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Review Paper

A Review Article On: Supercritical Fluid Extraction

Kiran Shende*, Aaditee Gore, Dr. Megha Salve

Shivajirao Pawar college of pharmacy, pachegaon.

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ABSTRACT

In simple terms, supercritical fluid extraction (SCFE) employs a liquid phase with properties that are a mix of gas and liquid to dissolve solutes in the matrix. The solvation performance of the SCFE, which is density controlled, can be adjusted within a wide range by changing the pressure, temperature, or both, allowing for selective tuning of the extraction process. In contrast to regular organic liquids that have a higher diffusivity and lower viscosity, SCFE offers much improved mass transfer of solutes from sample matrices. The article outlines research conducted on the extraction of valuable compounds from natural products using supercritical fluid extraction. These compounds are commonly used in industries such as food, pharmaceutical, agricultural, and dairy. It also talks about fine-tuning processing parameters from pilot scale testing to industrial implementation.

INTRODUCTION

Studies are being conducted globally to assess the efficiency of various new non-thermal techniques in food processing in order to minimize the negative effects of standard thermal methods like pulsed electric field[1]. Supercritical fluids have been used for extracting natural products since the late 1970s, focusing on a limited number of applications for an extended period of time. At present, businesses are showing more and more enthusiasm towards supercritical methods as they observe the benefits of improvements in procedures and machinery. The increasing number of patents filed in recent years is proof of the growing range of applications for supercritical fluid extraction (SFE) on a worldwide scale. The current landscape has already incorporated its use, primarily due to the growing need for top-notch products and the globalization of the economy. It also stands out in its use in the industries of pharmaceuticals, food, chemicals, and cosmetic ingredients. The increase in the utilization of this technology in the industrial sector is mainly due to its ability to selectively separate a wide variety of organic compounds easily. A lot of these compounds cannot be extracted using traditional

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***Corresponding Author:** Kiran Shende
Address: *Shivajirao Pawar college of pharmacy, pachegaon.*
Email ✉: kiranshende220@gmail.com

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methods or require costly high-resolution columns for purification, which may not be easily accessible in the domestic market, resulting in high expenses. The global discussion on the harmful effects of organic solvents on the environment stems from their extensive utilization in a range of industrial processes like fat and oil extraction, acquiring bioactive substances, heavy metal removal, polymer processing, and fuel production. With reference to this image, the Montreal Protocol was put into effect in 1987, and then the Kyoto Protocol in 1997, aimed at restricting or eliminating the production and consumption of ozone-depleting substances[3]. The concept of supercritical fluid technology entails utilizing the distinct properties of solvents in their supercritical phase. The mixture will change states based on the precise pairing of pressure and temperature. The solid, liquid, and gaseous states are the three basic states of matter. In thermodynamics, a phase diagram is a visual representation that displays the different physical states of a substance depending on varying temperature and pressure conditions[4]. The introduction of supercritical fluid extraction (SFE) represents an important milestone in this momentous journey. In the past twenty years, SFE has evolved from small-scale laboratory use to widespread adoption in industrial settings. Green chemistry advancements in extraction aim to reduce energy consumption and replace conventional solvents with eco-friendly alternatives. Green technologies such as ultrasound-assisted extraction, microwave-assisted extraction, supercritical fluid extraction, mechanical pressing, and détente instantanée contrôlée (DIC) are used in herbal extraction. The SFE utilizes CO2 at critical conditions to separate or extract chemical compounds from a matrix. Despite their low critical temperature and pressure values characteristic of other supercritical fluids, xenon (Xe) and sulfur hexafluoride (SF6) have restricted commercial application because of their costly production methods. Although they have low critical values, gases like nitrous oxide (N2O) or ethane are limited in use because of safety concerns[7].

Terminology:

Supercritical: The word "supercritical" describes a substance as a non-condensing, single-phase fluid when it exceeds its critical temperature (Tc) and critical pressure (Pc). Past this boundary, lies a supercritical area where the material exhibits the characteristic physical and chemical traits of gases or liquids, including elevated density, moderate diffusivity, and reduced viscosity and surface tension [8].

Supercritical Fluid: Highly compressed gases, known as supercritical fluids, exhibit a unique combination of gas and liquid properties. Supercritical xenon, ethane, and carbon dioxide provide a variety of unique chemical opportunities in synthetic and analytical chemistry [9].

Supercritical Fluid Extraction (SFE): Supercritical fluid extraction (SFE) is the process of utilizing supercritical fluids as the solvent for separating a specific component (the extractant) from another component (the matrix). Extraction usually entails taking out materials from a solid source, but it can also involve retrieving from liquids. SFE can be used to prepare samples for analysis or on a larger scale for tasks such as removing unwanted substances from a product (such as decaffeination) or extracting specific products (like essential oils). These essential oils might have limonene and other straight solvents. Supercritical carbon dioxide (CO2) is commonly used, sometimes with extra co-solvents such as ethanol or methanol. Supercritical carbon dioxide is obtained when the temperature is over 31 °C and the pressure is over 74 bar. Including modifiers could result in a minor change to this. The forthcoming conversation will primarily center on CO2 extraction, unless specified otherwise[6]. The diagram in Figure 1 depicts a fundamental

SFE system at process scale, showing a standard batch extraction process. The extraction tank is equipped with temperature controllers and pressure valves on both ends to ensure the desired extraction conditions while raw materials are added. Pumps must be used to apply pressure to the extraction tank with the liquid and move it throughout the system. The liquid and dissolved parts transfer from the reservoir to the divider, where the solvency of the liquid is decreased by increasing the temperature or decreasing the pressure in the system. Product recovery is accomplished by using a valve located at the bottom part of the separator(s) [10]. The extraction procedure's success is determined by how well the target compound dissolves in the selected solvent, which is influenced by the interactions between the solvent and the solute. Supercritical fluid extraction (SFE) is currently considered a superior option for retrieving bioactive substances from natural sources. This is because of its reduced extraction time, decreased organic solvent usage, ability to work with heat-sensitive materials, provision of cleaner extracts, and eco-friendly nature[12]. The curve marks the regions associated with gas, liquid, and solid phases. The critical point marks the end of the vapor liquid coexistence curve. Above the critical temperature, no phase transition occurs as the fluid remains unable to transition into a liquid phase even under increased pressure. In the supercritical state, there is a single phase with properties that lie between those of a pure liquid and gas, not falling under the classification of either [13].

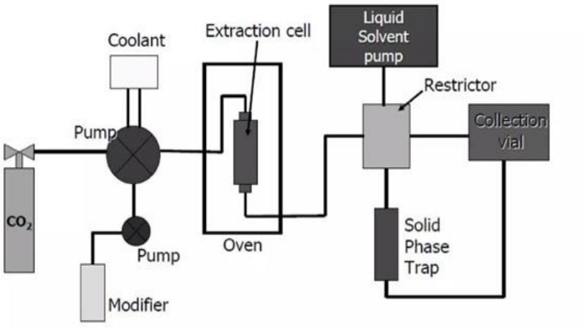

Fig: 1 Supercritical fluid Extraction[11].

Component Of SFE:

1. Fluid reservoir.
2. Pump.
3. Extraction cell/ column.
4. Restrictor
5. Collector.
6. Detectors[11].

Method development for SFE:

Table 1- Method development for supercritical fluid extraction[11].

Sample type	Intermediate volatility	Involatile non-polar	Involatile non-polar, higher MW	Involatile polar
Pressure or density	Low	Intermediate	High	High with polar modifiers
Temperature	Low near critical temperature	Low near critical temperature	Increase temperature	Increase temperature >modifier boiling point
Time	Generally short but will vary on sample matrix	Short, longer with less soluble analytes	Increase time as solubility decrease	Increase time as solubility decrease
Flow rate	Low	Increase to improve diffusion	Increase to improve diffusion	Low, allow interaction of modifier

Supercritical fluid as solvent:

Rapid Expansion of Supercritical Solution (RESS):

RESS includes utilizing supercritical fluid for both extraction and drug encapsulation in a traditional method. Rapidly decreasing the pressure of the saturated supercritical fluid on a solid substrate (transitioning from supercritical to ambient conditions) causes the supercritical fluid to rapidly expand, resulting in a swift reduction in solvation capability as it moves into a low-pressure chamber via a heated capillary or laser-drilled nozzle. Due to the decrease in solvation power, the solvent rapidly becomes super-saturated, resulting in the emergence of super fluid nucleation and particle formation. Adjustable variables encompass solute solubility in a supercritical fluid (commonly SC-carbon dioxide), temperature, pressure, capillary design angle, and the impact of the capillary jet striking the surface. This method produces dry particles that do not require further processing steps [14].

Rapid Expansion of a Supercritical Solution into a Liquid Solvent (RESOLV):

The RESOLV technique, a variation of traditional RESS, involves quickly introducing a supercritical solution into a liquid solvent to reduce the formation of aggregates in particle manufacturing. This technique includes releasing or expanding supercritical fluids with solid material into a collection chamber with room temperature aqueous solution through a laser-drilled opening. Furthermore, various water-soluble polymers or surfactants are added to the aqueous solution in order to function as a stabilizing agent[15].

Supercritical fluid As an Anti-Solvent:

Gas Anti-Solvent Recrystallization (GAS):

In this technique, a supercritical fluid acts as an anti-solvent. Initially, the solute is dissolved in an appropriate organic solvent. The organic solvent evaporates as the supercritical fluid is introduced into it. Therefore, the organic solvent's ability to dissolve substances decreases, making it an ineffective solvent for the solute. The general procedure supports the beginning of nucleation, leading to the formation of the solute. For optimal results using this method, it is best for the solute to have low solubility in the supercritical fluid and for the supercritical fluid to be mixable with the organic solvent[16].

Aerosolized Solvent Extraction System (ASES):

ASES has a strong connection with SAS. ASES utilizes SCFs as an antisolvent and can be handled by spraying the solution and antisolvent. The SCF entering the liquid droplets results in a significant increase in volume and a decrease in solvent power, leading to a sudden increase in supersaturation within the liquid mixture and the formation of small, uniform particles. A high-pressure pump is used to disperse the SCF into the high-pressure container. Once the system reaches a stable condition, the substance in liquid form is added to the container using a specific-sized opening. Getting small liquid droplets requires pumping the solution at a pressure higher than the vessel's operational pressure. The particles gather on the filter surface attached to the vessel's bottom[17].

Adventages of SFE:

1. The penetration power of supercritical fluid into porous solid materials is higher than liquid solvent due to its low viscosity and high diffusivity.
2. A complete extraction is possible in SFE as a fresh fluid is continuously forced to flow through the samples.
3. The solvation power of the supercritical fluid can be adjusted according to requirement by varying temperature and pressure resulting in high selectivity.
4. Suitable for thermo labile material.
5. It can be associated with various compounds detecting tool like gas chromatography and mass spectroscopy, which is useful in direct quantification in addition to extraction.

6. Extraction of natural raw material with supercritical CO2, allows the obtaining of extracts which flavour and taste are perfectly respected and reproducible.
7. The majority of the easily evaporated substances lost during hydrodistillation are found in the supercritical extracts, leading to a favored flavor and taste among taste testers[18].
8. Elimination of organic solvents i.e. reduces the risk of storage.
9. Rapid (due to fast back-diffusion of analytes in the SCF reduces the extraction time since the complete extraction step is performed in about 20 min).
10. Suitable for extraction and purification of compounds having low volatility present in solid or liquid.
11. Susceptible to thermal degradation (low operating conditions).
12. Complete separation of solvent from extract and raffinate[11].

Disadventages of SFE:

1.Although using Supercritical fluid extraction is time and organic solvent saving, but there is a lack of universal method that works for different types of matrices and analytes.
2. The Supercritical fluid extraction technique requires an experienced analyst to develop the method and run the sample. It requires the analyst to understand the mechanism and working mechanism and it’s not a day-to-day routine analysis[19].
3. Carbon dioxide could be an excellent solvent for non-polar analytes. However, it’s polarity might not be suitable to extract polar compounds due to the insufficient solubility of polar analytes in Sc-carbon dioxide.
4. Furthermore, Supercritical fluid extraction may not be appropriate for extracting compounds that are soluble in water or blood plasma. The use of a co-solvent as a modifier is necessary for extracting polar compounds. Included in this list are methanol, hexane, aniline, toluene, and diethylamine[20].
5. Prolonged time (penetration of SCF into the interior of a solid is rapid, but solute diffusion from the solid into the SCF).
6. Modeling is inaccurate.
7. Scale is not possible (due to absence of fundamental, molecular-based model of solutes in SCF).
8. Consistency & reproducibility may vary in continuous production[11].

Application of Supercritical Fluid Extration:

1. Food processing:

The attractive features of supercritical carbon dioxide, such as its lack of toxicity, affordability, lack of odor, lack of color, non-flammability, and having a critical temperature close to ambient, as well as low viscosity and high diffusivity compared to liquids, have established it as the preferred solvent for extracting essential oils and food industry oils. Further, the color, composition, aroma, and texture of the extracts are controllable, and the use of carbon dioxide in extraction aids in maintaining the product's fragrance. Supercritical fluid extraction is utilized in place of hexane for extracting soybean oil and has been tested for extraction from corn, sunflower, and peanuts. Supercritical fluid extraction has the advantage of replacing oils while also reducing iron and free fatty acid levels during extraction. Another application involves removing fat from food items. The whole procedure was devised exclusively for business applications, including the specified typical layout. The process of removing fat results in potato chips containing minimal to zero fat. SFE can effortlessly control the excess fat in potato chips according to the preferred flavor. A significant amount of research has been dedicated to the utilization of supercritical carbon dioxide for the purpose of decaffeinating coffee. Hence, it is not surprising that this was the first approach to be introduced to the market [21].

2. Nanoparticle formation using supercritical fluids:

SFE was used in different scenarios to produce organic systems that were micro-nanodispersed. Their distinctive ability to resist drastic temperature changes and their special solvent properties make them important for industrial use. Creating a sufficient super saturation for a precipitation reaction with conventional solvents is restricted by the low temperature dependency of solubility and the technical difficulty of rapid heat exchange. Taking this into account, it is important to mention the use of liquid CO2 as a refrigerant. In contact cooling, the active compound solution is sprayed at -78 °C into a CO2 stream, resulting in particle formation through crystallization within the droplets. Taking into account the toxicological compatibility, lack of combustibility, and favorable critical properties of CO2 (pc=74 bar, Tc=31°C), the RESS technique appears very attractive, since there may be no need for extra steps to remove any remaining solvent. However, SF-CO2 can function as an oxidizing agent against oxidation-sensitive substances such as β-carotene, making it unsuitable for use as a precipitation medium. SF-CO2 is utilized in place of water as the precipitation medium for organic solvents in both the GAS and PCA processes. During the SEDS procedure, the organic active-compound solution and SF-CO2 are quickly extracted by being combined in a coaxial mixing nozzle. However, only occurrences of particle formation in the micrometer scale have been recorded thus far [22].

3. Particle Design in Drug Delivery Applications:

The majority of pharmaceutical procedures for creating particles and preparing materials are fundamentally simple, inefficient, and highly limited. The traditional high-energy milling process for reducing particle size is inefficient and likely to cause changes in morphology and crystal structure. Modifications of that nature have the potential to alter the physical and chemical stability of the downsized material. Utilizing SFT in pharmaceutical materials and drug delivery systems shows promising potential for crystal and particle engineering in this area. The limitations hinder the capability to produce particles of various sizes, ranging from micro to submicron. Lately, the SAS technique has shown great potential in producing microparticles for different substances such as insulin, lysozyme, trypsin, methylprednisolone, and hydrocortisone [23].

4. Plant material extraction:

The extraction industry is utilizing supercritical fluid due to its numerous advantageous qualities that can be taken advantage of. In comparison to traditional solvent extraction methods, supercritical fluid extraction is a quicker process with greater precision, requiring fewer parameters to track. The solvents used are eco-friendly, leading to a higher quality of extraction yield. The processing of plant material is extremely intricate, taking into account factors such as plant nature, processing parameters, solvent physicochemical properties, and mass transfer phenomena. Supercritical fluids have been widely utilized for extracting plant materials. Fatty acid, essential oil, flavonoids, saponins, phenolic group, and carotenoid have been obtained from different plants through adjusting the extraction process[24].

5. Supercritical drying:

Supercritical drying surpasses the critical point of the working fluid to prevent the typical liquid-gas transition observed in regular drying. It is a method of eliminating liquid in a carefully controlled manner, much like freeze drying. It is typically utilized in making aerogel and in preparing biological samples for scanning electron microscopy. When a substance transitions from a liquid to a gas in the phase diagram, it evaporates causing a decrease in liquid volume. While this occurs, the tension on the surface of the solid-liquid connection resists any objects the liquid is clinging to. Fragile formations such as cell walls, dendrites in silica gel, and the small components of microelectromechanical devices are prone to breakage due to surface tension when the interface passes through. In order to prevent this situation, the sample can be transitioned from liquid to gas without crossing the liquid-gas boundary on the phase diagram; during freeze-drying, this involves going around to the left (low temperature, low pressure). Nevertheless, certain formations are disturbed by the solid-gas boundary. Alternatively, supercritical drying takes a different path by moving to the right side of the line, where both temperature and pressure are high. This transition from liquid to gas does not go through a phase boundary, but goes through the supercritical region where the difference between gas and liquid becomes irrelevant. Carbon dioxide and freon are appropriate fluids for supercritical drying. In its supercritical state, nitrous oxide acts as a potent oxidizer despite having physical characteristics like carbon dioxide. Supercritical water is a strong oxidizer due in part to its high critical point temperature and pressure of 374 °C and 647°K and 22.064 Mpa, respectively[25].

CONCLUSION: In the past two decades, there has been a rise in the utilization of supercritical fluid extraction in natural product research. SFE-based techniques show great potential in the field of analytical chemistry. They can also be used effectively as a tool to optimize and test the feasibility of non-analytical applications, such as exploring the possibility of expanding SFE for industrial use. Utilizing automated analytical SFE tools enables quick evaluation of SFE feasibility at a low cost and in a short amount of time. SFE techniques have been utilized for extracting an extensive variety of extracts, oils, oleoresin, and various bioactive compounds (such as alkaloids, terpenes, and phenolics), including individual compounds. SFE and SFC have a wide range of uses in qualitative analysis, such as in the analysis of various samples like food items, natural products, agrochemicals, environmental samples, fuels, lubricants, artificial polymers, oligomers, organometallic compounds, pharmaceutical agents, and chiral compounds essential for biology. SCF provides a more sustainable and selective option for qualifying and quantifying natural products compared to conventional methods. In collaboration, SCF-driven extraction techniques show significant potential and therefore deserve additional research.

REFERENCES

1. Odriozola-Serrano, I., Aguilo-Aguayo, I., Soliva- Fortuny, I. & Martín-Belloso, O. (2013) Pulsed electric fields processing effects on quality and health-related constituents of plant-based foods, Trends in Food Science and Technology, 29, 98-107.
2. Brunner, G., 2005. Supercritical fluids: Technology and application to food processing. J. Food Eng., 67: 21-33. DOI:10.1016/j.jfoodeng.2004.05.060.
3. Herrero M, Mendiola J, Cifuentes A, Ib´a˜nez E. (2010) Supercritical fluid extraction: recent advances and applications, J. Chromatogr, (16), 2495–511.
4. Carroll J. Natural gas hydrates: A guide for engineers: Gulf Professional Publishing. 2014.
5. Zhao B, Zhang Q, Lin H, Qingguo R, Kang Q, Zhang Y, et al. Effect of co-existent components in CO2 supercritical fluid extract of Angelica Sinensis Radix on metabolism of Z-ligustilide after oral administration in rats. Journal of Traditional Chinese Medicine. 2014; 1(2):126-134.
6. https://en.m.wikipedia.org/wiki/Supercritical_fluid_extraction.
7. Hill, J. H.; Petrucci, R. H. Chapter 11. In General Chemistry: An Integrated Approach,

3rd ed.; Prentice Hall: Upper Saddle River, NJ; 1996; (accessed at http://www.slidefinder.net/c/chapter-_states_matter_intermolecular_forces/12886275).

8. Spilimbergo, S. & Bertucco A. (2003) Biotechnol. Bioeng., 84, 627–638.
9. https://www.nottingham.ac.uk/supercritical/scintro.html.
10. Brunner, G., 2005. Supercritical fluids: Technology and application to food processing. J. Food Eng., 67: 21-33. DOI:10.1016/j.jfoodeng.2004.05.060.
11. https://www.slideshare.net/slideshow/supercritical-fluid-extraction-40257015/40257015.
12. Vigano, J., Machado, A. P. F., & Martínez, J. (2015) Sub- and supercritical fluid technology applied to food waste processing. The Journal of Supercritical Fluids, 96, 272-286.
13. Gopaliya P, Kamble PR, Kamble R, Chauhan CS. A review article on supercritical fluid chromatography. International Journal of Pharmaceutical Researchand Review. 2014; 3(5):59-66.
14. Phillips EM, Stella VJ. Rapid expansion from supercritical solutions: Application to pharmaceutical processes. International Journal of Pharmaceutics. 1993;94(1-3):1-10.
15. Meziani, M. J.; Pathak, P.; Beacham, F.; Allard, L. F.; Sun, Y. P. Nanoparticle formation in rapid expansion of water-in-supercritical carbon dioxide microemulsion into liquid solution. J. Supercrit. Fluids 2005, 34 (1), 91–97
16. Reverchon E, Adami R. Nanomaterials and supercritical fluids. The Journal of Supercritical Fluids. 2006;37(1):1-22.
17. Byrappa, K.; Ohara, S.; Adschiri, T. Nanoparticles synthesis using supercritical fluid technology towards biomedical applications. Adv. Drug Deliv. Rev. 2008, 60 (3), 299 –327.
18. Gopaliya P, Kamble PR, Kamble R, Chauhan CS. A review article on supercritical fluid chromatography. International Journal of Pharmaceutical Researchand Review. 2014; 3(5):59-66.
19. Zougagh M, Valcárcel M, Rıos A. Supercritical fluid extraction: A critical review of its analytical usefulness. TrAC Trends in Analytical Chemistry. 2004;23(5):399-405.
20. Yang Y, Gharaibeh A, Hawthorne SB, Miller DJ. Combined temperature/ modifier effects on supercritical CO2 extraction efficiencies of polycyclic aromatic hydrocarbons from environmental samples. Analytical Chemistry. 1995;67(3):641-6.
21. Perrut M. Supercritical fluid applications: Industrial developments and economic issues. Journal of Industrial & Engineering Chemistry. 2000; 39(12):4531-4535.
22. Herrero, M., A. Cifuentes, E. Ibanez and M. Herrero, et al., 2006. Sub- and supercritical extraction of functional ingredients from different natural sources: Plants, food-by-products, algae and microalgae. J. Food Chem., 98: 136-148. DOI:10.1016/j.foodchem.2005.05.058.
23. York, P. Strategies for particle design using supercritical fluid technologies. Pharm. Sci. Technol. Today 1999, 2 (11), 430 – 440.
24. Ibáñez E, Mendiola JA, Castro-Puyana M. Supercritical Fluid Extraction. In: Encyclopedia of Food and Health. Oxford: Academic Press. 2016;227-33.
25. Herrero, M., A. Cifuentes, E. Ibanez and M. Herrero, et al., 2006. Sub- and supercritical extraction of functional ingredients from different natural sources: Plants, food-by-products, algae and microalgae. J. Food

Chem., 98: 136-148. DOI:10.1016/j.foodchem.2005.05.058.

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