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A New Standard in Analytical Workflow Design

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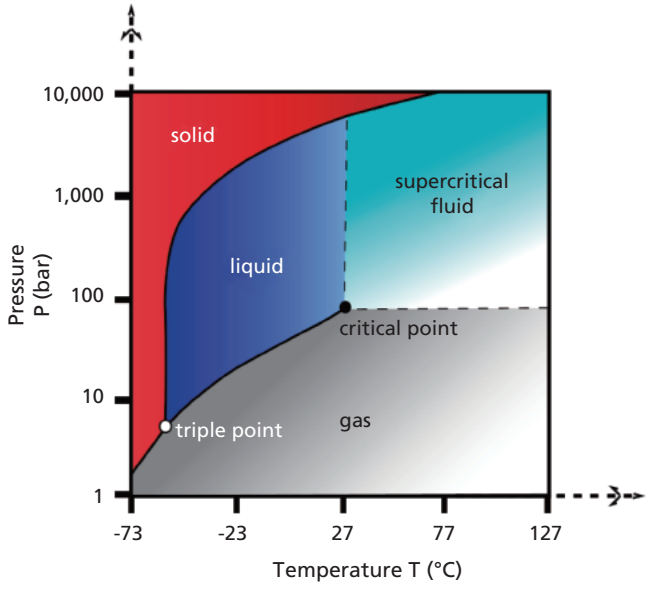
Introduction

Current analytical methodology typically consists of a separate off-line sample preparation technique that is followed by a chromatographic analysis. Sample preparation and manual transfer to the analytical instrument often consumes a majority of the analyst's time and effort. Recently, an innovative new concept was introduced that greatly reduces sample preparation times and the variability associated with manual procedures.

This new technique automates the sample preparation and analysis of samples by supercritical fluid extraction of compounds from the sample matrix, which are then transported to the analytical column for analysis without any human intervention. A number of applications that include food, environmental, and pharmaceutical areas will be shown that show the flexibility of this technique.

SFC Review

- Supercritical CO_2 is a fluid state of carbon dioxide where it is held at or above its critical temperature (31.1 °C) and critical pressure (1,070 psi)
- Rule-of-thumb: any molecule that dissolves in methanol (or less polar solvents) is compatible with SFC
- CO_2 at its critical point is non-polar, solvent strength is increased by using a polar co-solvent
- The benefits of supercritical fluids are still retained with the addition of co-solvents that greatly expand the application range. (subcritical fluid chromatography)



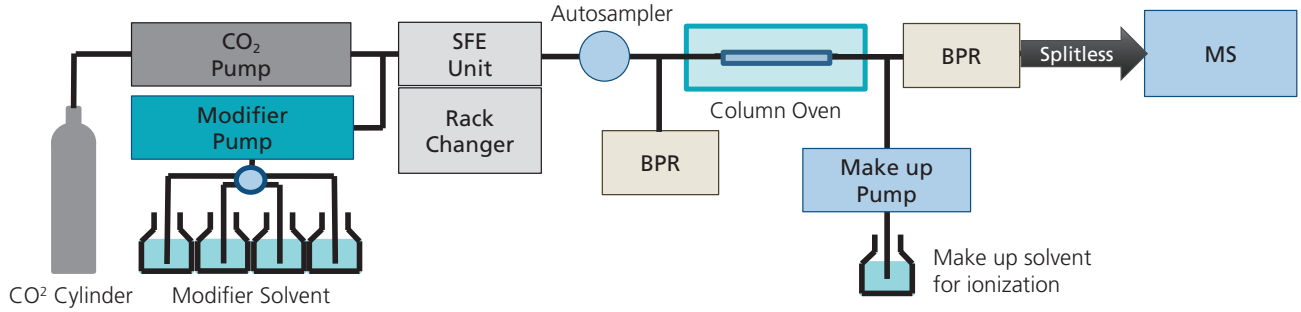
SFC Advantages vs. LC and GC

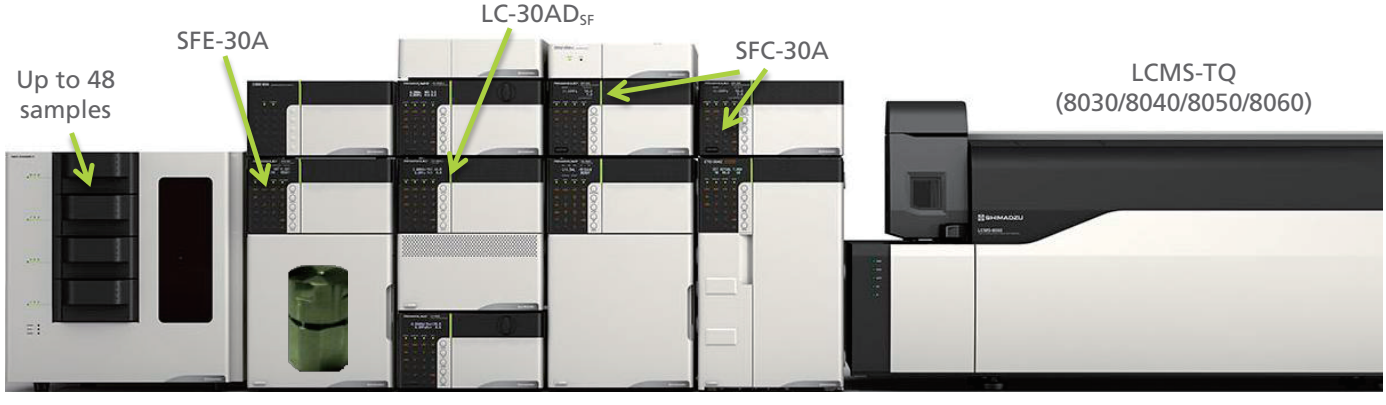
Lower viscosity of the mobile phase
- faster analysis (5 to 10 x faster)
- less pressure drop across the column
- better sensitivity

Greater separation efficiency than that of HPLC (chiral)
"Green" technique – reduced organic solvent usage/waste
Little residual solvent obtained in preparative chromatography
Analysis of non-volatile, polar or adsorptive solutes without derivatization
Analysis of thermally labile compounds
Preparative chromatography

System Configuration – SFE-SFC-MS/MS

Online SFE – SFC – MS System

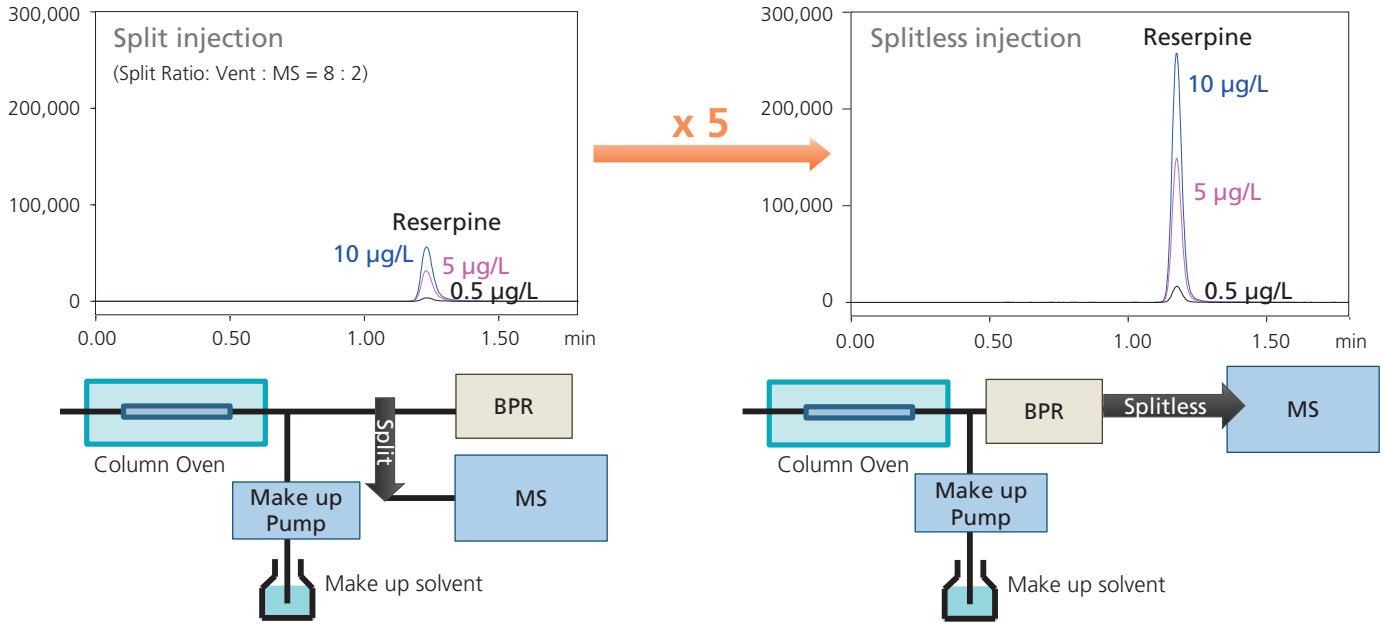




extraction vessel

Splitless BPR Improves Sensitivity

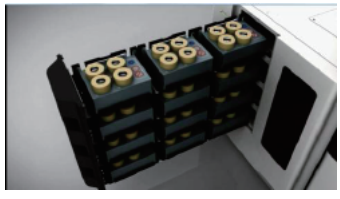
- High sensitivity detection
  - Improved sensitivity due to low dead volume BPR
  - Splitless injection into the MS without band broadening



Streamlined, On-line Sample Prep

- SFE (supercritical fluid extraction) sample preparation

Patented absorbent effective for dehydration of samples with high water content



Up to 48 samples can be extracted and analyzed in an automated workflow using the Rack Changer.

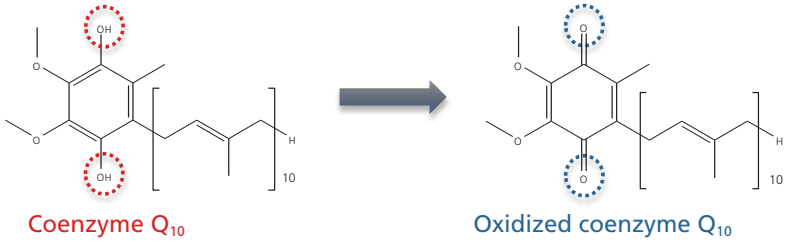
approx. 30 min time saving / sample

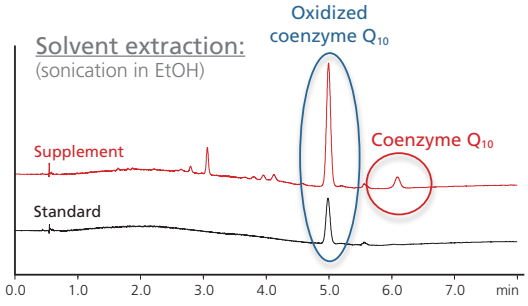
- Conventional sample preparation method (QuEChERS)

Preserves Labile Compounds

Analysis of coenzyme Q_{10} in supplements

- Conventional Method: Coenzyme Q_{10} is prone to oxidation

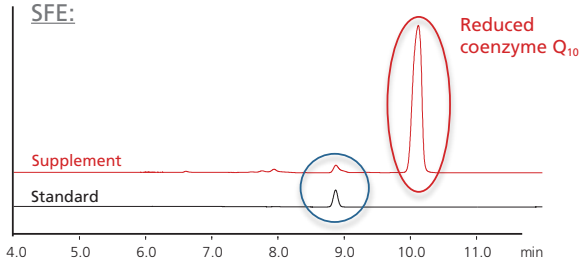




- Nexera UC: No oxidation with SFE

  Extraction with 5 % MeOH in CO_2 for 4 min

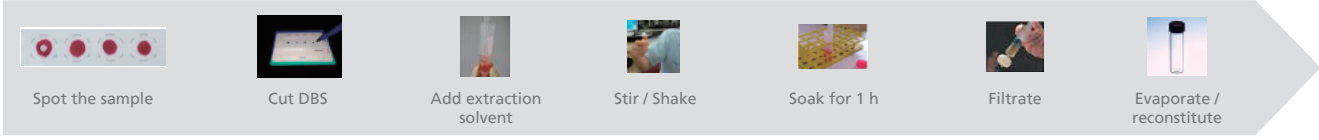
  Gradient: 5 %B (0 min – 4 min for SFE)
  5 % - 50 %B in 5 min



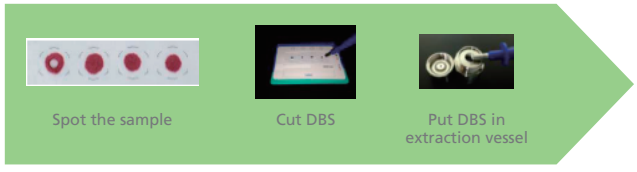
DBS Analysis

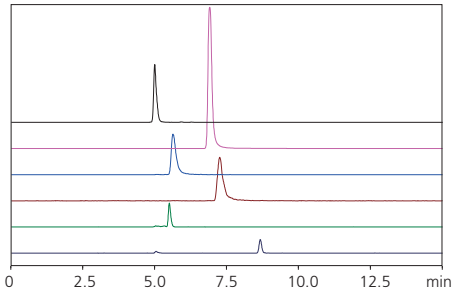
Analysis of biomarkers from dried blood spot (DBS)

- Conventional Method: time consuming



- Nexera UC:



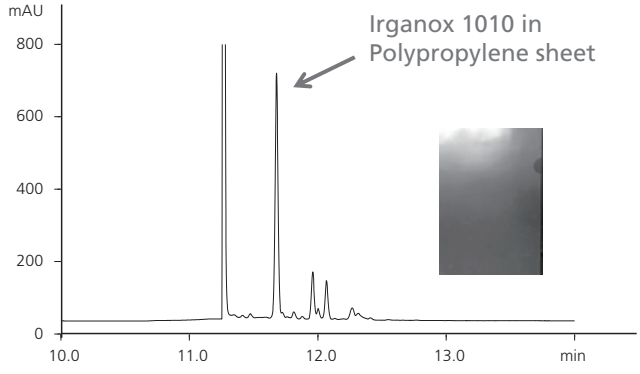


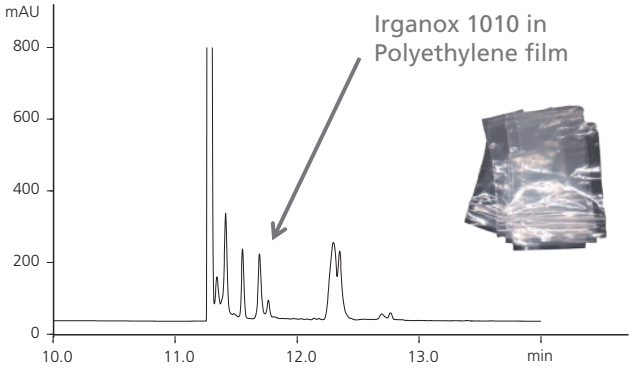
Extraction and analysis of 1 ppm phospholipid spiked into plasma on DBS

Polymer Additives Analysis

Extraction of polymer additives

- Conventional Method: 10 – 20 h soxhlet extraction
- Nexera UC: 7 min CO_2 extraction
  - Crushed polymer samples are placed in the extraction vessel
  - After 7 min CO_2 extraction, the sample is ready for SFC analysis

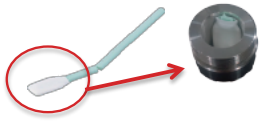


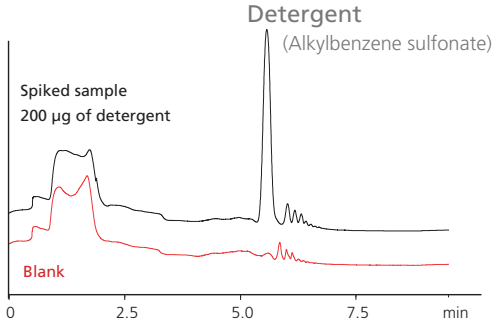


Cleaning Analyses

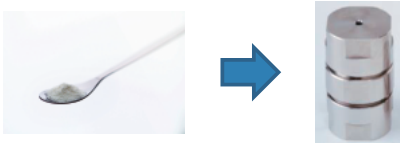
Cleaning validation

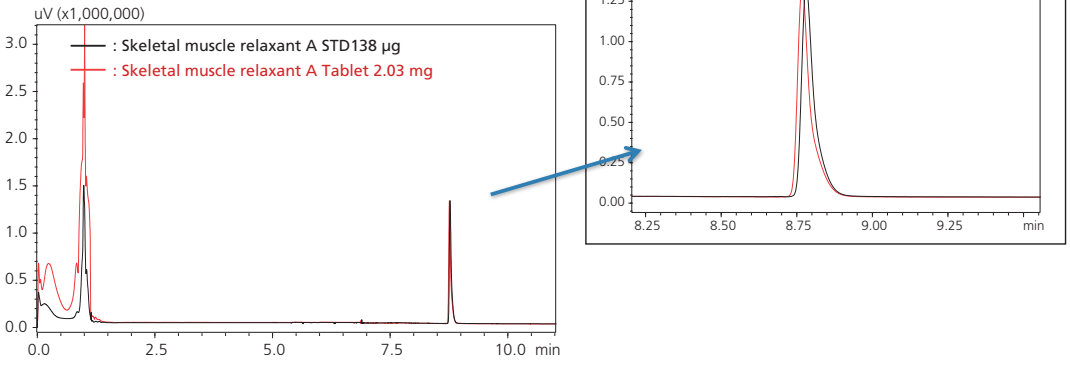
- Conventional Method:
  - Sampling – Solvent extraction – Concentration – HPLC analysis
  - Organic solvents can't be used for TOC analysis
- Nexera UC:
  - Swab is enclosed in the extraction vessel for SFE





Analysis of API in a Tablet





Sample	Area	Area converted to 2mg of sample	Recovery (%)
Tablet 2.27mg	4,508,728	3972447.577	100.1
Tablet 2.03mg	3,954,148	3895712.315	98.2
Tablet 2.10mg	4,378,007	4169530.476	105.1
Tablet 1.96mg	3,995,147	4076680.612	102.7
Tablet 2.25mg	4,473,899	3976799.111	100.2

Approx. 2mg of crushed tablet sample was weighed and transferred to the vessel for analysis. Recovery was calculated by comparing to the standard that is equivalent to the amount of API in 2mg of the tablet.

A New Standard in Analytical Workflow Design

Summary

- A new automated online sample preparation/chromatography system that uses supercritical fluids was recently introduced.
- The system can greatly reduce sample preparation times when compared to conventional methods like QuEChERS.
- Automated supercritical fluid extraction (SFE) can reduce solvent waste while improving reproducibility of results.
- SFE was shown to be a viable technique for a number of applications.

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