A Basic Rundown of Supercritical Fluid Chromatography

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Over the last several years, there has been an increased interest in SFC (Supercritical Fluid Chromatography). But can you blame people? It’s green. It’s cheap. And it’s fast. What’s not to like about it? To learn just what is it about SFC that people like, we will dive into column phases, considerations for column screen setup, and explore general method development.

The Plus Side of Supercritical Fluid Chromatography

We already know that SFC is fast. But thanks to the lower viscosity of CO2 versus your typical reverse phase, normal phase, or HILIC solvents, one can ramp up the flow rate and achieve satisfactory chromatography in a fraction of the time. Supercritical Fluid Chromatography is also a friend to our planet as it significantly reduces the amount of hazardous waste that often requires specific disposal methods. Another benefit is that there is virtually no dry down step required. It is also an orthogonal technique to LC, meaning it typically appeals to those chemists who need a confirmation analysis within their workflow.

The Down Side of Supercritical Fluid Chromatography

Traditional disadvantages include lack of reproducibility and low UV sensitivity; however, this is improving with newer systems coming onto the market. SFC also does not work for water soluble only compounds and it is limited for highly polar compounds and proteins. The CO2 tanks required for this analysis are large, and heavy. This becomes a bigger issue when
working with preparative SFC. Limited lab space and the weight capacity of the flooring of older buildings can make it difficult to store the larger tanks of gas.

**Popular SFC columns currently on the market—Achiral Columns**

An ethyl pyridine column is like the C18 for SFC. If an analyst runs SFC, they most likely have several ethyl pyridine columns in their column drawer from various suppliers. Other popular phases include diol, cyano, amino or amide phases, bare silica, imidazole and the relatively newer pentafluorophenyl phase (PFP) and biphenyl. There is also the school of thought of using chiral phases for achiral screens (as demonstrated in this poster we presented at Pittcon last year). I have found that the more experienced SFC analyst is already using chiral stationary phases (CSPs) in their routine screens.

**Polar SFC columns currently on the market—Chiral Columns**

Polysaccharide-based CSPs are widely popular for SFC. They have “undoubtedly conquered a dominant position, because of their easy accessibility and proven broad enantioselectivity”\(^2\). With the introduction of more CSPs, from various manufacturers, your “hit rate” increases as does adequate separation.

Immobilized polysaccharide-based CSPs also allow for harsh modifiers and harsh diluents, such as DMSO and THF, which have been thought to boost separation capabilities. Clearly, there are many options here. It’s easy to see how one could easily be overwhelmed when choosing the appropriate CSPs for method development. To relieve this confusion, here is a Technical Note which discusses a 98% success rate on 4 CSPs of 55 of 56 probes.

This is a good example of how important it is to test various modifiers, mobile phases and CSPs to maximize your chances of satisfactory separation.
Supercritical Fluid Chromatography (SFC) Pros and Cons

It is also important to point out that SFC is thought to be the truly best technique for chiral screening with its fast runtimes and quick equilibration times. With even making strides in different industries, chiral SFC used in the pharmaceutical industry is the reason we have the current modern instruments.

**Final Thoughts on SFC**

It’s probably obvious by now that things are not as “cut and dry” with supercritical fluid chromatography as it tends to be with standard reverse phase method development. The key is to test as many column phases, modifiers, additives, and mobile phases as possible. I like to sometimes refer to SFC as the “black magic” of chromatography as an explanation for what works and what doesn’t work is not always clear. SFC might not be as predictable or universally applicable as liquid phase chromatographic methods, but it has significant advantages when it is applicable.

Resources

Have questions about SFC or any of our products? Reach out through live chat with our Technical Experts nearly 24/7 globally!

Check out this easy to use SFC infographic for a rundown of everything discussed: SFC Infographic- All Your SFC Needs
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