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Supercritical fluid extraction: A new technology to herbals

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Abstract
In Pharmacognosy, extraction of phytochemicals is one of the most fundamental process, which have Witnessed Sea of changes over the period. From centuries, we are striving to develop more effective ways to extract valuable constituents. Starting with galanicals, different solvents, steam, microwave, heat, different methods and equipments all were tried at the best to extract as much as possible. The latest among these is Supercritical Fluid Extraction (SFE). In this advent, carbon dioxide (CO_2) is mainly used as mobile phase for separation of compounds. This technique is modern, fast and scalable, which can be used to extract, isolate and separate. SFE enjoys some advantages like ultra-pure quality, higher extraction yield and low solvent residue. SFE has been applied to wide variety of materials including natural products, drugs, foods, pesticides, herbicides, surfactants, polymers and polymer additives, fossils fuels, petroleum, explosives and propellants. In coming years, supercritical fluid extraction can give more impetus of crescendo and roll wheel of Pharmacognosy research at great velocity.

Keywords: Constituents, extraction, herbals, medicinal plant, supercritical, technology

1. Introduction
The plants are the most abundant natural entity on which folklore relies heavily for their pharmacological activity. Natural products are used as a source of cosmetics, food and traditional medicine. Various chemical extracted from plants parts are used to prevent or fight various disease such as cancer, neorological disorder, cardivascular disorder, antifungal or antibacterial and diabetes. Plants are rich source of secondary products like alkaloids, tannins, glycosides [1]. Extraction of these secondary metabolites is a very essential process in drug discovery and development of new medicine from plants. The process of extraction which involves separation of active element from crude drug by using suitable solvent is under metamorphosis. From last two decades, testified extraction of natural product is becoming more demanding. In Pharmacognosy, one cannot undermine importance of extraction technology. The journey of extraction, started with galanicals over the years is poised at ultramodern, use of supercritical fluids [2]. Journey towards better quality of herbal drugs is unrelenting as we are expecting better quality medicines. Thus extraction continues to be of substantial interest so as to get improved yields with low solvent residue extraction initially was manual affair with solvent as decoction, maceration, percolation, soxhlet and thereafter witnessed many more advances with respect to technique and technology. Such extraction methods are often simple and practical, as well as they have their drawbacks such as being tedious to operate, employing hazardous processing solvents requiring additional steps to remove, and many employing heat thereby resulting in the degradation of heat-labile molecules [3]. Many of these extraction methods are not completely effective but are expensive due to the need to dispose of large amounts of organic waste, which in itself can risk environmental [4].

Introduction of supercritical fluid extraction (SFE) has become milestone in this epic journey. During the past twenty years SFE evolves from a laboratory scale to industrial scale. The emergence of green chemistry for extraction purposes occurred with the aim of reducing energy consumption and replacing the conventional solvents with less environmentally harmful alternatives. Some of the green technologies used for herbal extraction are ultrasound-assisted extraction, microwave-assisted extraction, supercritical fluid extraction, mechanical pressing, and détente instantanée contrôlée (DIC). The SFE is the method of separating or extracting the chemical compounds from the matrix using carbon dioxide at critical temperature and pressure as the extracting solvent [5].The phase separation can facilitate the collection of pure CO_2 solvent (gas), such that it can be recirculated into storage, ready for re-use, thus reducing total energy costs (less CO_2 collection required) thereby reducing energy consumption and increasing the overall sustainability. SFE offer reduces processing energy and an alternative solvent approach. Till date, SFE is employed in coffee decaffeination, hops extraction, catalyst regeneration, extraction of organic wastes from water and soil. On this back ground, it would be interesting to look up and understand how this relatively new technique is becoming upcoming technology for herbal extraction.

2. Supercritical Fluid Technology

Supercritical fluid technology is in use from late 19th centrury for the extraction of different chemical constituents. It generally utilizes CO_2 as the mobile phase, the whole chromatographic flow path is pressurised. A fluid is said to be supercritical, when its pressure and temperature exceed their respective critical value (Tc- critical temperature and Pc- critical pressure). In the phase diagram, the critical point located at the right upper end and the phase area beyond of this point is the supercritical region. Above the Tc, it is not possible to liqueify a gas by increasing the pressure. In other words, a supercritical fluid technology can behave as either a liquid or a gas, but is actually neither. The characteristic properties of a supercritical fluid are density, diffusivity and viscosity [6]. The curve defines the regions corresponding to the gas, liquid and solid state. The critical point marks the end of the vapor liquid coexistence curve. Above the critical temperature there is no phase transition in that the fluid cannot undergo a transition to liquid phase, regardless of the applied pressure. 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 [6].

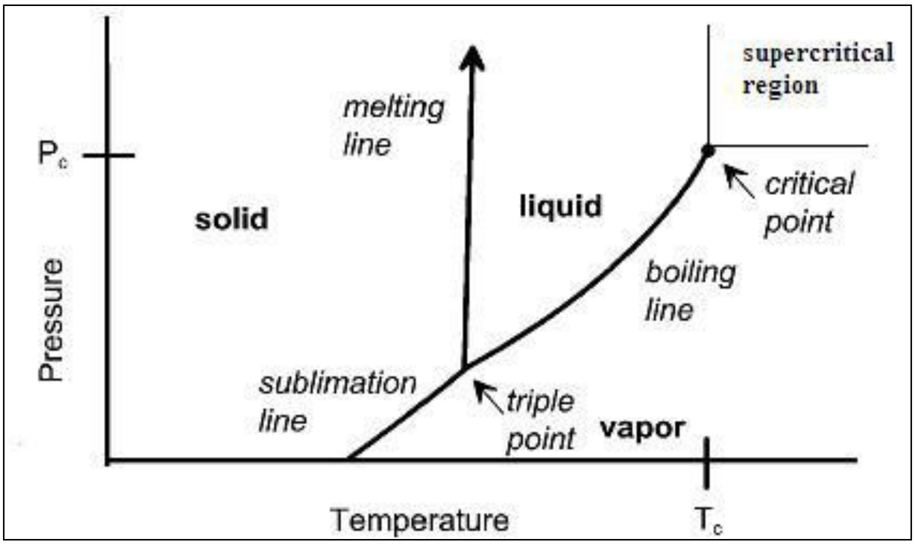

Fig 1: Phase Diagram

Table 1: List of compounds along with their critical temperature and pressure to be used as supercritical fluids

S. No	Compound	Critical temperature (°C)	Critical pressure (bar)
1	Carbon dioxide	31.3	72.9
2	Ammonia	132.4	112.5
3	Water	374.15	218.3
4	Nitrous oxide	36.5	71.7
5	Xenon	16.6	57.6
6	Krypton	-63.8	54.3
7	Methane	-82.1	45.8
8	Ethane	32.28	48.1
9	Ethylene	9.21	49.7
10	Propane	96.67	41.9
11	Pentane	196.6	33.3
12	Methanol	240.5	78.9

3. Herbal Plants Extraction

Extraction by supercritical fluid involves the dissolution of the desired component from sample of plant under the controlled condition of temperature and pressure followed by the separation of desired component from the supercritical fluid by a significant drop in solution pressure. Conventional extraction processes require large amount of hazardous solvent (hexane, chloroform, and methanol) and are generally cumbersome. Soxhlet extraction technique was developed in the intention to make extraction process continuous and was used for extraction of volatile oil and lipids. This process is associated with disadvantages such as requirement of highly pure solvents, use of hazardous and flammable liquid organic solvent, potential toxic emission during extraction, and finally, it is a time consuming process. Supercritical fluid extraction is routinely used for the extraction of lipids, essential oils, alkaloid and glycoside from plant or animal material because of its environmentally friendly nature. Supercritical fluid extraction is the simplest and economical way to extract valuable constituent botanicals. CO_2 is the most generally used supercritical fluid in food and pharmaceutical business as a result of obtained extract contains no organic residues [7]. Moreover, CO_2 is non-toxic, non-flammable, stable, cheap and includes a low critical point of temperature and pressure [8]. In principle, the low critical temperature of carbon dioxide could also be useful for thermally labile substances [9]. In recent years SFE has received enhanced attention as a vital alternative to traditional separation methods. Indeed, it's been demonstrated that SFE will turn out superior quality product characterised by the absence of artefact and by a more robust copy of the original flavour or fragrance. Supercritical fluids have adjustable extraction characteristics, because of their density, which may be controlled by ever-changing the pressure or temperature [10. 11]. Cocoa butter is exclusive among vegetable fats because of its composition and crystallization behavior. Cocoa bean contains substantial amounts (55%) of cocoa butter. There is a high demand for quality cocoa butter, particularly in foods, nutraceuticals, cosmetics and prescribed drugs. Compared with the traditional technique, SFE is the possible technique to supply higher yield and higher quality cocoa butter. Essential oils were traditionally extracted from seeds, roots, flowers, and leaves using hydrodistillation. Thermal degradation, hydrolysis and solubility of some compounds in water may alter the flavour and sometimes fragrance of essential oils. SFE technique is used to avoid these problems. The optimum operating conditions for extraction of essential oils by SFE method are: pressure in the range of 90-100 bar and temperature ranges from 40-50 ºC, since at these conditions all the essential oil compounds are highly soluble in supercritical fluid-CO_2. For instance, linalool, a terpene is completely miscible with supercritical CO_2 at temperature of 40 ºC and pressure more than about 85 bars. Seed oils were generally extracted using hexane. The major problem associated with this method was difficulty in hexane removal after extraction and thermal degradation during the extraction, which necessitates the use of SFE technique. There are hundreds of herbs which are still not extracted using this novel technique for high quality and enriched chemical constituents [12].

3.1 The major advantages of SFE over conventional solvent extraction process are [12]:

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 CO_2, allows the obtaining of extracts which flavour and taste are perfectly respected and reproducible.
7. Most of the volatile components, which tend to be lost in hydrodistillation, are present in the supercritical extracts and partly because of this extracts obtained in this way tend to have flavour and taste, which are well liked by tasty panels [6].

There have been a few technical issues that have limited adoption of SFE technology. First of which is the high pressure operating conditions. High-pressure vessels are expensive and bulky, and special materials are often needed to avoid dissolving gaskets and O-rings in the supercritical fluid. A second drawback is difficulty in maintaining pressure (backpressure regulation). Whereas liquids are nearly incompressible, so their densities are constant regardless of pressure, supercritical fluids are highly compressible and their physical properties change with pressure - such as the pressure drop across a packed-bed column. Currently, automated backpressure regulators can maintain a constant pressure in the column even if flow rate varies, mitigating this problem. A third drawback is difficulty in gas/liquid separation during collection of product. Upon depressurization, the CO2 rapidly turns into gas and aerosolizes any dissolved analyte in the process. Cyclone separators have lessened difficulties in gas/liquid separations. Carbon dioxide itself is non-polar, and has somewhat limited dissolving power, so cannot always be used as a solvent on its own, particularly for polar solutes. The use of modifiers increases the range of materials which can be extracted. Food grade modifiers such as ethanol can often be used [13].

Table 2: Application of superscritical fluid extraction technology in natural products

S. no.	Plant name	Bioactive Compounds	Temperature _(ºC)	Pressure (Mpa)	Time (min)	Reference
1	*Carica papaya* (Seeds)	Carpaine, pseudocarpaine, papain, chymopapain, benzyl isothiocyanate	40	100	20	[14]
2	*Artemisia sphaerocephala* (Seeds)	Polysaccharides, Sugars	45	45	120	[15]
3	*Schisandra chinensis* (Stems)	Deoxyschizandrin, γ-schizandrin, gomisin N, schizandrin, anwuweizic acid, (-)-dihydroguaiaretic acid, tetradecanoic acid	45	30	180	[16]
4	*Kniphofia uvaria* (Flowers and seeds)	Triglycerol, diacylglycerol, Fatty acids	60	29	-	[17]
5	*Mexican arnica* (Flowers)	Cadalene, polyphenols, sesquiterpenes, terpenes	60	10	80	[18]
6	*Mitragyna speciosa* (Leaves)	Ajmalicine, corynantheidine, isomitraphylline, mitraphylline, paynantheine, Palmitic acid	60	20	60	[19]
7	*Ammi visnaga* (Fruits)	Xanthotoxin, ammoidin, imperatorin, bergapten, marmesin,γ pyrones	45	200	90	[201
8	*Hybrid hibiscus* (Flower)	Alkaloids, L-ascorbic acid, anthocyanin, Beta-carotene, Beta-sitosterol, citric acid, arabins, arabinogalactans, quercetin, gossypetin	80	53.7	50	[21]
9	*Wedelia calendulacea* (Whole plant)	Wedelolactone, coumestans, flavonoids, steroids, triterpenoids	40	25	90	[22]
10	*Abelmoschus manihot* (Flowers)	Myricetin, cannabiscitrin, glycerolmonopalmitate, guanosine, adenosine, heptatriacontanoic acid, 1-triacontanol	40	10	30	[23-24]
11	*Vaccinium myrtillus* (Seeds)	Quercetin, catechins, tannins, ellagitannins, phenolic acids	60	45	45	[25]
12	*Wheat germ oil*	Hexanal, 2-methyl-2-butene, 2,4- heptadienal, limonene, linoleic acid	40	20	-	[26]
13	*Laurus nobilis* (Leaves)	1,8-Cineole, α-terpinyl acetate	40	25	-	[10]
14	*Benincasa hispida* (Fruits)	Volatile oils, flavonoids, glycosides, sacchrides, carotenes, vitamins, minerals, ß-sitosterin, uronic acid	60	25	180	[27]
15	*Capcicum frutescens* (Seeds)	Capsaicin, dihydrocapsaicin, nonivamide	40	25	320	[28]

16	*Cannabis sativa* (Seeds)	Cannabidiol, cannabichromene, cannabigerol, tocopherol	40	30		[29]
17	*Camelina sativa* (Seeds)	α-linoleic, oleic, eicosaenoic and erusic acid	70	45	510	[30]
18	*Chenopodium quinoa* (Leaves)	Carbohydrate, proteins, tocopherol	130	18.5	55–180	[31]
19	*Coffea arabica* (Seeds)	Caffeine, cafestol, chlorogenic acid, linoleic, oleic, strearic, arachidic acid	35.9	33.1		[32]
20	Cacao pod husk	Catechin, epicatechin, anthrocyanins, tannins	60	299	150	[33]
21	*Eucalyptus globulus* (Leaves)	1-8-Cineole, α-pinene, p-cymene, cryptone, aromadendrene, spathulenol	80	35	60-120	[34]
22	*Euterpe oleracea* (Roots and leaves)	Linolenic, linoleic, palmitic acids, caffeoylquinic acids, apigenin, luteolin. caffeoylshikimic acids	-	49	180	[35]
23	*Gynostemma pentaphyllum* (Leaves)	Gypenosides IV, VIII, XLVIII, XLIX, LXIX, LXXI, gylongiposidee I, allaotion, vitexin	43	32	160	[36]
24	*Juniperus communis* (Berries)	α-Pinene, β-myrcene, sabinene, D-limonene	55	30	60	[37]
25	*Moringa oleifera* (Seeds)	Carotenoids, nonacosane, heptacosane, Vitamin C, β-amyrin	60	50	120	[38]
25	*Ocimum basilicum* (Leaves)	Eugenol, linalool, α-begamotene, germacrene D, γ-cadinene, δ-cardinene, β-selinene	60	15	240	[39-40]
26	*Paullinia cupana* (Seeds)	Caffeine, cathechins, theophylline, theobromine, tannins	40	10	40	[41]
27	*Phyllanthus amarus* (Whole plant)	Phyllanthin, Hypophullantin, gallic acid, Ellagic acid	40	23.2	90	[42]
28	*Piper nigrum* (Fruits)	Piperine, β-caryophyllene, limonene, cabinene, 3-carene, α-pinene	50	30	80	[43]
29	*Rhodiola rosea* (Roots)	Lotaustralin, Rosavin, phenylethanoids, rosin, phenylpropanoids, glycosides, salidroside, p-tyrosol, rhodiolin, terpenes	62	31.7	90	[43]
30	*Zingiber officinale* (Rhizomes)	α-Zingiberene, β-sesquiphellandrene, α-farnesene, geranial, β-bisabolene, β-eudesmol	50	25	180	[45]
31	*Cynanchum paniculatum* (Whole plant)	Mudanoside, paeonolide, Santamarin, paeonol, annobraine, laricircsinol, α-asarone, 7-angelyheliotridine	55	150	20	[46]
32	*Ramulus cinnamoni* (Barks)	Cinnamic acid, taxifolin, protocatechuic acid, trans-o-methoxy cinnamic acid, 4-hydroxybenzoic acid, coumarin	40–50	230–410	120	[47]
33	*Cassia tora* (Seeds)	Chrysophanol, emodin, obtusifolin, obtusin, chryso-obtusin, auranto-obtusin	45	250	180	[48]
34	*Cucscuta reflexa* (Seed)	Coumarin, bergenin, kaempferol-3-O-glucoside, astragallin, myrecetin, benzopyrones	55	248	120	[49]
35	*Elettaria cardamomum* (Seed)	1,8-cineole, linalyl acetate, limonene, linalool, limonene, 1,8-cineole, terpinolene, myrcene	35	300	60	[50]
36	*Nigella sativa* (Seeds)	Essential oil, linoleic acid, oleic acid, palmitic acid, *t*erpinolene, myrcene	40	400	35	[51]
37	*Rhodiola rosea* (Roots)	Rosavin, rosin, salidroside, p-tyrosol, rhodiolin, terpenes	80	200	180	[52]
38	*Valeriana officinalis* (Roots)	Valerenic acid, acetoxyvalerenic acid hesperidin, linarin	37	360	60	[53]
39	*Anoectochilus roxburghii* (Whole plant)	Phytosterol, alkaloid	45	250	20	[54]
40	*Stevia rebaudiana* (Leaves)	Sesquiterpenes glycosides	50	150		[55]
41	*Baccharis dracunculifolia* (Leaves)	Artepillin, nerolidol, limonene, phenolics	60	400	20	[56]
42	*Borago officinalis* (Seeds)	Linoleic acid, oleic acid, palmitic acid, stearic acid, eicosenoic, erucic acid	50	200	150	[57]
43	*Matricaria chamomilla* (Flower)	Farnesene, chamazulene, apigenin, quercetin, patuletin, luteolin	40	250	90	[58]
44	*Vitex agnus-castus* (Fruits)	Diterpenes, triterpenes, casticin, luteolin	45	450	240	[59]
45	*Nelumbo nucifera* (Flowers)	Isoliensinine, liensinine, lotusine, methylocrypalline, neferine, nuciferine, galuteolin	50	320	120	[60]
46	*Eugenia uniflora* (Fruits)	γ-Bisabolene, β-bisabolene, γ-bisabolene, (*Z*)-α-bergamotene, carotenoids	60	250	120	[61]
47	*Garcinia mangostana* (Fruits)	p-Hydroxybenzoic acid, mangosteen, xanthones	40	200	100	[62]
48	*Curcuma longa* (Rhizomes)	Curcumin, ar-turmerone, β-sesquiphellandrene, curcumenol	35	220	180	[63]
49	*Satureja montana* (Leaves)	Thymol, p-cymene, linalool, carvacrol	30	120	120	[64]
50	*Peumus boldus* (Leaves)	1,8-cineole, trans-sabinene, pinocarveol, pinocarvone, 4-terpineol, ascaridole, piperitone oxide, limonene dioxide, n-eicosane	35	100	120	[65]

4. Applications of Supercritical Fluid Extraction

1. Food processing: Supercritical carbon dioxide has attractive properties (it is nontoxic, inexpensive, odourless, colorless, non-flammable and has near ambient critical temperature, low viscosity and high diffusivity compared to liquids) that it has become the preferred solvent in the processing of essential oils and oils in food industry. Further, the extracts color, composition, odor, texture are controllable and extraction by carbon dioxide retains the aroma of the product. Supercritical fluid extraction is used as a replacement for hexane in extracting soybean-oil and has been tested for extraction from corn, sunflower and peanuts. Supercritical fluid extraction provides a distinct advantage not only in the replacement but also extracts oils that are lower in iron and free fatty acid. Another application is removal of fat from food [66]. The process has been fully designed for commercial application, using the aforementioned standard design. The removal of fat process has the advantage of producing fat-free or fat reduced potato chips. According to the expected taste the amount of remaining fat in the potato chips can easily be controlled by SFE. A large amount of research has been concentrated on the decaffeination of coffee by supercritical carbon dioxide. Thus, it is not surprising to note that this was the first process to be commercialized [67].

2. Enrichment of vitamin from natural sources: Fat-soluble vitamins are organic molecules that are nutritionally essential to the human body. Lack of vitamins can lead to serious diseases such as night blindness (vitamin A), rickets and weakening of bones (vitamin D), rupturing of blood cells and cancer (vitamin E) and blood coagulation diseases (vitamin K) [68]. However, over consumption of vitamins can also be dangerous. These factors have resulted in strict regulations for vitamin use in food nutrition, requiring the need for continuous analysis of food products and pharmaceutical preparations [24]. New methods are constantly being developed regarding the extraction and enrichment of fat-soluble vitamins from natural sources such as plants, oilseeds and vegetables. For example, carotenoids (vitamin A) are used as antioxidants and natural pigments, to enhance the value of the food products and to provide color ranging from yellow and orange to red [69]. Moreover, vitamins A and E are thought to prevent skin damage, and are commonly found as additives in cosmetic creams and ointments [6]. The use of supercritical fluids in fat-soluble vitamin analysis provides an interesting alternative to the use of organic solvents. The main advantages of using supercritical fluids instead of conventional organic solvents are the minimal consumption of organic solvents, the exclusion of oxygen, and the reduction of heat. Modern supercritical fluid extraction offers shorter extraction times, potentially higher selectivity and increased sample throughput (due to available automated instruments) compared to conventional solvent extraction technology [7].

3. Removal of alcohol from wine and beer: Wine is one of the most complex alcoholic beverages; more than 800 volatile organic compounds (acids, esters, alcohols, aldehydes, lactones, terpenes, etc.) present in very low amounts were identified, which all together are responsible of each particular bouquet. Therefore, the production of an alcohol-free wine by removing ethanol while preserving the organoleptic properties of wine is a very complex and challenging problem. De-alcoholized wine or beer is achieved by removing ethanol from water [70]. Distillation is well known for this purpose with the disadvantage that aroma compounds will also be removed. SFE with CO_2 has appears as a promising alternative to other conventional de-alcoholized of beverages techniques [12].

4. Supercritical Fluid Chromatography and its analytical uses: Supercritical Fluid chromatography (SFC) is an environmental-friendly alternative for analytical use and in purification of hebal constituents. In SFC, greenhouse gas is employed as the mobile phase underneath precise conditions of pressure and temperature [71]. The ability to vary selectivity by programming the parameters pressure and temperature rather than by modifying the chemical composition of the eluent represents the technique’s major difference [72]. The low viscosity of the mobile phase permits an arrangement of several HPLC-type columns in series [4]. It's well known that SFC has become one amongst the favourite techniques for the gathering of focused fractions of pollutants like polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyls (PCBs), pesticides, dioxins or open-chain hydrocarbons from environmental samples, from biological samples like blood or urine so as to gather drug residues, from food samples like seeds, plants or crops to concentrate fats and oils, fragrance and flavours [73]. In recent years, there has been increasing interest within the development of supercritical fluid chromatographic technology and its application [SFC has been applied to a variety of applications for the detection and quantification of various analytes [74].

5. Conclusions

Over the last 20 years, the use of supercritical fluid extraction research has increased in the field of natural products. SFE-based methods have a promising future in analytical chemistry. Also they can be employed to considerable advantage as an aid in optimizing and testing the feasibility for non-analytical applications, i.e., to investigate the potential for scaling up SFE for industrial application. Using automated analytical SFE instrumentation for such purposes allows the rapid assessment as to whether a SFE will work at minimal expense and time. SFE methods have been used to harvest a large range of extracts, oils, oleoresin, groups of bioactive compounds (alkaloids, terpenes, and phenolic) as well as single compounds. The applications of SFE and SFC in qualitative analysis cover a broad spectrum of samples, together with food stuffs, natural products, agrochemicals, environmental samples, fuels and lubricants, artificial polymers and oligomers, organometallic compounds, achiral pharmaceutical agents and biologically necessary chiral compounds. SCF offers a more selective and environmentally sustainable alternative to traditional methods in natural products qualification and quantification. Collectively, SCF-based extraction methods are a technology with large potential and thus merit further investigation.

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