

Comparison of mass spectrometric platforms for the analysis of cytostatic drugs in water

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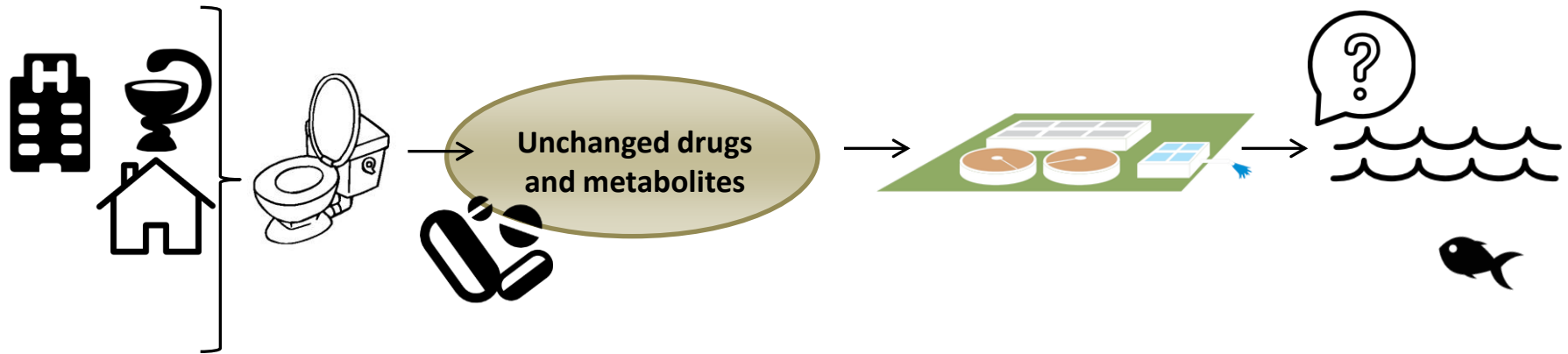


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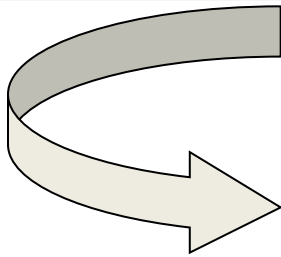
Comparison of mass spectrometric platforms for the analysis of cytostatic drugs in water



Cytostatic drugs in water

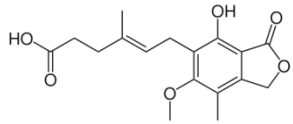


$$PECs \text{ (ng L}^{-1}\text{)} = \frac{\textit{consumption} \times F_{exc} \times (1 - F_{wwtp})}{WWinhab \times inhab} 10^9$$

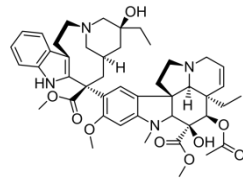


**Prioritization of anticancer drugs
in wastewater and river water**

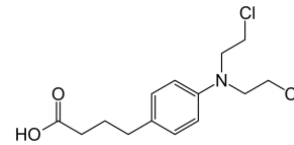
Compounds studied



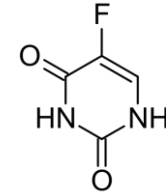
Mycophenolic acid



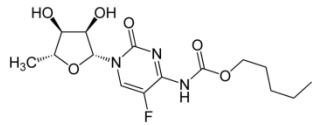
Vinblastine



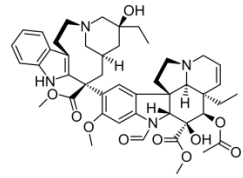
Chlorambucil



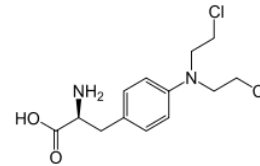
5-Fluorouracil



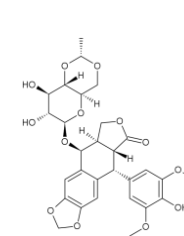
Capecitabine



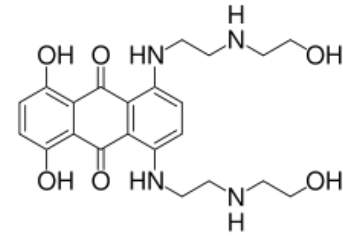
Vincristine



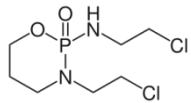
Melphalan



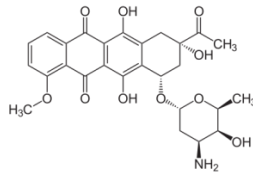
Etoposide



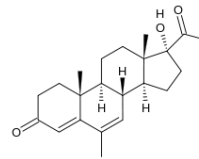
Mitoxantrone



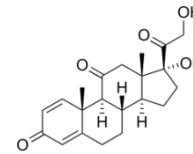
Ifosfamide



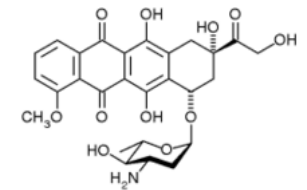
Danourubicin



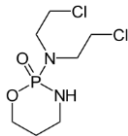
Megestrol



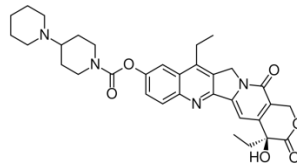
Prednisone



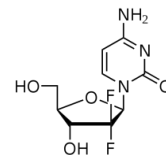
Epirubicin



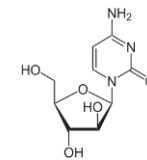
Cyclophosphamide



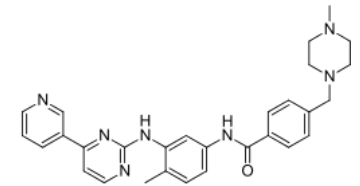
Irinotecan



Gemcitabine

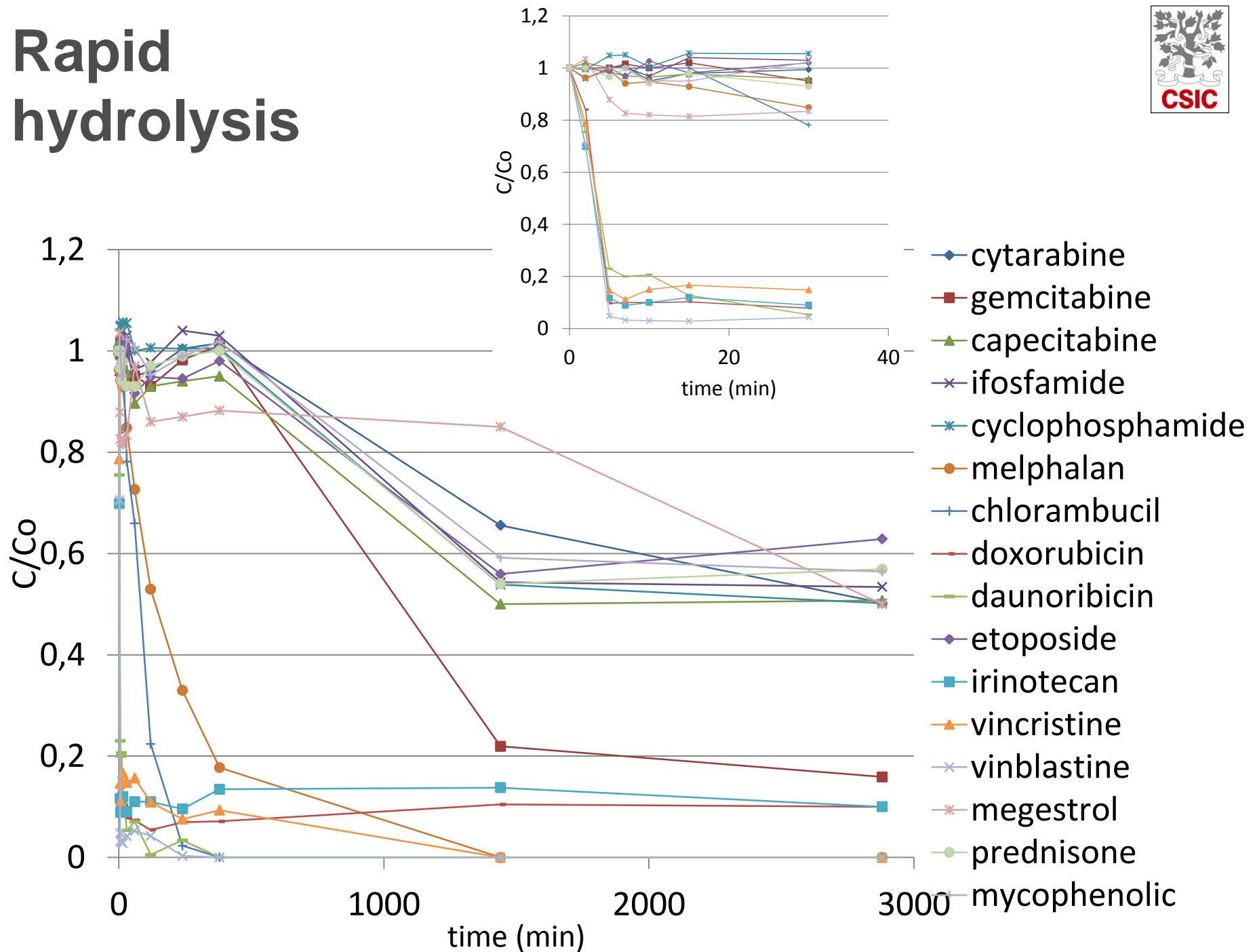


Cytarabine

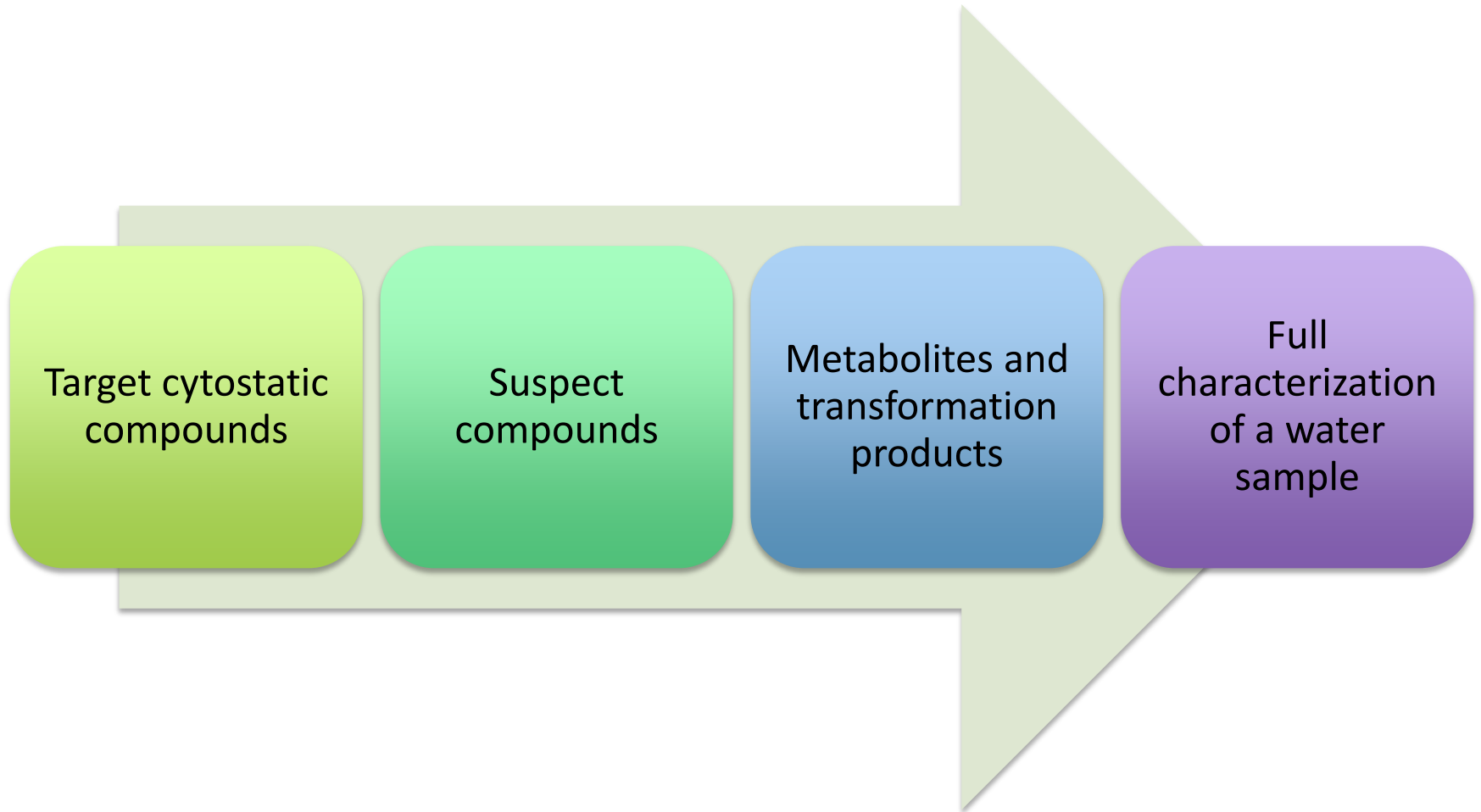


Imatinib

Rapid hydrolysis



Objectives and experimental pipeline



10 ng/L EMA threshold for risk assessment

Analytical platforms



Orbitrap: 100.000 FWHM



HPLC-HRMS

TOF: 50.000 FWHM, 50%



HPLC-(q)-TOF

MS/MS: Unit resolution



MS: Unit resolution



Platforms

Ultrahigh Resolution and Mass Accuracy

- Confirmation of Organic Compounds
- Good sensibility and Linearity
- Screening
- Identification of unknowns

Determine Elemental Formulae with confidence

Ultrahigh Resolution + Mass Accuracy + Accurate MS/MS

- Less interferences
- More confirmation criteria
- Excellent sensibility and Linearity
- Molecular Characterization of unknowns

Target Analysis and Quantification Structural information



Pilot: 5-FU in hospital effluents

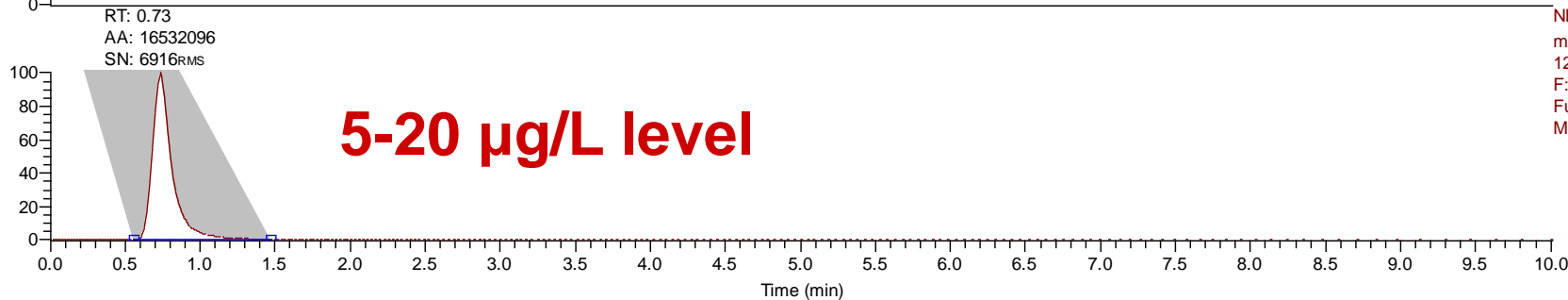
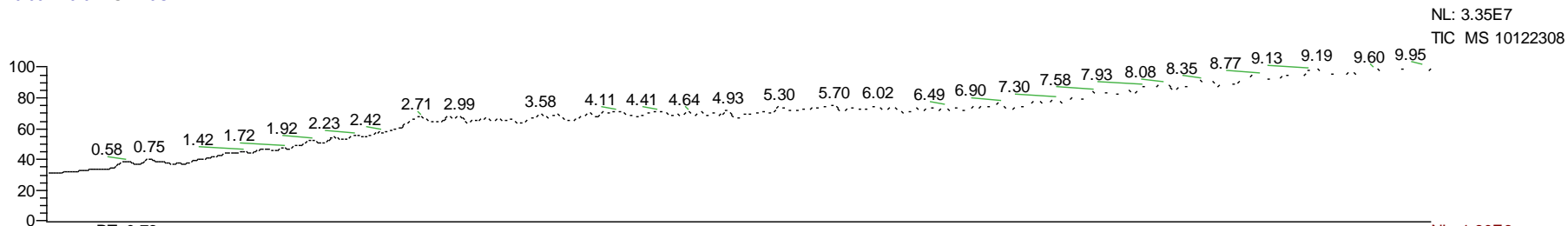


C:\Xcalibur\Data\Silvia_Lacorte\10122308

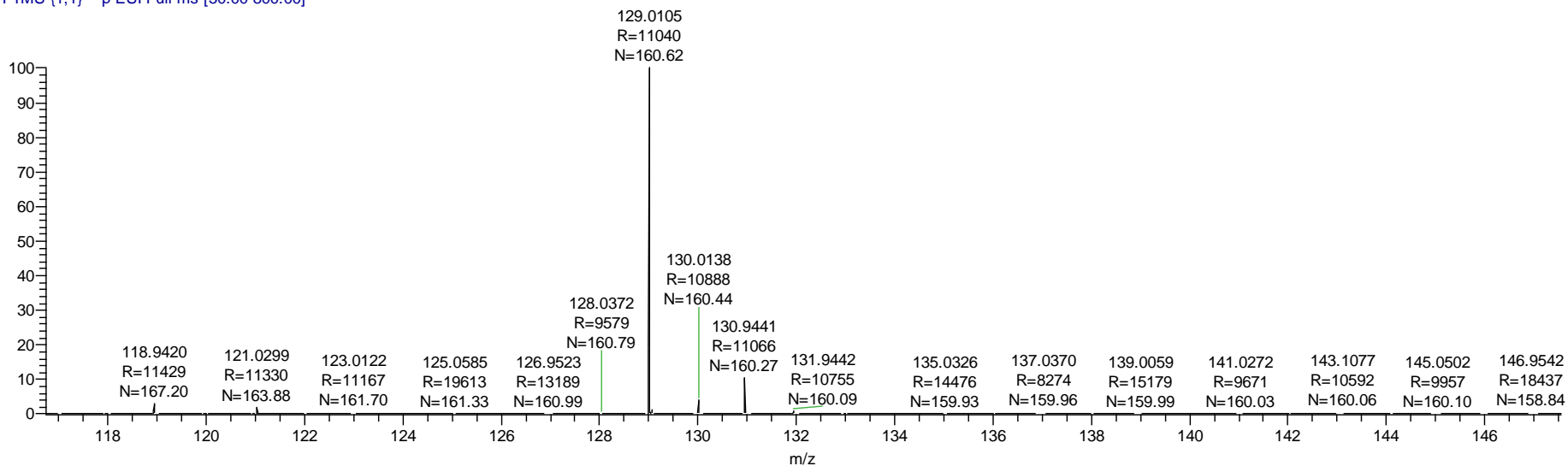
12/22/2010 12:00:56 PM

RC 5 500ppb x 5uL

RT: 0.00 - 10.02 SM: 9G



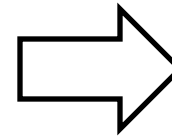
10122308 #36-47 RT: 0.66-0.85 AV: 12 SB: 385 0.10-0.51, 1.99-6.22 NL: 1.11E6
T: FTMS {1,1} - p ESI Full ms [50.00-800.00]



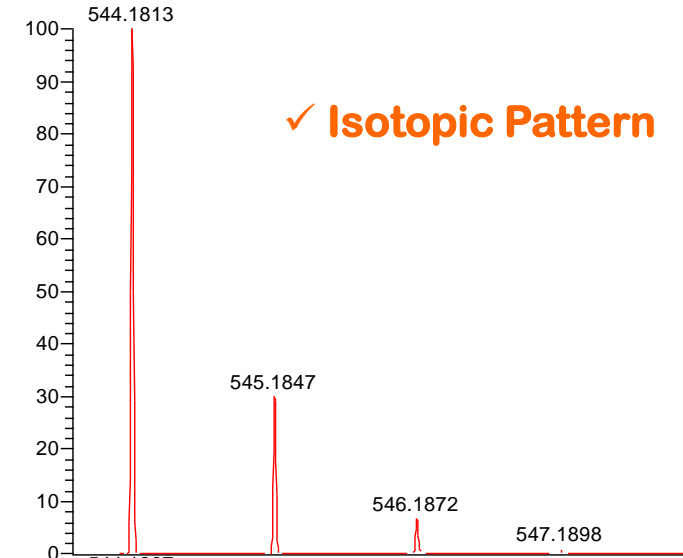
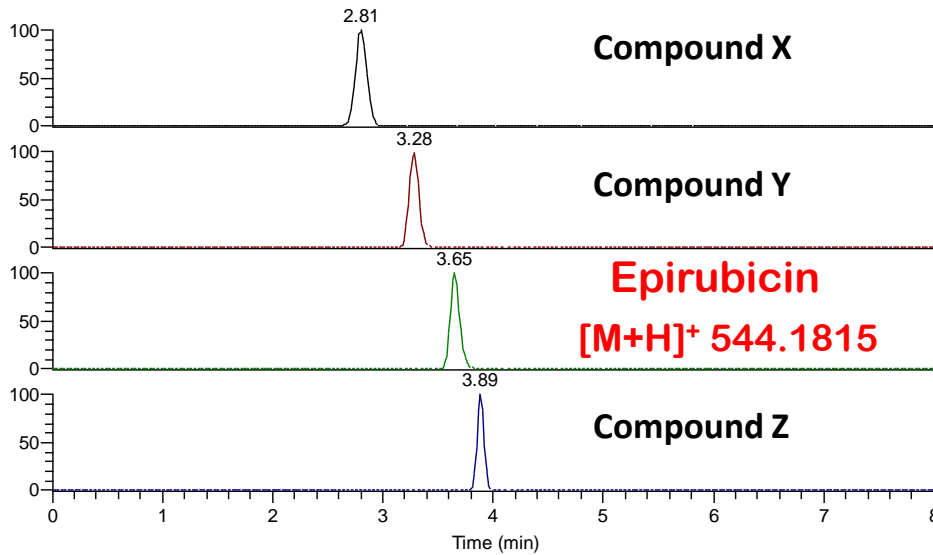
Target analysis and confirmation

criteria

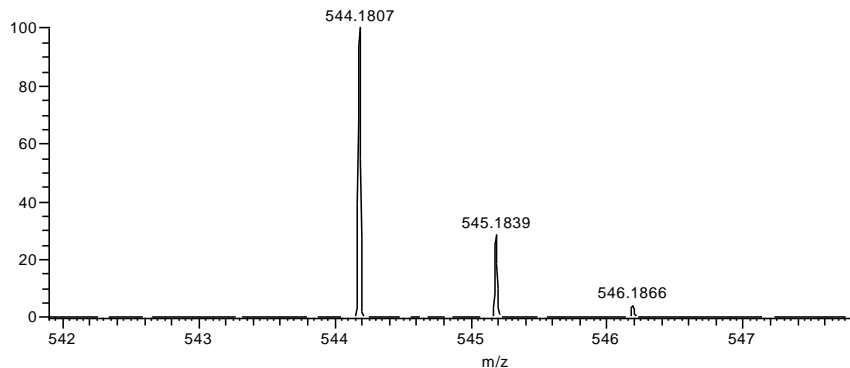
✓ Retention Time



Good linearity ($R^2=0.996$)
Good Sensibility



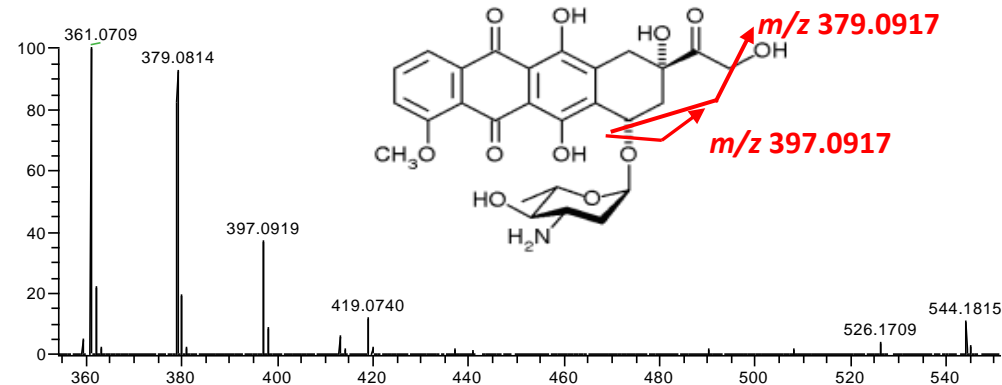
✓ Isotopic Pattern



✓ Mass Spectrum

✓ Accurate Mass Precursor Ion

HCD Spectrum 25eV
High Resolution Product Ions

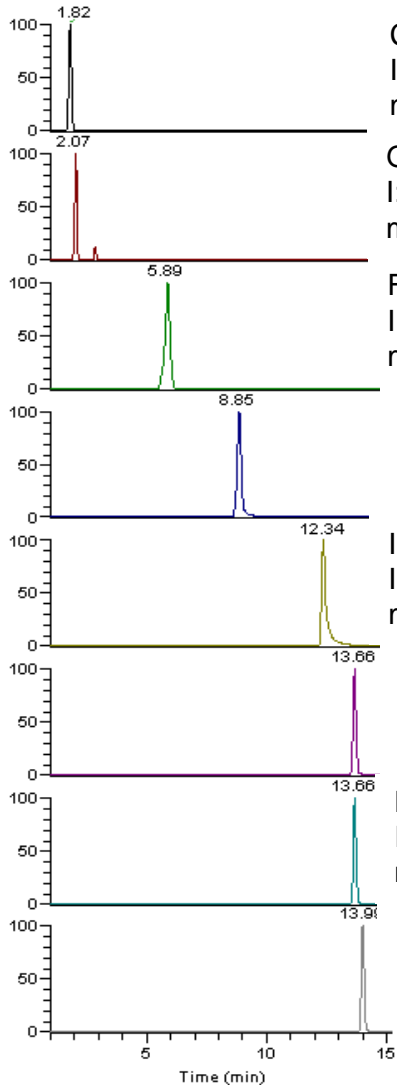


✓ Accurate Mass Products

HPLC-OrbitrapMS target analysis



Luna C18 (150 mm x 2 mm ID, 5 μm)



Citarabine
I:3.10e5
m/z= 244.0927

Gemcitabine
I: 2.29e6
m/z= 264.0790

Fludarabine
I:9.28e4
m/z=286.0944

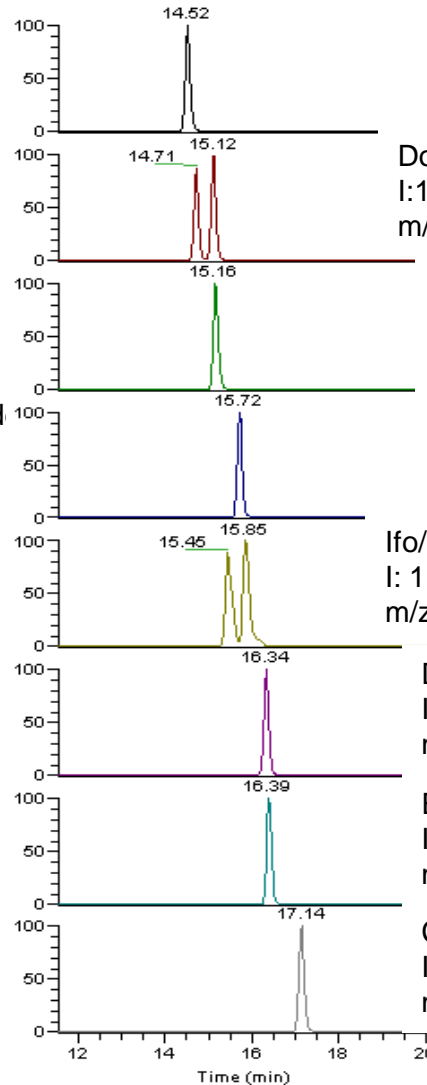
Aminoglutetimid
I:3.00e6
m/z= 360.1553

Imatinib
I:5.54e5
m/z= 494.2659

Goserelin
I:8.51e5
m/z= 635.3264

Leuprolide
I:1.11e6
m/z= 605.3294

Irinotecan
I:3.33e6
m/z= 587.2851



Vincristine
I:2.92e6
m/z= 825.4060

Doxo/Epirubicina
I:1.04e6
m/z= 544.1807

Vinblastine
I: 3.35e6
m/z= 811.4264

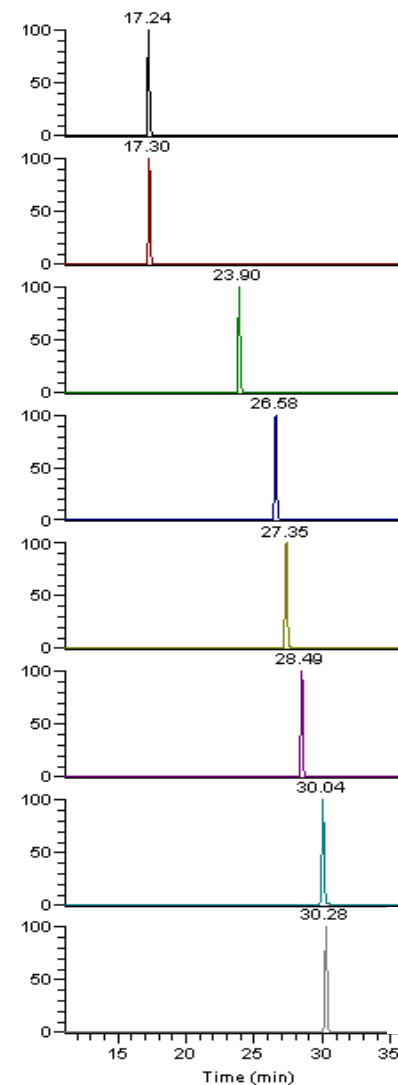
Melphalan
I: 1.43e6
m/z= 305.0810

Ifo/cyclofosfamida
I: 1.03e6
m/z= 261.0313

Daunorubicin
I: 7.77e5
m/z= 528.1863

Erlotinib
I: 6.51e6
m/z= 394.1753

Capecitabine
I: 5.90e5
m/z= 360.1553



Prednisone
I:9.31e5
m/z= 359.1841

Etoposide
I:1.38e5
m/z= 589.1911

Tamoxifen
I:1.41e7
m/z= 372.2314

Docetaxel
I:4.37e4
m/z= 808.3541

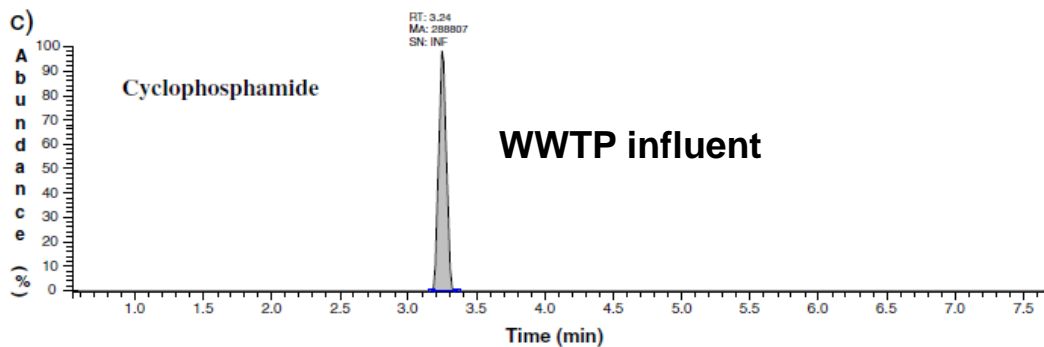
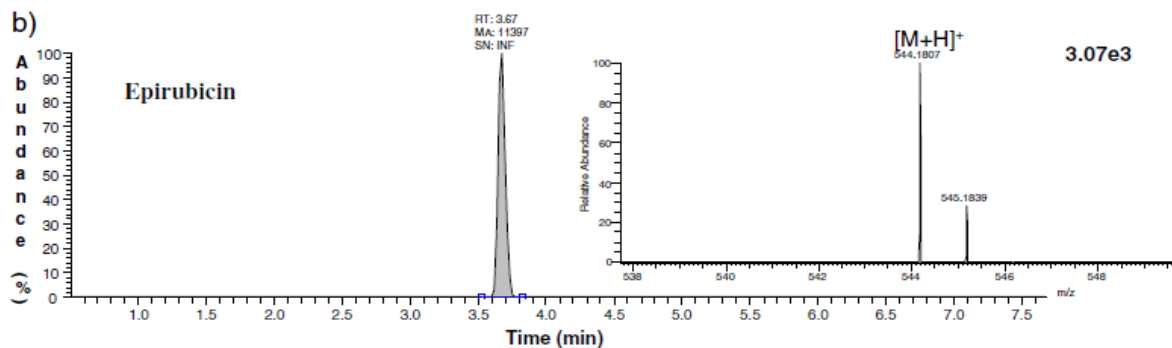
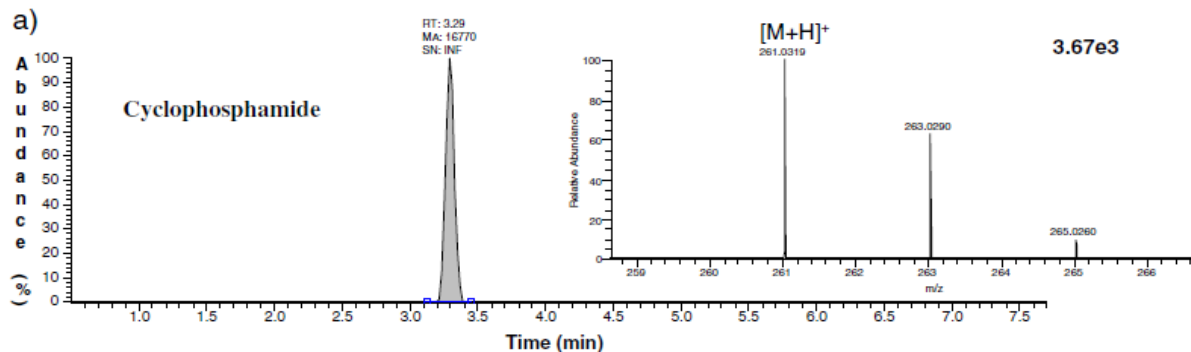
Paclitaxel
I:1.68e5
m/z= 854.3376

Chlorambucil
I:2.94e6
m/z= 304.0864

Ciproterone
I:1.39e6
m/z= 417.1823

Megestrol acetate
I:1.27e6
m/z= 385.2371

Monitoring



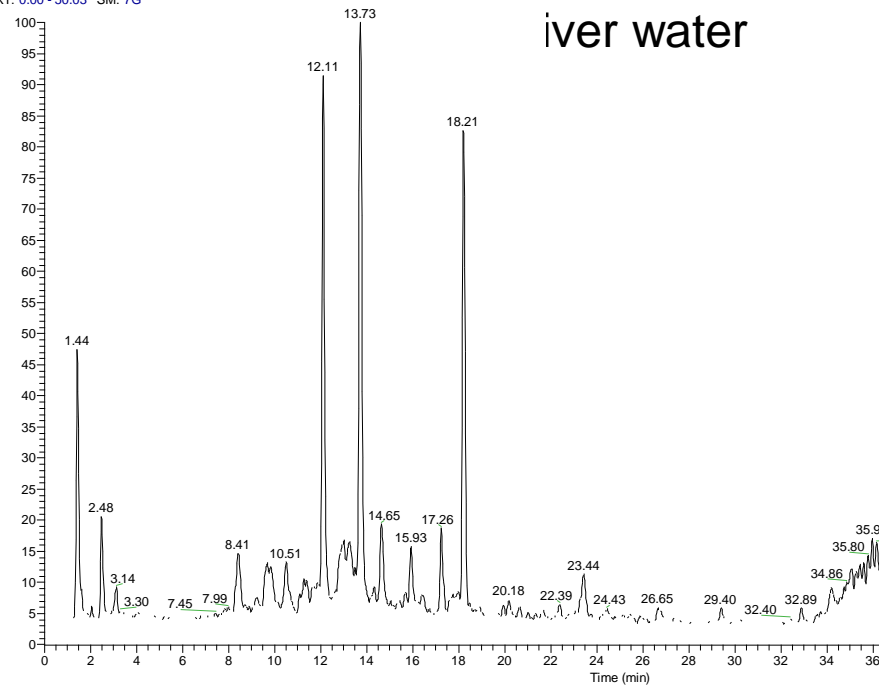
Hospital effluents
5.2-24.8 $\mu\text{g L}^{-1}$

WWTP influents
0.1-13 $\mu\text{g L}^{-1}$

WWTP effluents
0.01-2 $\mu\text{g L}^{-1}$

Rivers
0.001-0.6 $\mu\text{g L}^{-1}$

RT: 0.00 - 50.03 SM: 7G



iver water

Untargeted analysis

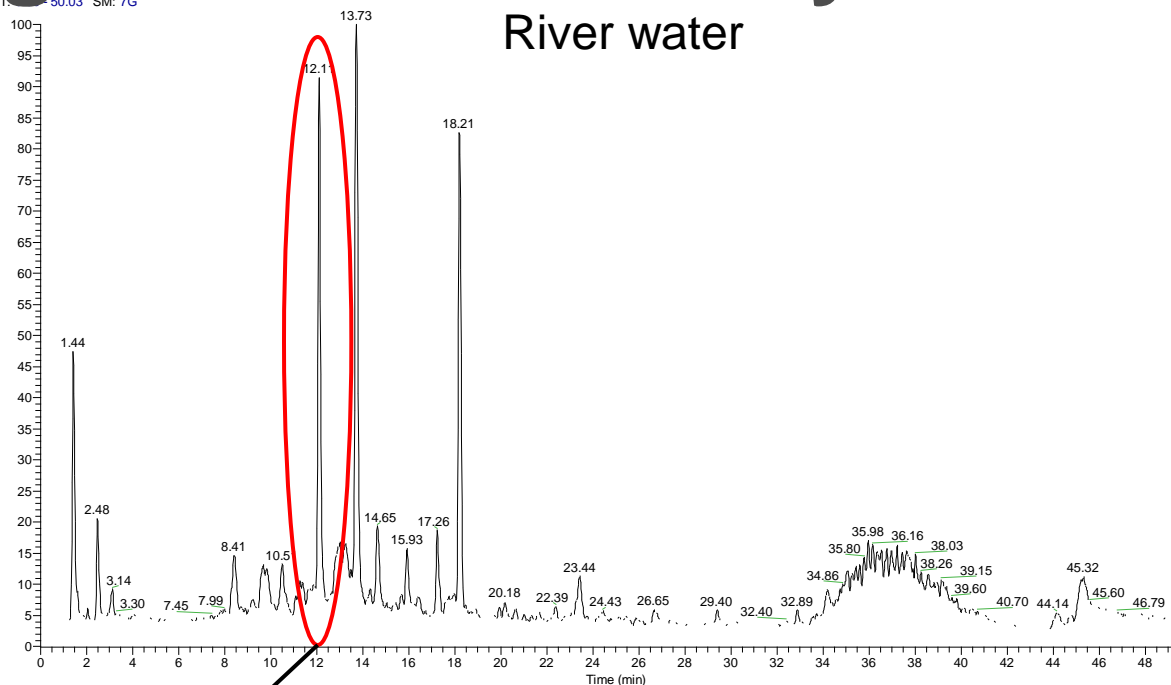


Lost...

Untargeted unknown analysis

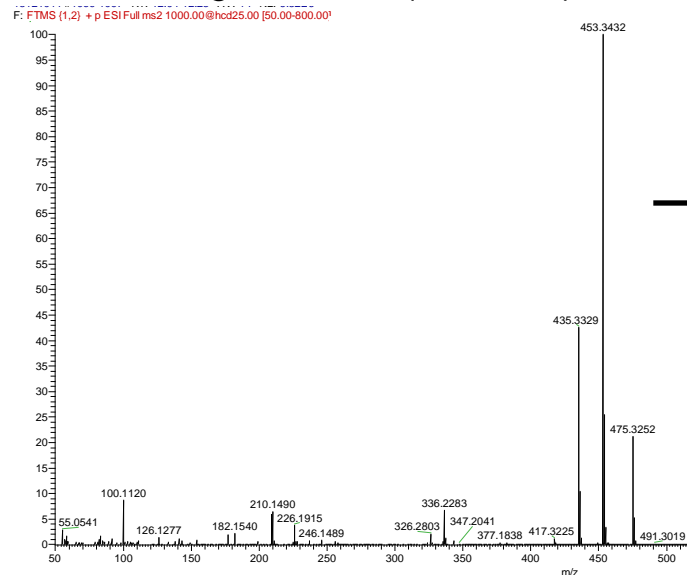
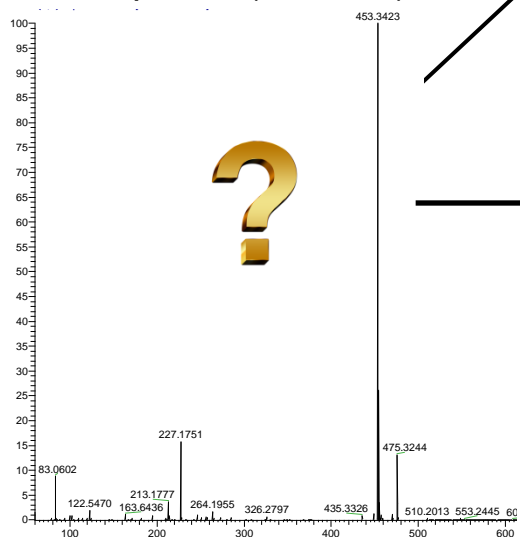


RT: 50.03 SM: 7G



Mass spectra (full scan)

Mass fragmentation (HCD cell)



TraceFinder™ 3.0
Optimized for Quantitation

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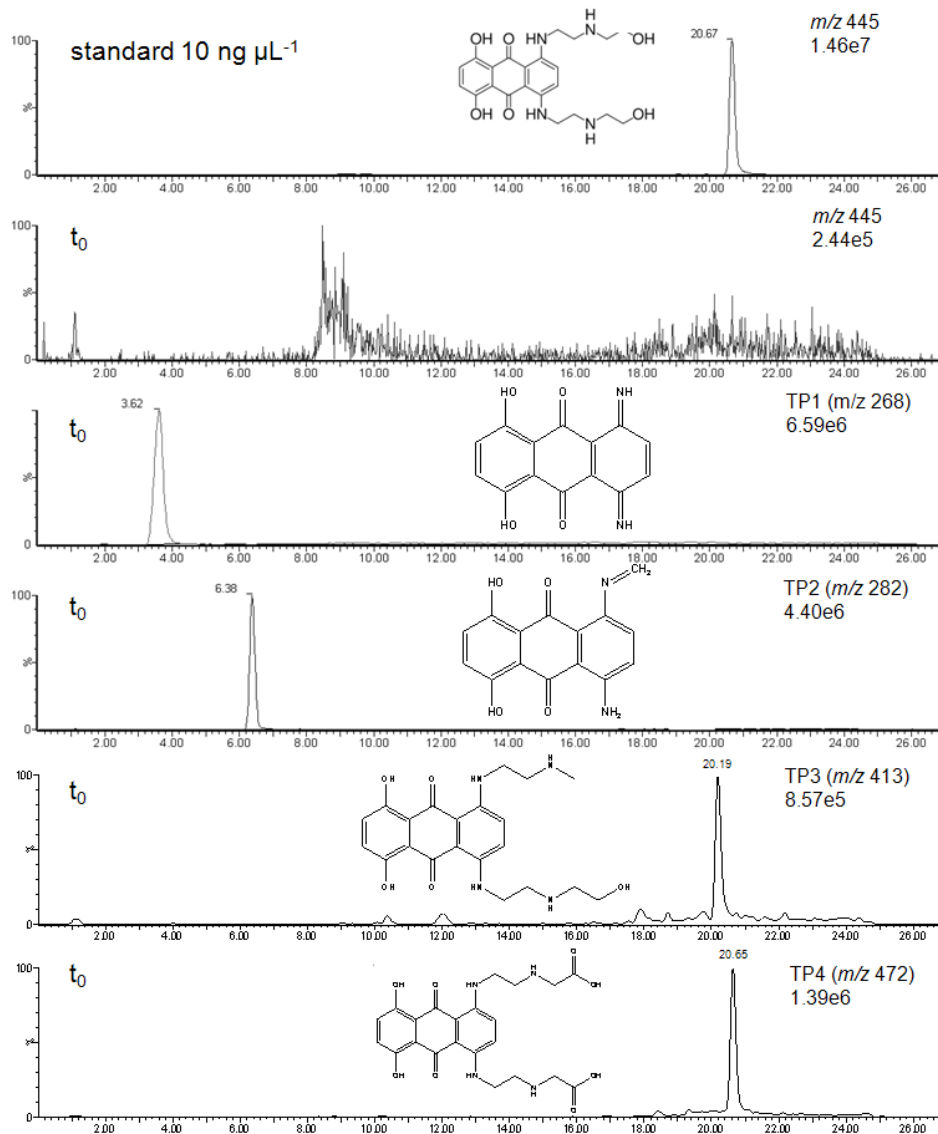


TraceFinder™
The Power to Know

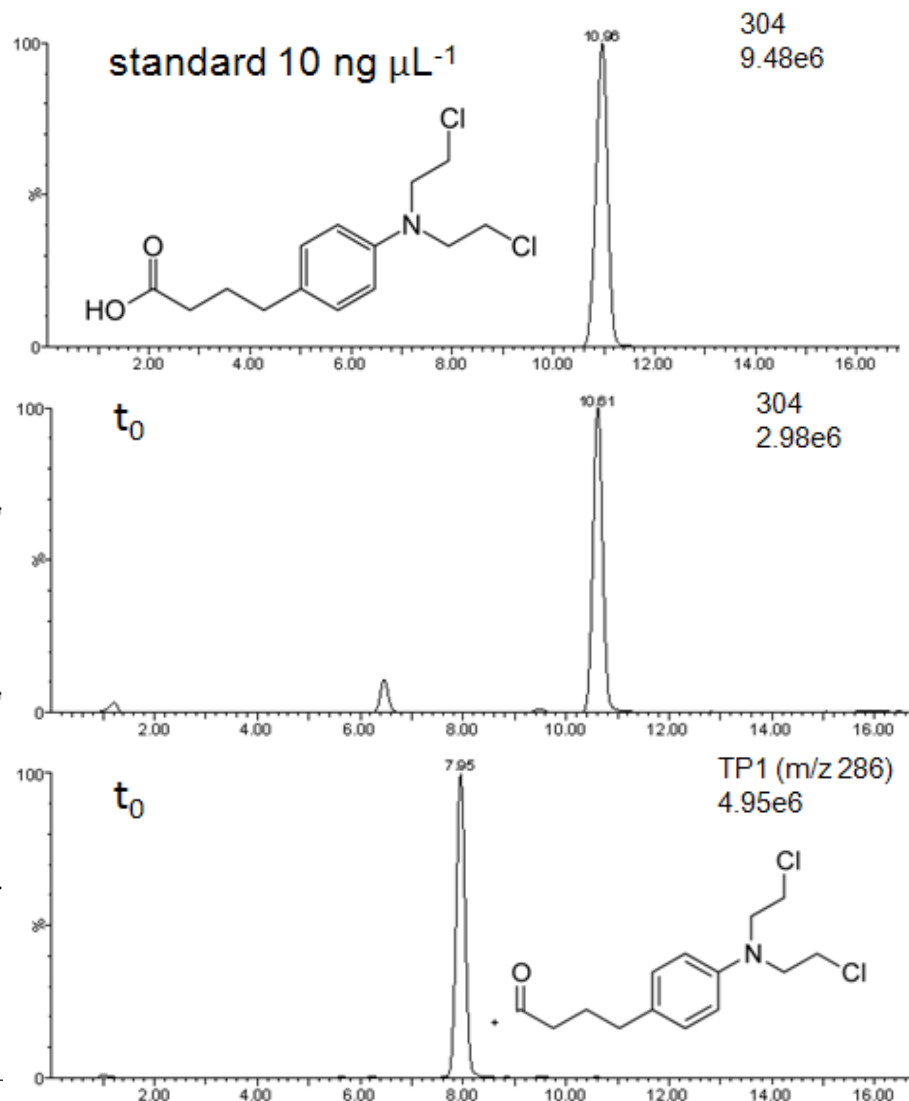
Untarget suspect: degradation products



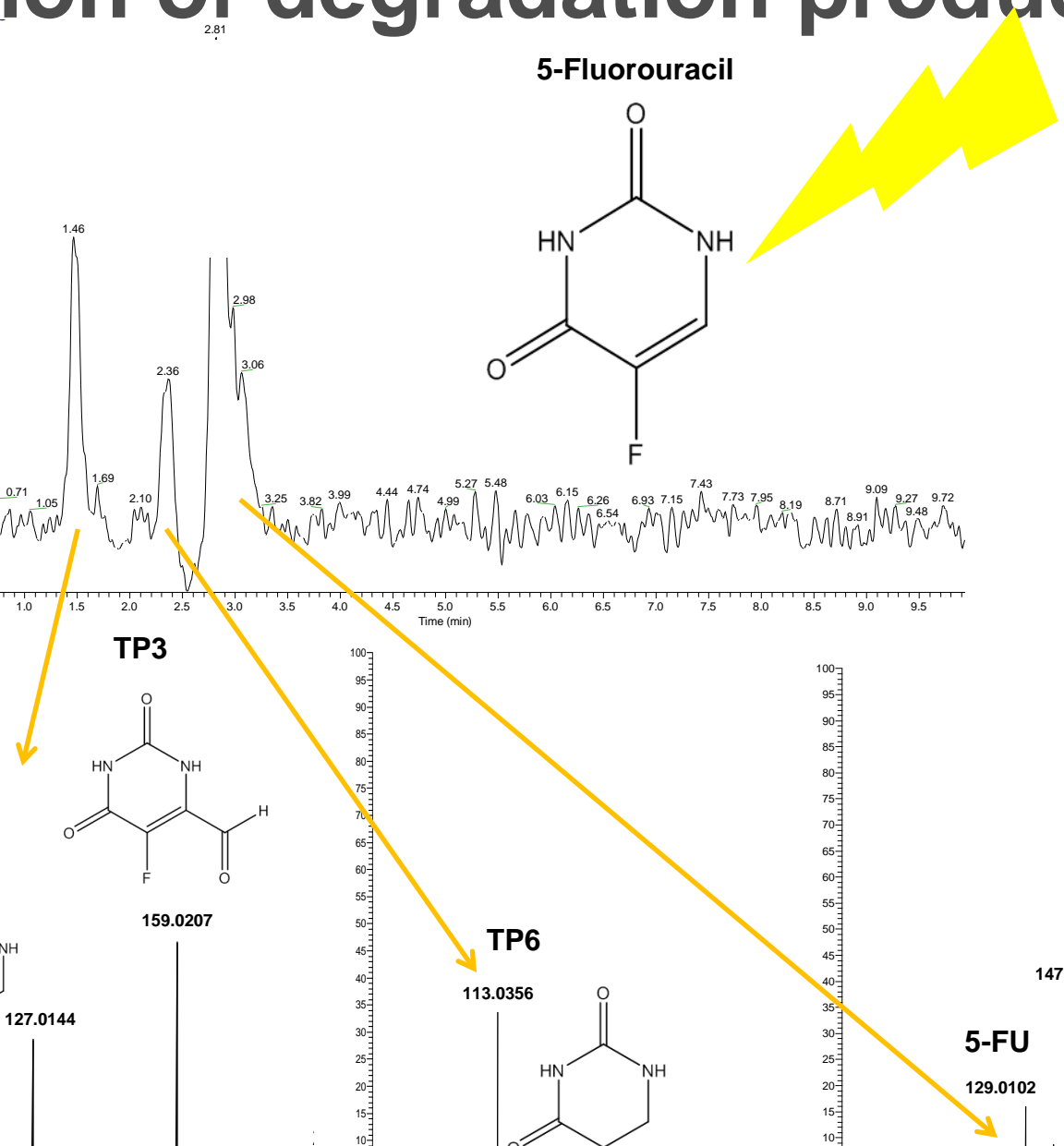
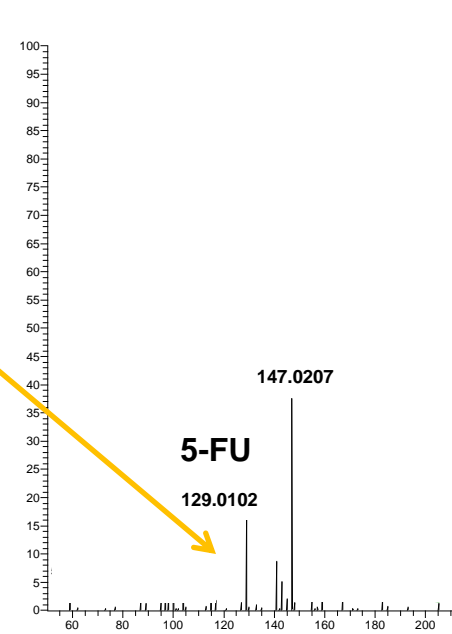
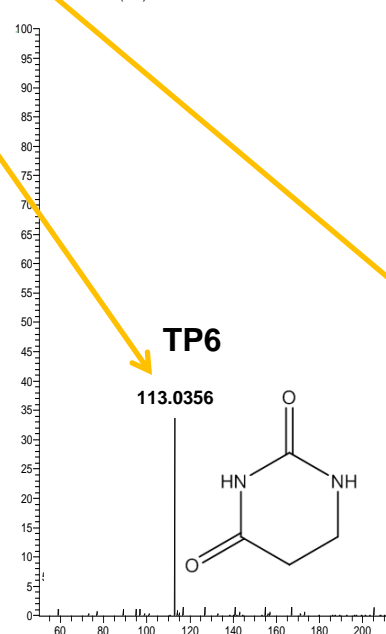
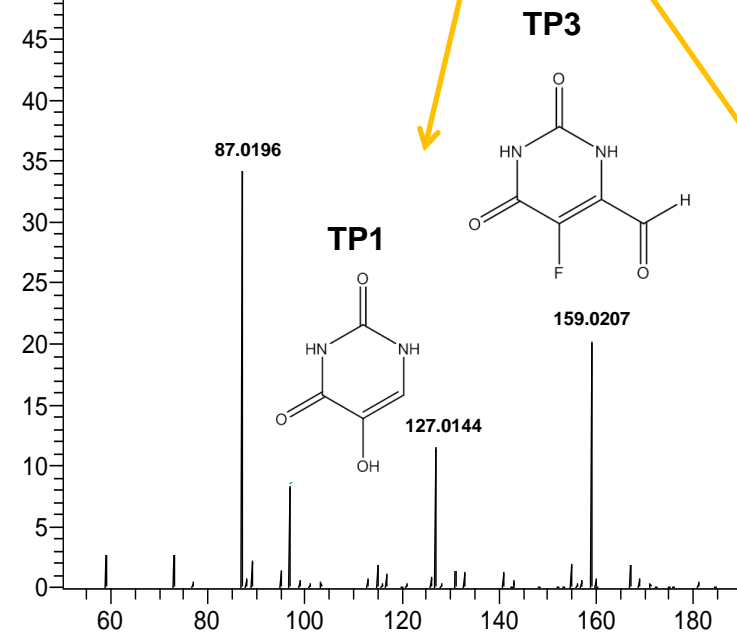
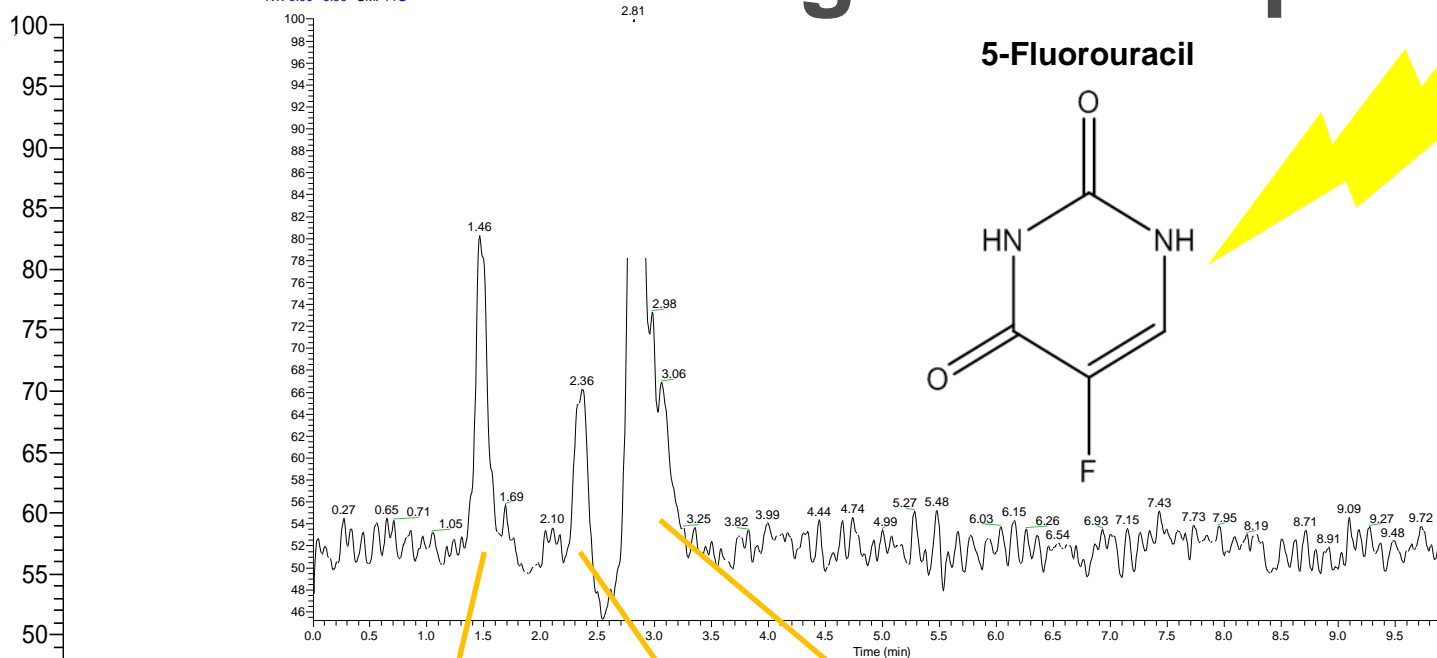
Mithoxantrone



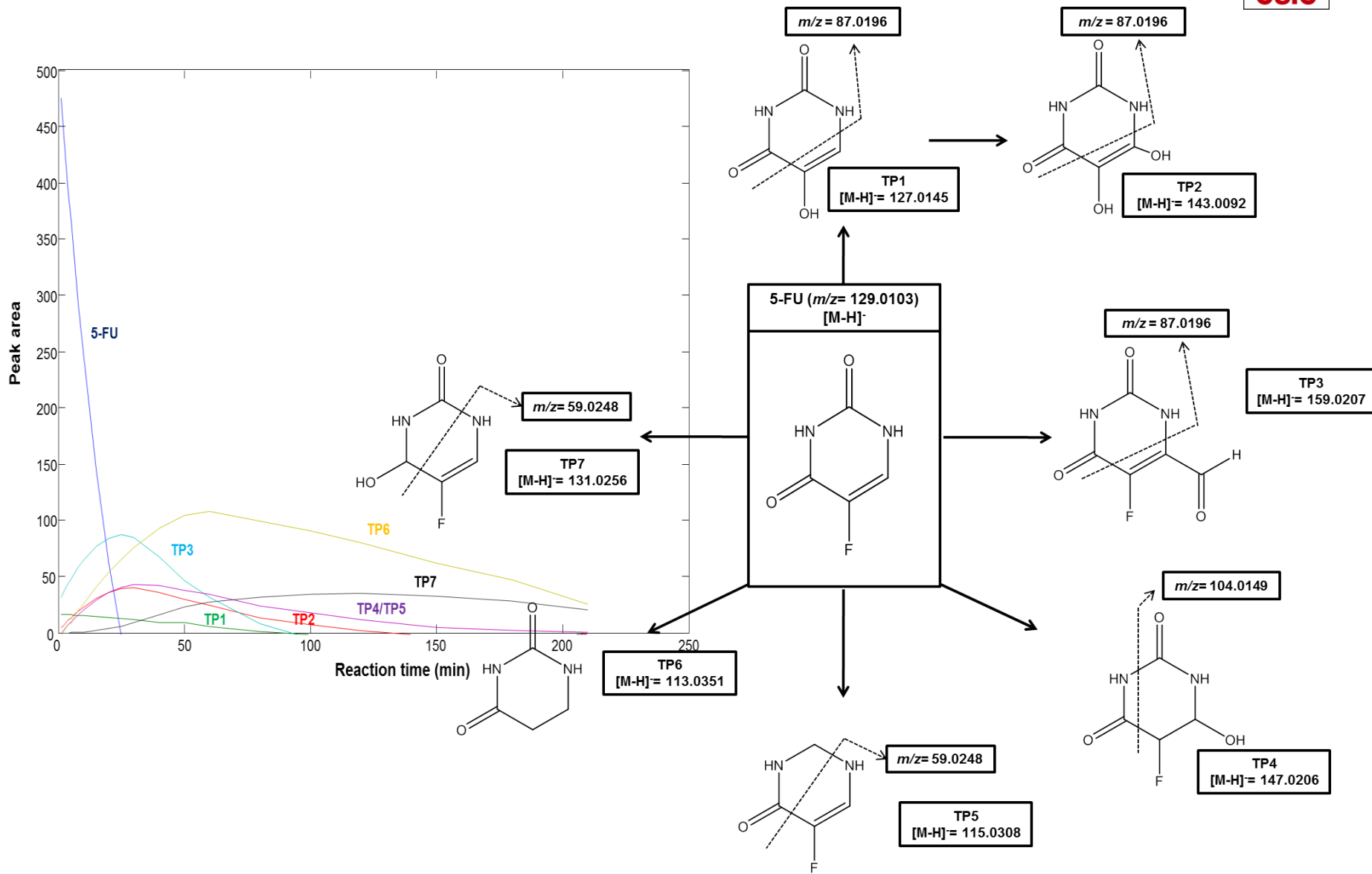
Chlorambucil



Identification of degradation products

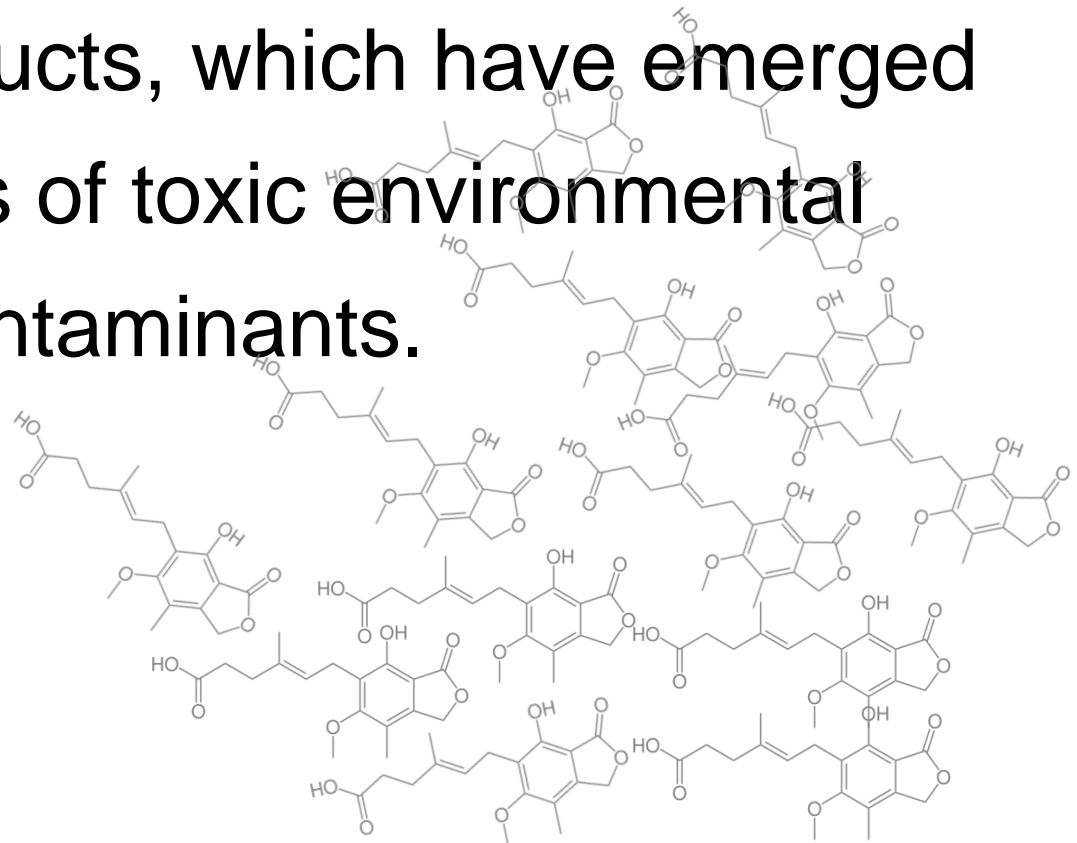


5-Fluorouracil



Conclusions

The MS potential is non-ending for the analysis of anticancer drugs and their degradation products, which have emerged as a new class of toxic environmental contaminants.





**Thank you for
your attention**

Questions?