

Observation of Charged ESI Droplets Aspirated into Commercial MS High Vacuum Systems under Analytical LC Conditions

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Introduction

Electrospray ionization (ESI) enables coupling between liquid chromatography (LC) and mass spectrometry (MS). Since it is considered a "soft" ionization technique, it is frequently used in analytical laboratories [1].

Several experimental setups have demonstrated that the use of ESI results in aspiration of charged droplets generated by the electrospray into mass spectrometers. The aspirated droplets pass through the individual vacuum stages of the instruments, causing a variety of potentially negative consequences, e.g. surface contamination [2,3].

References

- [1] Cole, R. B. (2010) *Electrospray and MALDI Mass Spectrometry. Fundamentals, Instrumentation, Practicalities, and Biological Applications*, 2nd ed.; John Wiley & Sons Incorporated: Hoboken
- [2] Markert, C.; Thinius, M.; Lehmann, L.; Heintz, C.; Stappert, F.; Wissdorf, W.; Kersten, H.; Benter, T.; Schneider, B. B.; Covey, T. R. Observation of charged droplets from electrospray ionization (ESI) plumes in API mass spectrometers, *Analytical and bioanalytical chemistry*, **2021**, *413*, pp. 5587–5600
- [3] Kang, Y.; Schneider, B. B.; Covey, T. R. On the Nature of Mass Spectrometer Analyzer Contamination, *Journal of the American Society for Mass Spectrometry*, **2017**, *28*, pp. 2384–2392

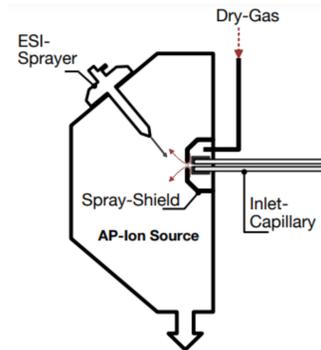


Fig. 1: Scheme of ES-Ion Source

Methods

1. Analyte

- Reserpine, ≥99.0 % HPLC (Sigma Aldrich)

2. LC-System

- Agilent Technologies
- Binary Pump Series 1200

3. Mass spectrometry

- Bruker Daltonic
- AmaZon ETD quadrupole Ion Trap
- Apollo Ion source (ESI)

4. Solvents

- Acetonitrile, ≥ 99.8 % HPLC (Fisher scientific)
- Ethanol, ≥ 99.8 % HPLC (Fisher scientific)

Variation of the liquid flowrate

Impact of different LC-flowrates

- Comparison of the flowrates: 100, 50, 20 $\mu\text{L}/\text{min}$
- The impact on the total intensity curve as shown in Fig. 2 is significant. The TIC is stable in some time slots (e.g. slot 4), however in others it displays an instable behavior. For example in slot 3, flowrates of 100 and 50 $\mu\text{L}/\text{min}$ present a different curve progression under otherwise identical conditions.
- The recorded isolation and fragmentation spectra, that consider the effect of different accumulation times, indicate that the release of the analyte ion is dependent on both the flow rate and the AccuTime

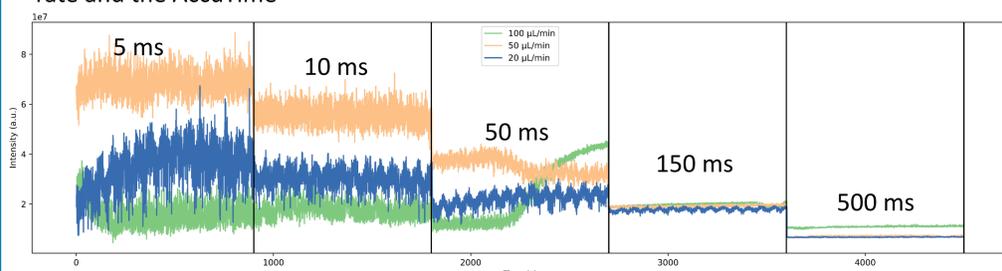


Fig. 2: Chromatogram of the TIC from a Reserpine (EtOH:H₂O:CH₂O₂, v/v/v, 50+50+0.1) measurement using different LC-flowrates, segmented in various time slots while using different accumulation times: 5, 10, 50, 150, 500 ms per 15 min slot

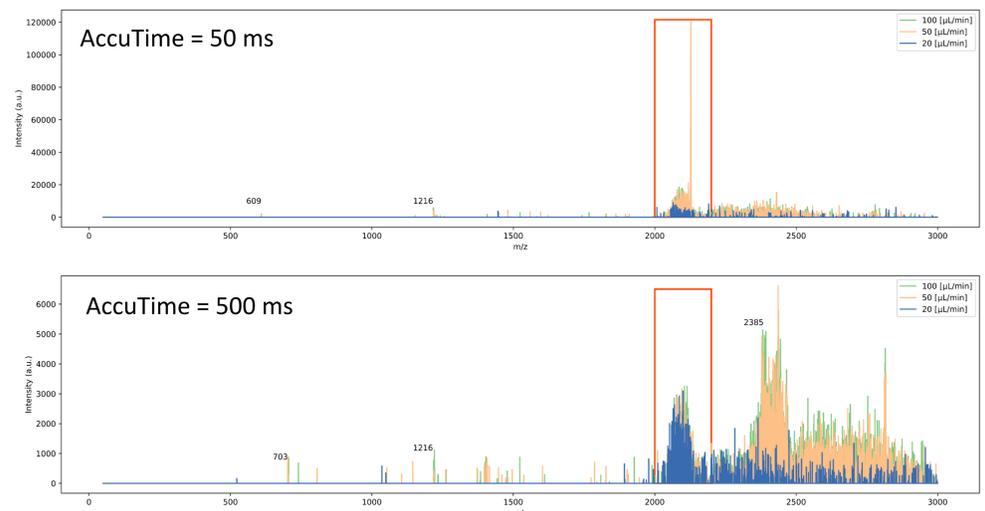


Fig. 3: Mass spectra of Reserpine (EtOH:H₂O:CH₂O₂, v/v/v, 50+50+0.1) with an isolation at $m/z = 2100$ with a width of 84 in positive mode. The signal pattern is clearly depended on the liquid flowrate and the accumulation time

Solvent dependency - Isocratic elution

- Variation of constant solvent ratio using different organic solvents for long-term observations
- When comparing the effect of solvent choice under the same conditions:
 - The overall droplet signature ($m/z > 2000$) intensity increases with ethanol as solvent
 - The general signal structure is similar but exhibits notable changes in dependence on the solvent
- Upon increasing the amount of organic solvent the intensity of the droplet signature ($m/z > 2000$) increases, but the effect is less pronounced when using ethanol instead of acetonitrile

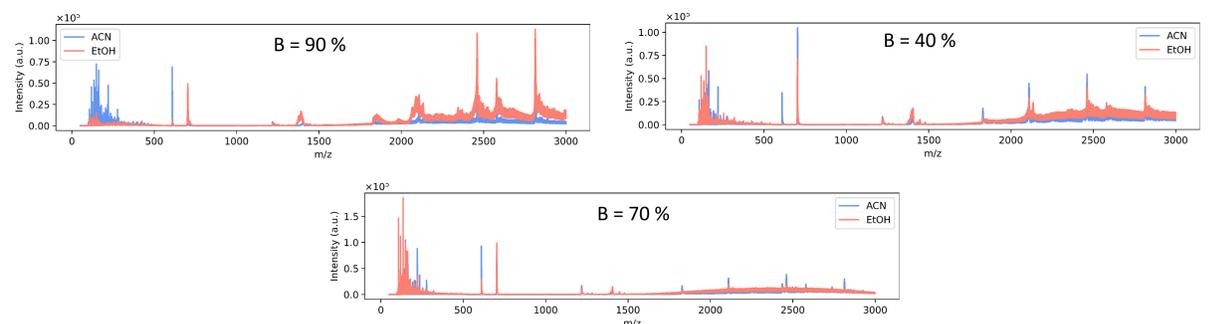


Fig. 4: Mass spectra of different isocratic elution with reserpine as analyte and using EtOH or ACN as organic solvent B.

Solvent dependency - Gradient elution

- Continuous change of the concentration of the organic eluent during the injection
- Overview gradient with a linear increase in the percentage of organic solvent from 5 to 95%
- By increasing the amount of acetonitrile, the intensity in the droplet signature region ($m/z > 2000$) increases
- The intensity of the analyte ($m/z = 609$) decreases, an adduct signal ($m/z = 703$) appears
- During re-equilibration the intensity of the signal complex with $m/z > 2000$ decreases, but the initial state is not recovered

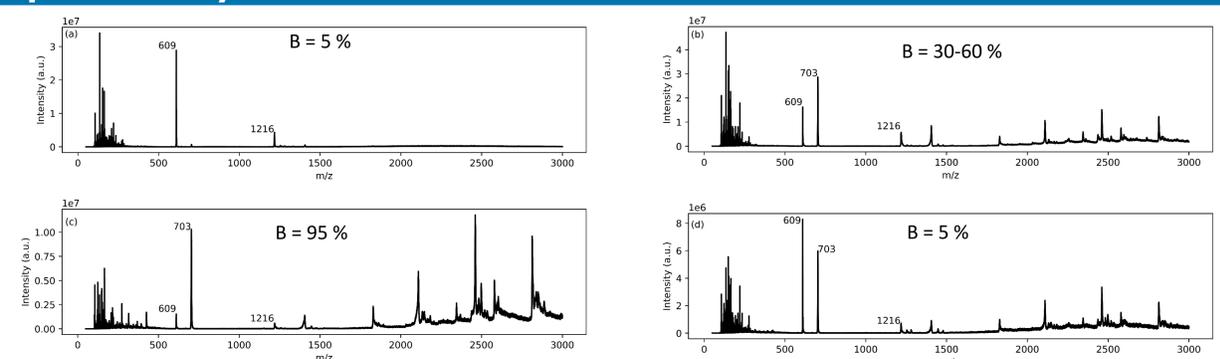


Fig. 4: Mass spectra of the overview gradient with reserpine as analyte and acetonitrile as organic solvent B. (a) Plateau of 5%-B for 5 min; (b) Linear increase within the gradient of 30-60%-B; (c) Plateau for the flush-out at 95%-B; (d) Re-equilibration (5%-B).

Conclusions

- Increasing of the LC-flowrate leads to more intense droplet signatures, resulting from the introduction of larger amounts of solvent into the system
- Reserpine isolation measurements (see Fig. 3) reproduced the results of Yang et al. [2] and Markert et al [3], in which analyte ions are released by collision-induced dissociations in the higher m/z range (>2000).
- The solvent dependency was investigated in order to estimate potential consequences for analytical applications. Here, different isocratic and gradient elutions have been considered, showing a clear dependence on the solvent choice and the solvent component ratios.