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A review: Supercritical fluid chromatography and it's applications

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Abstract

The discovery of supercritical fluid led to novel analytical applications in the fields of chromatography and extraction known as supercritical fluid chromatography. Supercritical fluid chromatography is accepted as a column chromatography method along with gas chromatography (GC) and high-performance liquid chromatography (HPLC).Supercritical fluid chromatography is a normal phase chromatographic technique in which the mobile phase is a supercritical fluid such as carbon dioxide as mobile phase. SFC is of importance because it permits the separation and determination of a group of compounds that are not conveniently handled by either Gas chromatography or High performance liquid chromatography. A solution of the sample is injected into a high-pressure flow stream that sweeps the sample into a tube or column filled with fine particles. The individual components in the sample interact differently with the surface of the particles, and are separated in time and space as they pass through the column. The components emerge from the column at different times, as Gaussian or pseudo-Gaussian peaks, and pass through a detector.Supercritical fluid chromatography is now commonly used for achiral separations and purifications in the pharmaceutical industry.

Keywords: Supercritical fluid, Supercritical fluid chromatography, Achiral separation, pharmaceutical industry.

Introduction: The use of a supercritical fluid mobile phase in chromatography was first proposed in 1958 by J. Lovelock. The first actual report use of this in a chromatographic system was in 1962 by Klesper et al, who used it to separate thermally-labile porphyrins. Supercritical fluid chromatography (SFC) is a form of chromatography in which the mobile phase is subjected to pressures and temperatures near or above the critical point for the purpose of enhancing the mobile phase solvating power [(1).] The critical point is defined by a critical temperature (T,) and a critical pressure (P,) above which the substance is neither a gas nor a liquid, but possesses properties of both. Critical temperature is the temperature at which a gas cannot become liquid as long as there is no extra pressure; and, critical pressure is the minimum amount of pressure to liquefy a gas at its critical temperature. A supercritical fluid is the phase of a material at critical temperature and critical pressure of the material. A supercritical fluid provides a gas-like characteristic when it fills a container and it takes the shape of the container [(2)].

The motion of the molecules is quite similar to gas molecules. As the supercritical phase represents a state in which liquid and gas properties converge, supercritical fluid chromatography is sometimes called as "**convergence chromatography**". The characteristic properties of a supercritical fluid are

density, diffusivity and viscosity. The formation of a supercritical fluid is the result of a dynamic equilibrium between liquids and gases. When a material is heated to its specific critical temperature in a closed system, at constant pressure, a dynamic equilibrium is generated. This equilibrium includes the same number of molecules coming out of liquid phase to gas phase by gaining energy and going into liquid phase from gas phase by losing energy. At this particular point, the phase curve between liquid and gas phases disappears and supercritical material appears. For a pure material, a phase diagram shows the fields where the material is in
the form of solid, liquid, and gas in terms of different temperature and pressure values. Curves, where two phases (solid-gas, solid-liquid and liquid-gas) exist together, define the boundaries of the phase regions. These curves, for example, include sublimation for solid-gas boundary, melting for solid-liquid boundary, and vaporization for liquid-gas boundary. Other than these binary existence curves, there is a point where all phases are present together in equilibrium; the triple point (TP)[3,4].

Physical Properties of Supercritical fluids:

1) Density: Density characteristic of a supercritical fluid is between a gas and a liquid as near liquid. In the supercritical region, density of a supercritical fluid increases when pressure rises at a constant temperature. When pressure is constant, density of the material decreases with increasing temperature. Dissolving effect of a supercritical fluid is dependent on its density value. Also, supercritical fluids are better carriers than gases thanks to their higher density. Therefore, density is an essential parameter for analytical techniques using supercritical fluids as solvents.

2) Diffusivity

Diffusivity of a supercritical fluid can be 100 times more than a liquid and 1,000-10,000 times less than a gas. Because supercritical fluids have more diffusivity than a liquid, a solute can show better diffusivity in a supercritical fluid than in a liquid. Diffusivity is parallel with temperature and contrary with pressure. Increasing pressure affects supercritical fluid molecules to become closer to each other and decreases diffusivity in the material. The greater diffusivity gives supercritical fluids the chance to be faster carriers for analytical applications. Hence, supercritical fluids play an important role for chromatography and extraction methods.

3) Viscosity

Viscosity for a supercritical fluid is almost the same to a gas and it is 10 times less than a liquid. Thus, supercritical fluids are less resistant than liquids towards the components flowing through themselves. The viscosity of supercritical fluids distinguish from liquids that temperature has a little effect on liquid viscosity while it can influence supercritical fluid viscosity in a considerable way. These three major properties are related to each other. The change in temperature and pressure can affect all of them in different combinations. For instance, increasing pressure causes a rise for viscosity and rising viscosity results in declining diffusivity[5].

Principle: It is a combination of GC and HPLC, the principle is based on adsorption and partition chromatography. The principle is also based on triple point, critical point, and supercritical fluid.

Instrumentation [6]:

SFC has a similar setup to an HPLC instrument. They use similar stationary phases with similar column types. However, there are some differences. Temperature is critical for supercritical fluids, so there should be a heat control tool in the system similar to that of GC.

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Also there should be a pressure control mechanism, a restrictor because pressure is another essential parameter in order for supercritical fluid materials to be kept at the required level. A microprocessor mechanism is placed in the instrument for SFC. This unit collects data for pressure, oven temperature, and detector performance to control the related pieces of the instrument.

1) Pumps:

In SFC, the CO_2 is usually supplied from steel cylinders containing liquefied CO_2 in contact with a gaseous headspace. The cylinder pressure in typically 55 to 85 bar near room temperature. Since the modifier is a normal liquid at room temperature and pressure, the mismatch in pressures requires separate pumps for the CO_2 and for the modifier. As a consequence, binary pumping systems are used. Reciprocating pumps have low compression ratios and cannot compress a low density gas. To pump CO_2 with such a pump, it must be liquefied. Most SFC systems use the liquid phase from the bottom of the cylinder to minimize power requirements. The liquid in the cylinder is in contact with a gaseous headspace. Any increase in temperature or decrease in pressure during a standard HPLC pump refill stroke would cause part of the liquid to vaporize, and the pump would create gaseous cavities in the liquid flow. Consequently, both the CO_2 and the CO_2 pump head are pre-chilled to 4 or 5°C. Most SFC systems first use that pump to pre-compress the fluid from cylinder pressure to the column head pressure, and then accurately meter the CO_2 flow. Chilling the pump head usually requires a bulky heat exchanger being bolted onto the front of the pump to pump cold glycol solution. Some pumps have a Peltier device mounted on the pump head, with a large finned heat exchanger with a fan. The fan draws lab air through the heat exchanger to carry away the heat. The cold side and the pump head need to be insulated to prevent excessive condensation of moisture out of the lab air. CO_2 is far more compressible than normal liquids, even when chilled and liquefied. At supply cylinder pressures and typical chiller temperatures, adiabatic compressibility can exceed 1200x10-6/bar, which is 8 to 27-times the compressibility of normal liquids. Fortunately, as the pressure is increased, the compressibility decreases, and by 400 bar, the compressibility of CO_2 is similar to some normal liquids. High-pressure pump used in SFC is determined by the column type. For packed columns, reciprocating pumps are generally used while for capillary SFC; syringe pumps are most commonly employed. Reciprocating pumps allow easier mixing of the mobile phase or introduction of modifier fluids.Syringe pumps provide consistent pressure for a neat mobile phase.

2) Injector:

Injection in SFC is usually achieved by switching of the content of a sample loop into the carrier fluid at the column entrance by means of a suitable valve. For packed column SFC, a conventional HPLC injection system is adequate, but for the capillary column SFC, the sample volume depends on column diameters and small sample volumes must be quickly injected into the column, therefore pneumatically driven valves are used. Auto sampler designs use the variable-loop or flow- through design concept, but SFC is incompatible with this approach. In a variable- loop auto sampler, a needle is connected to a high-pressure metering device (such as a syringe) with a piece of flexible stainless-steel tubing that acts as the sample loop. During sample loading, the mobile phase is diverted directly from the pump to the column by switching an injection valve into bypass (load) mode. Sample can then be withdrawn from a vial at atmospheric pressure into the needle and loop. After withdrawing the sample, the needle is pushed into a high-pressure needle seat, and the injection valve is switched (inject), diverting the mobile phase from the pump through the metering

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device, loop, needle and seat, then through the valve onto the head of the column. The needle and the sample loop can remain in the inject position to be flushed by mobile phase in order to minimize carryover. In SFC, the mobile phase behaves like a compressed gas. When the valve is switched to the bypass position, the contents of the metering device, connecting tubing (loop), needle and needle seat all expand up to 500-time their compressed volume, and rapidly vent through the waste port of the valve to ambient. After this expansion, the whole injection system is filled with a low density gas. Attempting to withdraw the next sample results in the cavitation of the metering device, so this results in it being unable to withdraw any further samples from the sample containers. Variable-loop auto samplers need to be modified for use in SFC by converting them to fixed-loop operation. An external fixed-volume loop is connected between opposite ports of a 2-position/6-port valve. The sample is withdrawn from a vial, and then pushed through the loop with the same high pressure metering device. When the injection valve is turned, only the loop and rotor groves experience the high pressure of the system. When using an injector program, the needle should be left in the needle seat, and withdrawn only after the valve returns to the bypass position. If the needle is prematurely withdrawn from the needle seat before the valve is switched, the contents of the metering device (about 200 μL), the loop and the needle all rapidly vent as a highly compressed gas into the interior of the sample compartment, contaminating all the surfaces with potentially harmful mobile phase components such as some additives. If the needle is left in the needle seat, all this fluid is vented out the waste line. The waste line should always be connected to a liquid trap and the vapour phase should be diverted into a fume hood. Before the next injection can be made, a wash pump mounted in the SFC module washes the metering pump, loop and needle with fresh solvent.

3) Oven:

A thermostated column oven is required for precise temperature control of the mobile phase. Conventional GC or LC ovens are generally used.

4) Columns[(6)]:

SFC columns are similar to HPLC columns in terms of coating materials. Open tubular columns and packed columns are the two most common types used in SFC. Earlier work employed absorbents such as alumna, silica or polystyrene or stationary phases insoluble in SC - CO_2 . More recent packed column work has involved bonded non-extractable stationary phases such as octadecylsilyl (C_{18}) or aminopropyl bonded silica. SFC columns consist of a stainless steel tube filled with the stationary phase. SFC columns use end-fittings that permit their connection to the rest of the chromatographic system, and are identical to those used in HPLC columns.

OPEN TUBULAR: Similar to HPLC fused- silica columns. These types of column contain internal coating of cross-linked siloxane material as stationary phase. The thickness of those coatings can be 0.05-1 μm. The length of these columns can be in the range of 10-20m.

PACKED COLUMN: Packed SFC columns are usually made of stainless steel; however, ceramic columns are also available. The stationary phase is retained at each end of the tube by a sieve or frit. Only carbon dioxide based systems are useful as SFC mobile phases; therefore, SFC applications typically require polar stationary phases such as silica amino and diol. Packed column is similar to HPLC columns (10, 5, or 3 μm porous particles) typically 10 cm long x 4.6 mm.

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5) Restrictor or back-

Pressure device:

Pressure restrictors are commonly used to meet pressure requirements in the column by a pressure-adjustable diaphragm or controlled nozzle irrespective of the mobile phase pump flow rate. The outlet of the pressure regulator is usually heated to prevent adiabatic cooling of the expanding supercritical fluid. Adiabatic cooling of SFC mobile phases could render dry ice (solid form of carbon dioxide) formation and flow path blocking. Pressure restrictor is placed either after the detector or at the end of the column. A typical restrictor for a 50 or 100 μm open tubular column consists of a 2-10 cm length of 5-19 capillary tubing attached to the column.

6) Microprocessor:

The commercial instruments for SFC are ordinarily equipped with one or more microprocessors to control such variables as pumping pressures, oven temperature and detector performance.

7) Mobile phase:

There is a wide variety of materials to be used as mobile phase in SFC. Mobile phase can be selected from the solvent groups of inorganic solvents, hydrocarbons, alcohols, ethers, halides; or can be acetone, acetonitrile, pyridine etc. The most common supercritical fluid which is used in SFC is carbon dioxide because its critical temperature and pressure are easy to reach. Carbon dioxide is the preferred fluid because it is:

- ✓ Readily available
- ✓ Inexpensive
- ✓ Has an accessible critical point
- ✓ Relatively safe
- ✓ Good solvent for non-polar molecules
- ✓ Considered green since it has been recycled and
- ✓ Miscible with a wide range of highly polar modifiers.

Other than carbon dioxide, ethane, n-butane, N_2O, dichlorodifluoromethane, diethyl ether, ammonia, tetrahydrofuran can be used.

Today, most SFC applications are performed on relatively polar stationary phases with CO_2 modified with an organic solvent and sometimes other highly polar components, such as acids and bases, called additives[6].

Effect of pressure:

Part of the theory of separation in SFC is based on the density of the super critical fluid which corresponds to solvating power. As the weight in the framework increases, the thickness of the supercritical liquid increases and correspondingly its solvating power increases. This in turn shortens the elution time for the eluent as pressure changes in SFC have a pronounced effect on the retention of analytes. This effect is general and similar to programmed temperature in GC or gradient elution in HPLC.

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Detector:

The choice of detectors will depend upon the mobile phase composition, column type, flow rate and ability to withstand the high pressures of SFC. Conventional gas- phase detectors such as Flame photometric detectors, Electron capture detector (ECD), Nitrogen phosphorous detector (NPD), Sulphur chemiluminescence detector (SCD) and Flame ionization detector (FID)[7-9] are a highly sensitive detector which can contribute to the quality of analyses of SFC with its good features. Liquid phase detectors like Refractive index detector, Ultraviolet – visible spectrophotometric detector, Evaporative Light scattering detectors[10-12] have been employed for SFC. Mass spectrometry and Fourier transform infrared spectrometry can also be used. Chiral detectors, which are capable of differentiating the right and left enantiomers can be used. SFC can be coupled with mass spectrometer, ultraviolet spectrometer, and infrared spectrometer. Some other detectors which are used with HPLC can be attached to SFC such as fluorescence emission spectrometer or thermionic [13-17].

Applications:

There are applications for nourishment, ecological and pharmaceutical products. Likewise, pesticides, herbicides, polymers, explosives and fossil fuels are different classes to be utilized. Chiral partitions should be possible for some pharmaceutical compounds. SFC is dominantly utilized for non-polar compounds on account of the weakness of carbon dioxide, which is the most widely, recognized supercritical liquid mobile phase, as far as dissolving polar solutes effectively. SFC can happen in petroleum industry with the applications on aggregate fragrant substance analysis or other hydrocarbon partitions. It is utilized for the analysis and separation [18, 19] of low to direct sub-atomic weight, thermally labile particles. It can likewise be utilized for the partition of chiral compounds. SFC is utilized as a part of industry essentially for partition of chiral particles, and uses same columns as standard HPLC frameworks. SFC is currently used for achiral divisions and purifications in the pharmaceutical business [24].

Applications in the material and polymer industry: Supercritical fluids are used extensively in the material and polymer industry. Rapid expansions from supercritical solutions across an orifice or nozzle are used commercially to precipitate solids. In this technique, a solute dissolved in supercritical fluid is depressurized rapidly. By controlling the operating variables carefully, the desired precipitated morphology can be attained. In a process, called gas anti-solvent, a supercritical fluid is rapidly added to a solution of a crystalline solid dissolved in an organic solvent. Since the solute has limited solubility in the fluid, the supercritical fluid acts as anti- solvent to precipitate solid crystals. Another process is the precipitation using a compressed fluid anti-solvent. In this process the solvent is sprayed through a nozzle into a compressed fluid and the solvent diffusesrapidly into the supercritical fluid while the fluid swells the solution to precipitate the solute. This process has been used commercially to form nanometric, monodisperse microspheres of polymers. Another process that has been commercialised is the usage of supercritical fluid carbon dioxide to produce foamed parts. Since supercritical fluids depress the glass transition temperature of the polymer, polymer foams can be formed at room temperature by directly adding the supercritical fluid into the extruder [20].

Application in food industry: Carbon dioxide is the most common supercritical fluid in the food industry. It can be used to extract thermally liable food components and the product is not contaminated with residual solvent due to non-toxicity and low critical temperature of CO_2. The extracts colour, composition, odour, texture are controllable and extraction by supercritical fluid CO_2 retains the aroma of the product. Supercritical carbon dioxide extraction is used as a replacement for hexane in extracting soybean-oil and has been tested for the extraction from corn, sunflower and peanuts. Supercritical fluid extracts oil that is lower in iron and free fatty acid. In addition, supercritical carbon dioxide has also been used to extract lilac, essential oils, black pepper, nutmeg, vanilla, basil, ginger, chamomile and cholesterol [(21)].

Pharmaceutical applications: The extraction of vitamin E from soybean oil and purification method for vitamin E has been well studied. The latter process avoids the step of vacuum distillation, which usually results in the thermal degradation of the product [(22)].

Environmental applications: As there are strict environmental regulations, supercritical fluids are used as replacements for conventional hazardous chemical such as hexane. Carbon dioxide has been used with entrains for the extraction of highly polar compounds. Chelating moieties that dissolve into carbon dioxide have been developed for the extraction of heavy metals from soil[(23)].

Conclusion:

In overall ranking of chromatographic techniques it can be judges that SFC falls somewhere between HPLC and GC. Supercritical fluid chromatography technique has the advantage of supercritical fluids and their unique physical properties to best other related methods in both chromatography and extraction fields. Sometimes, they are known as alternative instrumental analytical techniques, while in some other cases; they are used as complementary partners for binary systems.

Future perspective:

SFC is likely to be used to a much greater extent than in the past in food, fuels, and natural products in both research and in routine analysis. Fields other than pharma, including pesticides, are likely to perform many more chiral analyses. The 'green' aspects of SFC are likely to become more widely appreciated.

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References:

(1).MILTON L.LEE and KARIN E. MARKIDES.Introduction, Definition and Description of Supercritical Fluid Chromatography. In: Analytical Supercritical Fluid Chromatography and Extraction, pp.1, Chromatography Conferences, Inc. Provo, Utah.

(2).E. Klesper, A.H Corwin, D.A. Turner, 1962. High pressure gas chromatography above critical temperatures, Journal of Organic.Chemistry(27): 700 – 701.

(3).Chih Wu, Properties of Thermodynamic Substance. In: Thermodynamics and Heat Powered Cycles: a Cognitive Engineering Approach. New York, Copyright 2007 by Nova Science Publishers, Inc.

(4).Miguel Herrero, Alejandro Cifuentes Elena I Brarez 2005. Sub-and supercritical fluid extraction of functional ingredients from different natural sources: Plants food –by- products, algae and microalgae. Food Chemistry 98 (2006): 136 -148.
(5).T.L Chester 1986.The role of supercritical fluid chromatography in analytical chemistry.Journal of Chromatographic Science 24(6):226-229.
(6).Larry T. Taylor 2009. Supercritical fluid chromatography for the 21st century.The journal of Supercritical fluids 47 (3):566-573.
(7).Zhongpeng Xia, Kevin B. Thurbide 2006. Universal acoustic flame detection for modified supercritical fluid chromatography.Journal of Chromatography A, 1105 (1-2): 180-185.
(8). Nohoa P. Vela, Joseoh A. Caruso 2000. Element Selective detection for supercritical fluid chromatography. Journal of Biochemical and Biophysical Methods 43:45-58.
(9).T.A. Berger 2001. Simple Correction for Variable Post, Column Split Ratios using Pure Carbon Dioxide in Packed Column Supercritical Fluid Chromatography with Independent Pressure and flow control. Chromatographia, 54(11/12):783-788.
(10).Yukio Hirata, Yukinori Kawaguchi and Yasuhiro Funada 1996. Refractive Index Detection Using an Ultraviolet Detector with a Capillary Flow Cell in Preparative SFC. Journal of Chromatographic Science, 34(1):58-62.
(11). H. Shi, J.T.B. Strode III, L.T. Taylor, E.M. Fujinari 1996.Feasibility of supercritical fluid chromatography- chemiluminescent nitrogen detection with open tubular columns.Journal of Chromatography A, 734 (2):303-310.
(12). Roger M. Smith, Orapin Chienthavom, Nicholas Danks, Ian D. Wilson 1998. Fluorescence detection in packed- column supercritical fluid chromatographic separations. Journal of Chromatography A, 798 (1-2):203-206.
(13). Francis Rouessac and Annick Rouessac 2nd edition 2007. Supercritical Fluid Chromatography. In: Chemistry Analysis: Modern instrumentation Methods and Techniques, pp.127 -133, Johnwiley & sons Ltd.
(14). Douglas A. Skoog, F. James holler, Timothy A. Nieman, Supercritical Fluid Chromatography. In: Principles of instrumentation analysis, fifth edition, pp.768 -774, Saunders Golden Sunburst Series.
(15).Mustafa Salih Hizir, Andrew R. Barron 2014. Basic principles of supercritical fluid chromatography and supercritical fluid extraction.International Journal of Pharma Research & Review 3(5):59-66.
(16).Basic Principle of supercritical fluid aspects of supercritical fluid chromatography 1982, Analytical Chemistry,54:1090-1093.
(17).Dixon, D.J. an Johnston, K.P. Supercritical Fluids," In Encyclopedia of Sepaation Techonology; Ruthven D.M., John Wiley, 1544 – 1569.
(18).Akgerman, A. and Giridhar, M 1994. Fundamentals of Solids Extraction by Supercritical Fluids. In Supercritical Fluids – Fundamentals for Applications; Sengers, J.M.H.; Kiran, E.,Eds., Kluwer Academic Publishers, 669-696.
(19).Fangbiao, Li and Yunsheng Hsieh 2008. Supercritical fluid chromatographymass spectrometry for chemical analysis.Journal of Separation Science, 31(8): (1231-1237).
(20).Supercritical fluid chromatography Primer, Terry A.Berger, Agilent technologies.
(21).Nikolaos Botsoglou and Dimitrios Fletouris, Residual Antibacterial in Food 2011, Handbook of Food Analysis, Second Edition-3 Volume Set,10.1201/b11081-27: (931-1035).
(22). Preeti Gopaliya, Priyadarshani R Kamble, Chetan Singh Chauhan 2014.A Review Article on Supercritical Fluid Chromatography. International journal of Pharma Research & Review, 3(5):59-66.

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Cosmos Impact Factor-5.960

(23).Takashi Yarita, 2008. Development of Environmental analysis methods using supercritical fluid extraction and Supercritical fluid chromatography, Chromatography, 29 (1).
(24).Terry A Berger. "Separation of polar solutes by packed column supercritical fluid chromatography". Journal of chromatography A , 785:3 – 33.

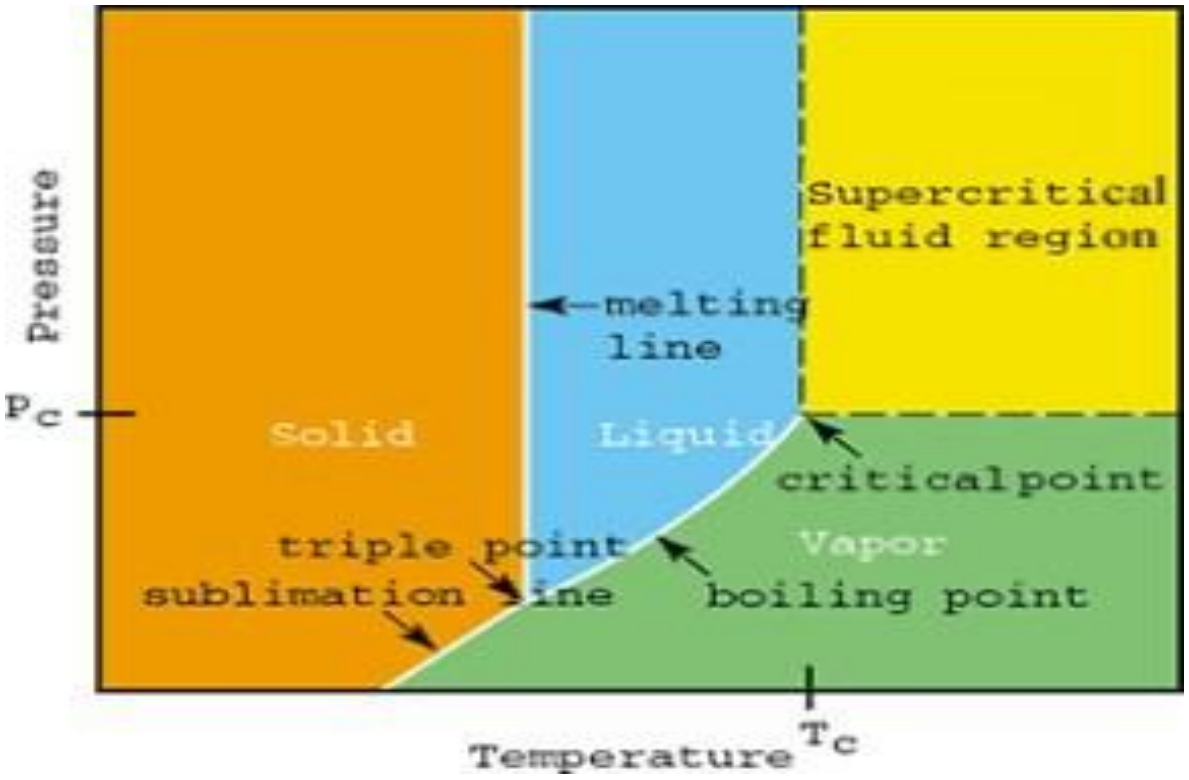

Figure 1: Definition of Supercritical fluid

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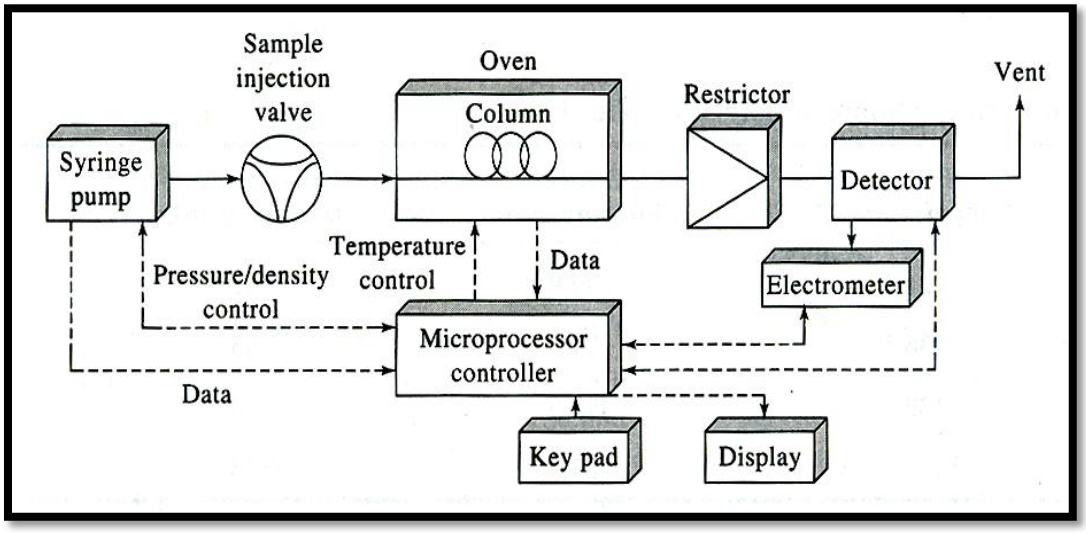

Figure 2: Instrumentation of SFC

Figure 3: Supercritical Fluid Chromatography

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Table 1: Properties of some solvents as mobile phase at the critical point.

SOLVENT	Critical temperature (° C)	Critical pressure (bar)
Carbon dioxide	31.1	72
N_2O	36.5	70.6
Ammonia	132.5	109.8
Ethane	32.3	47.6
n-butane	152	70.6
Diethyl ether	193.6	63.8
Tetrahydrofuran	267	50.5

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