



# **Selective Extraction And Analysis of Chemical Migrants from Packaging Material using Supercritical Fluids (SFE)**

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**International Symposium on GPC/SEC and  
Related Techniques**

# Market Specific terminology

## ■ Pharmaceutical packaging

- **Extractables** – Compounds that can be extracted from elastomeric, plastic components or coatings of the container and closure system when in the presence of an appropriate solvent(s)
- **Leachables** – Compounds that leach from elastomeric, plastic components or coatings of the container and closure system as a result of direct contact with the formulation

## ■ Food packaging

- **Intentionally added substances (IAS)** - compounds added to produce the final product
- **Non-intentionally added substances (NIAS)** - impurities from starting materials, reaction and degradation products formed during manufacturing process
- **Migrants** - compounds which partition from the packaging into the food



## Typical extractables & leachables

- Chemical additives, plasticizers, antioxidants and contaminants present in individual polymers
- Monomers and oligomers from incomplete polymerization reactions
- Volatile compounds from the secondary packaging such as inks and adhesives
- Residual compounds from the surfaces of the molding equipment, antistatics etc

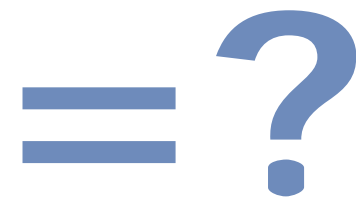
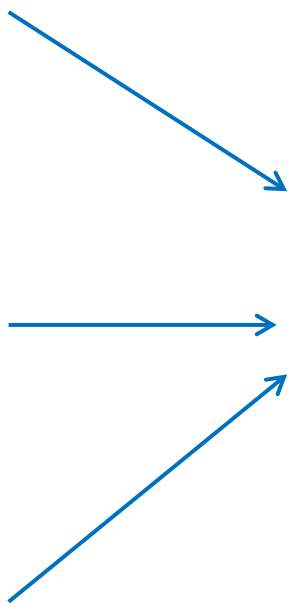


# Regulated areas for packaging

Food packaging and contact materials- European guidelines list detailed experimental conditions (simulant, T°, time) based on food type

Pharma- guidelines exist in Europe and USA

Cosmetics- only European regulations require testing



# Sample Preparation

## Major Source of Laboratory Costs



Grinding/Cutting



SFE



Soxhlet  
Extraction



Microwave



Migration cell

# Comparison study of 3 different extraction techniques

- **Microwave**


- Hexane, Isopropanol

- **Soxhlet**

- Hexane , Isopropanol

- **Supercritical Fluid Extraction (SFE)**

- Isopropanol



Compare extraction profiles of the same packaging materials by using UPC<sup>2</sup> (SFC)

- Multiple solvents to ensure polar and non-polar analytes extracted



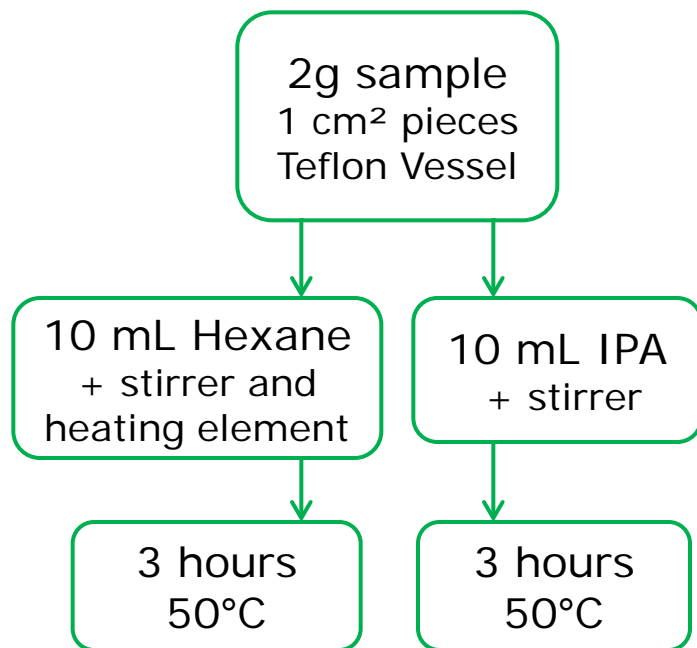
# Samples

- High Density Polyethylene pill bottle (**HDPE**)
- Low Density Polyethylene bottle (**LDPE**)
- Ethylene Vinyl Acetate plasma bag (**EVA**)
- Polyvinyl Chloride blister pack (**PVC**)

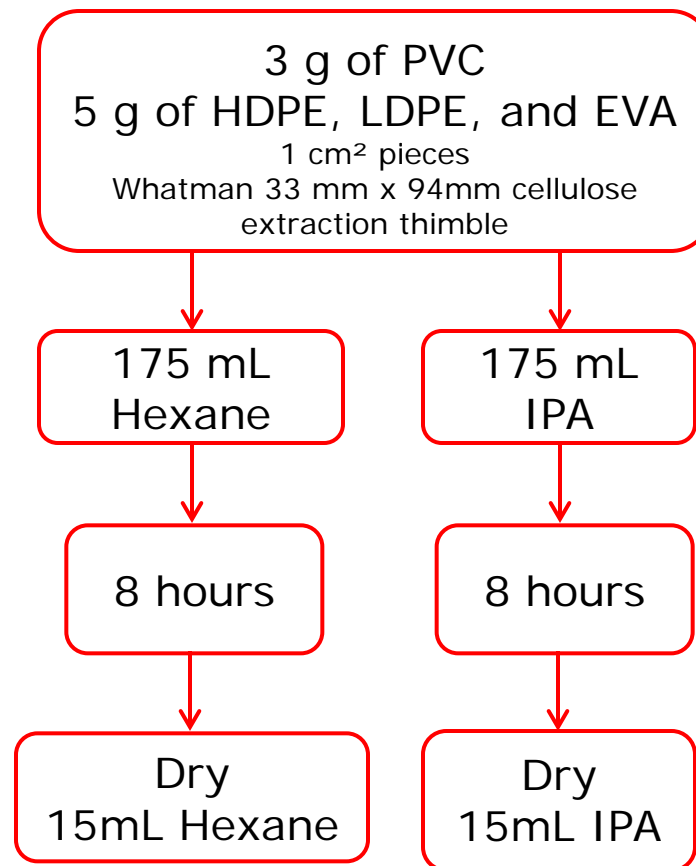
- Analytes :
  - Irgafos 168
  - 5-chloro-2-hydroxy-4-methylbenzophenone (5-Cl-2-OH-4-methyl BP)
  - 4-hydroxy-2-octyloxybenzophenone (4-OH-2-octyloxy BP)
  - Irganox 245
  - Lowinox 44B25
  - Naugard 445
  - Diphenyl phthalate
  - Tinuvin 328
  - Uvitex OB

# Extractions conditions

## Microwave extraction



## Soxhlet







# Why a Supercritical Fluid?

Why do Supercritical fluids make good mobile phases for chromatography?

	Diffusivity (cm <sup>2</sup> /s)	Viscosity (g/cm x s)
Gas	10 <sup>-1</sup>	10 <sup>-4</sup>
Supercritical Fluid	10 <sup>-4</sup> - 10 <sup>-3</sup> Liquid Like	10 <sup>-4</sup> - 10 <sup>-3</sup> Gas Like
Liquid	< 10 <sup>-5</sup>	10 <sup>-2</sup>

Diffusivity describes the rate at which one substance can move through another

Viscosity is resistance to flow

High diffusivity, and low viscosity combine in SFC to give **fast, efficient chromatography**

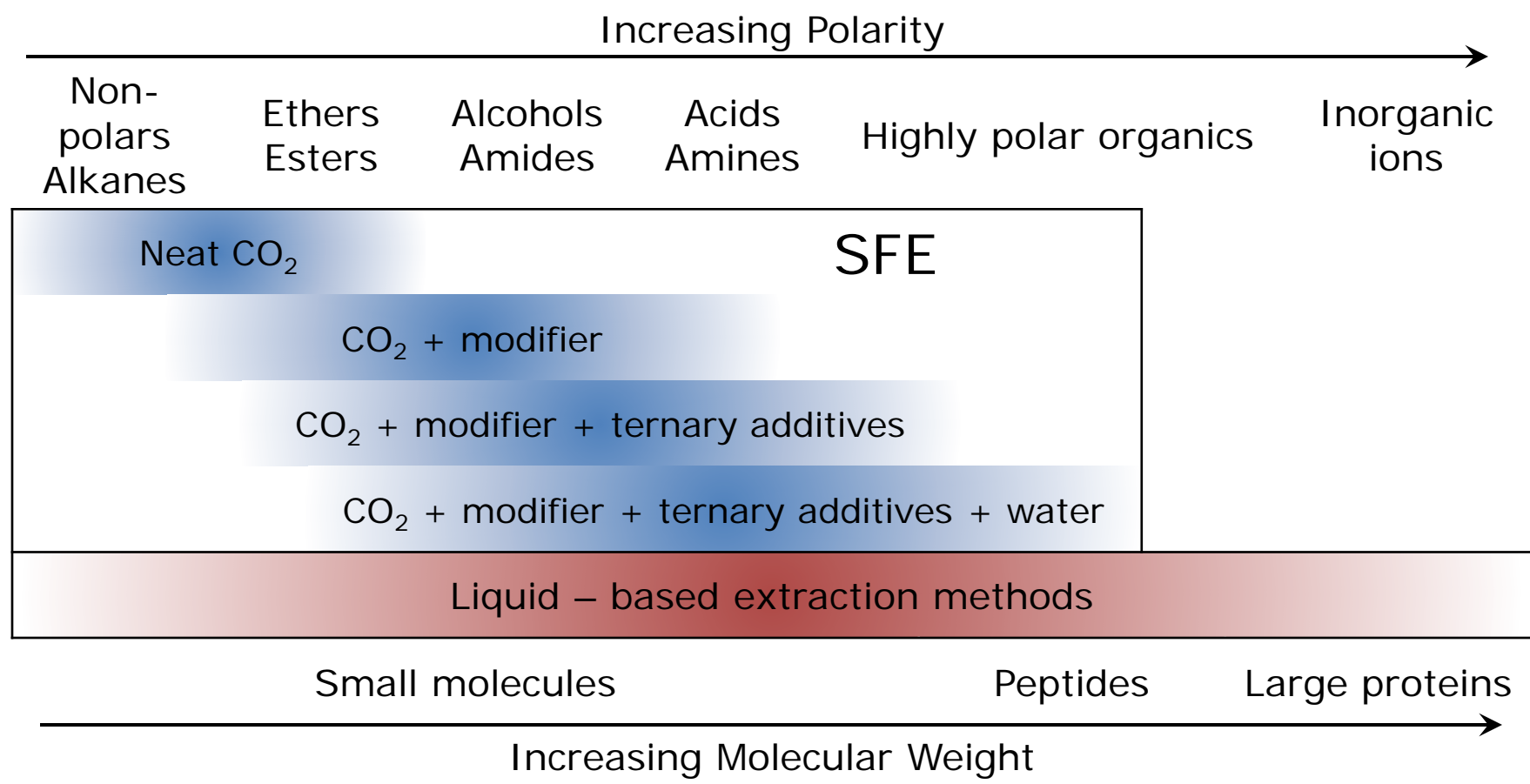


# What Is Supercritical Fluid Extraction

- Supercritical Fluid Extraction is the process of separating one or multiple components (**the extractant**) from another (**the matrix**) using supercritical fluids as the extracting solvent
- Extraction is usually from a **solid matrix**
- SFE can be used as :
  - A **sample preparation step for analytical purposes**
  - Or on a larger scale to either **strip unwanted material from a product**
    - (e.g. decaffeination)
  - Or **collect a desired product**
    - (e.g. essential oils)
- Carbon dioxide (CO<sub>2</sub>) is the most used supercritical fluid sometimes modified by co-solvents such as ethanol or methanol
  - > 31° C and 74 bar (1073 psi)
- Based on the principle that solubility in a supercritical fluid increase dramatically with increasing density and different solutes have different solubility at the same condition



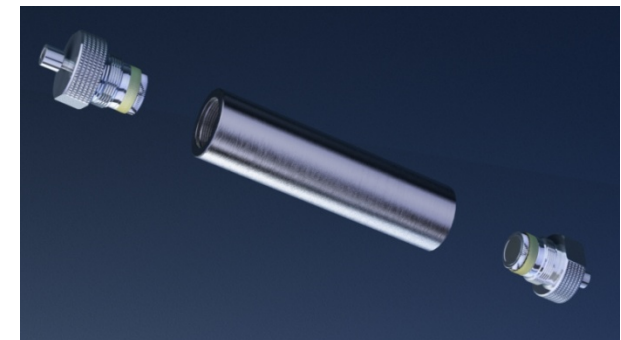
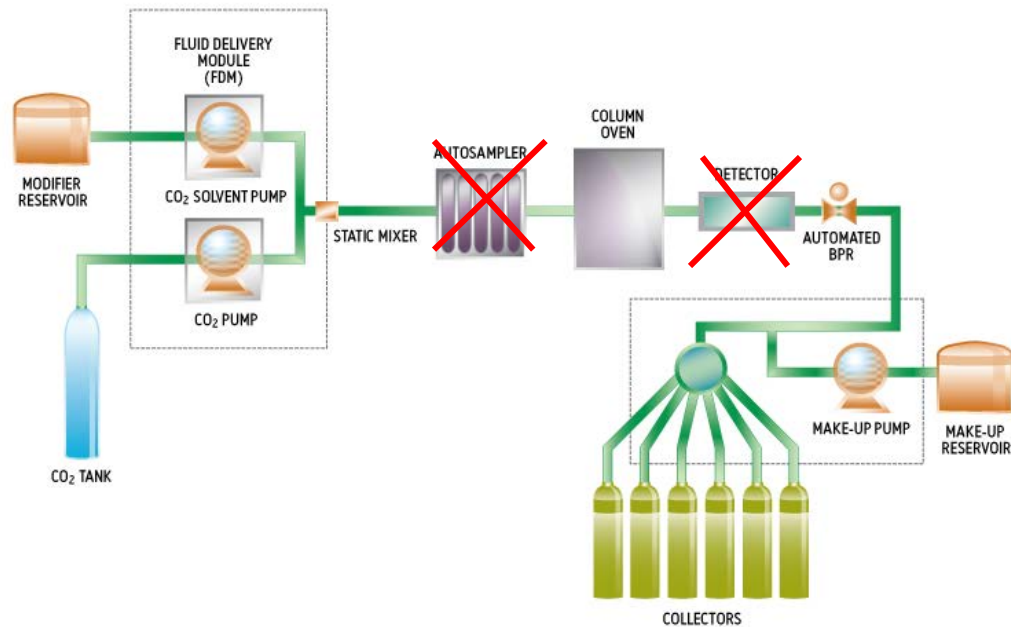
# Extractability Based on Polarity



**One of the largest advantages of SFE: Selectivity**

# Instrumentation

- An extraction technique **complementary/alternative to Soxhlet or liquid/liquid extraction**
  - CO<sub>2</sub> in combination with an organic solvent, most commonly alcohols, is used as the extraction solvent





# Extraction Modes

- Extractions are done in dynamic, static, or combination modes.
- In a **dynamic extraction** the supercritical fluid **continuously flows** through the sample in the extraction vessel and out the restrictor to the trapping vessel.
- In **static mode** the supercritical fluid is **held in the extraction vessel** for some period of time before being released through the restrictor to the trapping vessel.
- In **combination mode**, a static extraction is performed for some period of time, followed by a dynamic extraction.



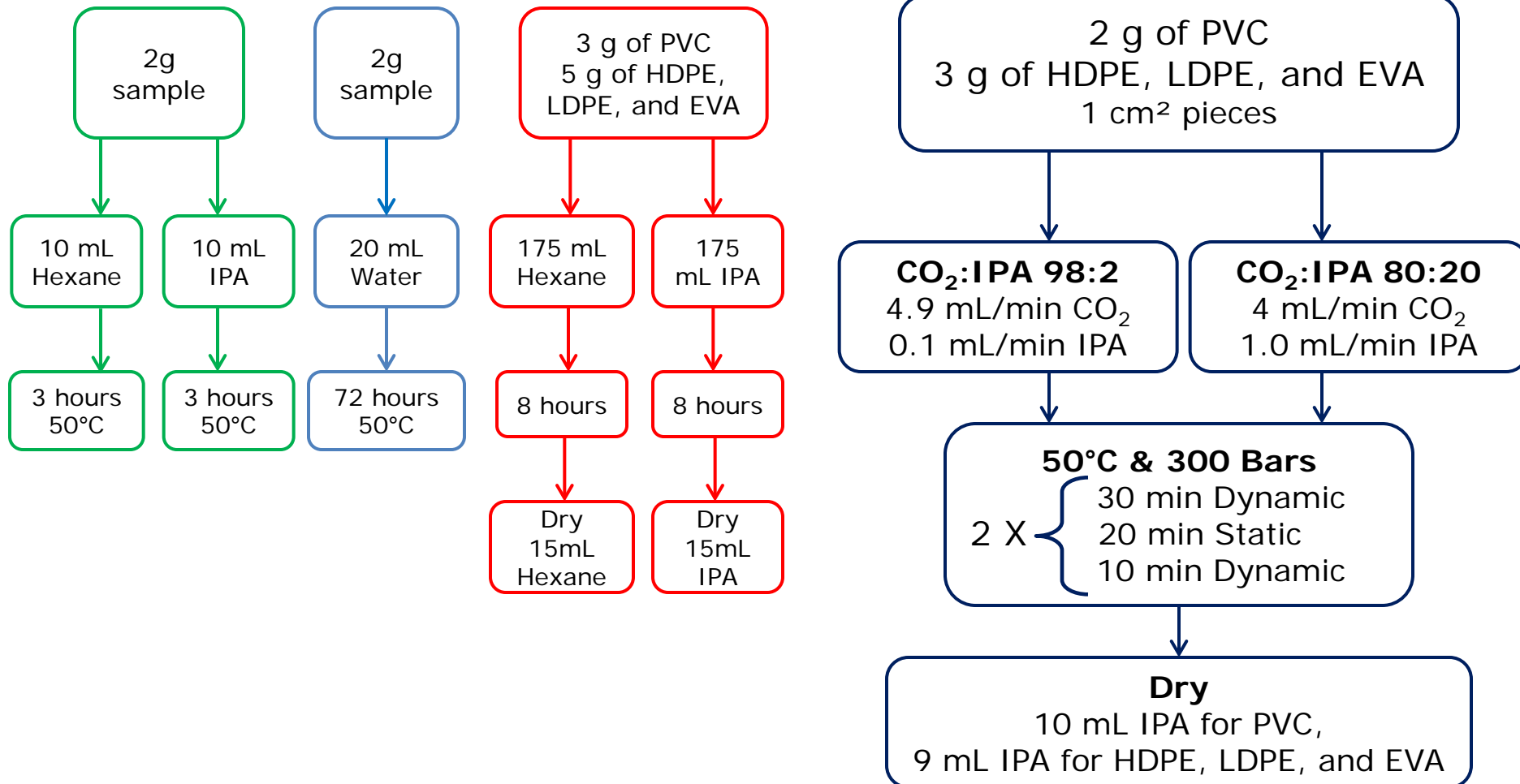
# SFE conditions

## Microwave extraction

## Water extraction

## Soxhlet

## Supercritical Fluid Extraction

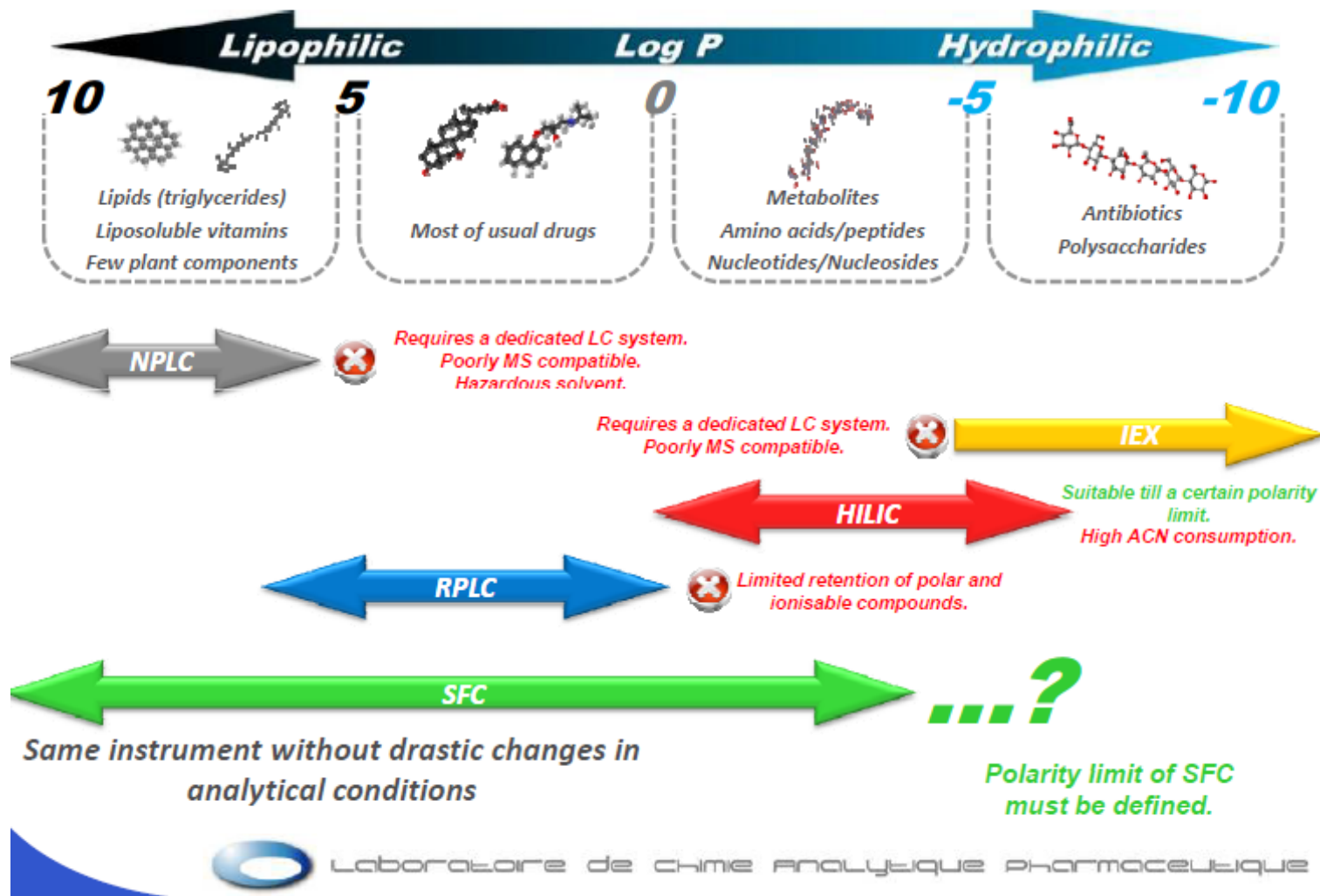


# Advantages of SFE

- **Increased selectivity and specificity**
  - Fine tune the extraction with changes in co-solvents (Method Dev)
- **Decreased cost** per sample
  - Minimal procurement or disposal cost of CO<sub>2</sub> in comparison to organic solvents
  - **Improves extraction efficiency and reduces extraction time** vs. other sample preparation techniques
- **Minimize exposure** to organic solvents
  - Lack of residual organic solvents
  - Is environmentally friendly
- **Accelerate** the extraction process
  - Extract analytes faster than comparative techniques
  - Eliminate cumbersome traditional solid/liquid extraction (ie. Soxhlet or solvent soak)
- Ability to handle **thermally labile compounds**
  - Operates at lower temperatures than PSE, MAE and soxhlet

# Broad Applicability of SFC Analysis

## Polarity limits of chromatographic techniques

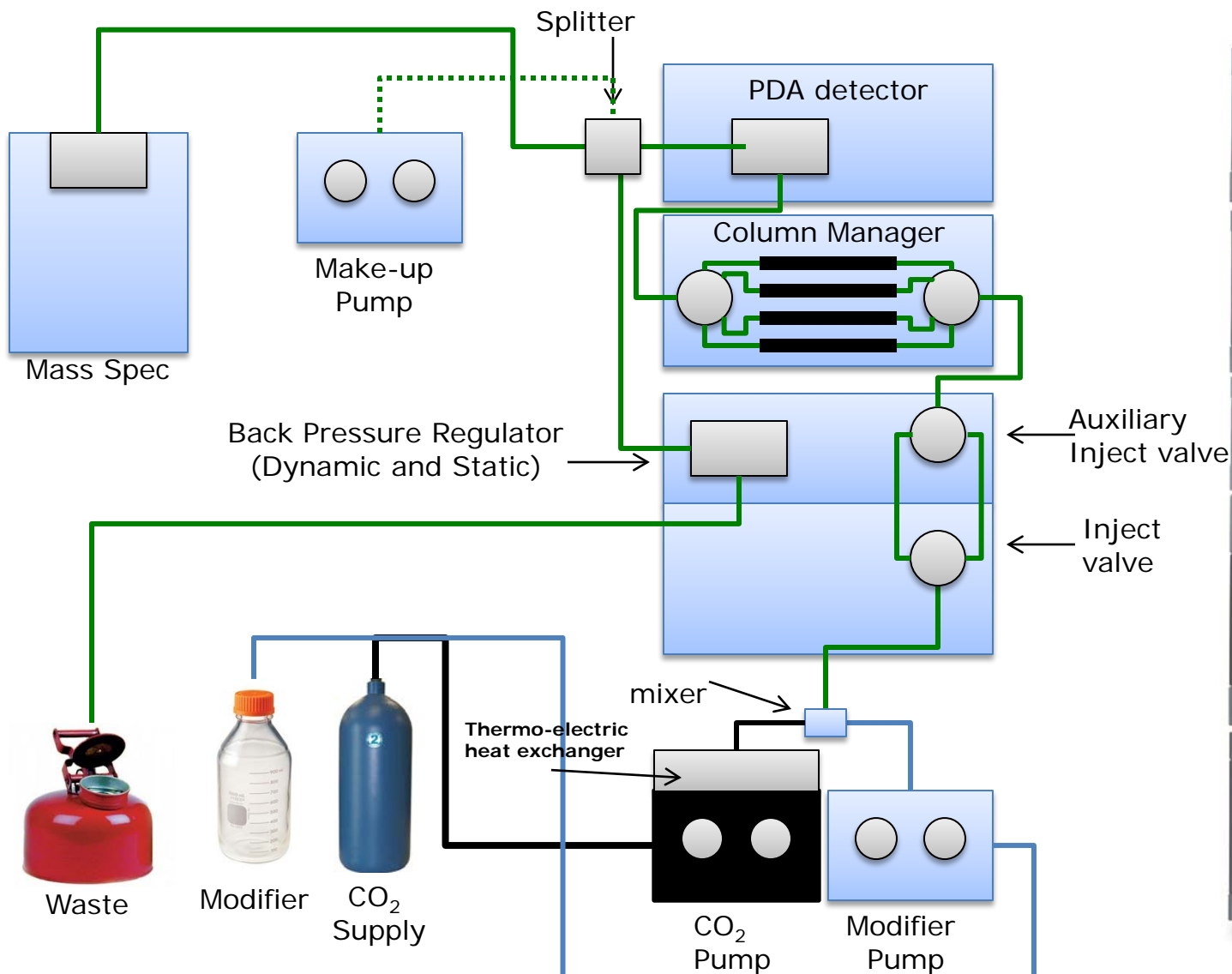


Courtesy of A. Grand-Guillaume Perrenoud, D. Guillarme, Pr J-L. Veuthey, University of Geneva



# The ACQUITY UPC<sup>2</sup>

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# UPC<sup>2</sup>: Compatibility with all MS Technologies

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**For ultimate CC-MS performance,  
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**ACQUITY QDa**

- Single quadrupole detector for robust and routine performance

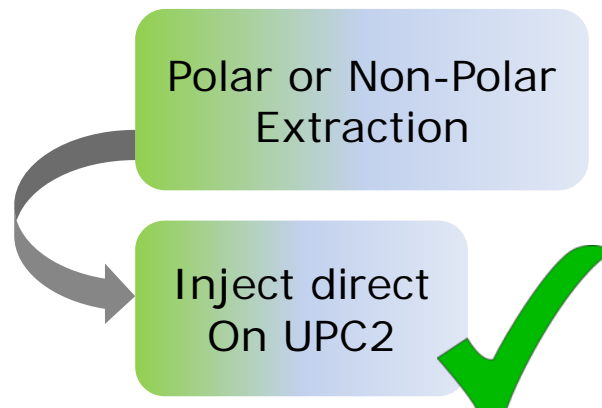
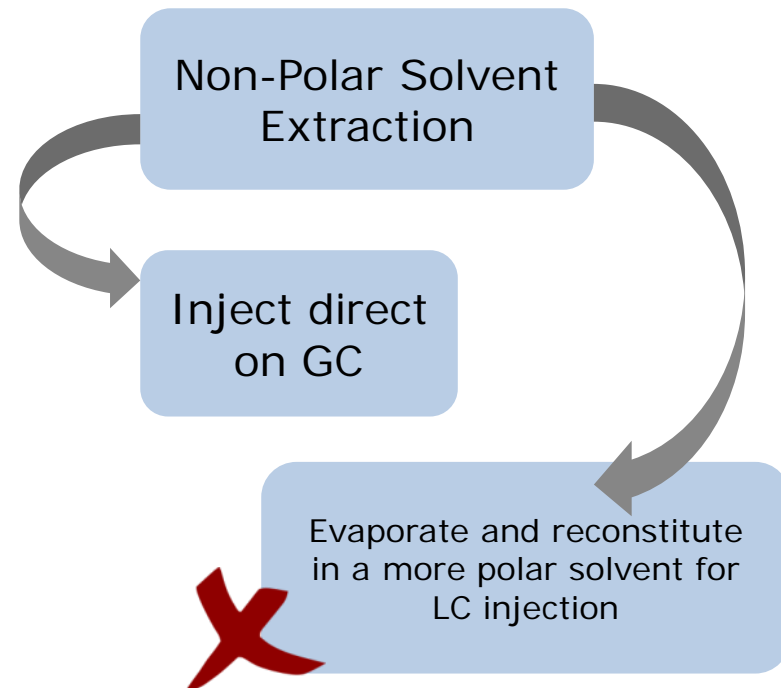
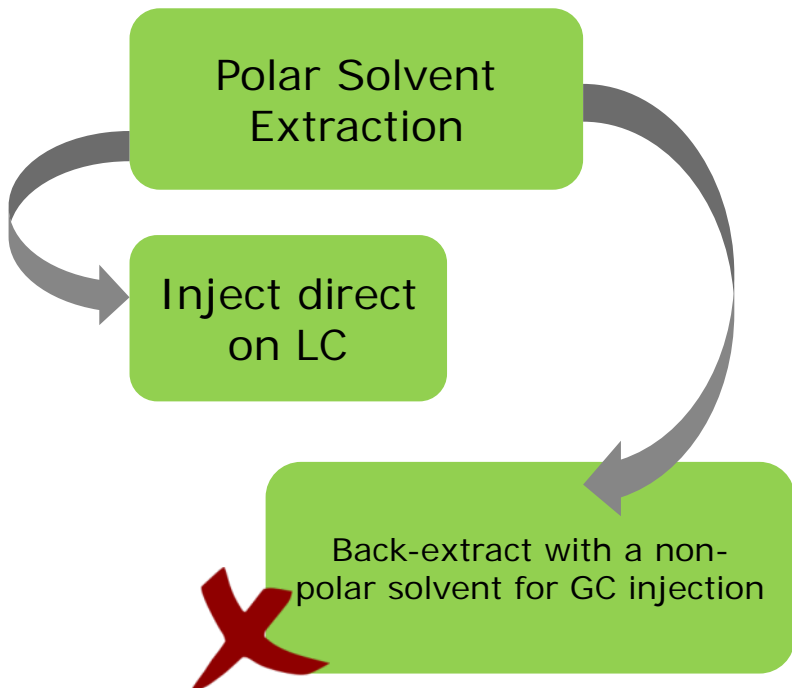
**Xevo TQ-XS**

- Ultimate sensitivity

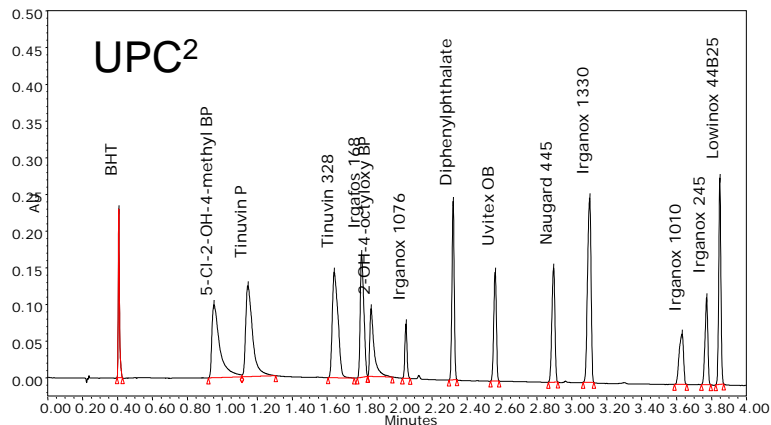
**Xevo G2-XS Qtof and Synapt G2-Si**

- Qualitative and quantitative results from a single platform

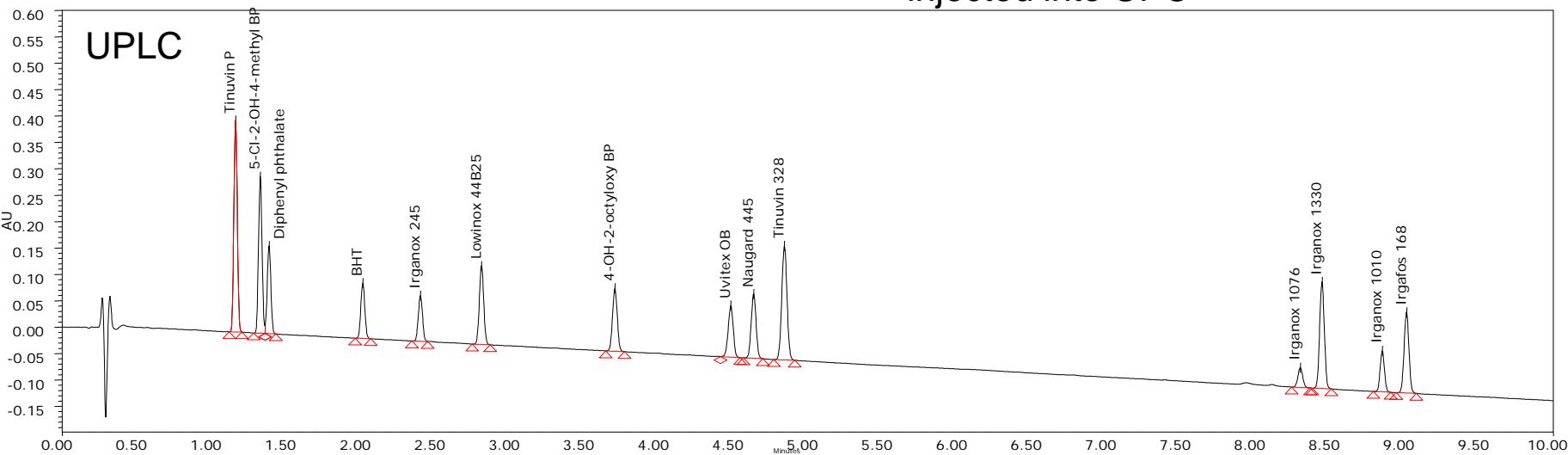
# Workflow Benefit of ACQUITY UPC<sup>2</sup> for the Analysis of Polymer Extracts



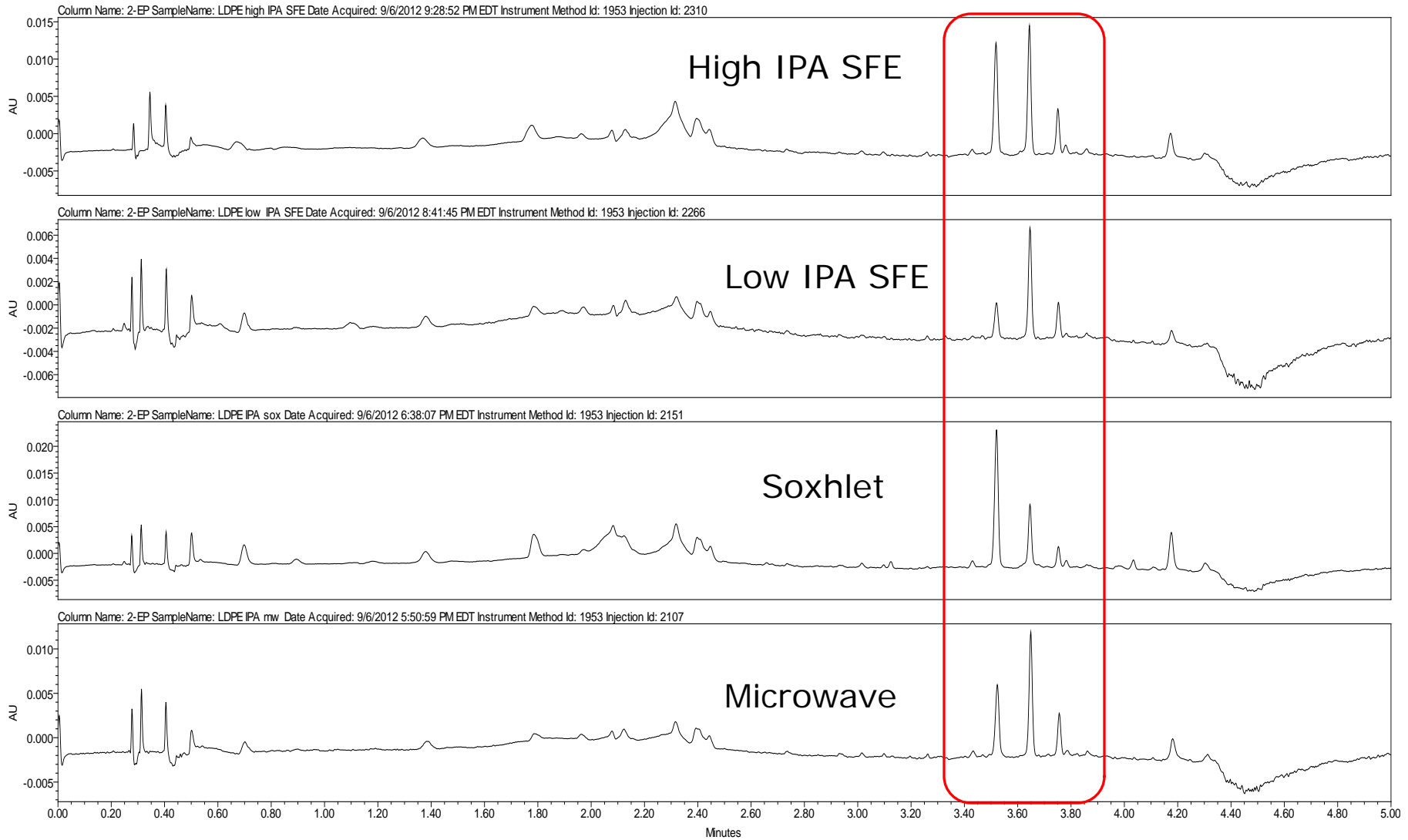
# Chromatographic separations



- 4 min separation by UPC<sup>2</sup> vs. 9.5 min by UPLC
- Orthogonality of techniques demonstrated by change in elution order
- Either of extraction solvents directly injected into UPC<sup>2</sup>

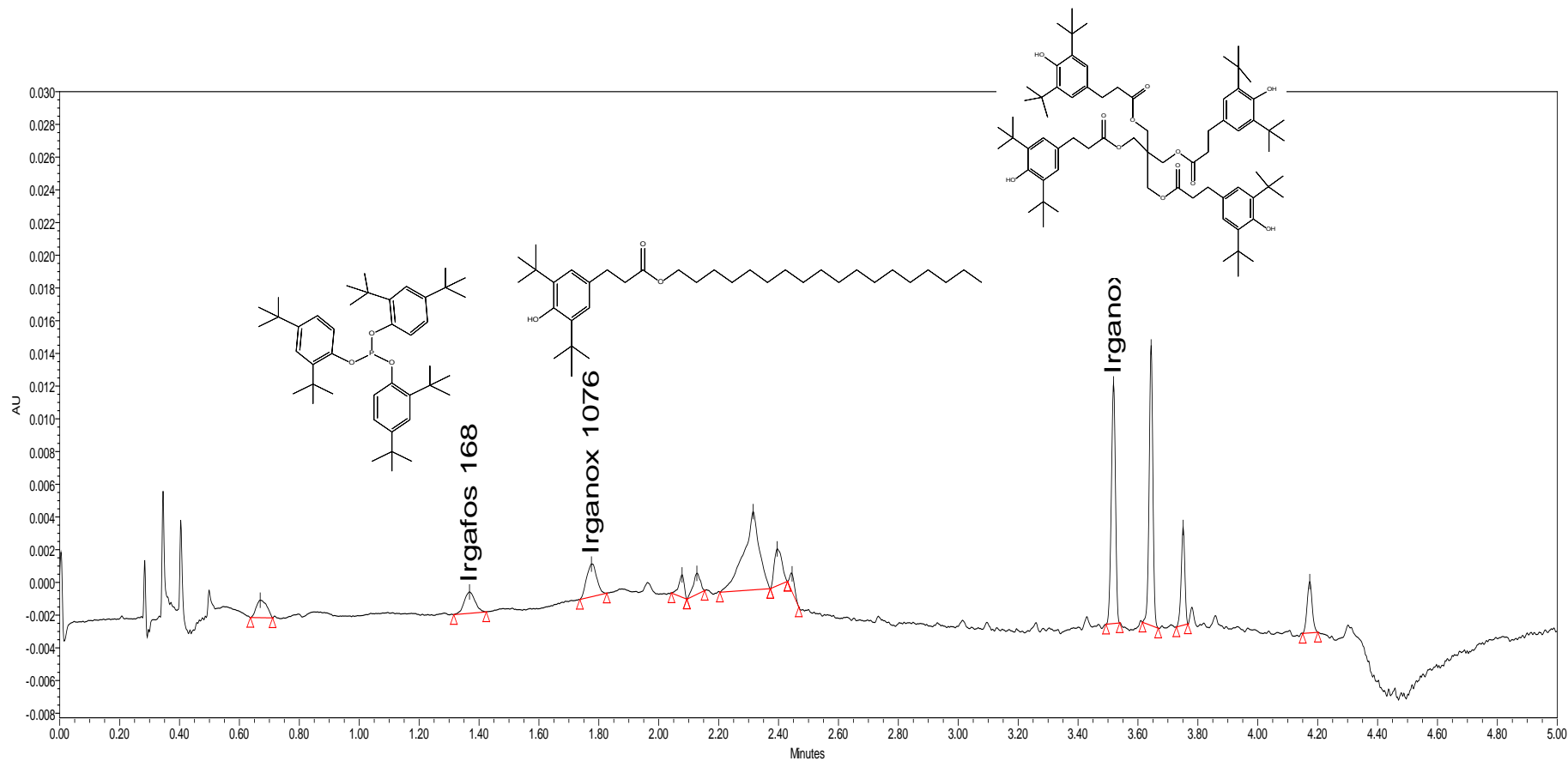


# LDPE, all IPA extracts

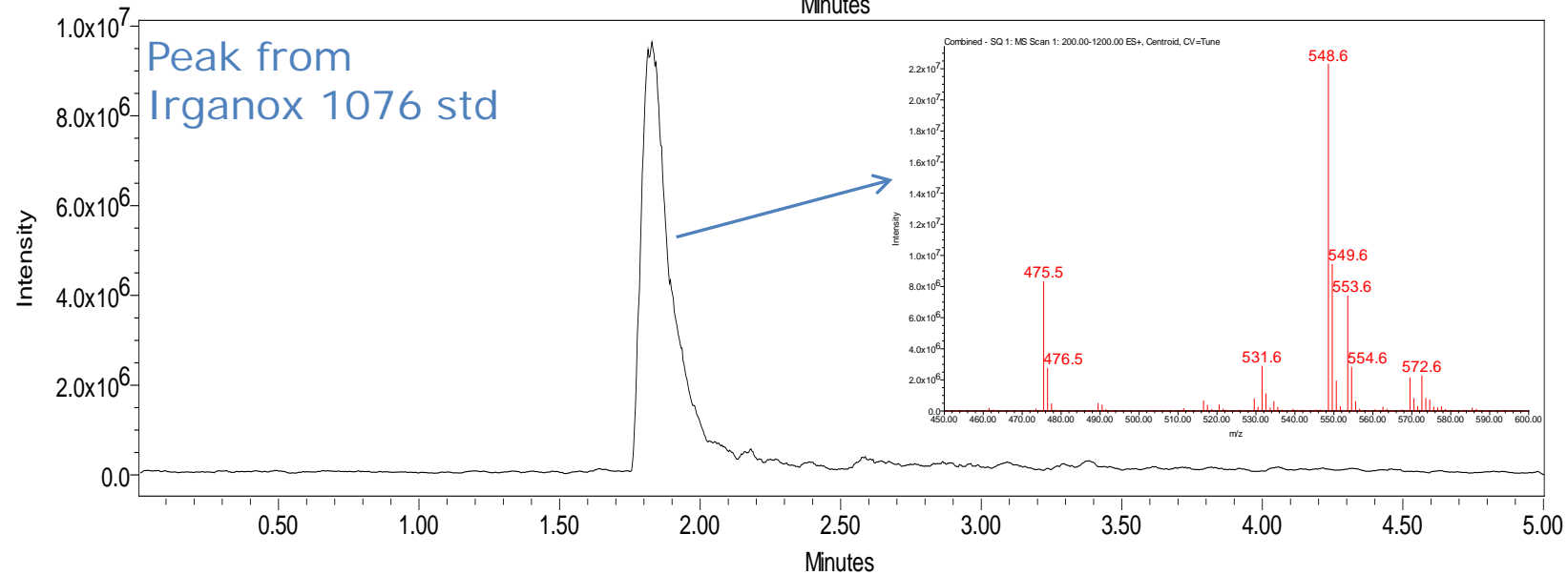
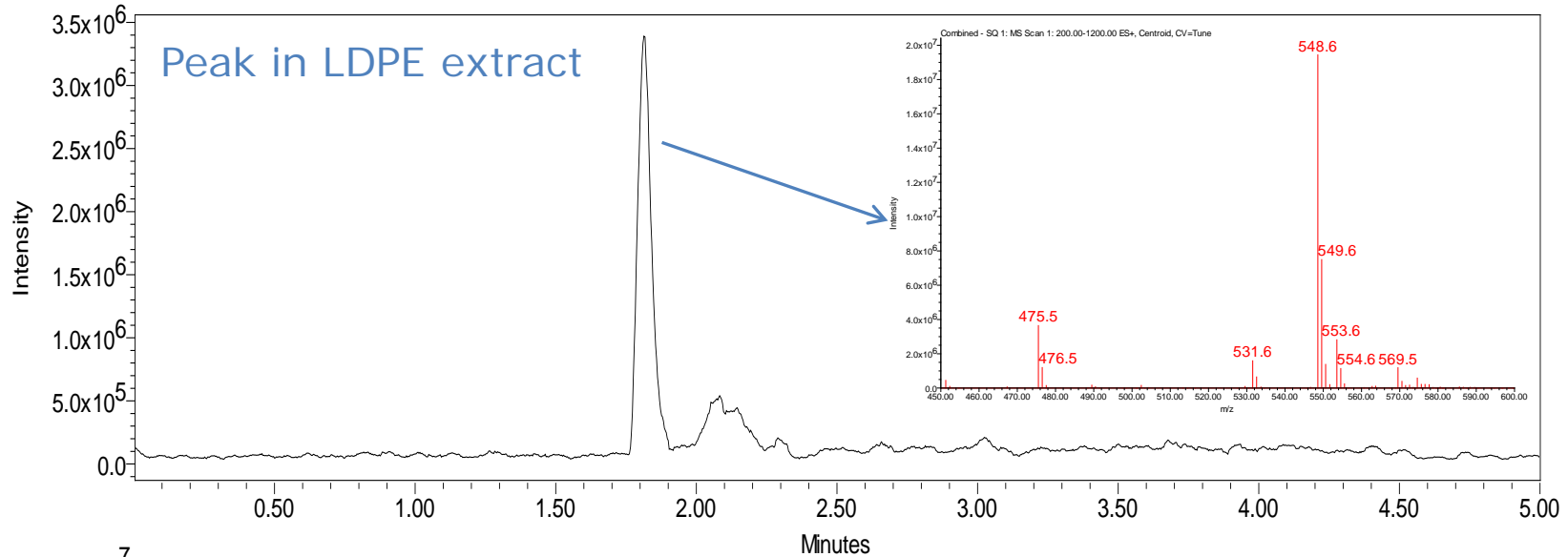


# UV chromatogram of LDPE SFE extract analysed by UPC<sup>2</sup>

- 3 target compounds identified



# Confirmation of identity using MS





## Conclusion

All extraction techniques provided similar extractable profiles but...

- SFE consumes much less solvent and is quicker than Soxhlet extraction
- The MV-10 SFE System has automated method development and extractions on 10 samples to simplify the process
- UPC<sup>2</sup> gives a fast, high resolution separation and has wide sample diluent compatibility





Thank You!

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