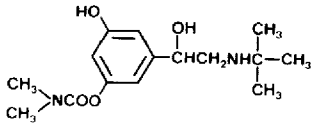
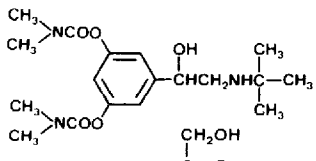
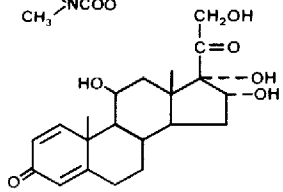
The structures of the test compounds used to optimize the TSP conditions are shown in Table I. A mixture of the test compounds, at a concentration of 20 μg/ml each, was prepared in 0.1 *M* ammonium acetate buffer (pH 5) containing 70% methanol. Ammonium acetate and acetic acid were purchased from Merck (Darmstadt, F.R.G.). Methanol of HPLC grade was obtained from Rathburn (Walkerburn, U.K.). Caffeine was obtained from Apoteksbolaget (Sweden) and 16-hydroxyprednisolone from Lark (Milan, Italy). D4030, D2439 and bambuterol were from Draco (Lund, Sweden). Water was filtered through a Milli-Q system (Millipore, Molsheim, France). The mobile phase (0.1 *M* ammonium acetate buffer, pH 5, containing 43% methanol) was filtered through a 0.22-μm Durapore filter (Millipore) and degassed with helium before use.

LC–MS

The LC equipment consisted of a Spectra-Physics 8700 pump, delivering 1.2 ml/min, a Valco pneumatic injector with a 25-μl loop and a 150 × 4.6 mm I.D. column packed with Nucleosil C_{18}, 5 μm.

TABLE I

STRUCTURES OF THE TEST COMPOUNDS

Name	*Structure*	*MH^+ ion*	*Fig. symbols*
Caffeine		195	×——×
D 4030		209	+---+
D 2439		297	□ · · · □
Bambuterol		368	○——○
16-Hydroxyprednisolone		377	△ · · · △

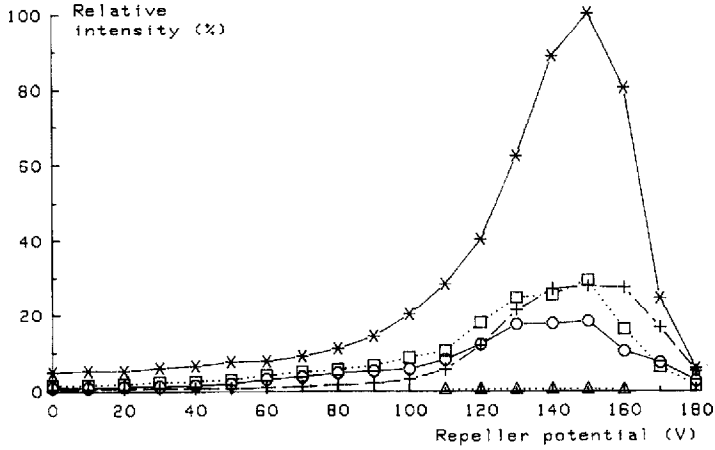


Fig. 1. Response of the test compounds as a function of repeller potential. The intensities are normalized to the highest value of *m/z* 195. The vaporizer temperature was set to 170°C and the jet temperature to 230°C. Symbols as in Table I.

A Finnigan TSP interface (without a filament) was used with a Finnigan 4500 mass spectrometer connected to an Incos data system. The vaporizer temperature was varied between 120 and 190°C and the jet temperature between 200 and 230°C. The repeller potential was measured on the PCB with a digital voltmeter (10 MΩ input impedance) and was varied in the range 0–180 V. Background ions were scanned from *m/z* 10 to 150 and spectra of the test compounds were acquired from *m/z* 150 to 450 at a rate of 2 s per scan. The ion intensities of the test compounds were measured as the peak heights on the respective mass chromatograms, after smoothing by the data system, regardless of noise and peak shape.

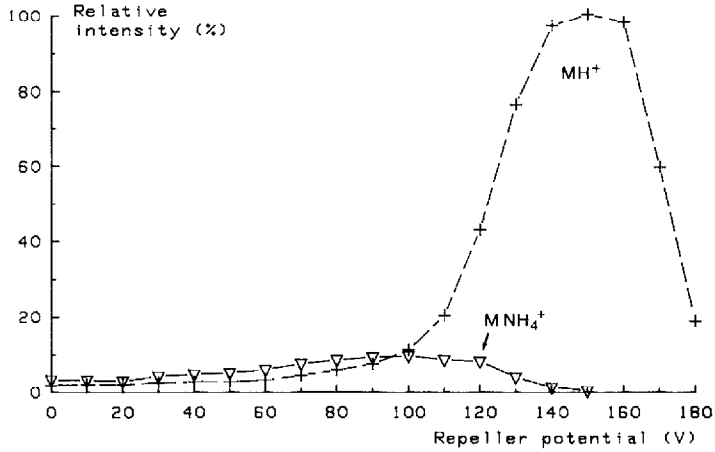


Fig. 2. Relative intensities of the protonated molecular ion and the ammonium adduct ion of D 4030 as a function of repeller potential. The intensities are normalized to the highest value of the MH^+ ion. The vaporizer temperature was set to 170°C and the jet temperature to 230°C.

RESULTS AND DISCUSSION

Effect of repeller potential

Fig. 1 shows the MH^+ ion intensities of the five test compounds plotted *versus* repeller potential. All MH^+ ions reached a maximum in the same region (130–160 V), but the response of the compounds differed considerably. Large variations in sensitivity to TSP ionization have been reported for different compounds[1,4]. As gas-phase ion–molecule reactions, similar to conventional chemical ionization with ammonia, probably play an important role in the TSP ionization process[5,6], molecules with a high proton affinity should give high sensitivity. The response of the two test compounds in this study containing a basic amino group (D 2439 and bambuterol) was not greater than that of the two non-basic xanthine derivatives (caffeine and D 4030). The gas-phase proton affinities of these compounds are not known, however.

TSP mass spectra of D 4030 recorded at different repeller potentials were completely different. The results displayed in Fig. 2 show that, depending on the repeller voltage, the intensity of the ammonium adduct ion could be changed from 0% to 180%, relative to the MH^+ ion. A similar, although not so pronounced, behaviour was found for the MNH_4^+ ion of caffeine. This effect of the repeller potential resembles to some extent the effect of the repeller in discharge ionization TSP. It was recently reported[7] that with this ionization technique the fragmentation can be enhanced by increasing the repeller potential.

A spectrum of the background ions was also highly dependent on repeller potential (Fig. 3). The only background ion maximizing in the same region as the test compounds was that at *m/z* 60. This ion is probably the MH^+ ion of acetamide, an impurity in the solvent–buffer system used[8]. The intensity of the MNH_4^+ ion of acetamide (data not shown), relative to its MH^+ ion, was found to vary with repeller

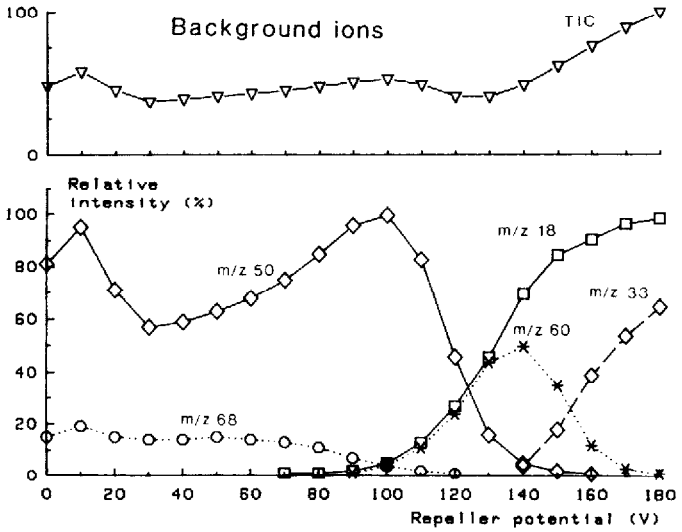


Fig. 3. Relative intensities of the solvent–buffer ions as a function of repeller potential. The intensities are normalized to the highest value of *m/z* 50. The total ion current curve is independently normalized. The vaporizer temperature was set to 170°C and the jet temperature to 230°C.

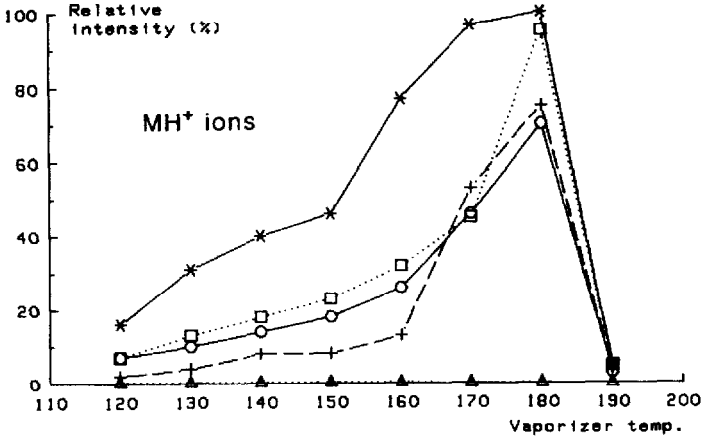


Fig. 4. Response of the test compounds as a function of vaporizer temperature. The intensities are normalized to the highest value of *m/z* 195. The repeller potential was set to 140 V and the jet temperature to 200°C. Symbols as in Table I.

potential in the same way as the corresponding pair of ions of D 4030 (Fig. 2). The data in Fig. 3 show that the solvent–buffer ion signal cannot be used uncritically to optimize TSP performance.

Effect of vaporizer temperature

The profile of MH^+ ion intensity *versus* vaporizer temperature (Fig. 4) was similar for four of the test compounds. Increasing temperature afforded higher ion intensity up to a certain point, at which a dramatic drop occurred. The fifth compound, 16-hydroxyprednisolone, behaved differently, showing only a weak MH^+ ion

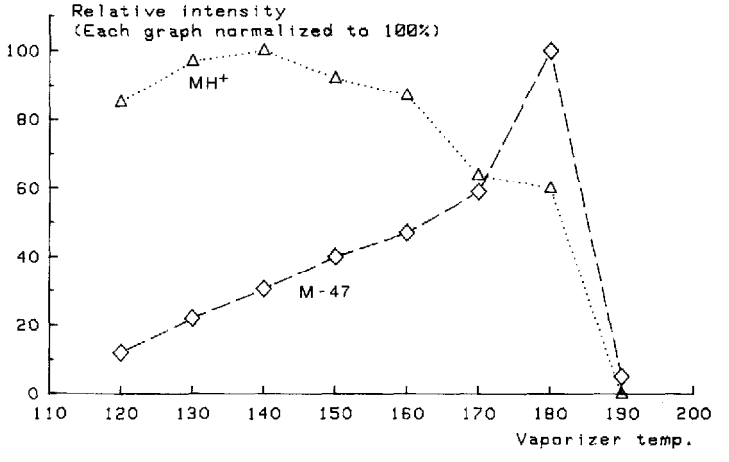


Fig. 5. Relative intensities of the protonated molecular ion and a fragment ion of 16-hydroxyprednisolone as a function of vaporizer temperature. The repeller potential was set to 140 V and the jet temperature to 200°C.

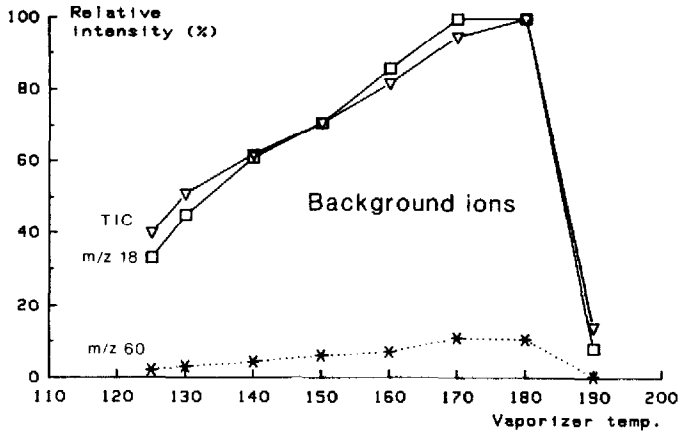


Fig. 6. Relative intensities of the solvent–buffer ions as a function of vaporizer temperature. The intensities are normalized to the highest value of *m/z* 18. The total ion current curve is independently normalized. The repeller potential was set to 140 V and the jet temperature to 200°C.

with a maximum at relatively low temperature. This thermally labile compound fragmented into an M − 47 ion (presumably $MH^+ - H_2O - CH_2O$), which maximized at about the same temperature as the MH^+ ions of the more thermally stable test compounds (Fig. 5). The intensity of the MH^+ ion, relative to the M − 47 ion, decreased from 12% at a vaporizer temperature of 120°C to only 1% at 180°C. The maximum intensity of the solvent–buffer ions was found at roughly the same vaporizer temperature as that of the stable test compounds (Fig. 6).

CONCLUSIONS

Optimum values of repeller potential and vaporizer temperature are similar for many compounds. However, the MH^+ ion intensities of thermally labile compounds seem to maximize at a lower vaporizer temperature, a higher temperature increasing the extent of fragmentation. The solvent–buffer ions can be used to optimize vaporizer temperature but not repeller potential. For the identification of unknown compounds, e.g. drug metabolites, acceptable thermospray performance can be achieved by optimization on model compounds. In quantitative analysis, when maximum sensitivity is required, optimization should be performed on the compound of interest.

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