From measuring ionization efficiencies to ion source design – taming the electrospray ionization

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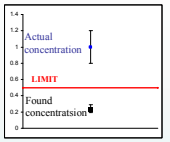
Matrix effects in ESI

Matrix effect is known to be the biggest drawback of the ESI/MS analyses. Therefore a large number of different approaches – both for reducing and correcting for it – have been proposed and used in LS/ESI/MS literature.



Matrix effect has been investigated as the function of dilution. It is demonstrated that in some cases dilution can eliminate matrix effect, but often it is just reduced. Based on these findings we propose a new quantitation method based on consecutive dilutions of the sample. If dilution does not fully eliminate the matrix effect (for excample quantitation limit might be reached before, Figure A.1) extrapolation to matrix-free solution should be made. This approcache has been validated for 4 pesticides in 5 matrices at 2 concentration levels. We demonstrate that in terms of accuracy of the obtained results the extrapolative dilution approach works distinctly better than simple sample dilution.For more information see ref 4.

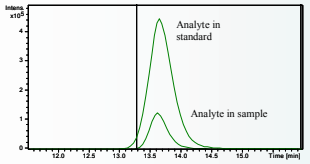
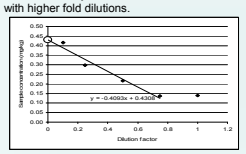
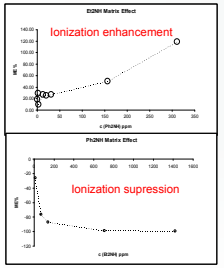


Figure A.1 For 0.49 mg/kg aldicarb in apple the dilution decreases the matrix effect – the calculated analyte concentration increases with higher fold dilutions.





Gas phase processes

$Ph_2NH_2^+ + Et_2NH \rightarrow Ph_2NH + Et_2NH_2^+$

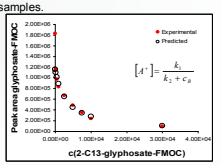
Gas phase processes occur if a protonated compound with a low proton affinity but with high ionization efficiency (such as diphenylamine) donates proton to a stronger gas phase base (for example diethylamine).

Figure A.2 Diethylamine supresses the signal of diphenylamine (on the right) at the same time showing itself ionization enhcamet (on the left).

Supression of isotope labelled compounds

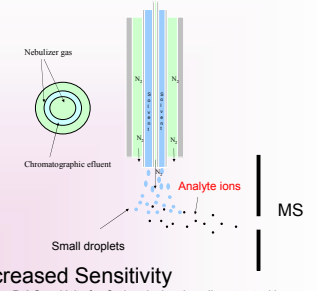
On the otherhand protonated compounds also compeat for the surface of the droplets. This is also observed for analyte and its isotope labelled analogue. It has been observed on the excample of glyphosate-FMOC and 2-C^{13}-glyphosate-FMOC that even ver similar compounds supress eachother.

Figure A.3 Change of glyphosate-FMOC MS signal while changing the concentration of 2-C^{13}-glyphosate-FMOC concentration in the samples.



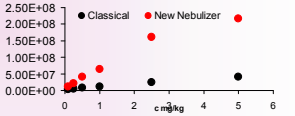
Enhancing Ionization via novel nebulizer

A novel electrospray nebulizer has been designed for electrospray mass spectrometry, which includes an additional nebulization gas capillary inside the liquid capillary. We demonstrate that this design offers significantly enhanced ionizationefficiency compared to the classical electrospray nebulizers and as a result leads to improved sensitivity (by 3 to 10 times) and decreases the detection limit (by up to 250 times, on an average 8 times). We see the current results as the first step in the design of ESI nebulizers potentially offering improved sensitivity and higher robustness. Possible future developments would include optimization of the dimensions of the capillaries as well as testing the nebulizer for other matrices and analytes.



Increased Sensitivity

Figure B.1 Sensitivity for Carbendazime in galic extract with classical nebulizer and with the novel nebulizer.



The nebulizer has been tested for pesticides in fruits and vegetables as well as for farmaceuticals in blood serum.

Reduced LoD values

Table B.1 LoD values together with the S/N ratios (in brackets) for two different nebulizer designs (in µg/kg).

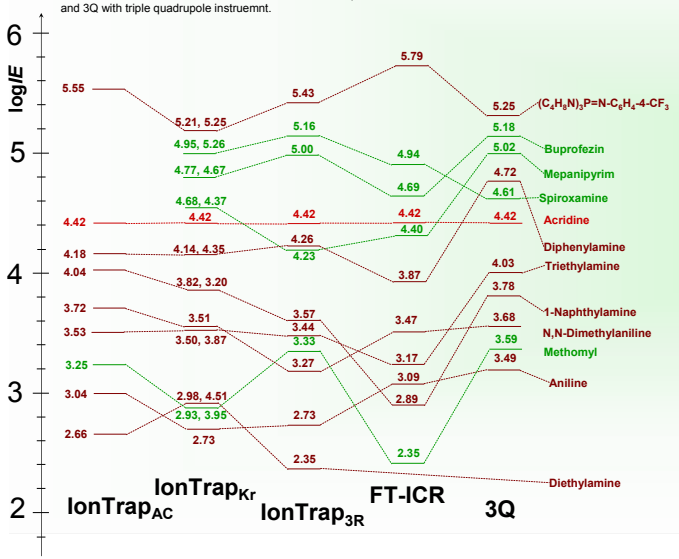
	Classical			New Nebulizer		
	Solvent	Apple extract	Garlic extract	Solvent	Apple extract	Garlic extract
Carbendazim	10.0 (21)	NA	25.0 (7.1)	5.0 (18)	NA	0.1 (7.3)
Thiabendazole	1.0 (9.2)	1.0 (12)	25.0 (17)	0.2 (8.9)	0.1 (5.9)	0.2 (6.3)
Imazalil	1.0 (6.9)	1.0 (16)	25.0 (6.9)	0.2 (8.0)	0.1 (7.9)	25.0 (22)
Methiocarb	50.0 (75)	50.0 (43)	>50.0	5.0 (7.9)	10.0 (5.8)	>50.0

References:

1. M. Oss, A. Kruve, K. Herodes, I. Leito "Electrospray Ionization Efficiency Scale of Organic Compounds" *Anal Chem* 82 (2010) 2865
2. I. Leito, K. Herodes, M. Huopolainen, K. Virro, A. Künnapas, A. Kruve, R. Tanner "Towards the electrospray ionization mass spectrometry ionization efficiency scale of organic compounds" *Rapid Commun Mass* 22 (2008) 379
3. A. Kruve, A. Künnapas, K. Herodes, I. Leito "Matrix effects in pesticide multi-residue analysis by liquid chromatography-mass spectrometry" *J Chrom A* 1187 (2008) 58
4. A. Kruve, K. Herodes, I. Leito "Extrapolative dilution as an effective quantization method to account for matrix effects in pesticides LC/ESI/MS analyses" *Analytica Chimica Acta* 651 (2009) 75

Ionization Efficiency Measurements

Table C.1 Results on log*IE* scale validation. Each column represents a different setups.IonTrapAC refers to the scale publised in ref 1, IonTrapKr refers to the measurements with the same intstrument from 2010 to 2012, IonTrap3R refers to the same instrument with different ESI nebulizer, FT-ICR refers to the measurements with ICR instrument and 3Q with triple quadrupole instruemnt.



Ionization efficiency (IE) of different compounds in electrospray ionization (ESI) source differs widely, leading to widely differing sensitivities of ESI-MS to different analytes. An approach for quantifying ESI efficiencies (as log*IE* values) and setting up a self-consistent quantitative experimental ESI efficiency scale of organic compounds under predefined ionization conditions (ionization by monoprotonation) has been developed.

Combining the *RIE* values of pairs of compounds it was possible to establish an *ionization efficiency scale*. The *relative ionization efficiency (RIE)* of a compound B_1 relative to B_2 is:

$$RIE(B_1/B_2) = \frac{IE(B_1)}{IE(B_2)} = \frac{K'_1}{K'_2} = \frac{R_1 C_2}{R_2 C_1}$$

Using this approach a log*IE* scale containing 62 compounds of different chemical nature and ranging for 6 orders of magnitude has been established.

Also the scale has been validated over 4 different instrumental setups using 12 compounds. The IE data from different instruments seem to indicate that the log*IE* parameter measured according to the proposed procedure is a universal parameter across ion sources and instruments provided that certain instrumental conditions are similar.

The log*RIE* values have been correlated with several physicochemical parameters. A model describing the dependence of log*IE* on p*K*a and logarithm of the molecular volume (logMV) was found. However, several other physico-chemical parameters may also be influential, but their influence may be masked by non-negligible correlation between them and p*K*a or logMV.

$$\log IE^s = (0.3941 \pm 0.0752)\, pK_a^{\ s} + (0.6599 \pm 0.0752) \log MV^s$$

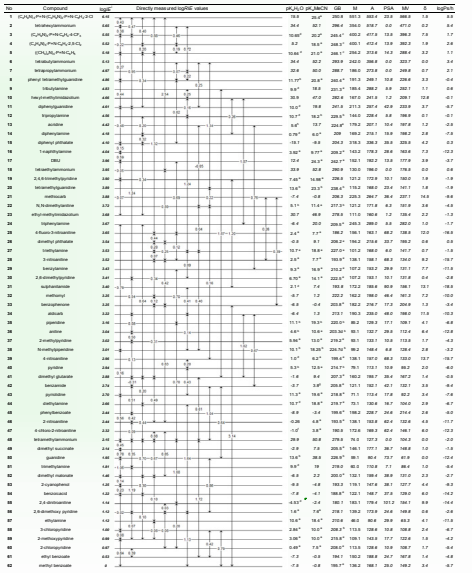



Table C.2 Studied compounds, their obtained log*IE* values, scale containing 116 measurement results, pKa value in water (pKa H2O), pKa value in acetonitrile (pKa MeCN), gas phase basicity (GB) (kcal/mol), molecular mass of ion (M) (g/mol), molecular area of ion (A) (Å2), polar surface area of ion (PSA) (Å2), molecular volume of ion (MV) (Å3), dipole moment of ion (δ) (debye) and log of distribution coefficient of solvent/hexane for ionic form of the compound (logPs/h). Values in italic are computational.