REVIEW ARTICLE

Accepted 7 October 2005
Revised 9 June 2005
Received 5 Feburary 2005
Indian J. Pharm. Sci., 2005, 67(5): 532-539

Supercritical Fluid Extraction: a New Milestone in Extraction Technology

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Supercritical fluid extraction is two-step process, comprising of feed of fluid into extraction vessel at above its critical temperature and critical pressure and depressurization of fluid after extraction. Supercritical fluid has both gas like properties (diffusivity, viscosity and surface tension) and liquid like properties (density and solvating power), which are favorable for diffusion coefficient as well as mass transfer. Carbon dioxide is most useful supercritical fluid ($T_c=31^0$ and $P_c=74$ bars) as it is safe, inexpensive, non-toxic, non-inflammable, inert to materials and solvating strength is adjusted by modifier (methanol) as well as extraction parameters (time, temperature and pressure). Supercritical fluid extraction is useful in extraction, separation and refining, cleaning and disinfection, synthesis and processing, optimization of drug particles and environmental application such as soil remediation and treatment of municipal waste.

Extraction is the process of the removal of soluble material from an insoluble residue, either liquid or solid, by treatment with a liquid solvent[1]. Traditional extraction method like solid-liquid extraction, Soxhlet extraction, homogenization, sonication and dissolution have number of disadvantages like lower efficiency, lower yield, lower purity of product, longer processing time[2]. There is also an increasing public awareness of the health, environment and safety hazards associated with the use of organic solvents in food processing and the possible solvent contamination of the final product. The high cost of organic solvent and the increasingly stringent environmental regulation, together with the new requirements of the medical and food industries for ultra pure and high added value products, have pointed out the need for the development of new and clean technologies for the processing of food products. Supercritical fluid extraction (SFE) technology has been developed, in which the sample is placed in flow through container and supercritical fluid is passed through sample; after depressurization, extracted material is collected in solvent or trapped on adsorbent, followed by desorption by rinsing with solvent[3-5].

Supercritical fluid:

A fluid is termed supercritical fluid when the temperature and pressure are higher than the corresponding critical values. Phase diagram describing physical state of a substance has three curves as sublimation curve, melting curve and boiling curve. The curve defines the regions corresponding to the gas, liquid and solid state (fig.1). The critical point (CP) marks the end of the vapour-liquid coexistence curve. Above the critical temperature (Tc) there is no phase transition in that the fluid can not undergo a transition to a liquid phase, regardless of the applied pressure. Critical pressure (Pc) is the highest pressure at which a liquid can be converted to a gas by an increase in temperature. In the supercritical environment only one phase exists and as it is termed, is neither a gas nor a liquid and characterized by physical and thermal properties that are between those of the pure liquid and gas. Under thermodynamic equilibrium conditions, the visual distinction between liquid and gas phases, as well as the difference between the liquid and gas densities, disappear at and above the critical point. Similar drastic changes exist in properties of a liquid mixture as it approaches the thermodynamic critical loci of the mixture.

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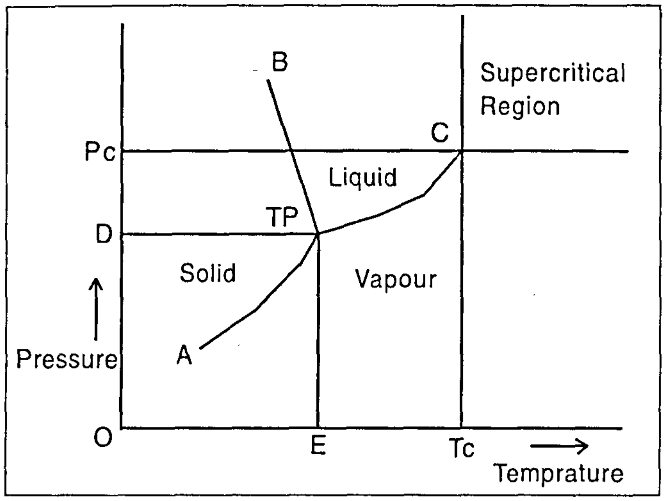

Fig. 1: Phase diagram of water and its supercritical region[1,14].

TP=Triple point (D=610N/m^2 and E=273°K), C=Critical point, Pc=Critical pressure (22.291×10^6N/m^2), Tc=Critical temperature (647°K), A-TP=Sublimation curve, B-TP=Melting curve, and C-TP=Boiling curve (figure is not in scale).

Other properties of a liquid that change widely near the critical region are conductivity, surface tension, constant-pressure heat capacity and viscosity. In comparing a liquid sample with a supercritical fluid sample of the same fuel density, thermal conductivity and diffusivity of supercritical fluid are higher than the liquid; its viscosity is much lower, while its surface tension and heat of vaporization have completely disappeared. These drastic changes make a supercritical fluid appreciably preferred over that of a liquid with the same density for extraction[6-10,15]. A comparison of typical values for density, viscosity and diffusivity of gases, liquid and its supercritical fluid is presented in Table1 (http://sunny.vemt.bme.hu/sfe/angol/supercritical.html, accessed on Oct 11, 2004). Various super-critical flu-

TABLE 1: COMPARISION OF PHYSICAL AND TRANSPORT PROPERTIES OF GAS, LIQUID AND SUPERCRITICAL FLUID

State	Density (kg/m^3)	Viscosity (cp)	Diffusivity (mm^2/s)
Gas	1	0.01	1-10
Supercritical Fluid	100-800	0.05-0.1	0.01-0.1
Liquid	1000	0.5-1.0	0.001

cp = centipoises, kg./m^3= kilogram/cubic millimeter and mm^2/ S = millimeter square/second

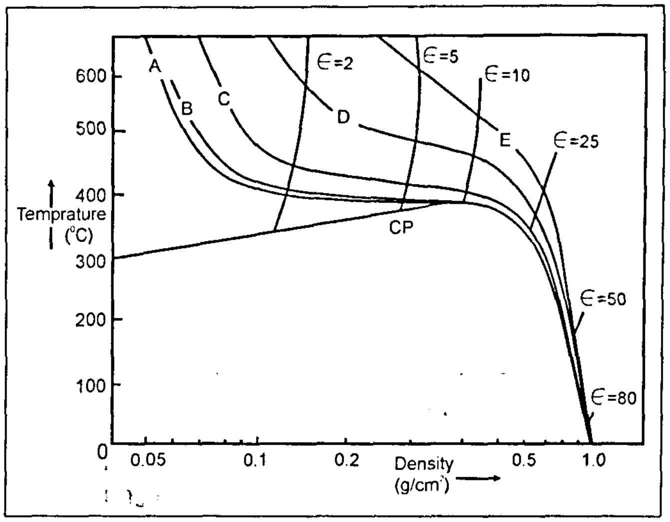

Fig. 2: Relationship of dielectric constant of water with temperature, pressure and density.

CP=Critical point, ε =Dielectric constant, A=220 Atm., B=250 Atm., C=350 Atm., D=500 Atm., E=1000 Atm (figure is not in scale).

TABLE 2: COMPARISION OF CRITICAL CONSTANTS FOR COMMONLY USED FLUIDS[6,12,16]

Fluid	Critical Temperature(°)	Critical Pressure(Atm)
Carbon dioxide (CO_2)	31.1	72.8
Methane (CH_4)	-82.1	45.8
Ethane (C_2H_6)	32.3	48.2
Propane(C_3C_8)	96.7	41.9
Argon (Ar)	122.3	48.0
Nitrous oxide (N_2O)	36.5	72.5
Water (H_2O)	374.1	218.3
Ethanol (C_2H_5OH)	243.0	63.0
Ethene (C_2H_4)	9.9	72.9
Ammonia (NH_3)	132.5	112.5
Pentane (C_5H_{12})	196.6	33.3
Butane (C_4H_{10})	152.0	37.5
Trifluro methane (CHF_3)	25.9	46.9
Di-chloro difluro methane (CCl_2F_2)	111.8	40.7

Atm = atmosphere pressure

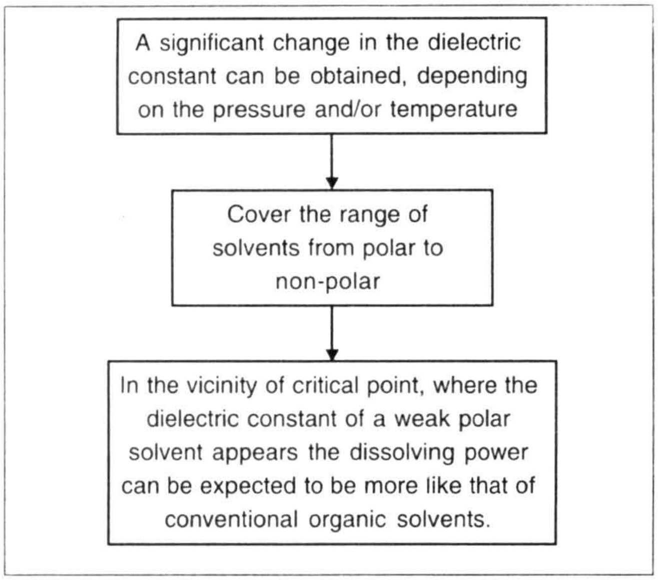

Fig. 3: Effect of temperature and pressure on dielectric constant and its relationship with solubility range.

ids with their critical temperature and critical pressure are given in Table 2.

In supercritical region, solvating strength is a direct function of density, which in turn is dependent on system pressure (at constant temperature). Solvating strength can be fine-tuned by minutely adjusting the pressure and/or temperature, using the solvent anywhere in the range of ideal gas to nearly pure liquid. Because of non-compressibility of liquid, this phenomenon is unique to supercritical fluids. It is even possible, by adding small quantities of co-solvent; to custom design a supercritical fluid for a specific application[11]. Fig. 2 shows the temperature/pressure dependency of the dielectric constant of water and fig. 3 shows its relationship with solubility range. The dielectric constant of supercritical water is in the range of from 2 to 30, which is similar to the range from a non-polar solvent such as hexane (with a dielectric constant about 1.8). In other words, with supercritical water it becomes possible to dissolve organic substances that do not dissolve in water under atmosphere conditions[17]

Carbon dioxide as supercritical fluid:

Carbon dioxide achieves a supercritical state above the temperature 31° and pressure 74 bars. In this state the density is similar to that of a liquid, and offers higher dissolving capability for various substances. Because the viscosity is similar to that of a gas and the diffusion coefficient is larger than that of a liquid, substances extraction is faster.

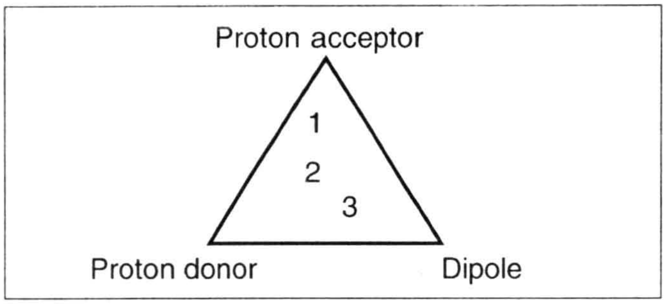

Fig. 4: Snyder rule for polarity and nature of solvents.

1. 2-popanol, 2. aetonitrile and 3. dchloromethane

For the extraction of natural products, carbon-dioxide is the preferred solvent since it offers the following advantages-mild process conditions (has near ambient critical temperature), generally regarded as safe (GRAS), inexpensive, easily available, inert to most materials, easily adjustable solvent strength, rapid diffusion due to low viscosity, fast and complete solvent recovery and environmentally acceptable with creating minimal waste[18-21]

The main disadvantage of carbon dioxide is its inability to elute very polar or ionic compound. This can be overcome by adding a small portion of a second fluid called a modifier fluid, which is generally an organic fluid (alcohols, cyclic ether, dimethylamine, methyl cyanides), which is completely miscible with carbon dioxide but can be almost any liquid including water. Modifier changes in solvent polarity and nature as per Snyder rules (fig. 4) (http://ull.chemistry.uakrom.edu/chemisep/slide.html$chap-ter=/chemsep/su-

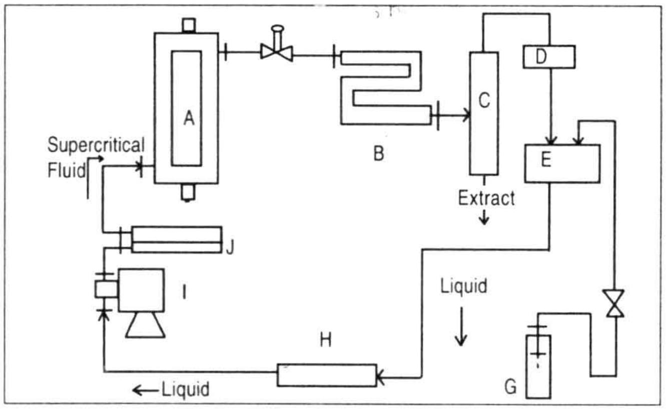

Fig. 5: Schematic flow of supercritical fluid extraction process.

A=Supercritical fluid extractor, C=Gas liquid separator, E=Receiver, G=Carbon-dioxide bomb, I=High pressure pump, B=D=H=J=Heat exchanger, and arrows show the flow of supercritical fluid/liquid/gas.

TABLE 3: COMPARISION OF PHYSICAL PROPERTIES OF CARBON-DIOXIDE IN GAS SUPERCRITICAL FLUID AND LIQUID.

Property	Gas P=0.1M Ps T=15-30^0	Supercritical Fluid		Liquid P=0.1 M Ps T=15-30^0
		Tc, Pc	Tc, 4Pc	
Density (g/cm^2)	0.0006-0.002	0.2-0.5	0.4-0.9	0.6-1.6
Viscosity(μ Pa-S)	10-30	10-30	30-90	200-3000
Diffusion coefficient (cm^2/sec)	0.1-0.4	0.0007	0.0002	(0.2-2)x10^{-5}

P = pressure, Ps = Pascal, T =temperature, Tc = critical temperature, Pc = critical pressure

per/&last=29 &lide=28, accessed on Oct 11, 2004).

The addition of the modifier fluid improves the solvating ability of the supercritical fluid and sometimes enhances selectivity of separation. It can also help to improve separation efficiency by blocking some of the stationary phase. Modifier fluids are commonly used, especially in packed column supercritical fluid chromatography. The environment benefits of supercritical carbon dioxide are well known. It has potential as a replacement for many undesirable organic solvent, which present a threat to the environment, health and safety in the work place, although most of the ozone destroying chemicals are now banned, other organic solvents contribute to photochemical smog, water pollution, and health problems for workers. Supercritical carbon dioxide is non-toxic, non-flammable and greenhouse neutral[23-25]

Extraction process:

Supercritical fluid extraction is two step process which uses a dense gas e.g. carbon-dioxide, as a solvent for extraction, above its critical temperature (31^0) and critical pressure (74 bar)[20,22,24] The feed, generally ground solid, is charged into the extraction vessel. Carbon dioxide is fed to the extraction vessel through a high-pressure pump (100 to 500 bars). The extract rich carbon dioxide is then sent to a separation vessel, which maintained at reduced pressure and temperature conditions, and the extract precipitates out in the separation vessel. The extract free carbon-dioxide stream, leaving the separation vessel is then recycled back to the extraction vessel till the end of the batch (figs. 5 and 6)[6]

Extraction process may be static (sample and fluid sealed in an extraction vessel), dynamic (fluid flows through the vessel), off-line (analytes are collected for later analysis) or on-line (analytes are directly transferred to a coupled instrument, such as a gas chromatography) modes. Static extraction is preferred in situations dealing with low concentration of active constituents strongly bound to matrix. The efficiency SFE depend upon the modifier (type and amount) and extraction parameters (time, temperature and pressure)[26].

Advantages:

SFE is environment-friendly process as its working is in a closed loop and it is not a new generator of carbon dioxide that is a growing concern in global warming (Green House Effect). Extracts are delicaceous and fresh close to natural i.e. superior in quality with higher yield and no residual solvent as solvent is gas (CO$_2$). SFE generally uses carbon dioxide as solvent, which is regarded as safe for extraction of natural products, thus avoid the use of organic solvents (used in conventional processes), which are suspected to be carcinogens. Extracts are free of biological contamination as well as heavy metals and longer shelf life

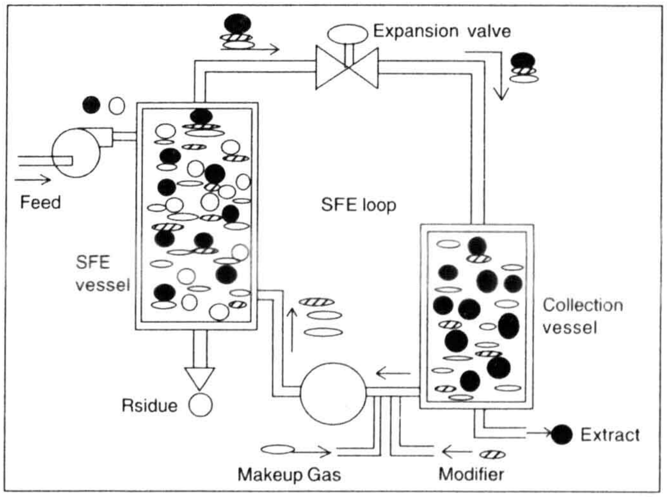

Fig. 6: Molecular basis of supercritical fluid extraction. (→) Arrows show the flow of supercritical fluid/liquid/gas.

TABLE 4: APPLICATIONS OF SUPERCRITICAL FLUID EXTRACTION.

APPLICATIONS	REF.
EXTRACTION:	
Oil and fats:	
Cocoa Butter from *Brazilian cocoa*	30
Fatty acid and sterols from plant tissues and sediments.	31
Nanacosan-10-ol, α-amyrin acetate from aerial part of *Ephedra sinica*	32
Squalene and stigmasterol from root bark of *Morus alba.*	32
Volatile oils (flavors and fragrance)	
Z-sabinene hydrate –rich essential oil from *Romanian mentha* hybrids.	33
Volatile oil from *Eucalyptus camaldulensis var. brevirostris* leaves	08
Essential oil (frenchone and camphor) from lavender flowers.	34
Volatile flavor from roasted peanut.	35
Marjoram essential oil from *Marjoram* leaves.	36
Carvone and limonene from caraway seeds (*Carum carvi* L.).	37
Natural colours	38
Herbal Medicines:	
Artemisinin, artemisinic acid from *Artemisia annua* L	39,40
Ginkgolide A, B, C, J and bilobalide from ginkolide standard extracts	41
Podophyllotoxin from *Dysosma pleiantha* roots	24
Steviol glycosides from *Stevia rebaudiana.*	42
Taxicin from *Taxus baccata*	43
Schisanadrol (A and B), and schisadrin (A, B and C) from *S. Chinesis* fruits	44
Hyoscyamine and scopolamine salts from *Scopolia japonica*	45
Flavanones and xanthones from roots of *Maclura pomifera.*	46
Pyrrolizidine alkaloid's from *Sensecio* species	47
Pharmaceutical agents:	
Cocaine and its metabolites from blood and urine	08
Vitamin E (tocopherols) from deodorized distillate (biomass)	48
SEPARATION AND REFINING:	
Fractionation of wax	49
Fractionation of butter oil.	23
Fractionation of essential oils.	50
Refining of petroleum and lipids.	03
Refining of physiologically active compounds and pigments	51
Separation of enatiomers:	
Optical resolution of 6- fluoro-2- methyl – 1,2,3,4 –tetrahydroquindine	52
Resolution of tetramisole	53
Resolution of cis –chrysanthemic acid by S–(+) benzylamino -1- butanol.	54

Removal of pesticides and herbicides:	
Organochlorine pesticides from vegetable sample.	55
2,4-Dichlorophenol from spiked control crop tissues	56
Organochlorine pesticides from Chinases herb medicine and dairy	57
Food technology:	
Cholesterol free food products	23
Degreasing of dairy products and food products	58
Deoiling of wheat glutin	59
Decaffeination of coeffee and tea	20
Deodorization of food products	23
Nicotine/ tar free tobacco	55
CLEANING AND DISINFECTION:	
Medical equipment and material	60,61
Removal of impurities from CDs and equipments	62
SYNTHESIS AND PROCESSING:	
Particle design	
Ultra-fine particles production	63
Whisker –shaped fine particles	64
Supercritical water oxidation and synthesis	65
Polymer processing; Hydrolysis of PET (polyethylene terephalate) pellets using supercritical water.	65
OPTIMIZING DRUG PARTICLES:	
Improved dissolution for insoluble compounds	63
Controlled release drug formulations	66
Crystallization of pure polymorphic forms of drugs	66
Generation of micro and sub-micro particles of amoxicillin	67
MISCELLANEOUS:	
Analysis of food products	07
Dyeing in textile industry	68
Cell breaking in biotechnology	03
Catalysis and chemical reaction	65
Environmental applications	69
Soil remediation	65
Oxidation of municipal waste	70
Microbial inactivation.	

with high potency of active components[18-20,24]

Solvating ability and selectivity are enhanced by addition of modifier and changing the operating conditions (time, temperature and pressure) i.e. it provide variety of flexibility to select the active component. Operating conditions (for carbon dioxide) are suitable for thermo-labile components and eliminate the unwanted side reactions. No need of extra unit operation to fractionate the component as it have precipitation cyclone separator[22,25]

SFE also can be integrated with various techniques viz. chromatography, mass spectrometry, Fourier transform IR, reactive reaction, textile processing, impregnation of product in solid matrix which provide faster processing time, increased productivity for analysis as well as other applications[26,28,29].

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