DESI-MS
in food contaminants control

Michel Nielen, Hans Mol

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Outline

Introduction

Principle

Experimental parameters

Instrumentation

Food contaminant applications

Summary/outlook

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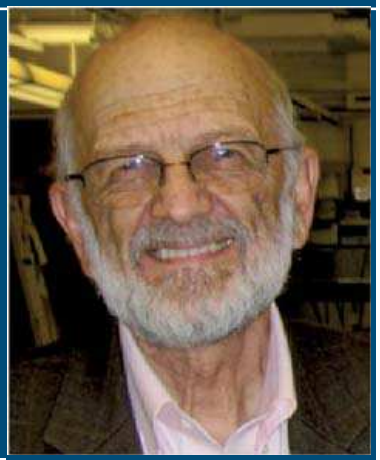
DESI-MS

Desorption electrospray ionization

First ambient MS technique invented by Graham Cooks from Purdue University, USA

Mass spectrometry



Mass Spectrometry Sampling Under Ambient Conditions with Desorption Electrospray Ionization

Zoltán Takáts, Justin M. Wiseman, Bogdan Gologan, R. Graham Cooks*

Science 306, 471 (2004)

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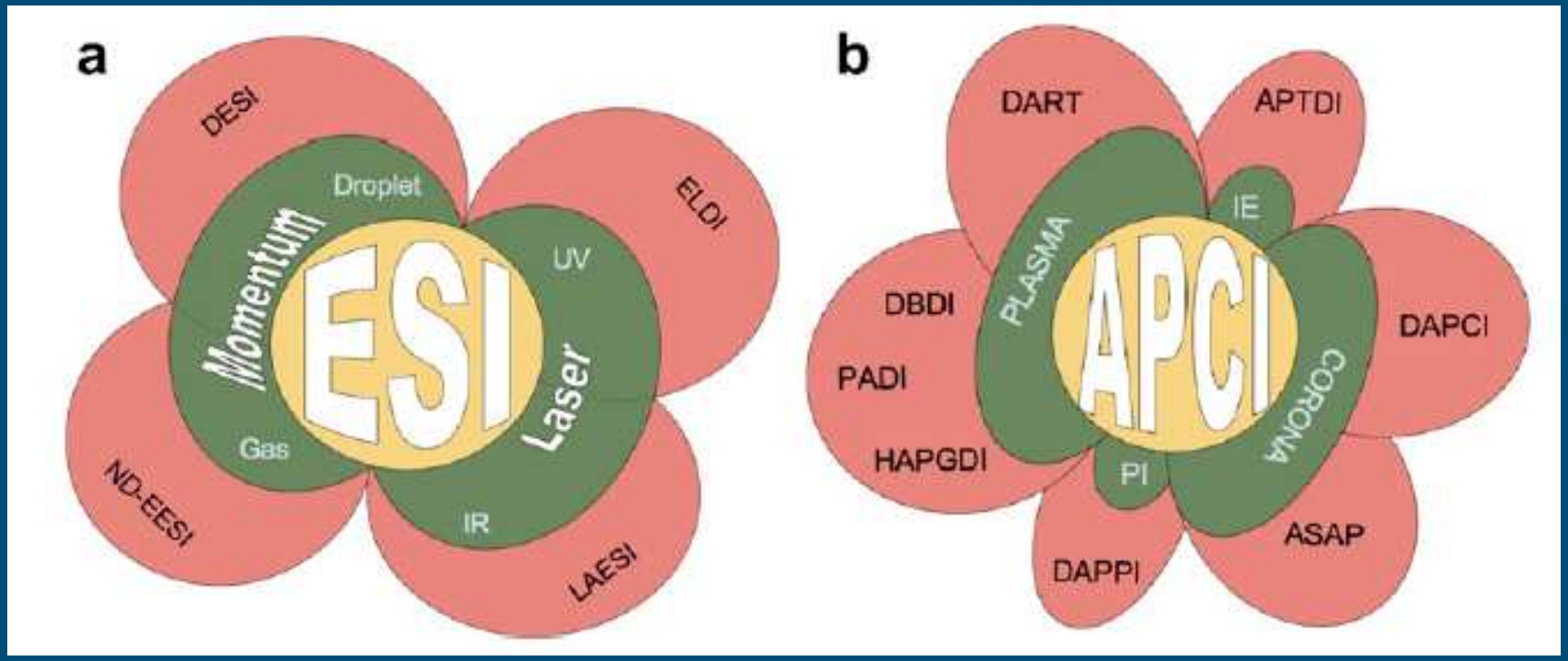
Ambient MS techniques



Venter, Nefliu, Cooks, Trends in Anal. Chem. 27 (2008) 284-290

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Ambient MS

Table 1 Chronology and perceived impact of developments in ambient ionization MS

Weston, Analyst, 2010, 135, 661-668

Method name	Acronym or abbreviation	Year of introduction	Research papers (papers/year)[a]
Desorption electrospray ionization	DESI[1]	2004	188 (31)
Surface sampling probe	SSP[20]	2004	5 (1)
Direct analysis in real time	DART[2]	2005	65 (16)
Atmospheric solids analysis probe	ASAP[21]	2005	7 (1.4)
Electrospray laser desorption ionization	ELDI[22]	2005	6 (1.5)
Fused droplet electrospray ionization	FD-ESI[23]	2005	2 (0.5)
Direct atmospheric pressure chemical ionization	DAPCI[24]	2005	89 (22)
Matrix-assisted laser desorption electrospray ionization	MALDESI[25]	2006	8 (2.7)
Jet desorption electrospray ionization	JeDI[26]	2006	1 (0.3)
Extractive electrospray sonization	EESI[27]	2006	22 (7)
Desorption sonic spray ionization	DeSSI[28]	2006	2 (0.7)
Atmospheric pressure thermal desorption ionization	APTDI[29]	2006	3 (1)
Helium atmospheric pressure glow discharge ionization	HAPGDI[30]	2006	1 (0.5)
Plasma-assisted desorption ionization	PADI[31]	2007	1 (0.5)
Dielectric barrier desorption ionization	DBDI[32]	2007	2 (1)
Neutral desorption extractive electrospray ionization	ND-EESI[33]	2007	5 (2.5)
Laser diode thermal desorption	LDTD[34]	2007	1 (0.5)
Laser ablation electrospray ionization	LAESI[35]	2007	1 (0.5)
Desorption atmospheric pressure photo-ionization	DAPPI[36]	2007	2 (1)
Infra red laser ablation electrospray ionization	IR-LAESI[37]	2008	7 (3.5)
Flowing atmospheric-pressure afterglow	FAPA[38]	2008	2 (2)
Easy ambient sonic spray ionization	EASI[39]	2008	5 (5)
Remote analyte sampling transport and ionization relay	RASTIR[40]	2008	1 (1)
Laser ablation flowing atmospheric-pressure afterglow	LA-FAPA[41]	2008	5 (5)
Low temperature plasma	LTP[42]	2008	7 (7)
Desorption electrospray metastable-induced ionization	DEMI[43]	2009	1 (–)
Liquid micro-junction surface sampling probe/electrospray ionization	LMJ-SSP/ESI[44]	2009	3 (–)
Surface activated chemical ionization	SACI[45]	2009	1 (–)
Single particle aerosol mass spectrometry	SPAMS[46]	2009	1 (–)

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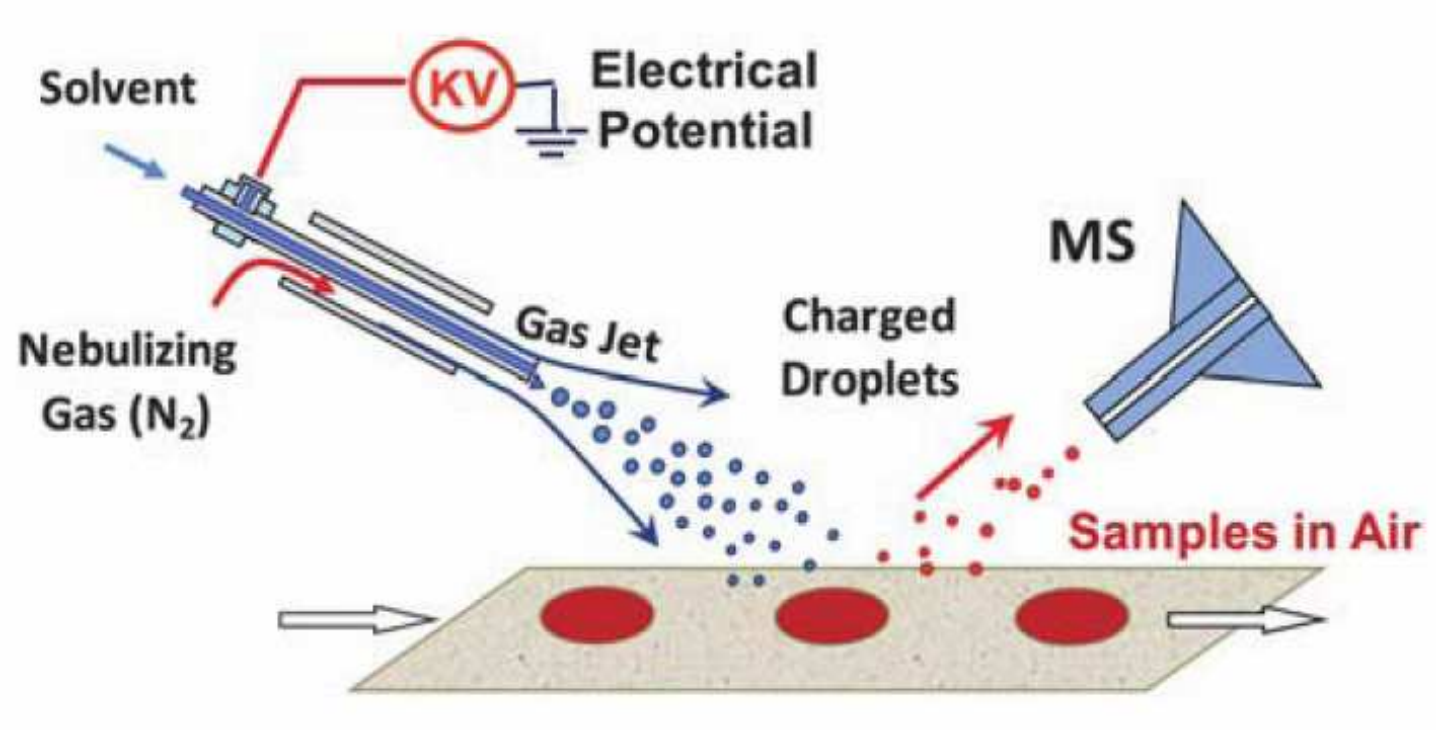
DESI: principle and processes

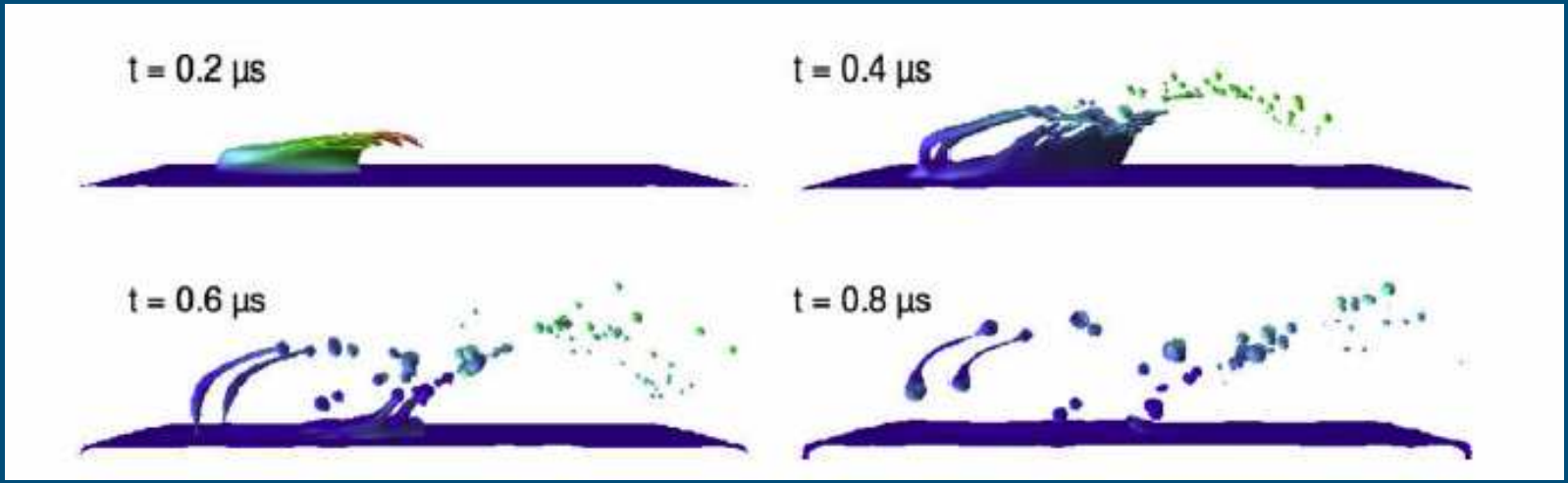


Ifa et al, Analyst, 2010, 135, 669–681

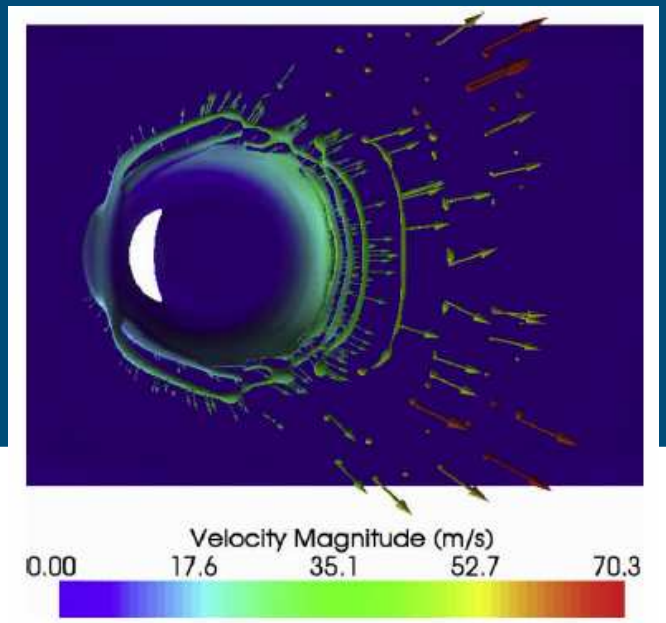
From surface deposit to ion:

1. Formation of charged primary droplets by electrospray source
2. Flight of droplets to surface, wetting of surface, dissolvation
3. Collision of charged droplets with surface => smaller droplets
4. Takeoff of secondary droplets, ablated material, free ions
5. Transport through atm. pressure interface
6. Shrinking of droplets, electrostatic fission => free ions

Formation of secondary droplets



Costa, Cooks, Chemical Physics Letters 464 (2008) 1–8



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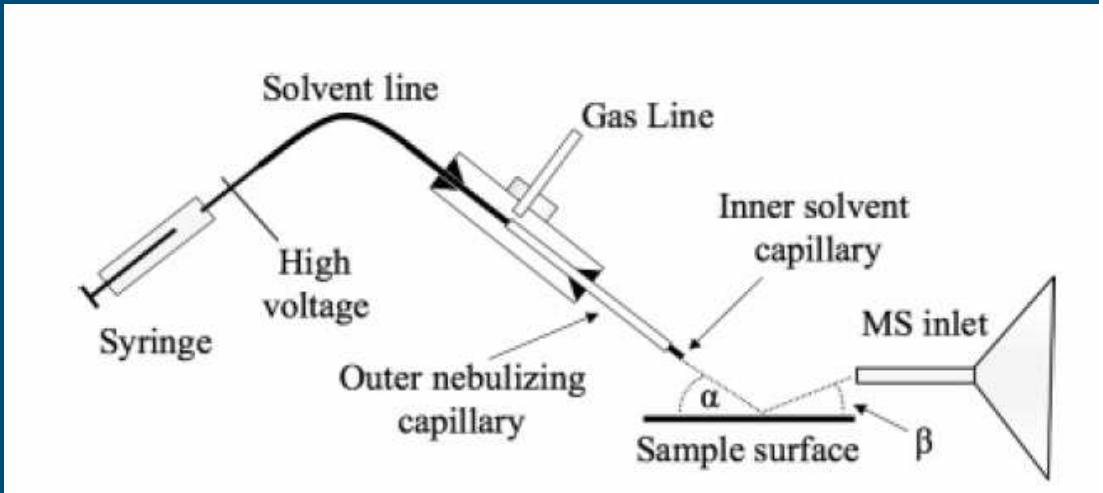
Experimental parameters

- Solvent
- Solvent flow
- Gas flow
- Spray angle
- Capillary voltage
- Distance to sample surface
- Angle ion collection MS
- Sample surface
- Distance to MS inlet
- MS parameters (incl. source temp)



Venter et al, Anal. Chem. 2006, 78, 8549-8555

Solvent and spray

Dissolution of analyte in microdroplets / solvent film

Ionization; similar to LC-ESI-MS solvents
$\Rightarrow$ MeOH or ACN with water/acid

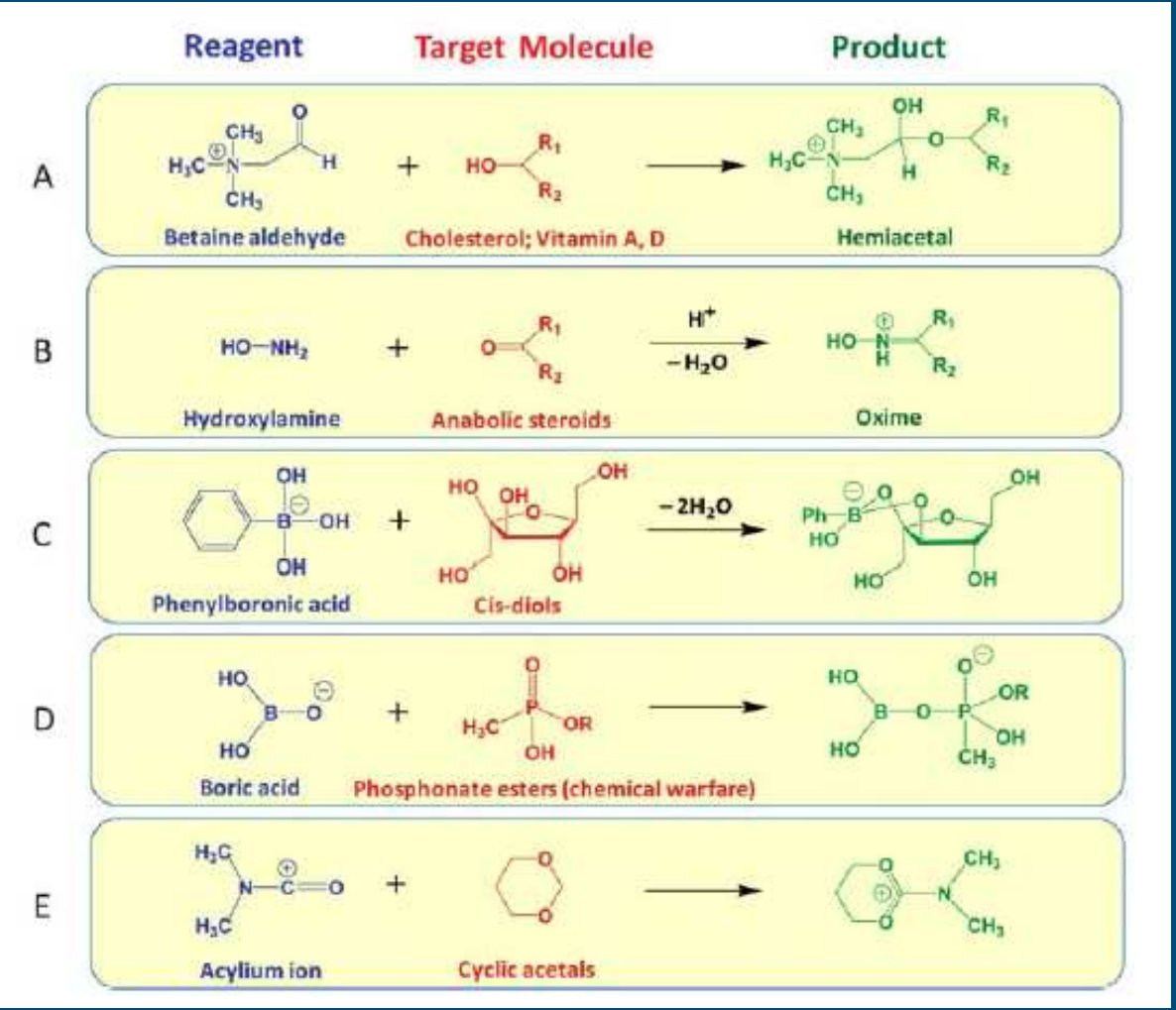
Option to add reagents (reactive DESI)

Flow rate: 1-5 µl/min

Nebulizer gas: 8-40 L nitrogen/min

Spray droplets: ≤ 10 µm (2-4), v ≥ 100 m/s (120)

Reactive DESI



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Ifa et al, Analyst, 2010, 135, 669–681

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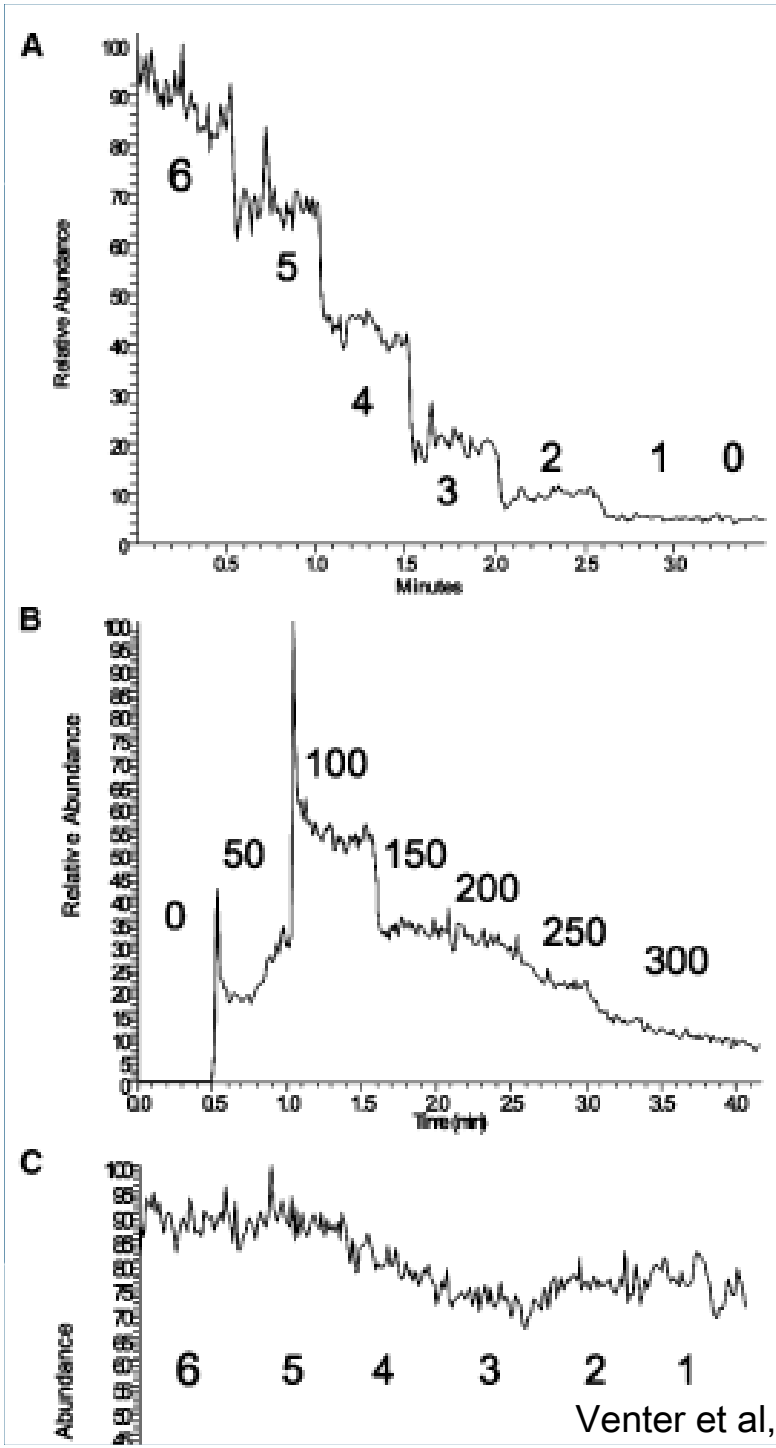


Spray voltage (kV)

Higher V => more charges on droplet surface

Levels off around 5 kV (=> default)

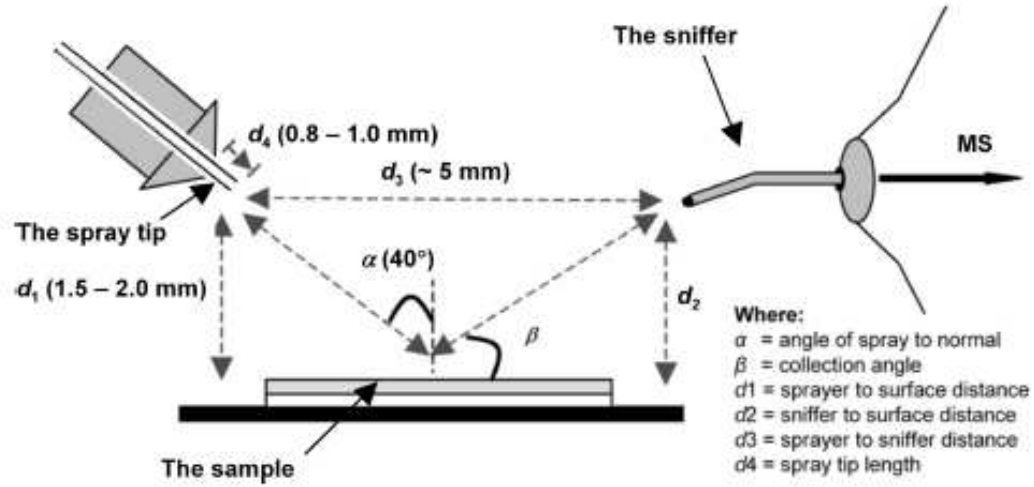
Nebulizer gas pressure (psi)

Solvent flow rate µl/min

Venter et al, Anal. Chem. 2006, 78, 8549-8555

Geometry

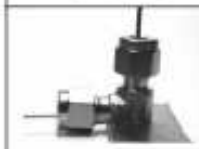
Standard configuration DESI sources



Green et al, Anal. Chem. 2009, 81, 2286-2293

α = 25-80°
β = ~5-10°
Spray tip to surface= 1-10 mm
Surface to MS inlet = 1-5 mm

Alternative configurations

Configuration	Incident/Collection angle	Mean Rhodamine intensity*
	90°/90°	1546±630
	90°/10°	739±250
	50°/10°	1375±510
	45°/45°	2974±1040
	50°/10°(Open)	1490±525

Venter et al, Anal. Chem. 2007, 79, 6398

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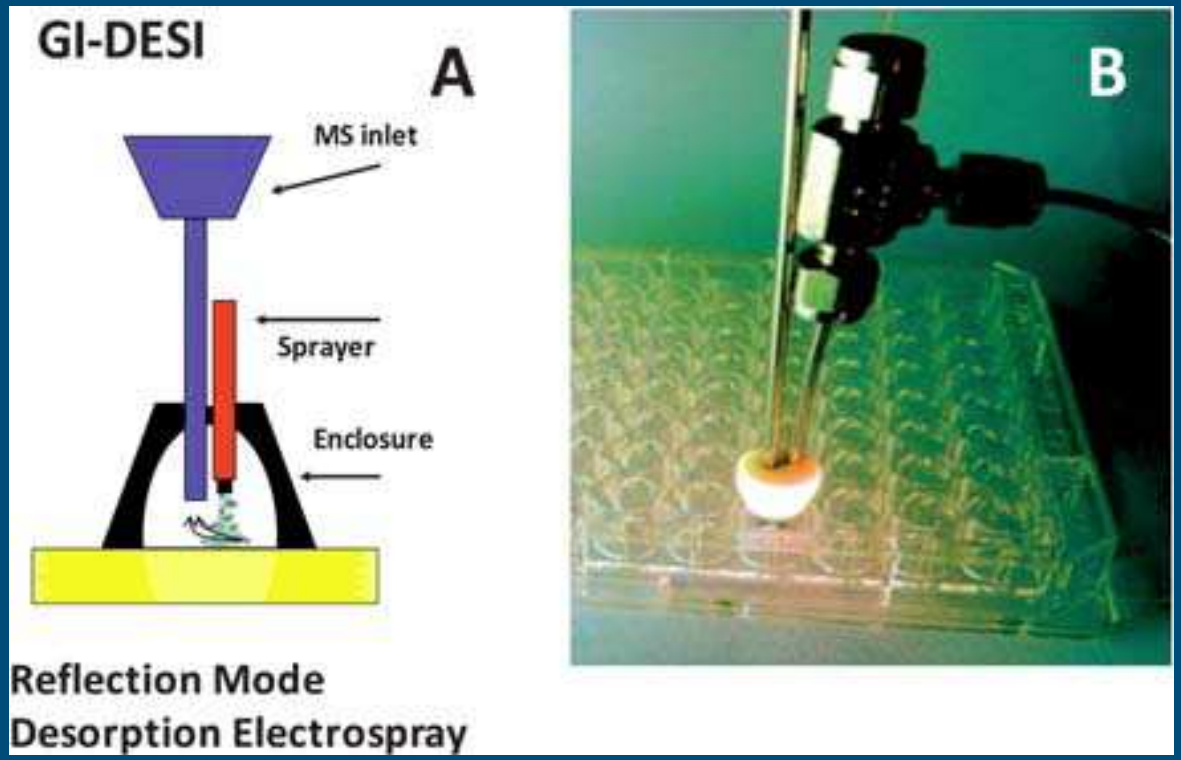
Geometry independent configurations



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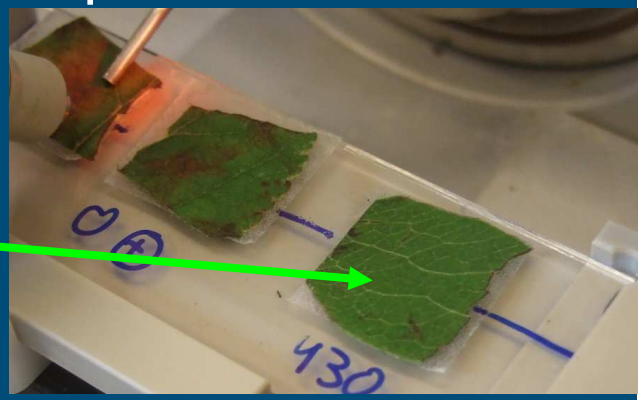
Sample surface (substrate)

Wettability: solvent formation/dissolution
Electroconductivity: more charge maintained by substrate, more charge in sec. droplets

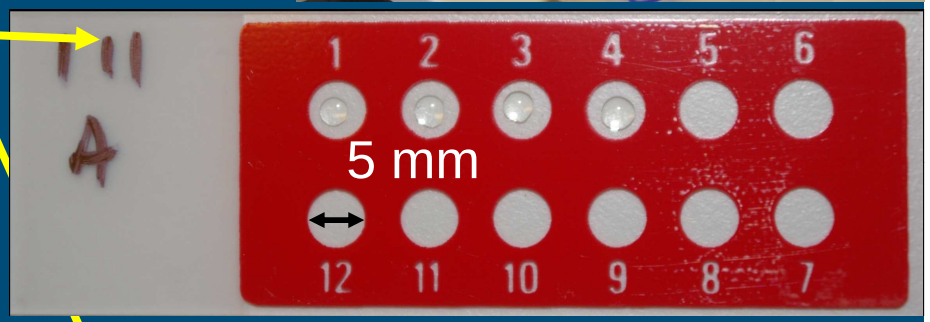
Surfaces:

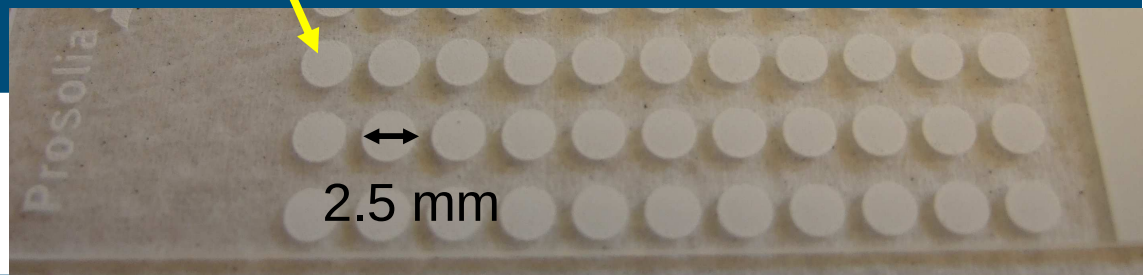
Sample itself

Pear leaf



Substrates for liquids/extracts:
- Glass
- PTFE (teflon)
- PMMA (polymethylmethacrylate)
- Filter paper
- TLC plates





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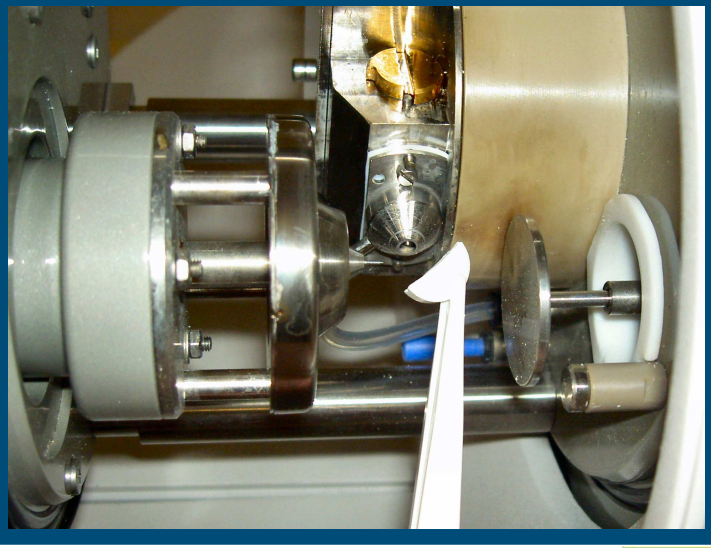
DESI, instrumentation

In principle…….you can misuse a Z-source….

Paracetamol



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DESI, instrumentation

Ion source assembly

OmniSpray ion source

Prosolia Inc.

Mass spectrometer

Agilent Technologies

Applied Biosystems

MDS SCIEX
Science advancing health

BRUKER DALTONICS

Thermo
ELECTRON CORPORATION

Waters

MICROMASS
MS TECHNOLOGIES

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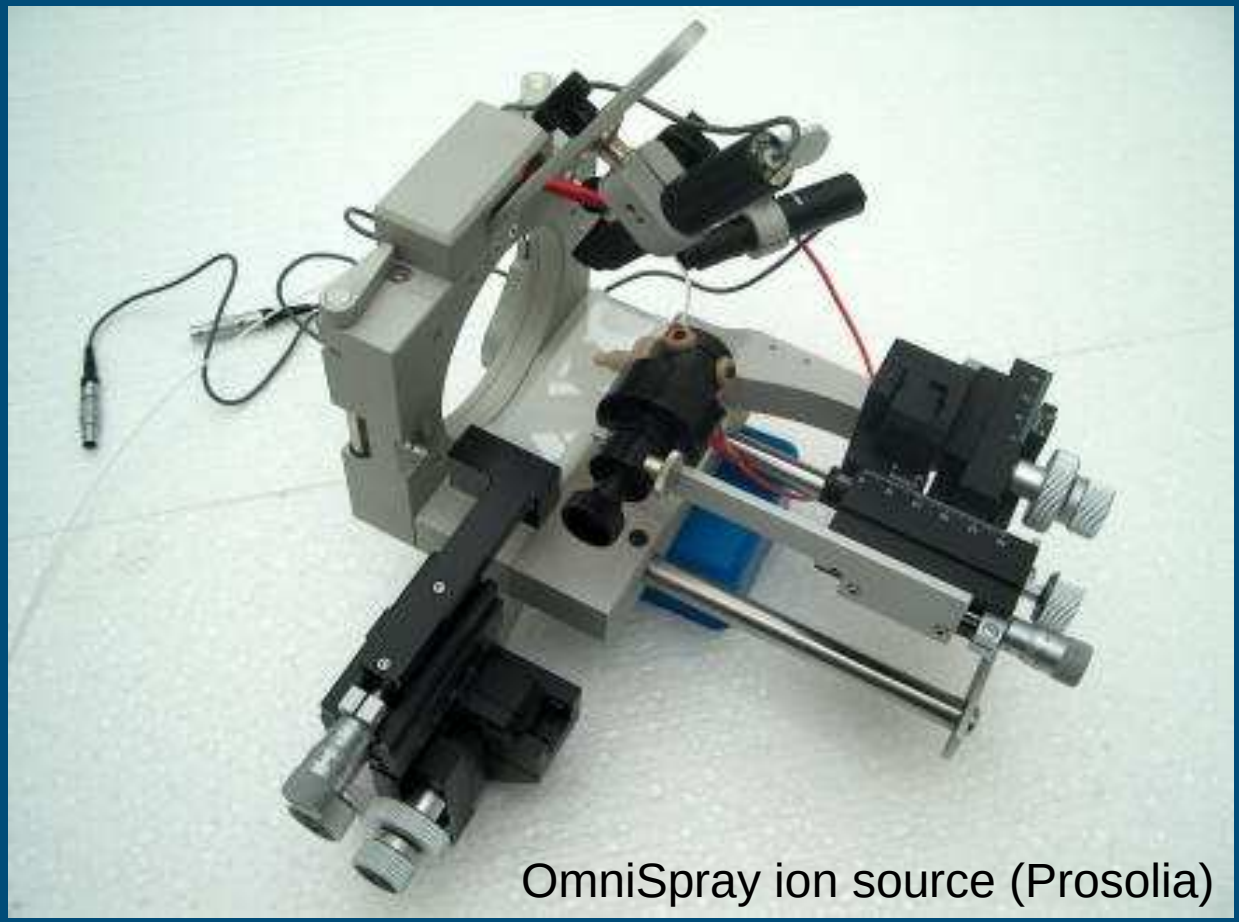
DESI, instrumentation

Top view DESI source assembly



OmniSpray ion source (Prosolia)

DESI-MS/MS (LXQ, linear ion trap)

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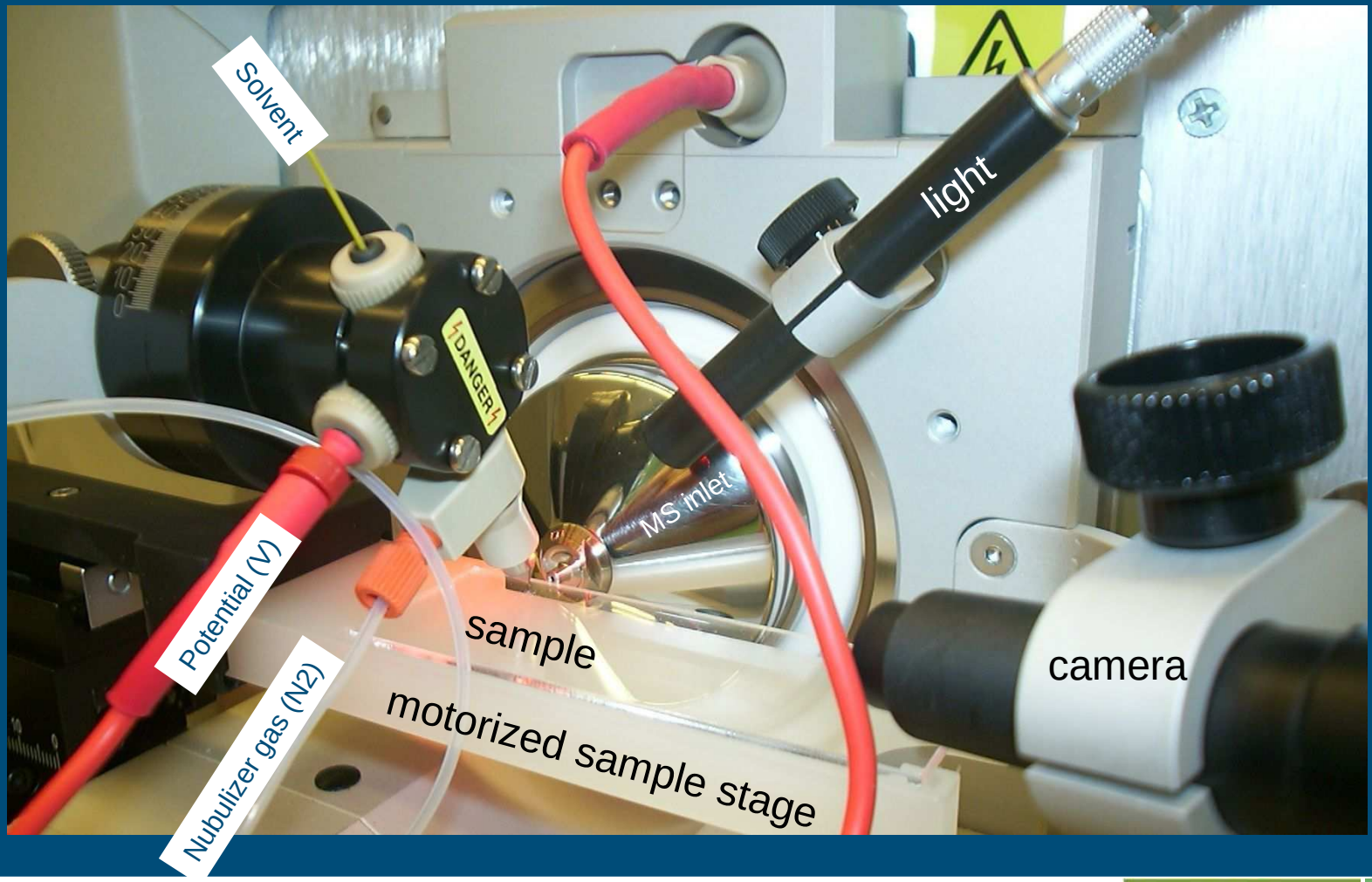
DESI, instrumentation



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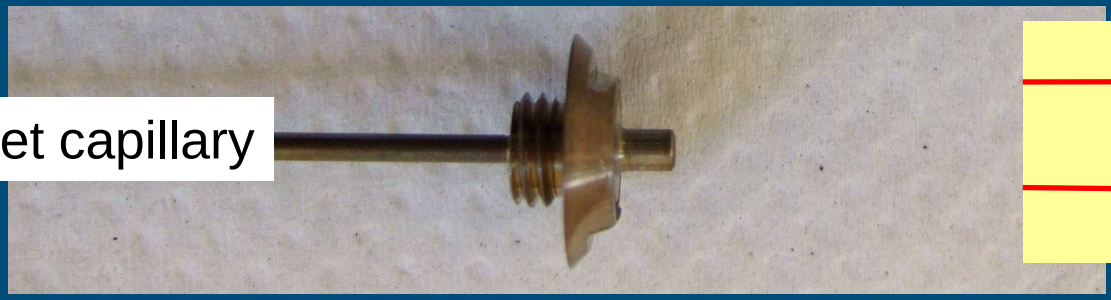
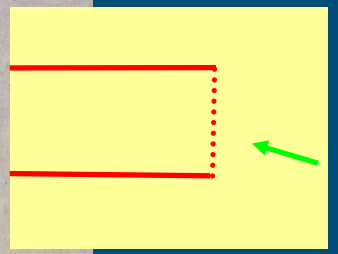
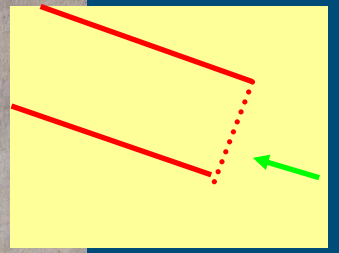
DESI, MS inlet (sniffers)

Standard LXQ MS inlet capillary

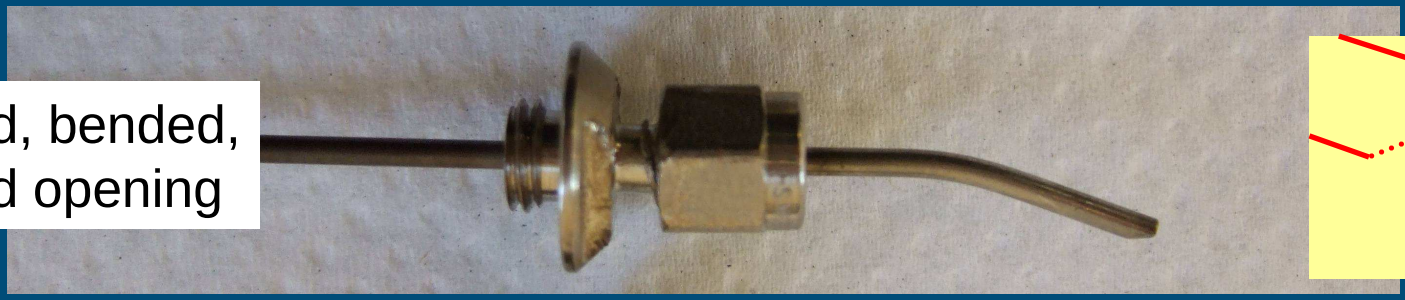


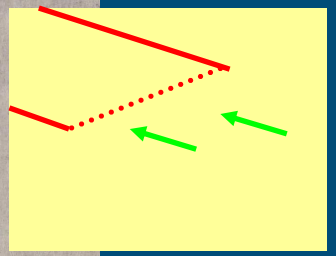


Extended, bended



Extended, bended, enlarged opening





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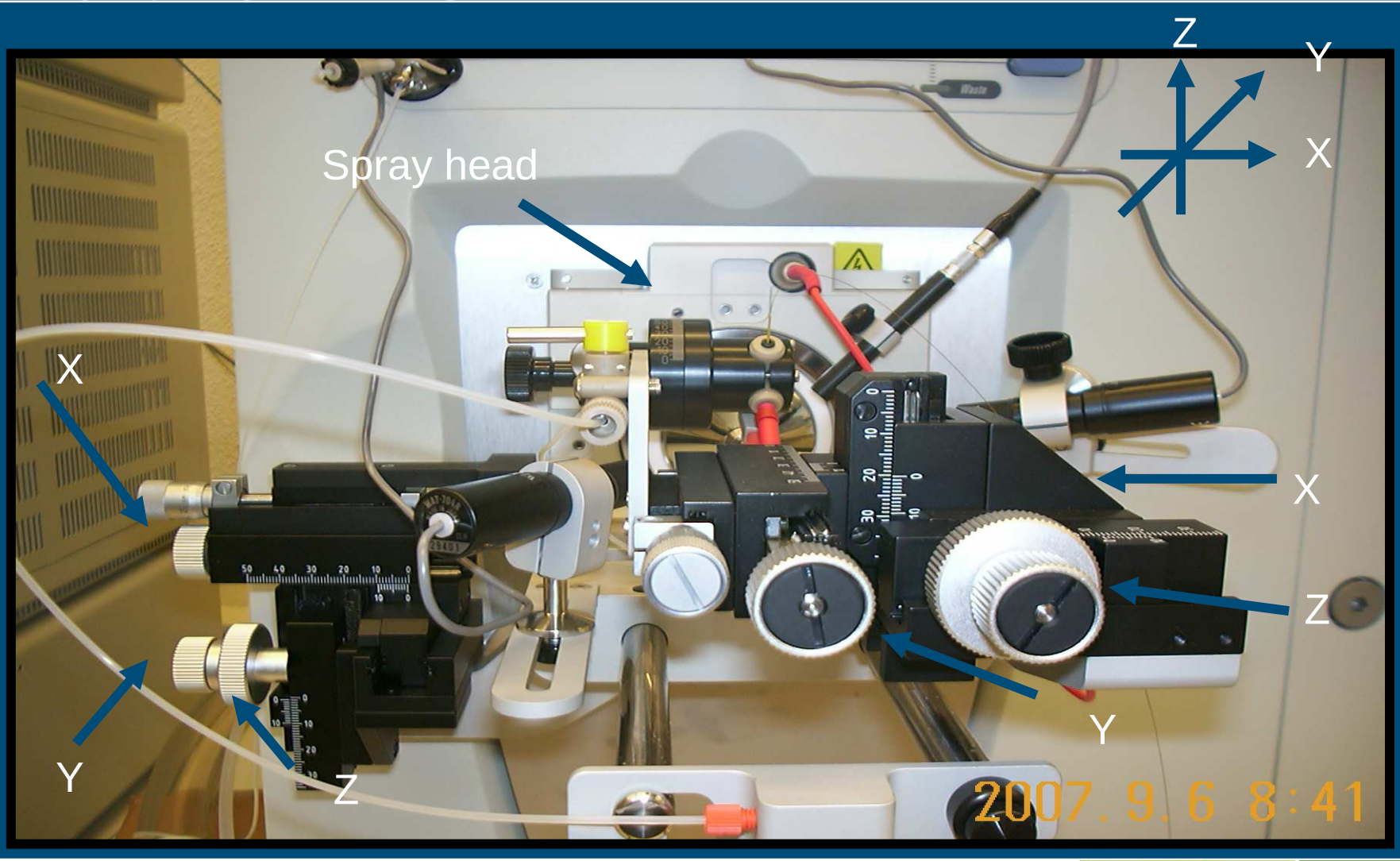
Front view DESI



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DESI applications

DESI and related ESI approaches by far most utilized ambient MS technique*

Rapid analysis pharmaceutical product
Explosives
Biological imaging
Forensic imaging of inks
Illegal and counterfeit drugs
Drug metabolites in biological matrices
Chemical warfare agents
Textiles
Peptides and proteins
Proteomics
Metabolomics
Plants / natural products
Food contaminants
…….

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*Weston, Analyst 135 (2010) 661-668

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DESI in food contaminants control

Consideration MRL verification
⇒ MRLs expressed in mg/kg whole product
⇒ requirements minimum sample size

Test MRL compliance:
Homogenisation (+extraction) => deposit on spots/slides
(semi) Quantitative analysis

In laboratory
DESI for fast high throughput analysis of extracts

Test presence (screening, yes/no)
Direct detection from sample surface or cross-sections of tissues
No sample preparation
Qualitative

In laboratory
Fast high throughput analysis of sample Distribution on surface/cross sections
In-field
DESI as on-site detection tool
Food forensics
crops, swops, clothing, containers, syringes

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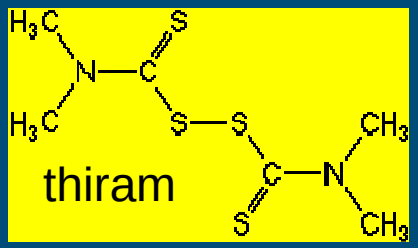
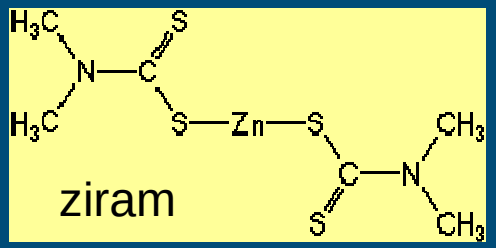
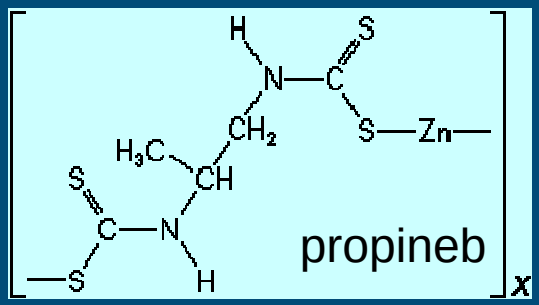
Feasibility Dithiocarbamates by DESI

Fungicides, widely used, high application rates
Non-systemic (residues on surface only)

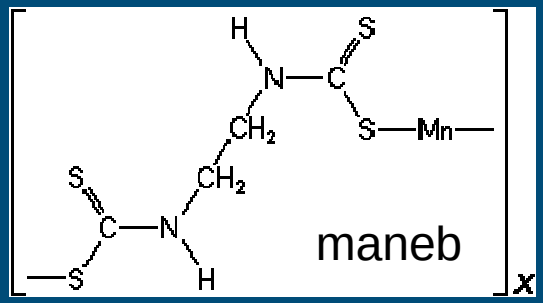




DMDC = bis(dimethyldithiocarbamate)



PBDC = propylenebis(dithiocarbamate)



EBDC = ethylenebis(dithiocarbamate)

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Dithiocarbamates

Solubility issues

Stability issues

Current method: hydrolysis to CS_2

Legislation (396/2005): CS_2 (sum) but specific MRL for 3 DTCs

Groups and examples of individual products to which the MRLs apply (a)	Dithiocarbamates (dithiocarbamates expressed as CS2, including maneb, mancozeb, metiram, propineb, thiram and ziram)	Propineb (expressed as propilendiamine)	Thiram (expressed as thiram)	Ziram
Apples	**5**	**0,3**	**5**	**0,1***
Pears	**5**	**0,3**	**5**	**1**
Strawberries	**10 (ft)**	**0,05***	**10**	**0,1***
Lettuce	**5**	**0,05***	**2**	**0,1***

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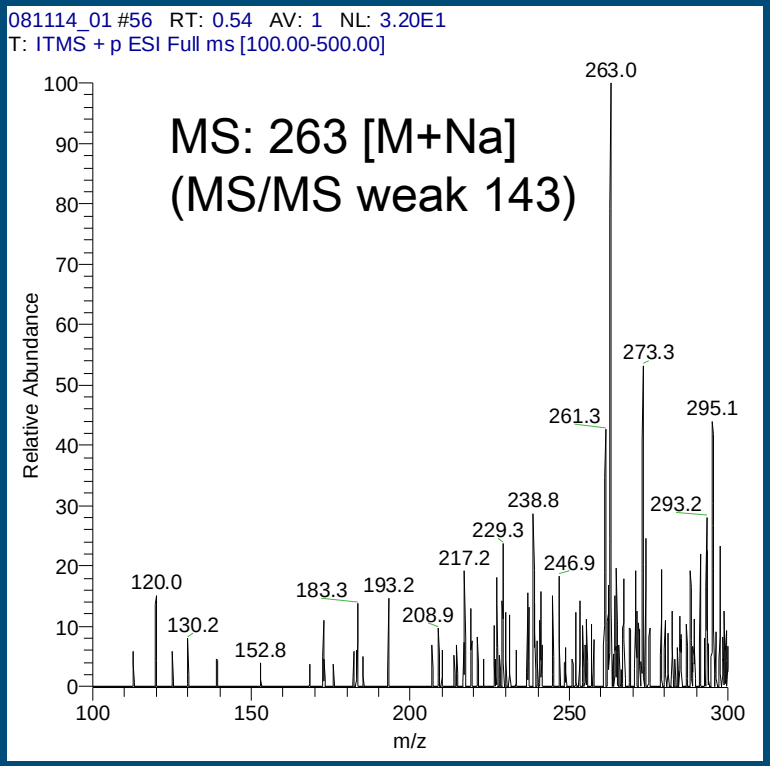
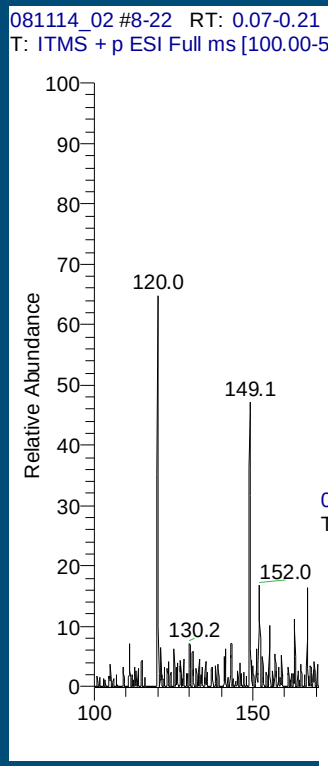
MS/MS optimization (thiram)



MeOH/water 1:1 , 0.1% FA



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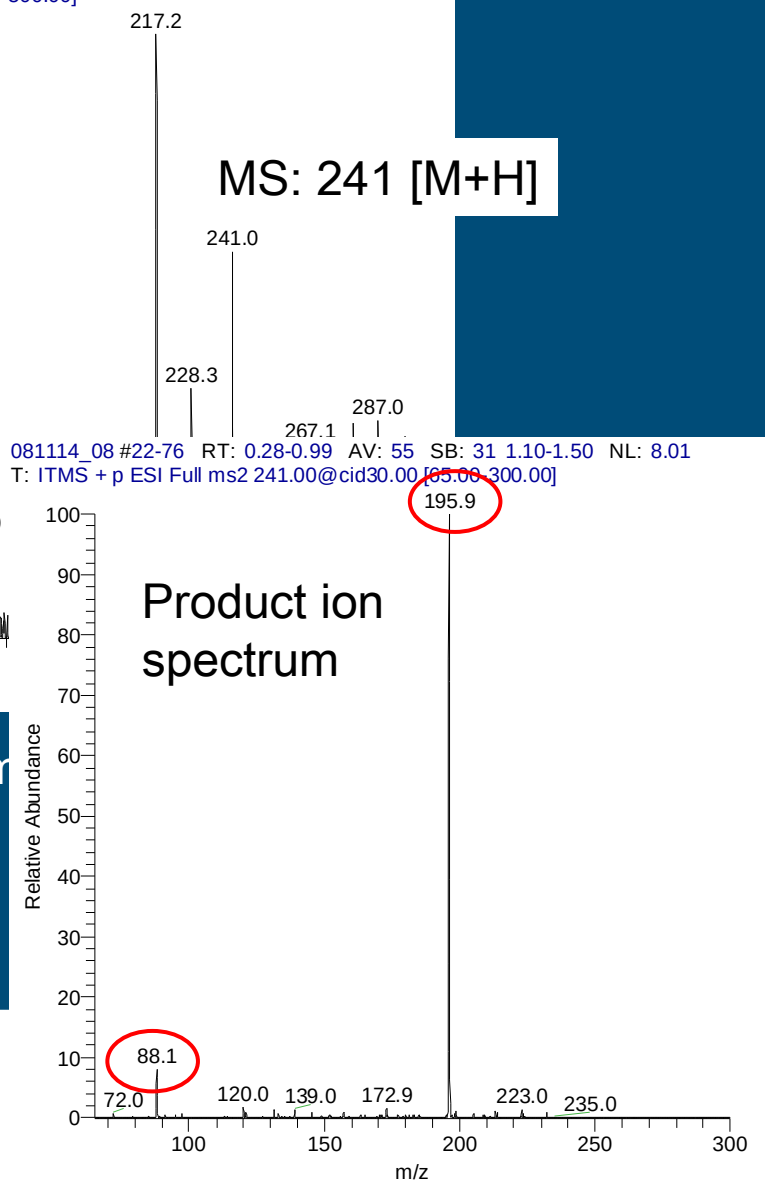

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DESI parameters

Nitrogen sheath gas	120 psi (9 bar)
Incident angle	55^{o}
Spray tip-to-surface distance	5 mm
Surface to MS-inlet distance	1 mm
Scattering angle	ca. 10^{o} to surface
DESI spray	MeOH/water 1:1 + 10 mM NH4For. + 0.1% FA
Flow	5 µl/min
Scanning of the surface	250 µm/sec
Heated capillary MS (LXQ)	50^{o}C
Substrate	PTFE printed on glass

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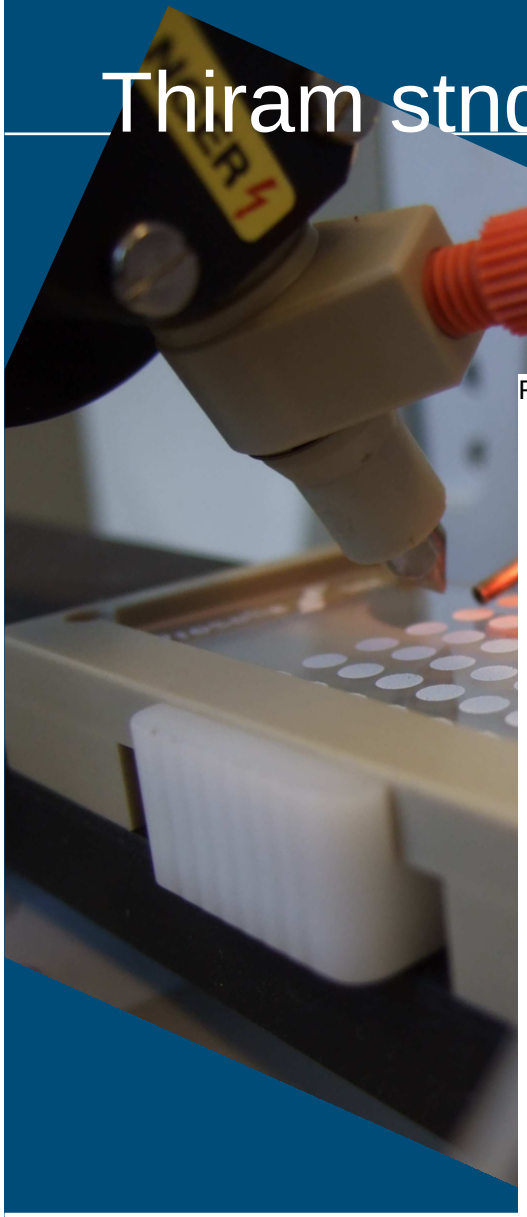
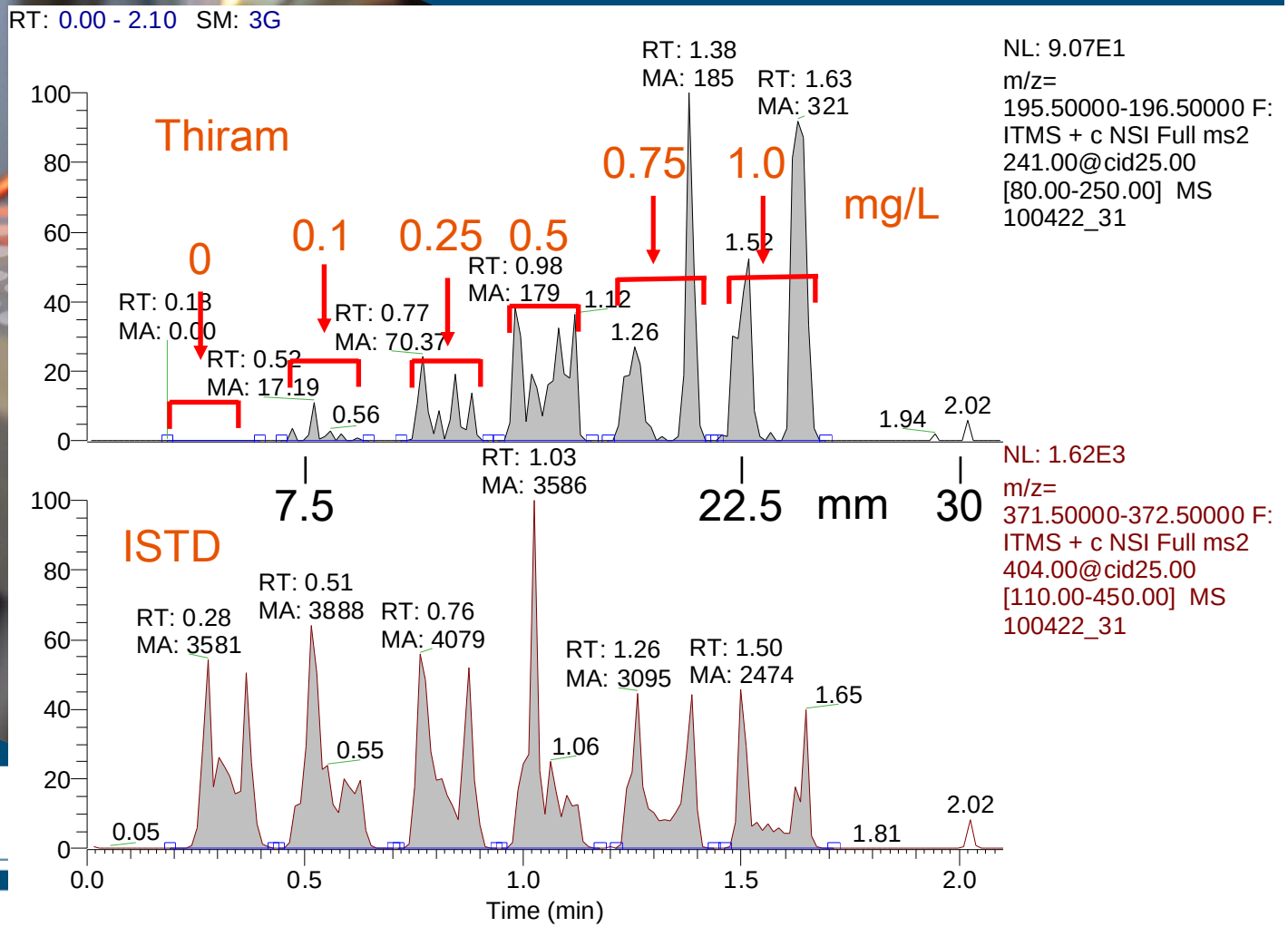
Thiram stnd solutions (teflon spots on glass)





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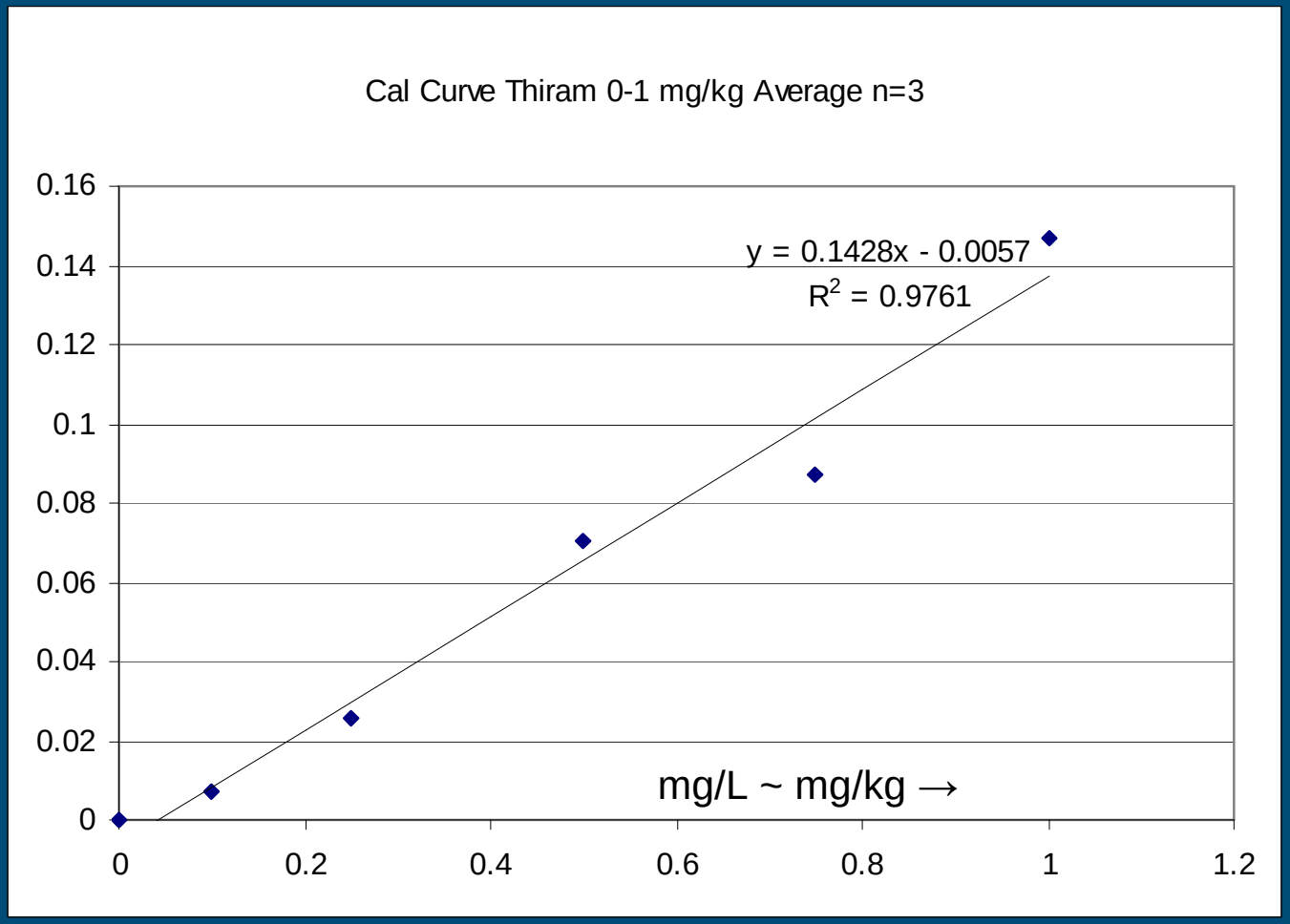
Quantitative analysis?



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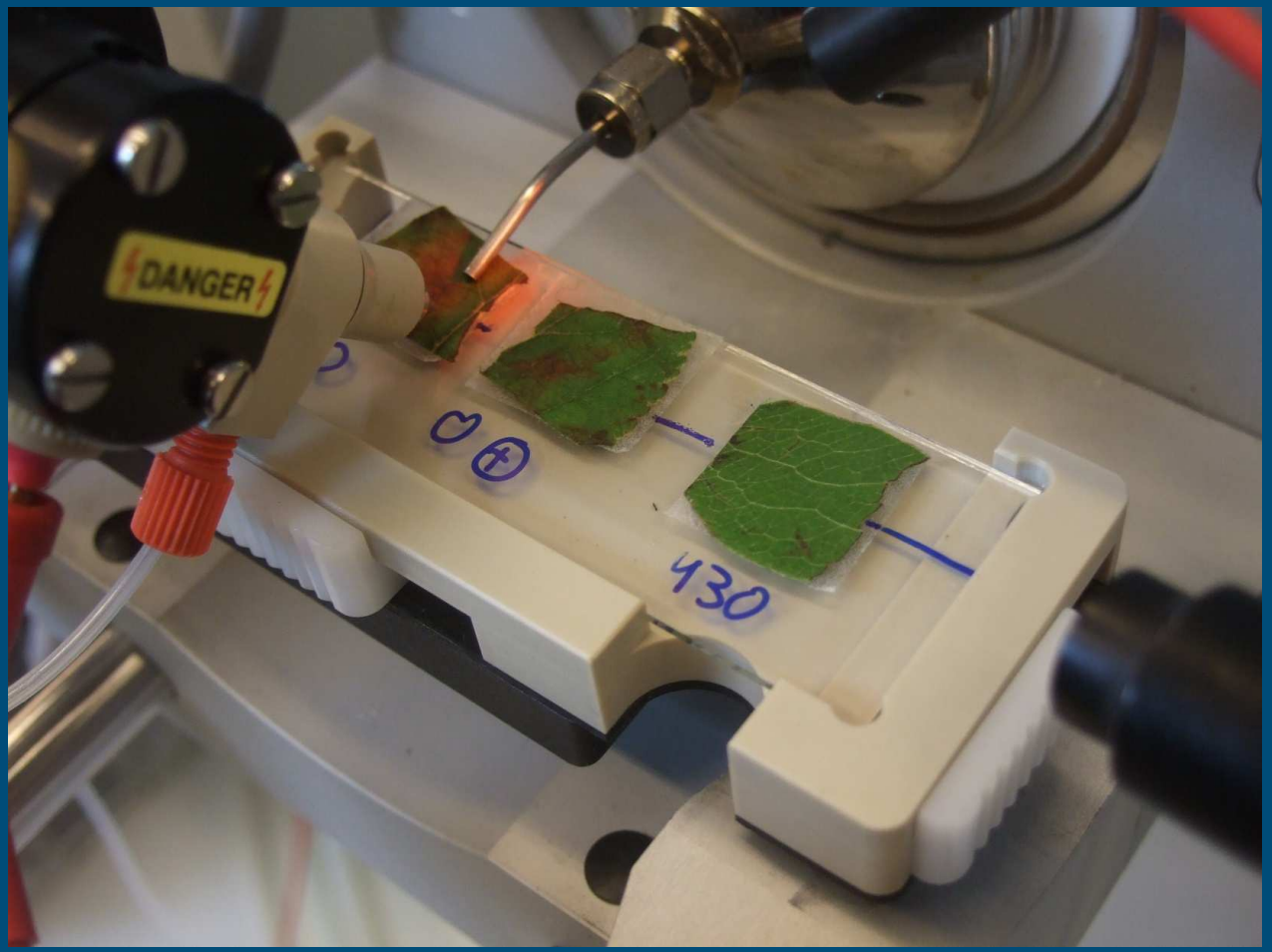
Direct analysis from sample surface



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Alternative to direct analysis

Homogenization (plant juices); simple extraction procedure followed by rapid DESI detection

Options extraction:

Systemic: QuEChERS or other

Non-systemic: solvent rinse of intact product

QuEChERS: 1. Initial Extraction Step

Weigh 10 g Sample

Add 10 mL MeCN

Shake Intensively

for 1 min

Slides from Anastassiades et al, (JAOAC, 2003)

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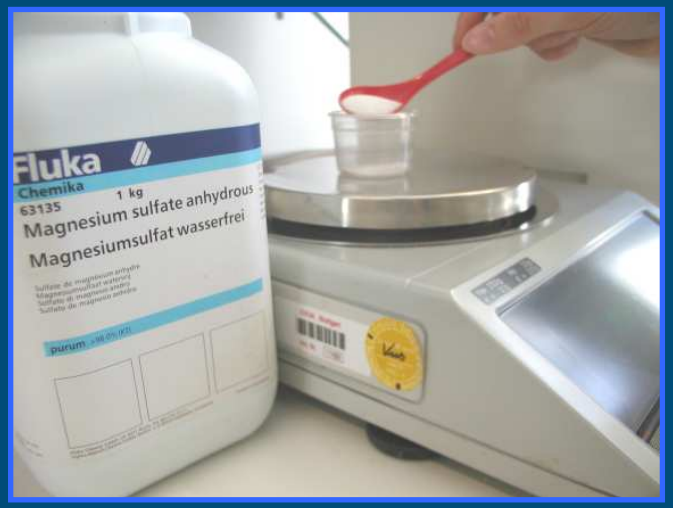
2. Extraction/Partitioning Step



(Pre-)Weigh
4 g $MgSO_4$ + 1 g NaCl

Add to the Tube

Shake Intensively

for 1 min

Slides from Anastassiades et al, (JAOAC, 2003)

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3. Addition of ISTD and Centrifugation

Add ISTD

Shake for 30 s

Centrifuge (ca. 5 min)

Separated Raw Extract

Slides from Anastassiades et al, (JAOAC, 2003)

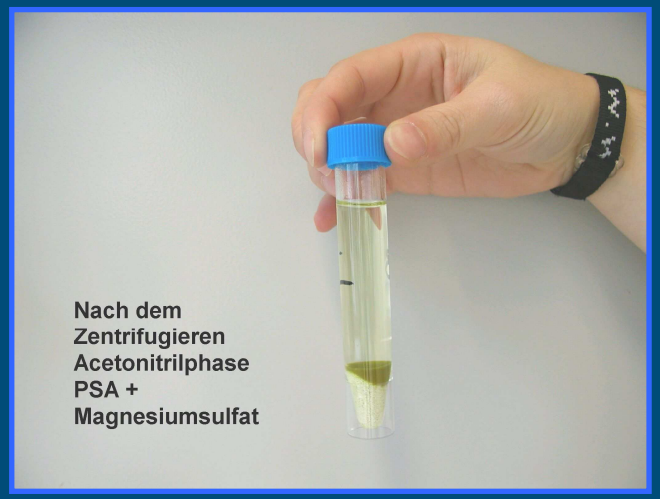
4. Dispersive SPE Step

(Pre-) Weigh $MgSO_4$ and PSA

Add Extract to Tube and Shake ca. 30 s

Centrifuge (ca. 2 min)

Cleaned up Extract



Slides from Anastassiades et al, (JAOAC, 2003)

Surface extraction

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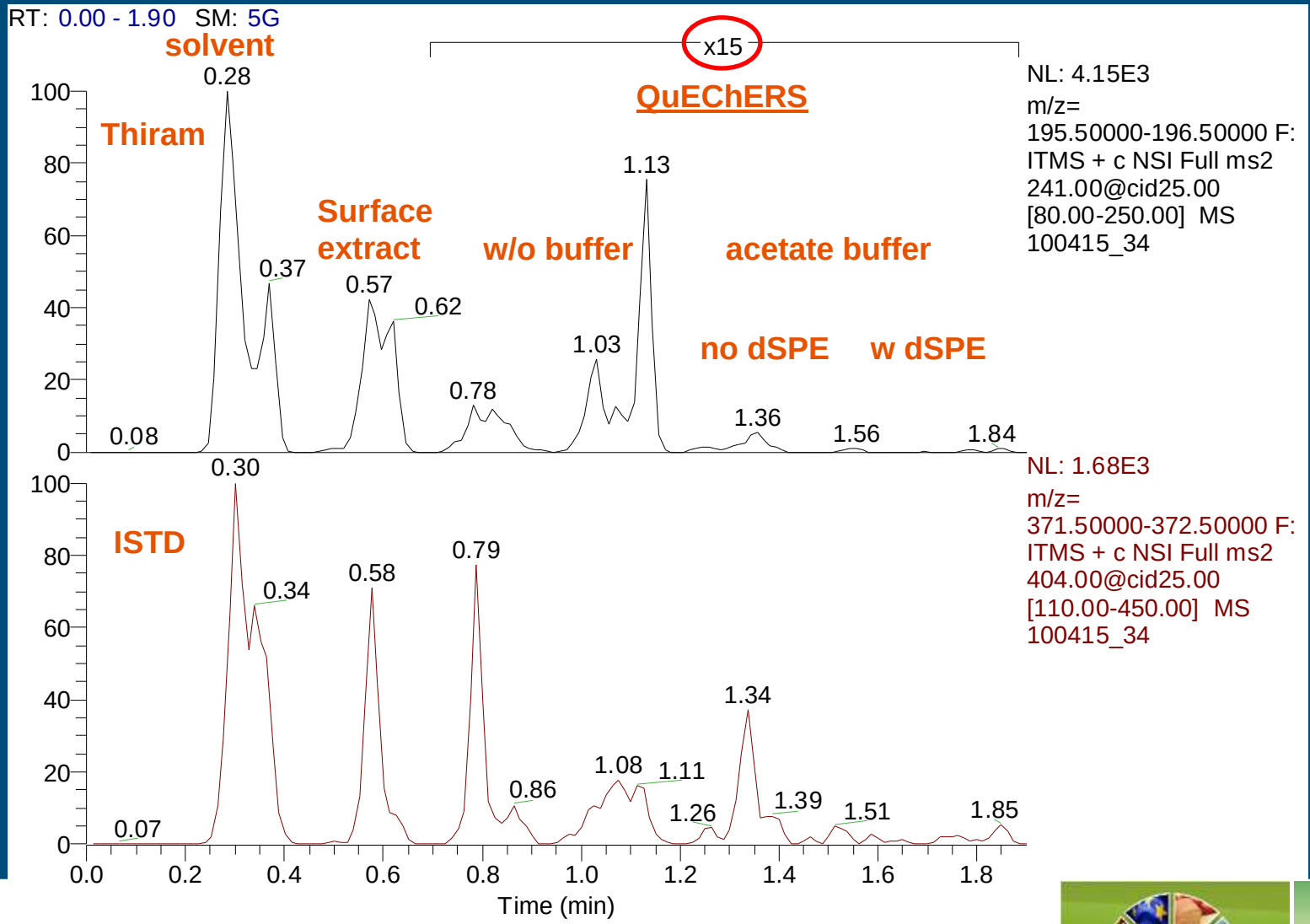
Comparison of extraction methods (pear)



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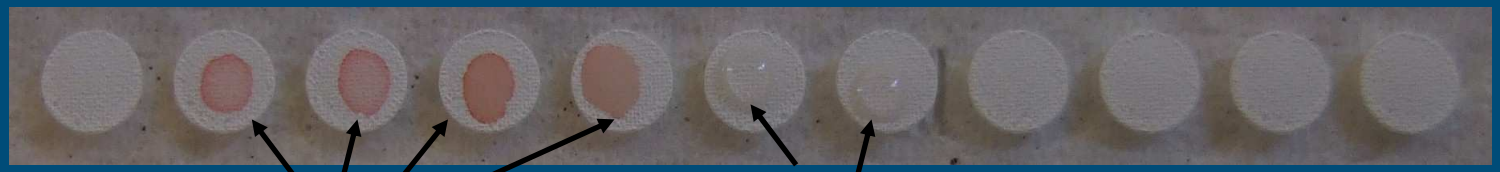
Spike experiments

Vegetables/fruits spiked with thiram std and commercial PPP (TMTD)



1.5 µl strawberry extracts Ref. std thiram

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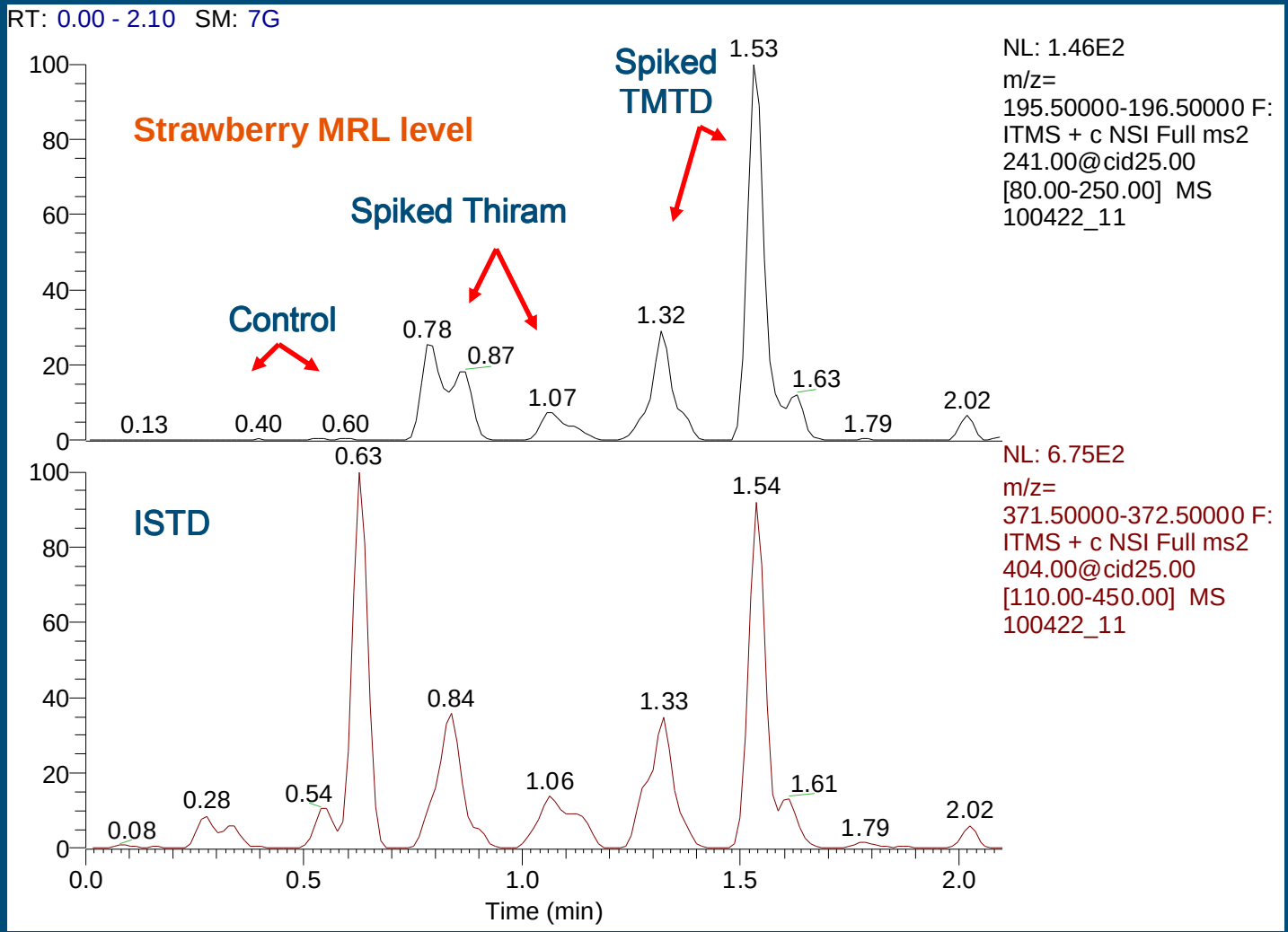
Results



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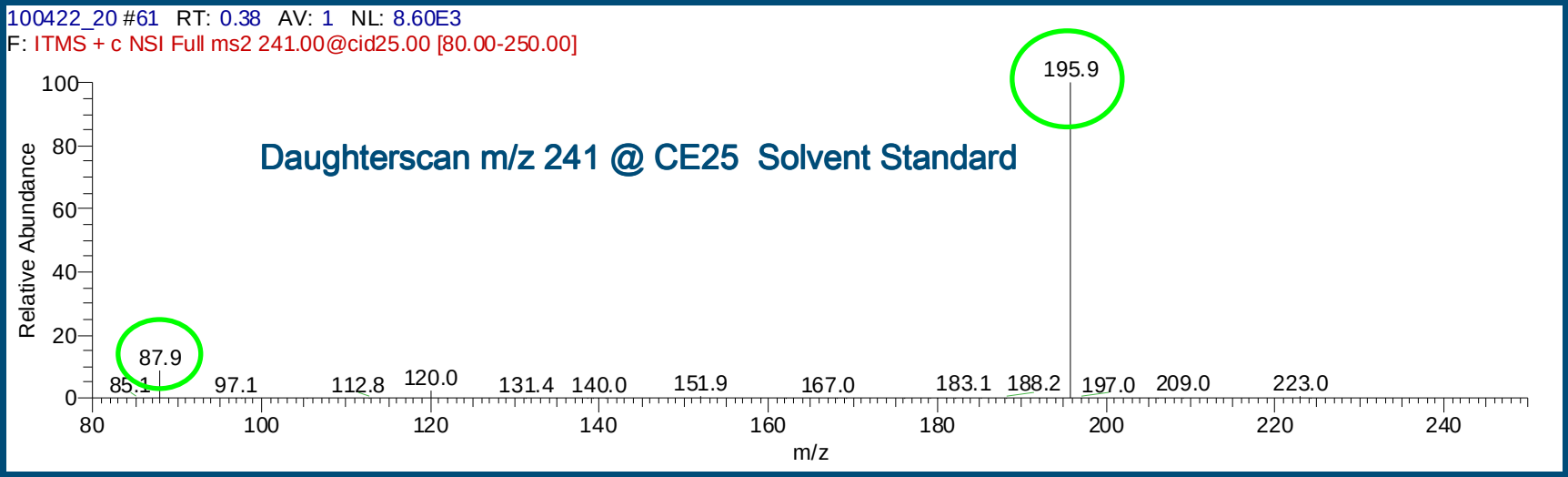
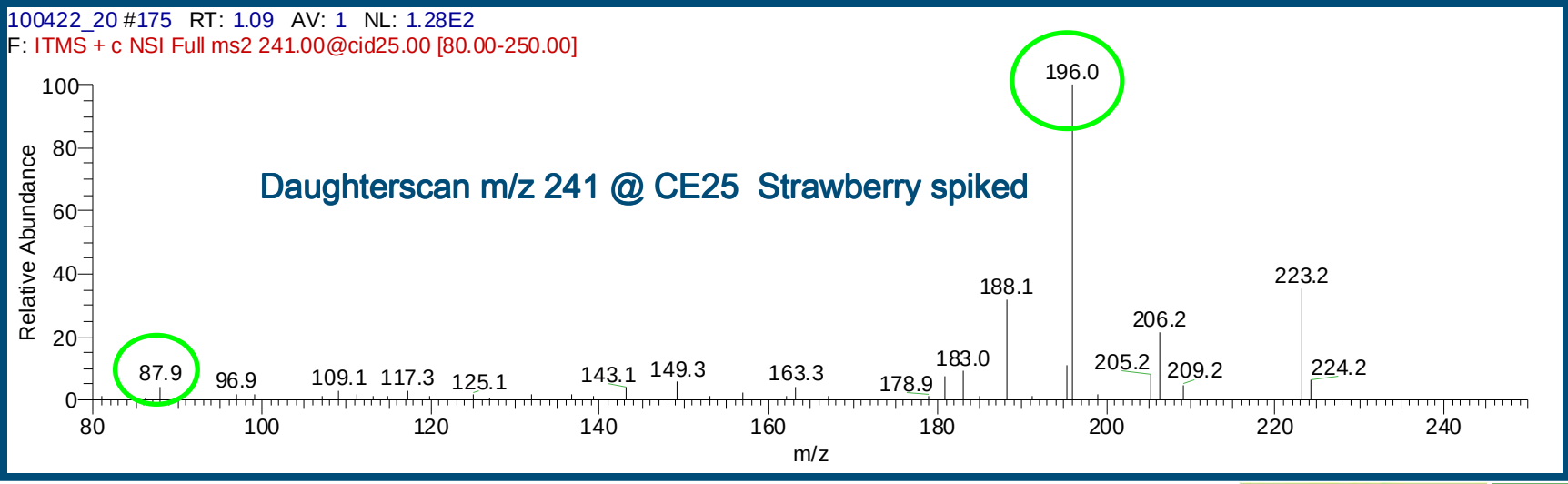
Results





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Results

Recovery and repeatability (matrix-matched calibration)

Pears spiked (10 mg/kg)

	thiram	ISTD	ratio
1	3333	5568	0.60
2	9398	7561	1.24
3	6124	5759	1.06
4	6552	6623	0.99
5	3414	5054	0.68
6	5117	5490	0.93
average	5656	6009	0.92
RSD%	40	15	**26**
av. Rec.%			**85**

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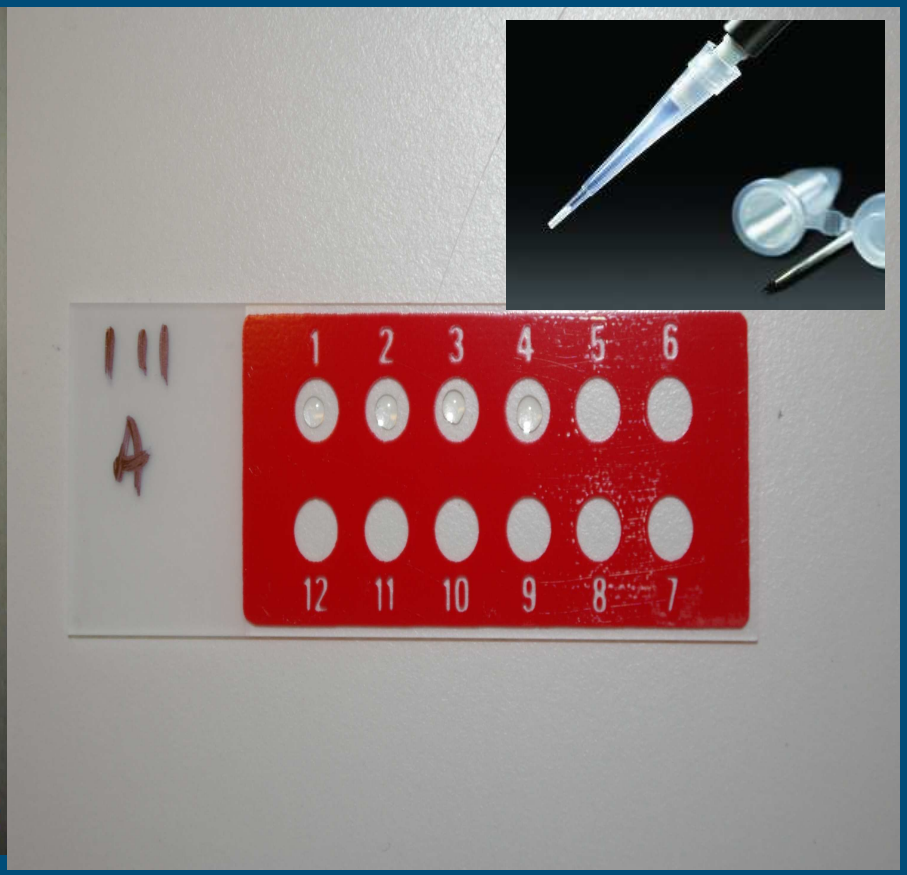
Strobilurin fungicides (Biocop)



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Schurek et al, Anal. Chem. 80 (2008) 9567-9575

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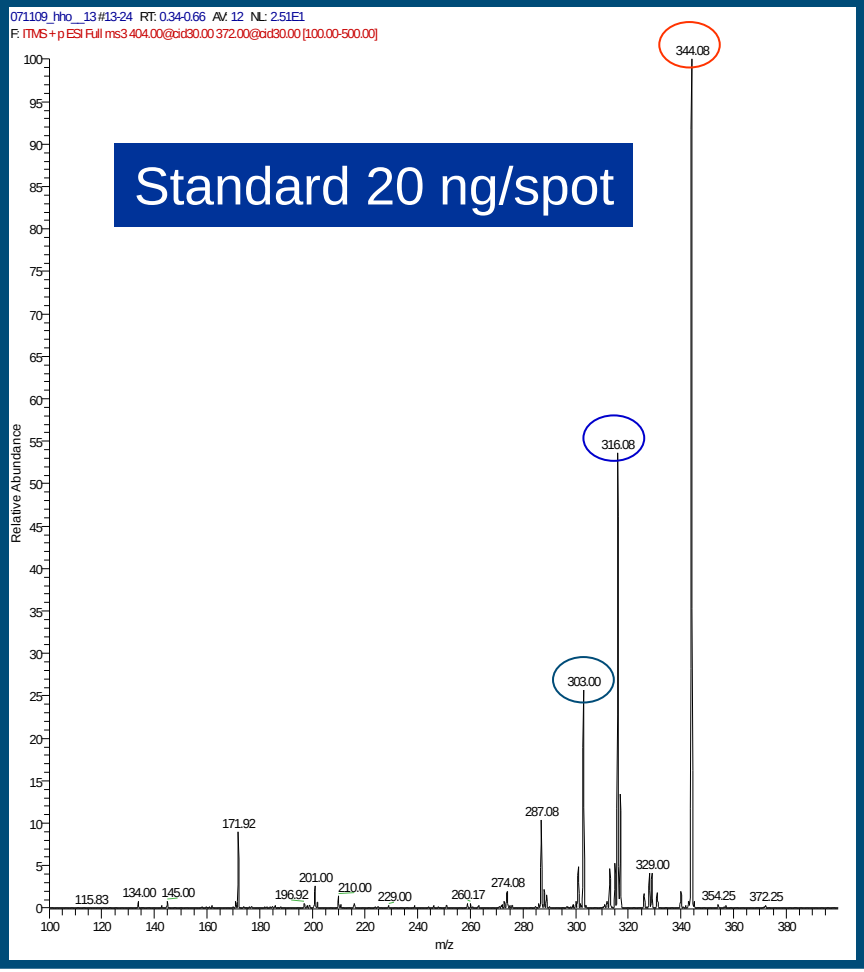
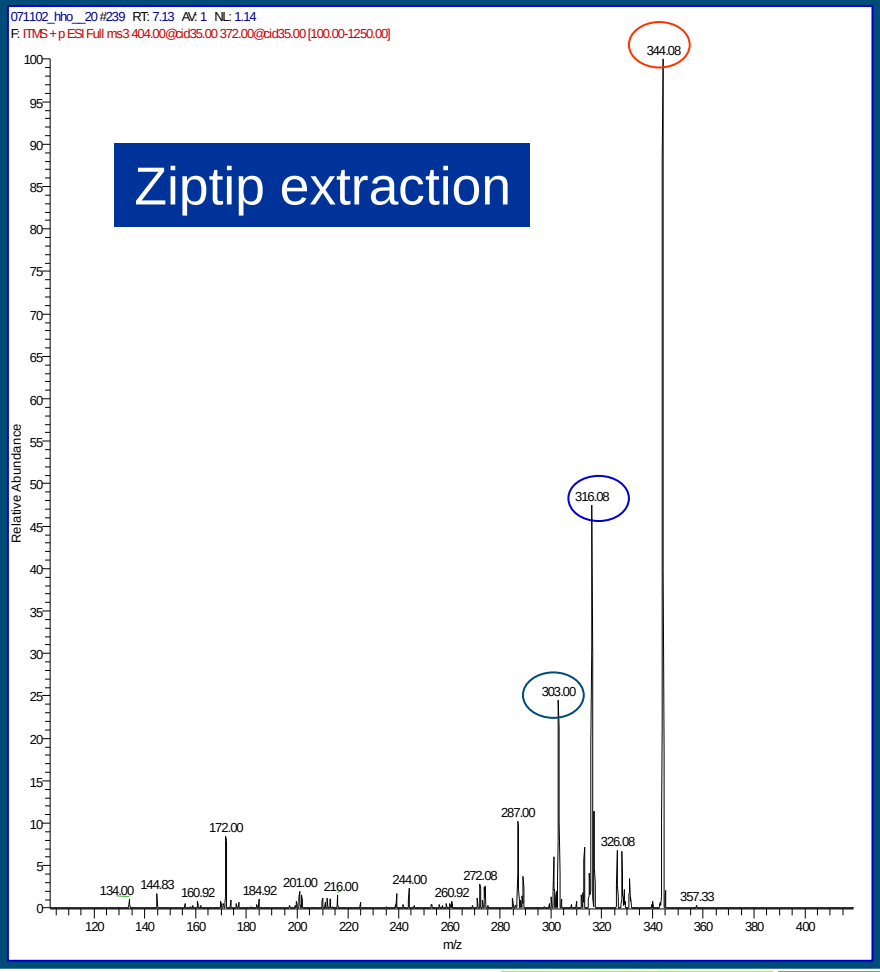
Azoxystrobin MS/MS on m/z 404





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Strobilurins: Reactive DESI

strobilurin	DESI from PTFE	Reactive DESI silver cationization
Metominostrobin "Z"	+	+
Metominostrobin "E"	+	+
Fenamidone	+	+/-
Kresoxim-methyl	-	+
Dimoxystrobin	+/-	+
Epoxiconazole	+	+/-
Famoxadone	-	+/-
Pyraclostrobin	-	+
Orysastrobin	-	+
Azoxystrobin	+	+
Trifloxystrobin	-	+
Fluacrypyrim	-	+
Fluoxastrobin	+	+
Picoxystrobin	+	+

DESI: ACN/water/FA (80:20:0.1)
reactive DESI: ACN/water (75:25) + 5 mg/ml AgCF3COOH flow 2.5 ul.min-1

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Pesticides in/on vegetables/fruits

Optimization of spray solvent

Compound	Limit of detection / ng ml^{-1}					
	MeOH: H_2O 50:50[a]	MeOH: H_2O 80:20[a]	AcN: H_2O 50:50[a]	AcN: H_2O 80:20[a]	AcN: H_2O 95:5[a]	AcN: H_2O 80:20 (1% FA[b]) [a]
Ametryn	30	10	5	2.5	5	2.5
Amitraz	65	150	30	30	30	30
Atrazine	120	200	100	80	35	35
Azoxystrobin	16.5	35	25	25	65	16.5
Bitertanol	1000	400	250	300	500	250
Buprofezin	35	65	10	35	100	10
Imazalil	16.5	35	20	10	25	10
Imazalil metabolite	330	500	16.5	16.5	35	16.5
Isofenphos-methyl	200	200	130	35	200	35
Malathion	200	330	330	35	100	35
Nitenpyram	500	2000	50	100	100	50
Prochloraz	200	1650	150	150	250	150
Spinosad	30	35	130	35	330	30
Terbuthylazine	150	250	130	130	65	65
Thiabendazole	165	400	330	100	50	50
Thiacloprid	300	1000	330	225	300	225

[a] All the experiments were performed using 3µl of solvent standards deposited on PTFE surfaces
[b]: FA: formic acid

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Garía-Reyes et al, Anal. Chem. 81 (2009) 820-829

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DESI parameters garcia et al

Nitrogen sheath gas	150 psi (10 bar)
Incident angle	55^{o}
Spray tip-to-surface distance	5 mm
Surface to MS-inlet distance	1.5 mm
Scattering angle	ca. 10^{o} to surface
DESI spray	acetonitrile/water 8:2+1% FA
Flow	5 µl/min
Scanning of the surface	?
Heated capillary MS (LTQ)	200^{o}C
Substrate	PTFE

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Pesticides in/on vegetables/fruits

limits of detection (LOD)

compound	LOD ($\mu g\ L^{-1}$) DESI-MS (optimized solvent)[c]	LOD ($\mu g\ L^{-1}$) DESI-MS/MS (solvent)[d]	LOD ($\mu g\ kg^{-1}$) DESI-MS/MS (tomato)[e]	LOD ($\mu g\ kg^{-1}$) DESI-MS/MS (orange)[f]
ametryn	2.7	0.1	1.0	1.5
amitraz	30	3.0	60	80
atrazine	30	0.16	1.5	1.5
azoxystrobin	15	2.0	18	18
bitertanol	265	6.5	60	80
buprofezin	10	2.0	80	80
imazalil	10	0.5	5.0	5.0
imazalil metabolite	17	5.0	90	90
isofenphos-methyl	35	3.5	80	60
malathion	35	3.0	30	40
nitenpyram	50	3.5	70	70
prochloraz	150	0.7	10	10
spinosad	30	8.0	80	80
terbuthylazine	65	0.16	2.0	2.0
thiabendazole	50	3.3	45	50
thiacloprid	225	5.0	50	60

QuEChERS w/o buffer + PSA clean up; extract diluted 1:3 in acetonitrile

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Garía-Reyes et al, Anal. Chem. 81 (2009) 820-829

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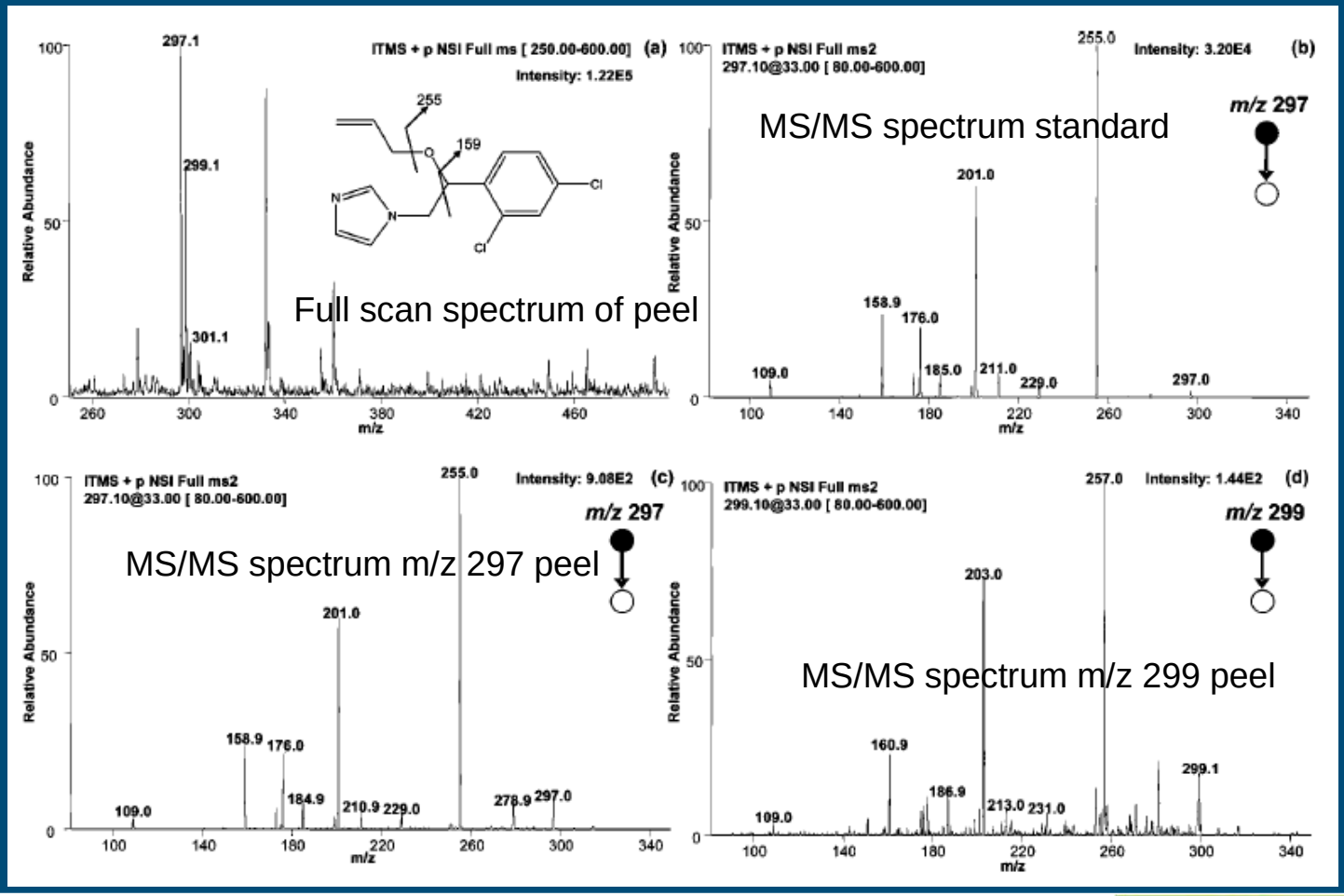
Pesticides in/on vegetables/fruits

Direct detection of imazalil from lemon peel



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Pesticides in/on vegetables/fruits

Table 4. Quantitation of Imazalil Residues in Citrus Fruits by DESI-MS/MS and Comparison with the LC−MS Reference Method

		imazalil concentration ($\mu g\ g^{-1}$)		
no.	sample	LC−MS ($\mu g\ g^{-1}$)	DESI-MS ($\mu g\ g^{-1}$)	RSD (%) ($n = 5$)
1	orange	0.19	0.16	12.8
2	lemon	0.35	0.38	11.2
3	lemon	0.44	0.48	9.6
4	orange	0.67	0.58	8.1
5	grapefruit	0.33	0.30	12.1
6	orange	0.15	0.12	14.5

using deuterated imazalil as ISTD

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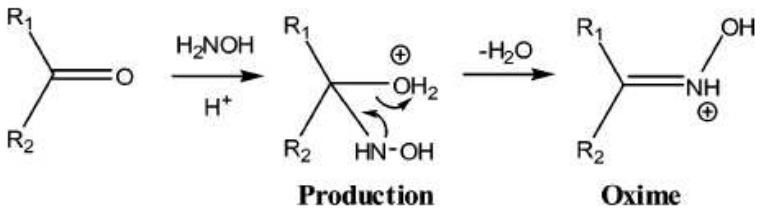
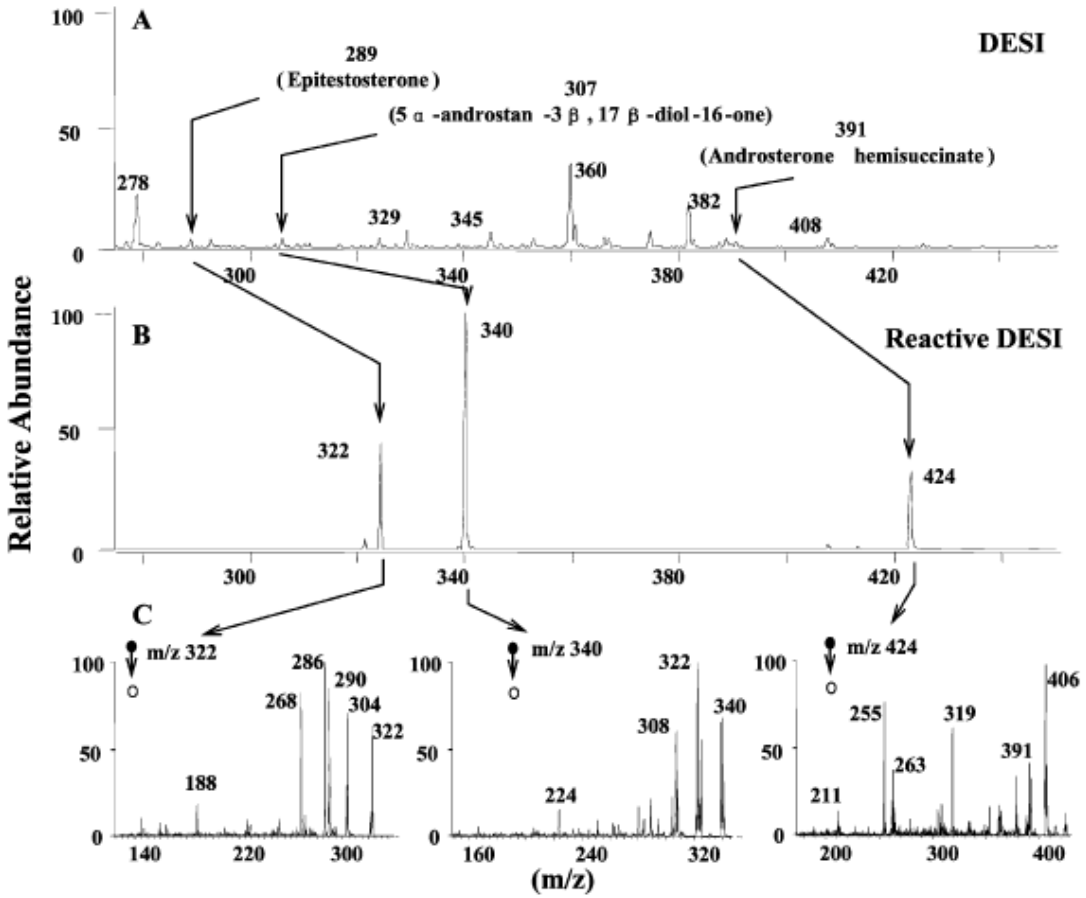
Reactive DESI analysis on steroids

Steroids in urine
SPME enrichment
Direct detection from fiber

Spray 3µl/min:
MeOH/water 1/1 0.05% HAc,
5% hydroxylamine





Huang et al, Anal. Chem. 79 (2007) 8327-8332

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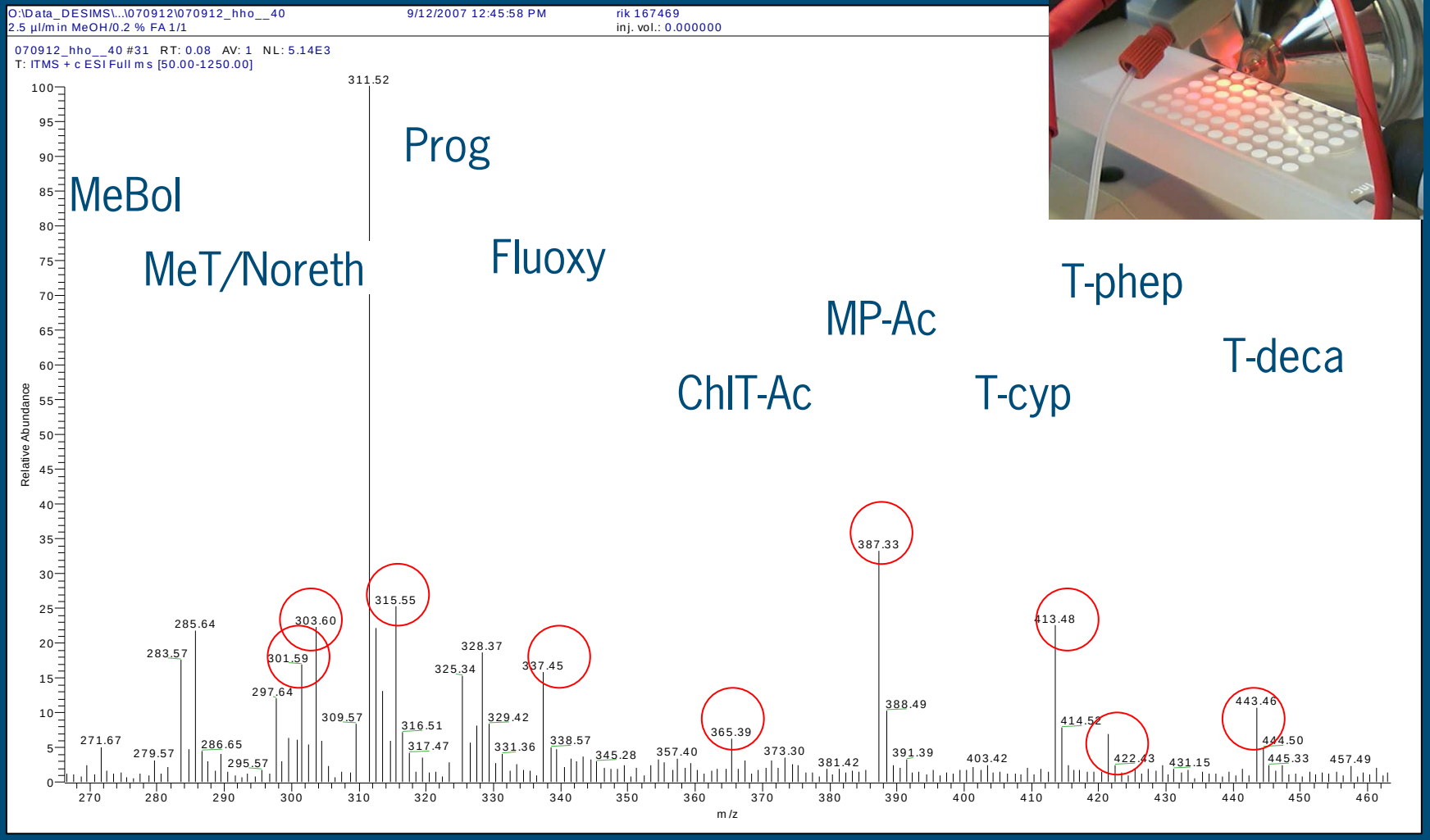
Steroid cocktail



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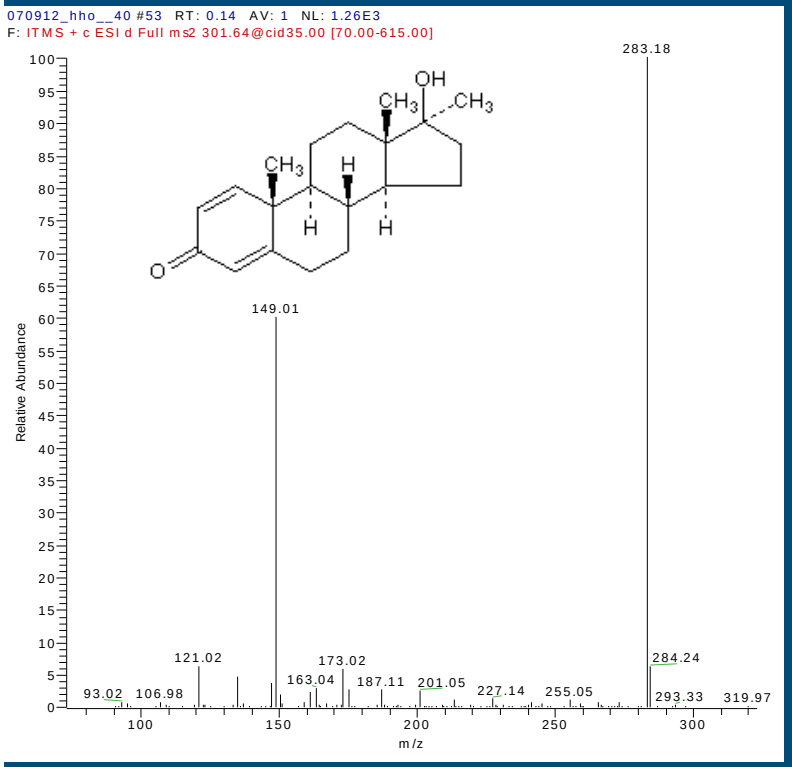
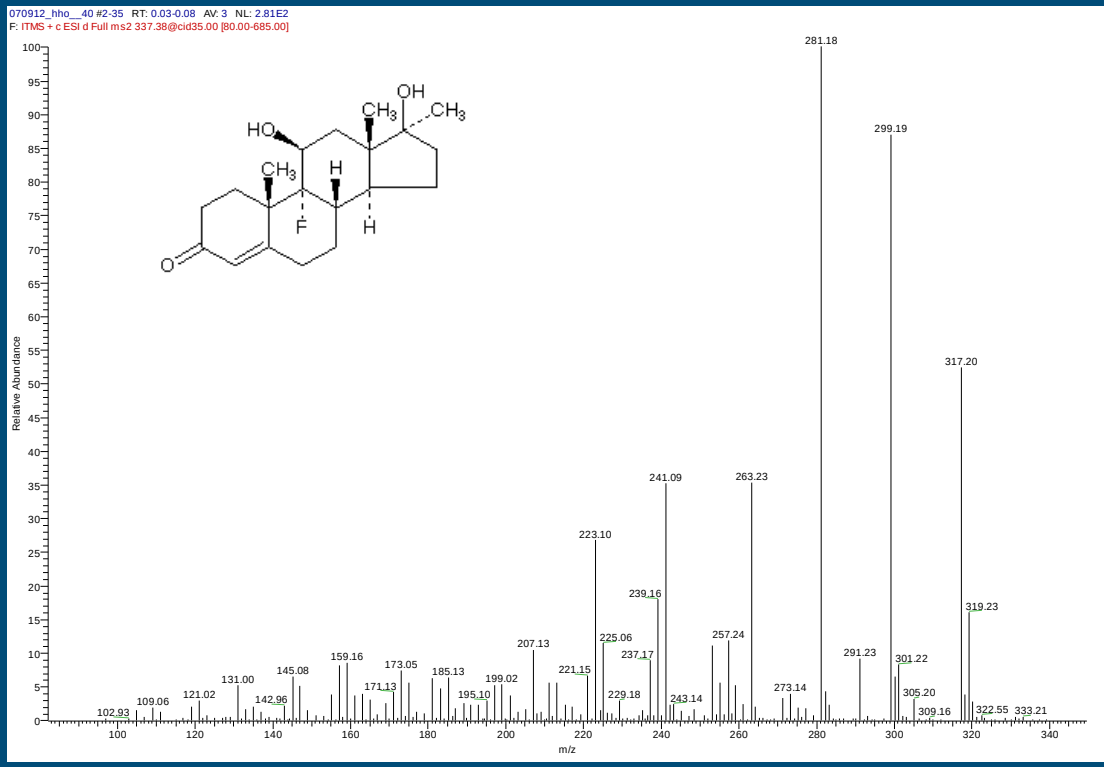
Steroid cocktail

Methylboldenone MS/MS m/z 301



Fluoxymesterone MS/MS on m/z 337



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Direct detection of IA captured fluoroquinolone

SPR biosensor chip
Immunoaffinity bound enrofloxacin

DESI conditions

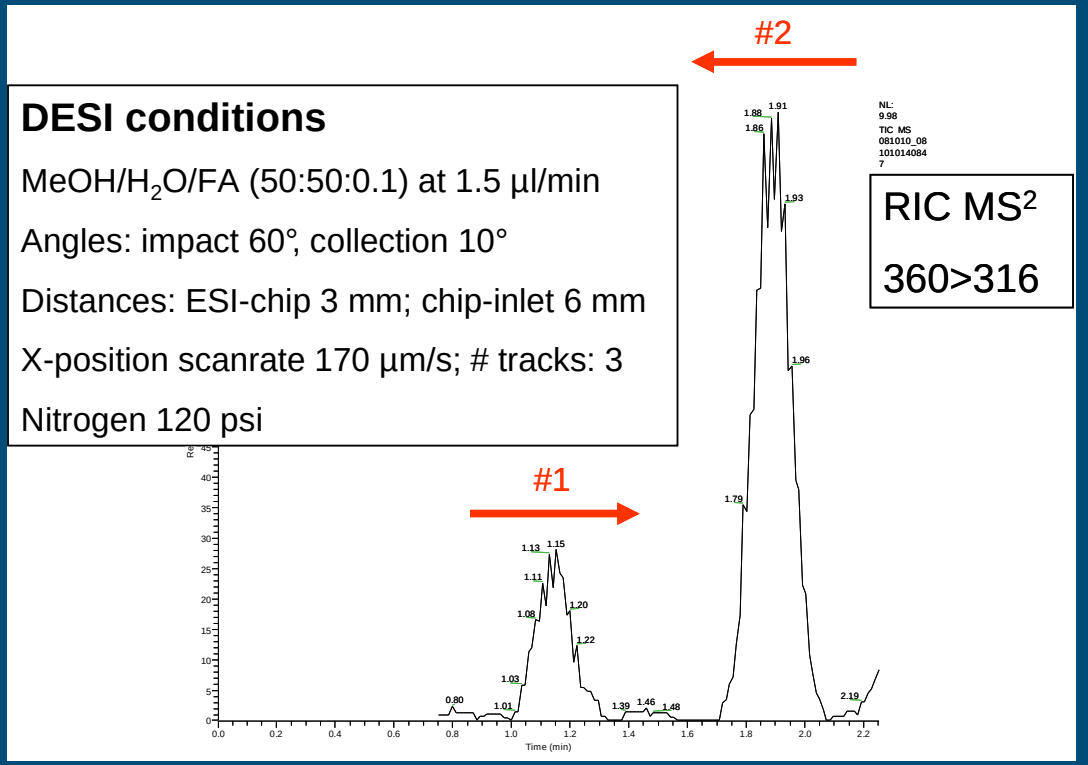
MeOH/H_2O/FA (50:50:0.1) at 1.5 µl/min

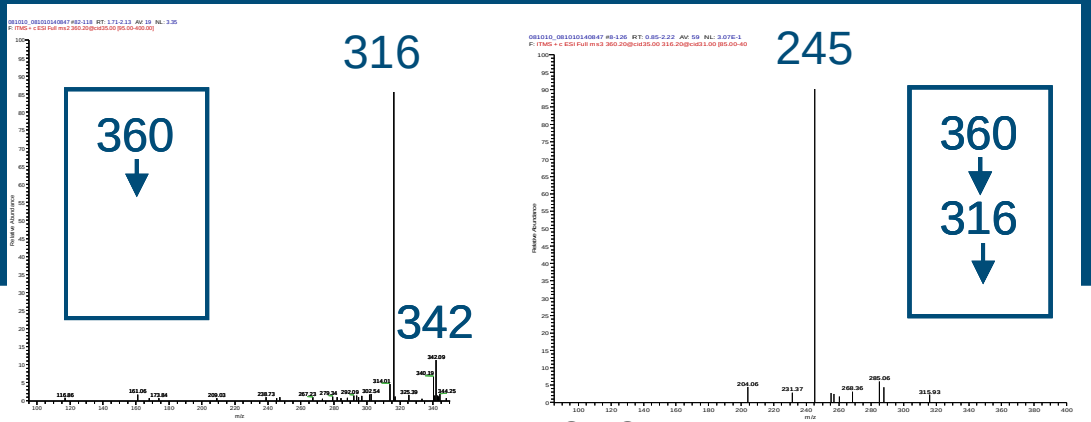
Angles: impact 60°, collection 10°

Distances: ESI-chip 3 mm; chip-inlet 6 mm

X-position scanrate 170 µm/s; # tracks: 3

Nitrogen 120 psi





Nielen et al, Poster ISMS, Bremen, 2009

Alkaloids on *Senecio jacobaea* L. Stinking Willie

Senecionine N-oxide

Unable to passively permeate membranes

Nontoxic

Metabolically safe

Senecionine

Able to passively permeate membranes

Toxic after bioactivation

Metabolically unsafe

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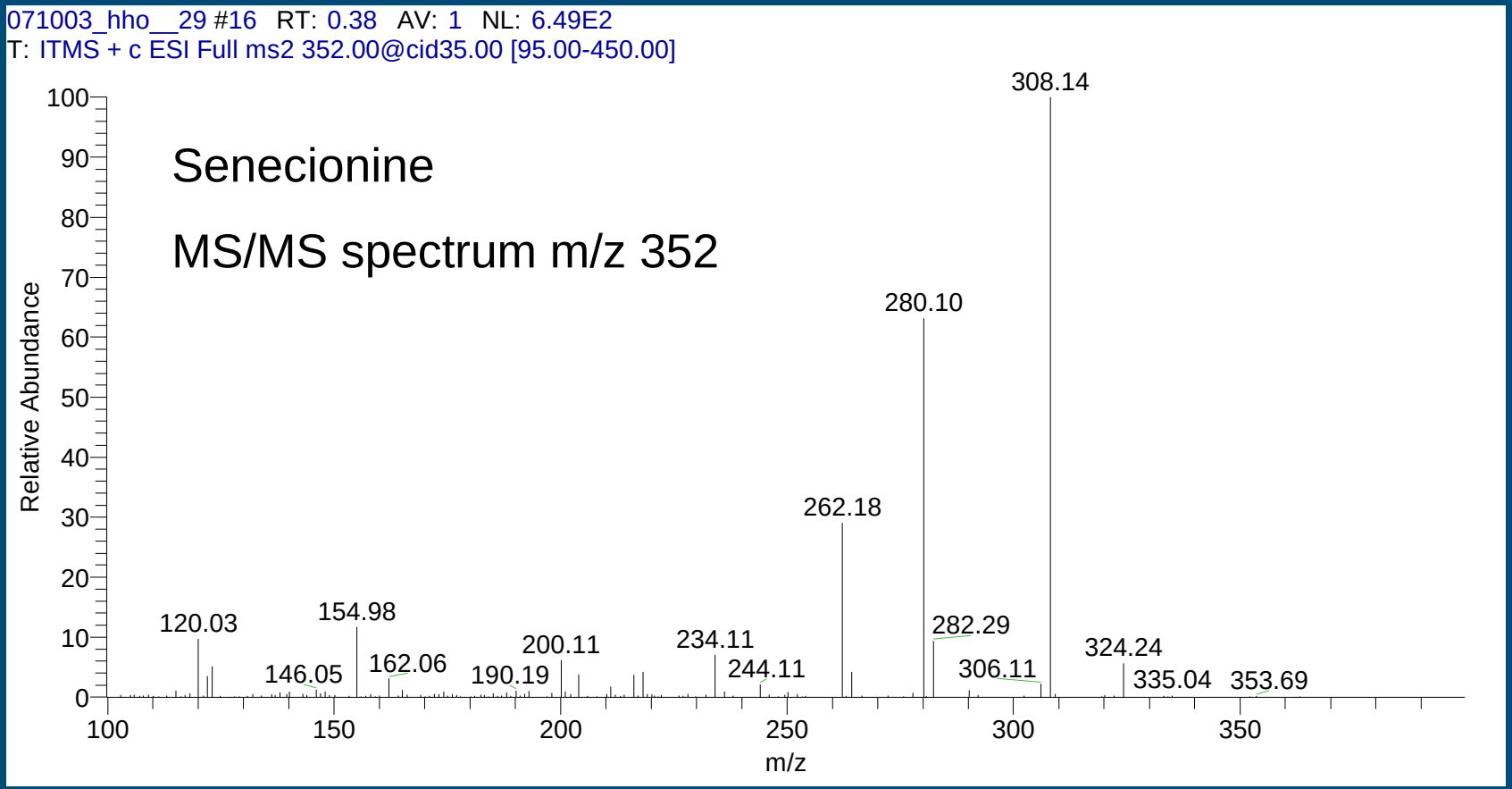
Alkaloids on *Senecio jacobaea* L. Stinking Willie



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Summary

DESI a useful option for food contaminant analysis/control
Lots of research in progress, many papers appearing
Like other ambient techniques, pro's and con's

Features:
- Direct detection from substrates, TLC, sensor chips, sample surface
- Reactive DESI
- Spatial resolution
- Rapid detection/high throughput of sample(extracts)

Quantitative determination possible with use of internal standard

Limitations:
- Sensitivity (matrix suppression)
- Reproducibility
- MS^n or high res required
- residues => targeted detection

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Outlook

In lab analysis:

- Further improvement robustness
- Rapid straightforward and selective extraction
- More applications
- Combi sources to extent scope

ASAP+DESI (Lloyd et al, Anal. Chem. 81, 2009, 9158)

Towards in-field:

- optimization of nongeometry dependent DESI source
- coupling of DESI with portable MS instruments
- …..

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Too much, too little, too fast, not clear?

DESORPTION ELECTROSPRAY IONIZATION MASS SPECTROMETRY IN THE ANALYSIS OF CHEMICAL FOOD CONTAMINANTS

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[1], RIKILT Institute of Food Safety, P.O. Box 230, 6700 AE Wageningen, The Netherlands

[2], Wageningen University, Laboratory of Organic Chemistry, Dreijenplein 8, 6703 HB Wageningen, The Netherlands. E-mail: michel.nielen@wur.nl

Submitted to Trends in Analytical Chemistry (March 2010)

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Thank you for your attention

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FOOD-CT-2004-06988 "BIOCOP (New Technologies to Screen Multiple Chemical Contaminants in Foods)" coordinated by Queen's University (Belfast, UK)

FP7-211326-CP "CONffIDENCE (Contaminants in Food and Feed: Inexpensive Detection for Control of Exposure)" coordinated by RIKILT – Institute of Food Safety (Wageningen, The Netherlands)

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DESI, spray video

DESI spray on surface video clip.wmv

Venter, Nefliu, Cooks, Trends in Anal. Chem. 27 (2008) 284-290

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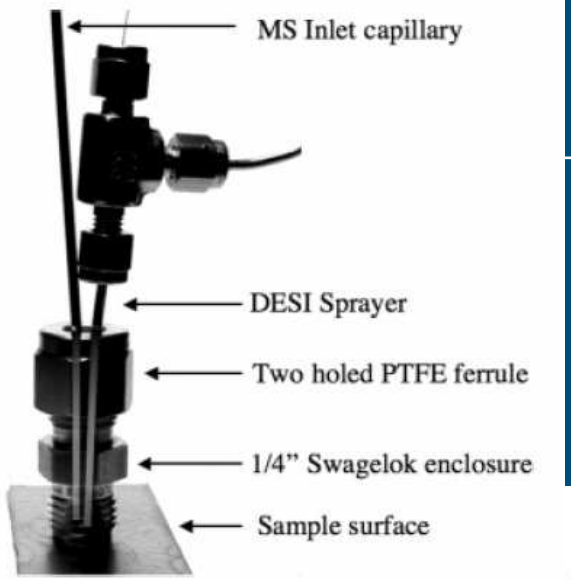
DESI, Alternative geometries



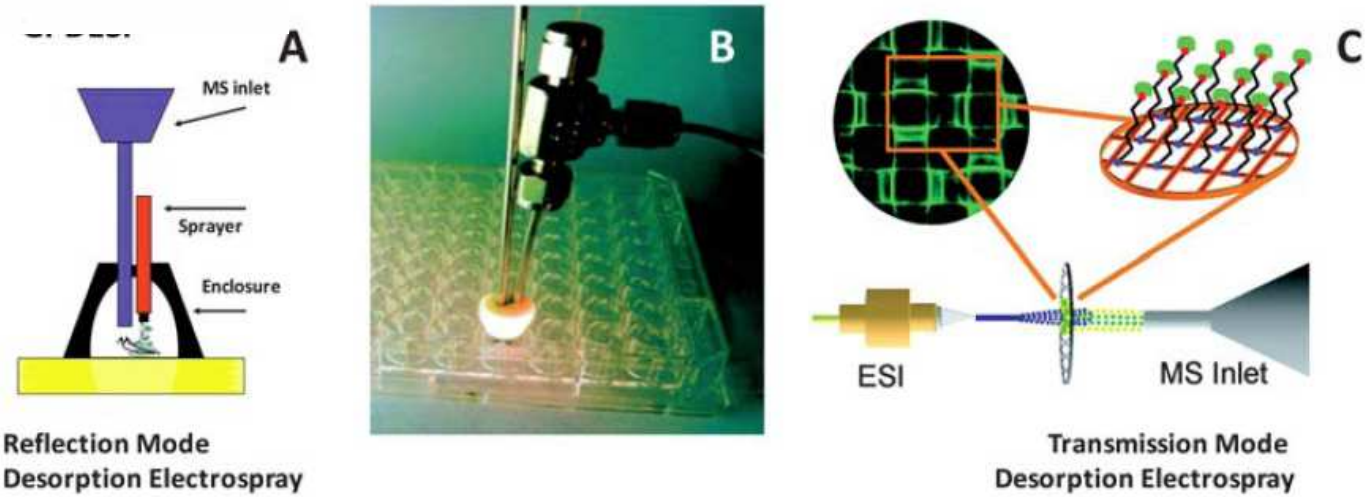


Fig. 4 Two simplified geometries for DESI. (A) and (B) Reflection mode (geometry independent) GI-DESI and its use in high-throughput analysis of metabolites in a bacterial matrix on a 96-well plate.[24] (C) Transmission mode (TM-DESI).[27]

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Ifa et al, Analyst 135 (2010) 669-681

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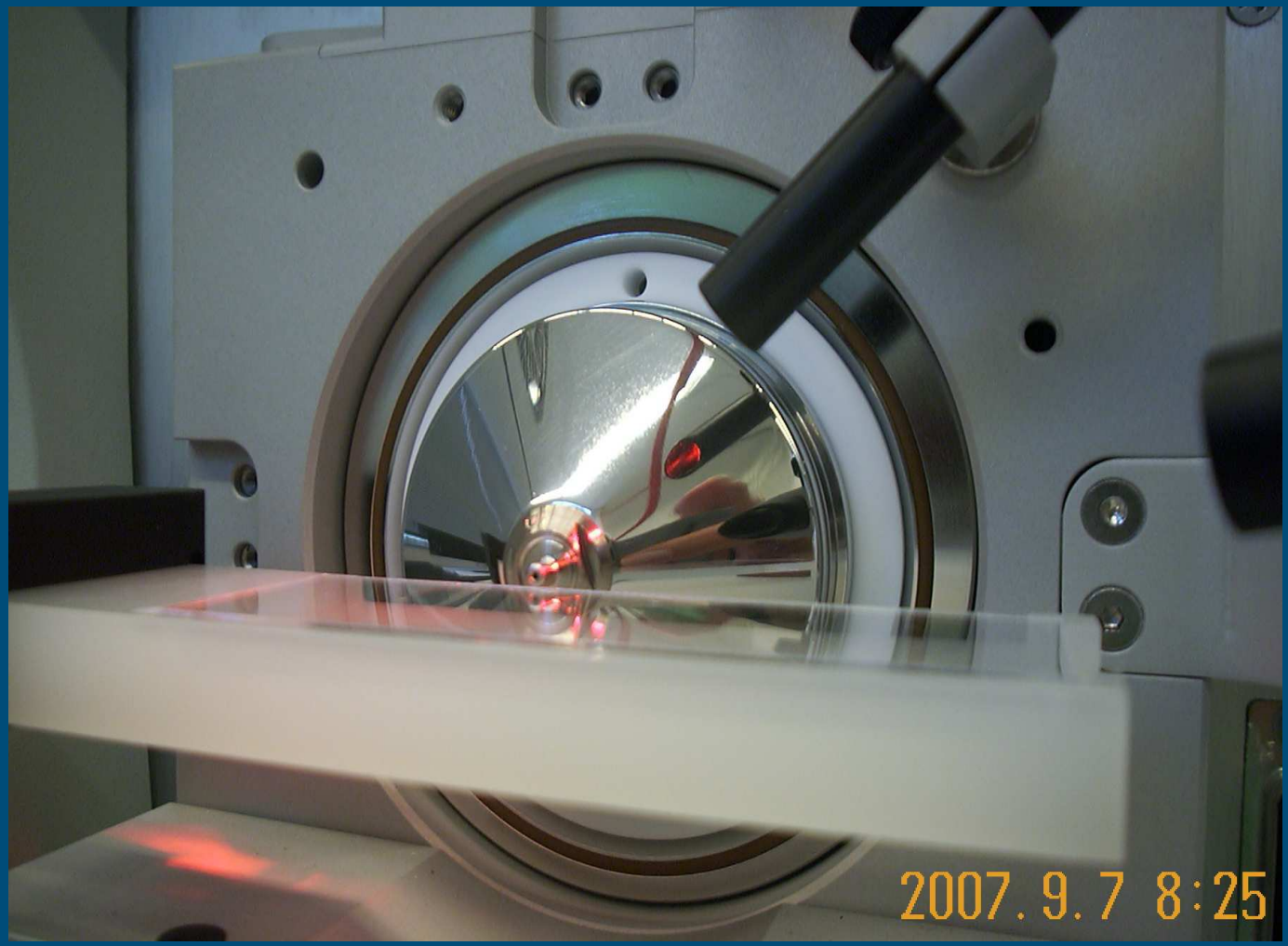
DESI, instrumentation



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