

# An Overview on Supercritical Fluid Chromatography: Current Trends and Applications

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**Abstract:** *The normal phase chromatography variation supercritical fluid chromatography (SFC) was introduced in 1962. Pressurization is needed along the chromatographic flow path since SFC uses carbon dioxide as the mobile phase. The convergence of liquid and gas characteristics in the supercritical phase makes supercritical fluid chromatography known as "convergence chromatography." After GC and HPLC, supercritical fluid chromatography is a key column chromatography technology. Supercritical fluids combine gaseous and liquid advantages. Viscosity, diffusivity, and density define supercritical fluids. In SFC, a supercritical fluid drives the sample down a separating column, where the mélange is partitioned into bands based on the stationary phase's interaction with the analytes. A detector identifies and quantifies these bands as they leave the column. SFC, a gas-liquid chromatography hybrid, works as LC when the mobile phase is below its critical pressure and temperature. It becomes a liquid when the mobile phase exceeds its critical pressure and temperature. Supercritical fluid chromatography equipment is versatile since it works with numerous detectors. SFC has been used to natural goods, medicines, cereals, pesticides, herbicides, surfactants, polymers, polymer additives, fossil fuels, petroleum, explosives, and propellants.*

**Keywords:** Supercritical fluid chromatography (SFC), Analytical techniques, Separation science

## I. INTRODUCTION

SFC has been used to evaluate and purify thermally labile, low-to-moderate molecular weight molecules since 1962. Separating chiral compounds is another use. SFC employs carbon dioxide as the mobile phase, hence the chromatographic flow channel must be pressurized. The concepts resemble HPLC. Why is supercritical fluid chromatography termed "convergence chromatography"? It combines liquid and gas characteristics.

Supercritical fluids (SF) dissolve liquids, have low viscosities, and increase diffusion. Thus, SF mobile phases should behave as solvents in HPLC and carriers of chemicals in GC.

A 1962 research investigated the separation of thermo-labile porphyrin derivatives using supercritical chlorofluoromethanes at 150-170°C and 140 bar pressure. More researchers developed and employed this method in the 1960s. Unfortunately, HPLC's chaotic rise cannot be compared to SFC's. After 20 years, SFC saw its first major boom in the 1980s. A material's critical temperature and pressure form a supercritical fluid. A supercritical fluid combines liquid and gas advantages. They act like liquids and gasses. Supercritical fluid acts like a gas when it fills and shapes a container. Dynamic equilibrium produces supercritical fluid. In a closed system, heating a material to its critical temperature under constant pressure creates dynamic equilibrium. This equilibrium occurs when equal amounts of gas-phase molecules enter the liquid phase and lose energy to depart. Supercritical material eliminates the liquid-gas phase curve. A phase diagram defines a surface field.

A phase diagram illustrates a material's solid, liquid, or gas states at various temperatures and pressures. The solid-gas, solid-liquid, and liquid-gas curves constitute phase zones. This curve exhibits liquid-gas boundary vaporization, solid-liquid barrier melting, and solid-gas interface sublimation. Triple Point (TP), when all three phases are balanced, connects these binary existence curves.

**Table 1: Comparison of densities, viscosities and diffusivities for liquid, supercritical fluid and gas**

State	Density (g/ml)	Viscosity (poise×10)	Diffusivity (cm <sup>2</sup> /s×10 <sup>3</sup> )
Liquid	0.8-1	3-24	0.005-0.02
Sup.fluid	0.2-0.9	0.2- 1	0.01-0.3
Gas	0.001	0.05-0.35	10-1000

### Physical Properties of Supercritical Fluids

#### Density

A supercritical fluid's density is as close to a liquid as it is between a gas and a liquid. When pressure rises at a steady temperature, the density of a supercritical fluid increases in the supercritical zone. The density of the substance drops with temperature while the pressure remains constant.

A supercritical fluid's ability to dissolve depends on its density. Additionally, because of their greater density than gases, supercritical fluids are excellent transporters. Density is thus a crucial factor in analytical methods that use supercritical fluids as solvents.

#### Diffusivity

Diffusion in a supercritical fluid can be 100 times higher than in a liquid and 1,000–10,000 times lower than in a gas. A solute may exhibit more diffusivity in a supercritical fluid than in a liquid because supercritical fluids have higher diffusivities than liquids. Diffusivity is parallel to temperature and inversely correlated with pressure. Pressure decreases a material's diffusivity by causing supercritical fluid molecules to move closer to one another. Supercritical fluids have the potential to be quicker carriers for analytical applications because to their higher diffusivity. Supercritical fluids are so vital to extraction and chromatography procedures.

#### Viscosity

Almost similar to a gas, supercritical fluids have 10 times lower viscosity than liquids. Supercritical fluids have less resistance to flowing components than liquids. Temperature has a large effect on supercritical fluid viscosity but none on liquid viscosity. Three main qualities are related. Temperature and pressure might affect them differently. In particular, increasing pressure increases viscosity, which decreases diffusivity.

#### Supercritical Fluid Chromatography (SFC)

After HPLC and GC, SFC is the third column chromatography method. SFC may offer greater advantages compared to HPLC and GC in the analysis of compounds that undergo high-temperature decomposition (as detected by GC) and lack detectable functional groups by HPLC detection systems. Certain properties can be altered via SFC during the chromatographic procedure. The ability to tune provides a benefit in terms of optimizing the analysis. SFC also possesses a greater variety of detectors than HPLC. Three primary characteristics distinguish column chromatographies:

- Selectivity
- Efficiency
- Sensitivity

GC is far more responsive and efficient. Various mobile and stationary phases improve HPLC selectivity. SFC has good sensitivity and efficiency but less selectivity than HPLC. Like solvents in liquid chromatography (HPLC), SF mobile phases in chromatography should carry and dissolve compounds. Supercritical fluid chromatography describes this method. In 1962, supercritical chlorofluoromethanes were used to separate thermo-labile porphyrin derivatives at temperatures of 150-170°C and pressures of up to 140 bar. This approach was improved theoretically and experimentally by 1960s researchers. Unfortunately, SFC's growth at this period was not comparable to HPLC's chaotic expansion. Thus, the company's first major growth occurred in the 1980s.

#### Instrumentation for SFC

SFC instruments are remarkably comparable to HPLC instruments in terms of hardware. In particular, they employ comparable stationary phases and column configurations. Certain distinctions exist. As temperature is of the utmost importance for supercritical fluids, the system should include a thermal control mechanism similar to that of GC. Additionally, it is imperative to incorporate a pressure control mechanism, such as a restrictor, as pressure is a critical parameter that must be maintained at the designated level for supercritical fluid materials.

### **Pumps**

By column type, the high-pressure pump utilized in SFC is determined. In the context of stacked columns, reciprocating pumps are frequently utilized, whereas syringe pumps are the most frequently employed for capillary SFC. The introduction of modifier fluids or the blending of the mobile phase is facilitated by reciprocating pumps. Syringe pumps ensure that an orderly mobile phase is subjected to a constant pressure.

### **Injector**

Injection in SFC is typically accomplished through the utilization of an appropriate valve at the column entrance to convert the contents of a sample loop into the carrier fluid. A conventional HPLC injection system is sufficient for packed column SFC. However, in the case of capillary column SFC, where the sample volume is dependent on column diameters and small sample volumes must be injected rapidly into the column, pneumatically driven valves are utilized.

### **Oven**

For exact temperature regulation of the mobile phase, a thermostated column oven is necessary. In general, conventional GC or LC furnaces are utilized.

### **Columns**

Due to the potent solvating capabilities of the mobile phase in SFC, it is critical to select stationary phases with extreme care. SFC primarily employs two varieties of analytical columns: packed and capillary. In the past, absorbents such as aluminum, silica, polystyrene, or stationary phases that were insoluble in SC-CO<sub>2</sub> were utilized. In more recent studies, bonded non-extractable stationary phases, such as aminopropyl bonded silica or octadecylsilyl (C18), have been utilized in packed column research.

With regard to coating materials, SFC columns are comparable to HPLC columns. In SFC, two distinct categories of columns are utilized.

Open tubular columns

packed columns

#### **Open tubular**

These are the most favored and resemble fused-silica columns used in HPLC. As the stationary phase, this category of columns is internally coated with cross-linked siloxane material. These coatings may have a thickness of 0.05-1  $\mu$  m. The dimensions of those columns may vary between 10 and 20 meters.

#### **Microprocessor**

Standard equipment for SFC measurement includes one or more microprocessors for regulating hydraulic pressures, oven temperature, and detector performance, among other parameters.

#### **Detector**

SFC uses gases or liquids as mobile phases. This ensures HPLC and GC detector compatibility. SFC uses liquid-phase detectors such refractive index, ultraviolet-visible spectrophotometric, and light scattering detectors instead of gas-phase detectors like flame ionization and flame photometric detectors. SFC also works well with Fourier transform infrared and mass spectrometry. Mobile phase composition, column type, flow rate, and SFC pressure tolerance will determine detector selection. Detector technology makes SFC better than HPLC. A flame ionization detector, common in GCs, may be installed on SFC. SFC analyses may benefit from this detector's qualities.

#### **Mobile phases**

A diverse range of materials can be employed as mobile phases in SFC. The mobile phase can be chosen from a variety of solvent groups, including hydrocarbons, ethers, halides, inorganic solvents, acetone, acetonitrile, pyridine, and so forth.

Carbon dioxide is the prevailing supercritical fluid utilized in SFC due to its readily achievable critical temperature and pressure. Additionally, carbon dioxide is readily available, inexpensive, UV-inert, non-toxic, and an effective solvent for non-polar molecules. Ethane, n-butane, N<sub>2</sub>O, dichlorodifluoro-methane, diethyl ether, ammonia, and tetrahydrofuran are all viable alternatives to carbon dioxide.

#### **Effect of Pressure**

The relationship between the solvating power and the density of the supercritical fluid is a component of the theory of separation in SFC. An increase in pressure within the system results in a concomitant rise in the density of the supercritical fluid, which in turn enhances its solvating capability. As a consequence, the eluent's retention duration is

reduced, given that pressure variations in SFC significantly impact analyte retention. Comparable to gradient elution in HPLC or programmed temperature in GC, this effect is widespread.

#### **Comparison of SFC with Other Types of Chromatography**

Since its physical characteristics are between gases and liquids, SCF contains certain gas and liquid chromatographic features. As with GC, SFC is faster than LC because to the higher flow rates needed to accommodate lower viscosity. SCFs have intermediate gas-liquid diffusion. Band widening is somewhat larger in SCFs than gases. Due to their intermediate viscosities and diffusivities, SCFs separate faster than LC and have less zone broadening than GC. GC, LC, and SCF mobile phases have different roles. The mobile phase causes GC zone movement. In LC, the mobile phase carries and interacts with solute molecules, altering selectivity. Supercritical mediums dissolve molecules like volatilization at far lower temperatures than GC. At a given temperature, a big molecule in SCF may have a 10-10 higher vapor pressure than without it. A column at a low temperature may elute high-molecular-weight chemicals, polymers, big biological molecules, and thermally unstable species. SFC can isolate thermally unstable chemicals better than GC. The pharmaceutical industry values this since it represents 20% of all medication prospects. SFC enables mobile phase variation to impact selectivity, unlike GC.

#### **SFC in chromatographic techniques**

SFC has promise for different applications. One key advantage of this approach is the ability to adjust selectivity by adjusting pressure and temperature, rather than changing the chemical makeup of the eluent. Series HPLC-type columns are possible due to the mobile phase's low viscosity. SFC analyzes substances with molecular masses above 1000, including lipids, oils, emulsifiers, oligomers, and polymers that cannot be investigated in GC. SFC is faster and more efficient than HPLC. Using supercritical carbon dioxide as a mobile phase allows for easy connection with mass, infrared, and NMR spectrometers.

#### **Drawbacks**

There have been a few technical issues that have limited adoption of SFC technology,

The first is high pressure operating circumstances. Large, costly high-pressure containers need specific materials to prevent gaskets and O-rings from disintegrating in supercritical fluid.

Back pressure control is another issue. Supercritical fluids, unlike liquids, are very compressible and exhibit physical features that alter with pressure, such as pressure drop over a packed-bed column.

This difficulty is mitigated by automatic backpressure regulators, which maintain column pressure regardless of flow rate.

Third, gas/liquid separation during product collection is problematic. CO<sub>2</sub> quickly transforms into gas and aerosolizes dissolved analytes upon depressurization. Gas/liquid separations are easier using cyclone separators.

#### **Applications of SFC**

Pharmaceutical, environmental, and food applications exist. Also used are insecticides, herbicides, polymers, explosives, and fossil fuels. This method can analyze antibiotics, prostaglandins, steroids, taxol, vitamins, barbiturates, and non-steroidal anti-inflammatory drugs. Chiral separation is achievable for many medicinal substances. Carbon dioxide, the most common mobile phase of supercritical fluids, can not dissolve polar solutes, hence SFC is mostly used for non-polar molecules. SFC might be used in petroleum for total aromatic content analysis and hydrocarbon separations. Thermally unstable low-to-moderate molecules are analyzed and purified using it. Additionally, it can separate chiral substances. SFC is mostly used in industry to separate chiral compounds using HPLC columns. Modern pharmaceutical achiral separations and purifications use SFC.

#### **Applications in the material and polymer industry**

Material and polymer industries employ supercritical fluids extensively. Rapid expansion from supercritical fluids via an aperture or nozzle commercially precipitates solids. This method quickly depressurizes supercritical fluid-dissolved solutes. Controlling operation factors carefully yields the required precipitated morphology. In gas anti-solvent, a supercritical fluid is quickly applied to an organic solvent-dissolved crystalline solid. Supercritical fluid precipitates solid crystals as an anti-solvent since the solute is poorly soluble. Final crystal particle size distribution may be carefully regulated by fluid density. Compressed fluid anti-solvent precipitation is another method. The solvent diffuses fast into the supercritical fluid as the compressed fluid expands the solution to precipitate the solute after the solution is sprayed via a nozzle. This method produces nanometric, monodisperse polymer microspheres economically. Another

industrial procedure for foamed components uses supercritical fluid carbon dioxide. Supercritical fluids lower the polymer's glass transition temperature, therefore they may be added straight to the extruder to make foams at ambient temperature.

#### **Food applications**

Most food industry supercritical fluids are carbon dioxide. It may extract thermally labile food components without solvent contamination due to its non-toxicity and low critical temperature. Controllable color, composition, odor, and texture, supercritical fluid carbon dioxide extraction keeps product fragrance. Supercritical carbon dioxide extraction has been explored for maize, sunflower, and peanut oil extraction instead of hexane. For replacement and low-iron and free-fatty acid oils, supercritical fluid extraction is advantageous. Supercritical extraction of oils from potato chips and other snack foods is being developed to meet market demand for 'lighter' diets. Also extracted using supercritical carbon dioxide include lilac, essential oils, black pepper, nutmeg, vanilla, basil, ginger, chamomile, and cholesterol.

Coffee decaffeination by supercritical carbon dioxide has been extensively studied. It's hardly unexpected that supercritical extraction was the first marketed technique in 1978. Water must be added to dry coffee beans to extract caffeine. To extract caffeine from coffee beans using supercritical carbon dioxide, soak for 2 hours. Kraft General Foods in the US and some German processes decaffeinate coffee.

#### **Pharmaceutical applications**

Given the critical significance of the residual solvent discovered in the extracted material within the pharmaceutical industry, supercritical fluid carbon dioxide has been utilized in a variety of contexts. Thorough research has been conducted on the extraction of vitamin E from soybean oil as well as a purification method for vitamin E. By skipping the vacuum distillation phase, which typically leads to thermal degradation of the product, the latter method circumvents this drawback. In supercritical fluids, the solubilization and recrystallization of numerous pharmaceuticals have been demonstrated.

#### **Environmental applications**

As a result of stringent environmental regulations, conventionally hazardous compounds like hexane are being substituted with supercritical fluids. Supercritical fluid extraction has been suggested as a potential substitute methodology for the regeneration of activated carbon and soil remediation. The majority of organic compounds, exceeding 99%, can be eliminated from contaminated soil. Among the organic compounds that have been extracted successfully are toxophene, PCBs, PAHs, and DDT. Entrainers have been utilized in conjunction with carbon dioxide to extract highly polar compounds. An oil separation process from refinery wastewater and contaminated soil has been developed commercially by CF Systems Corporation, based in the United States of America. The development of chelating moieties that dissolve in carbon dioxide has facilitated the removal of heavy metals from soil.

## **II. CONCLUSION**

Fluid supercritical Chromatography techniques leverage the distinctive physical properties of supercritical fluids to outperform other comparable methods in the domains of chromatography and extraction. In certain instances, they are implemented as supplementary instruments for binary systems, whereas at other times, they function as alternative instrumental analytical methods. The efficacy of an analytical approach in resolving practical challenges serves as an indicator of its utility.

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