

# Supercritical Fluid Chromatography

## What is supercritical fluid?

- It's a phase that exists at only above a certain temperature, regardless of what the pressure is.
- Its density and viscosity are between those of gas and liquid.
- It has the ability to act as a solvent.
- An example of a supercritical fluid is SF<sub>6</sub> (sulfur hexafluoride), water, methanol, ammonia.

## How does it work?

- SFC with a mixture of CO<sub>2</sub> and organic solvent is “green” technology that reduces organic solvent use by up to 90% for the separation of kilograms of compounds and enantiomers in the pharmaceutical industry.
- The low viscosity of the supercritical fluid allows for faster flow, which consequently increases productivity.
- Although CO<sub>2</sub> is a weak solvent, when mixed with some organic solvent, it is capable of dissolving a lot of compounds.

## What are its features?

- It provides increased speed and resolution with regards to liquid chromatography.
- This is because of its higher diffusion coefficients of solutes in supercritical fluids.
- When pressure is released.

## What are the equipment used in SFC?

- asdf

## Applications of SFC

- asdf

## Now, main points for the presentation

### A brief statement describing the technique (what it is)

- asdf

### Its significance (why should we care?)

- asdf

### How does it work?

- asdf

### Important Instrumental Details (what do you need for it to work?)

- asdf

### An Application (what's it good for?)

- asdf
- state about SFC columns.
- state that people probably moved to SFC from HPLC because of its speed and fast method development, and not necessarily because it is environmentally friendly.
- talk about how to increase elution strength, and compare it as to how you would do it in a GC and LC.
- talk about how you know that people prefer GC over LC, unless the solute is non-volatile, and state when would people really prefer SFC over GC.

### Pics to include

- CO<sub>2</sub> phase diagram
- Schematic of a SFC

## Blueprint of my Presentation

### Open up with a joke or two

### Explain what SFC is in a nutshell

- Supercritical fluid chromatography (SFC for short) is chromatography in which the mobile phase is a supercritical fluid.
- In most circumstances, the mobile phase chosen is CO<sub>2</sub>.
- SFC is extremely similar to high performance liquid chromatography, or HPLC for short, in terms of its equipment/instrumentation as well as the software used.
- In fact, the hardware can be used to rapidly switch back and forth between SFC and either normal or reversed phase HPLC, in just a few minutes!

### Explain what a supercritical fluid is, and reference the graph

- Its a phase that exists at only above a certain temperature, regardless of what the pressure is.
- critical point is the temperature at which only a single phase can exist.
- However, it is not recognized as a separate state of matter
- Just means a liquid can be converted to a gas and vice-versa without a phase transition.
- However, the conditions used are subcritical.
- Its density and viscosity are between those of gas and liquid.
- It has the ability to act as a solvent.
- An example of a supercritical fluid is SF<sub>6</sub> (sulfur hexafluoride), water, methanol, ammonia.
- Basically, it moves like a gas but dissolves like a liquid, think of it like that

### How does it work?

- Explain the need for modifiers
  - major difference with SFC from HPLC is the fact that the mobile phase is a denser, compressed gas instead of a liquid.
  - At extremely high pressures greater than 80 bar, CO<sub>2</sub> acts like a solvent.
  - CO<sub>2</sub> is nonpolar solvent
  - So for more polar solutes, an organic modifier (cosolvent), mostly alcohol, is added to the mobile phase.
  - Gradient elution from low to high modifier concentration is the norm.
  - Peaks elute from lower to higher polarity.

- However, for many highly polar solutes, interactions with stationary phase is too intense
  - Consequence: solutes fail to elute, or elute with poor peak shape
  - Solution: include a highly polar additive (strong acid or base) dissolved in the modifier.
- why CO<sub>2</sub>?
  - readily available
  - cheap
  - has an accessible critical point
  - relatively safe
  - green as it can be recycled
  - miscible with a wide range of highly polar modifiers
- Why use methanol as a cosolvent?
  - completely miscible with CO<sub>2</sub>
  - availability
  - inexpensiveness
  - relatively low toxic
- Stationary phases for different circumstances
  - for polar solutes
    - \* polar stationary phases are used bare silica or several ethylpyridines
  - for nonpolar solutes
    - \* reversed-phase columns such as C18, C8, C4 and methyl are used.
- Reference the figure 2 in your handouts and presentation
  - CO<sub>2</sub> in its vapour phase is supplied from a cylinder at room temperature
  - The SFC conversion module contains a chiller
    - \* it cools the incoming fluid and the pump head of the booster pump
  - it then moves to the binary pump section
    - \* in it, the CO<sub>2</sub> and the modifier is mixed in a compartment called a mixer
    - \* essentially, the job of the mixer is to homogenize the two solvents
- Because the mobile phase is a compressed gas, the backpressure regulator is there in the system outlet to make sure that the CO<sub>2</sub> remains a single dense phase throughout the chromatograph.
- As a consequence, the detectors (UV or DAD) need to be able to be operated at high temperatures.
- After passing through the detector, the mobile phase is returned to the backpressure regulator in the SFC conversion module
  - there, it is allowed to drop to atmospheric pressure
  - after the pressure is stabilized, the fluid breaks down into two phases
    - \* liquid goes to trap
    - \* gas goes into a fume hood.
- state that the SFC conversion module is the only new thing added to the HPLC

## Why should you care (As in, why use SFC and not just LC)?

- remember that LC is preferred over GC when
  - one wants to analyze thermally unstable compounds
  - one wants to analyze non-volatile compounds
- start off with the van Deemter equation
  - draw the equation on the board
    - \* A is Eddy diffusion
    - \* B is longitudinal diffusion
    - \* C is mass transfer
  - state that increased temperature and diffusion coefficient increases the B term, while increased viscosity decreases it
  - B is neglected in liquid chromatography because the mobile phase velocity is much higher than the diffusion coefficient of the component in solution.
- However, in SFC, the B term is not negligible
  - the intermolecular interactions in gaseous CO<sub>2</sub> are weak
  - when it is compressed, the resulting dense fluid acts like a solvent.
  - Yet, the intermolecular forces are still weak, despite the increased density.
  - So, other compounds dissolved in CO<sub>2</sub> can diffuse rapidly through it.
  - In addition, the diffusion coefficient of CO<sub>2</sub> is extremely high.
  - As a consequence, SFC is like three to five times faster than HPLC, and run times are shorter.
  - Also, re-equilibration is faster
- Other advantages:
  - Lower operating costs, as CO<sub>2</sub> is cheap
  - Environmentally friendly

## Applications, including one detailed description, if you can

- As a general rule, any compound soluble in methanol or a less polar solvent is a good candidate for separation by SFC.
- commonly used in the pharmaceutical industry to separate chiral compounds
- usually, normal phase HPLC is used to separate chiral compounds as they rely on mostly polar-polar interactions, and can better differentiate small differences in shape.
- RP-HPLC relies on different hydrophobic interactions to separate compounds.
- Most drugs are chiral, meaning they have pairs of isomers that are mirror images of each other called enantiomers.
- SFC is more superior in separating chiral compounds than NP-HPLC, in

terms of speed and resolution.

- **Draw a pic of increasing polarity types of mobile phases used**

## **A Summary**

- SFC is a good alternative for HPLC.