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An Overview on Supercritical Fluid Extraction of Herbal Medicines: Process and Methodology

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Abstract

The chemistry of natural products has gained improvement in the last years due to rapid progress of new chromatographic and spectroscopic methods. Supercritical fluid extraction (SFE) is considered as a promising alternate technology to traditional extraction methods since it has majority of distinct characteristics. Recently, SFE of bioactive components from plants has been gained wide applications in different medicinal, industrial and pharmaceutical fields. This article try to cover the fundamental concepts related to SFE like definition, properties, chosen of supercritical fluids (SCF) for extraction, the process, advantages and disadvantages of SFE, employment of SFE in the extraction of herbal medicines and finally the novel applications of SFE in Chemistry and industry.

***Keywords**: Supercritical Fluid Extraction (SFE), Supercritical Fluid (SCF), Modifier, Process, Applications.*

1. Introduction

The Herbs medicine is one of the important science in which the plants are used for solving the health care problems. It is also called phyto-medicine or botanical medicine. People are using the allopathic drugs due to their fast therapeutic actions as compared to herbal drugs [1] but now- a- days there is a great interest in the herbs medicine, which can be called "Return to Nature". Since old ancients, plants have been considered as a source of medicinal agents which called nutraceuticals due to their considerable effects on the human health. In addition, many of the new drugs have been derived from natural sources [2]. This became possible in the 19th century when man started to isolate the active components of medicinal plants prior to the second world war. Number of natural products isolated from plants used as clinical agents and they are still in use [3]. Furthermore, these compounds have been gained recently a wide interest to prove their possible use as ingredient for the industrial preparation of functional foods or cosmeceuticals. Plants are also good source of many different constituents such as phenolic compounds, vitamins, terpenoids and some of secondary metabolites, which are found to have valuable bioactivities such as anti-inflammatory , anti-bacterial, anti-oxidant or anti-carcinogenic. The drugs which were taken from the plant considered as "green medicine " due to their safety, more dependable and less side effects comparing with the costly synthetic drugs[4]. Extraction is the process of separation the effective constituents medically of herbs or plants from the inert or the components which are not active, by employing suitable solvents and conducting standard steps [5]. The improvement of new technologies has resulted in more development in health through the production of new and more functional medicine. It has shared in the progression of the science and the evolution of complicated and precise apparatus and methods to discover new effective constituents and methods [6]. The number of the active components recovered from plant samples affected by the type of plant and the applied extraction technique [7]. Traditional laboratory extraction methods such as decoction, sonication, digestion, percolation, infusion, maceration and Soxhlet extraction have different shortcomings like consuming long time, losing volatile compounds, degrading thermolabile compenents, low yield and low extraction efficiency [50,51]. On the other hand these methods require high amounts of organic solvents which may affect health negatively if these toxic solvents are not eliminated completely from the extract [52]. Recently, Supercritical fluid extraction is considered as the most advanced and green technology which employ to extract bioactive constituents. This novel technique provides a lot of unusual properties compared with the traditional solvents extraction techniques. Supercritical fluids have the ability to penetrate into the pores of solid materials with more efficiency than liquid solvents so the rate of mass transfer increases considerably and consequently the extraction can be performed rapidly [8]. SFE has been used perfectly to extract different bioactive constituents from herbs and other plants [9]. The combined liquid-like solvating power and gas-like transport properties of supercritical fluids make it particularly suitable for the extraction of diffusion-controlled properties like the tissues of the plants and therefore it has achieved more attention in foods, pharmaceuticals and cosmetic industries [10].

2. Supercritical Fluid Extraction

2.1 Supercritical fluids Definition and properties

The Supercritical fluid state is defined as the state of a compound, element or mixture above its critical pressure (PC) and critical temperature (TC) but less than the pressure which needed to condense it into a solid [11]. However, the last sentence of the definition ("but less than the pressure which needed to condense it to a solid") was mostly deleted since the pressure needed to condense a SCF into a solid is very high [12]. Each gas possess a temperature above which cannot be liquefied without taking into account the applied pressure. This temperature is known as the critical temperature whereas the pressure needed to convert the gas to liquid is known as the critical pressure. The critical point indicated the highest temperature and the highest pressure where the substance can find as a vapor and liquid phases in equilibrium and they are indistinguishable. The pressure-temperature diagram (phase-diagram) is generally used to explain the compound phases and the conditions in which every phase exists. Components near to or above their critical point, which follow the boundary between the liquid and the gas phases up to reaching an intermediate state will exhibit the properties and characteristics of both states (liquids and gaseous). The phase diagram curves show coexistence between two of the phases. Both temperature and pressure increase while moving upward along the gas-liquid co-existence curve which is a plot of vapor pressure vs. temperature. Due to thermal expansion the liquid becomes less dense and the gases become denser, as result of increasing the Pressure. At the Critical point the densities become identical. The Curve comes to the end at the critical point where the distinction between the gas and liquid disappear, and a supercritical fluid is created. The boundary of gas liquid does not find when both pressure and temperature become higher than their critical values. The phase diagram for a pure compound explains that the compound trans-fer directly from a liquid phase to a gas phase with no phase sepa-ration easily by crossing through the supercritical region of the phase diagram. The carbon dioxide phase-diagram is shown in figure (1). As appear a substance becomes a supercritical fluid (SCF) when compressed to pressure and elevated to a tempera-ture higher than of its critical point. The fluid shows properties of both a liquid and a gas.

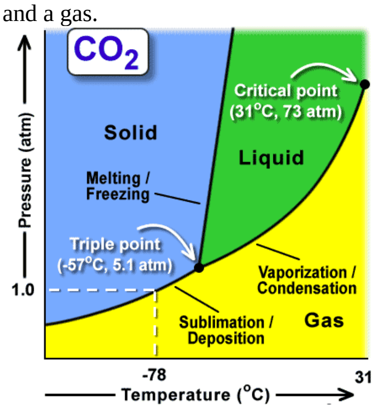

Figure 1 Phase diagram of carbon dioxide.

2.2 Extraction using CO_2

Selection of a SCF in order to extract the natural constituents is very necessary for yield of the product and its selectivity, availa-bility, polarity, safety and the critical temperature and pressure are always taking into account. Table (1) showed the critical properties of some common solvents.

Table 1 Critical properties of various solvents

Solvent	T_c (°C)	P_c (bar)
Ethylene	10	50
Carbon dioxide	31	74
Ethane	32	49
Propane	97	43
Ammonia	132	114
Methanol	240	81
Ethanol	241	61
Toluene	319	41
Water	374	221

Among the various solvents suggested, carbon dioxide (CO_2) is chosen to be the most desired and favorable solvent for SFE for natural compounds for many reasons include its critical temperature which is only 31°C that makes it suitable for the extraction of heat sensitive components since the temperature of the process is so low and does not change the physico- chemical characteristics of the extract. It has no toxicity so it is accepted as GRAS (Generally Recognized A Safe) ingredient in food and pharmaceuticals, CO_2 is also inert in nature, therefore there is no risk of any side reactions will be expected, it exhibit a law polarity which is near to that of hexane and pentane solvents that used commonly in liquid extrac-tion. Therefore a similar range of components can be extracted; furthermore CO_2 has no flammability and no explosivity. It is also cheap, odorless, colorless, clean solvent which does not leave any residue in the extract [13]. In addition, CO_2 is considered as envi-ronmentally friendly or green solvent since it does not cause any pollution. It is reported also that CO_2 can enhance diffusivity or mass transfer, it is chemically stable and there is no difficulty in the separation of the extract. Supercritical carbon dioxide is a linear-non-polar molecule which allows poor solubility for polar or ionic constituents. Although CO_2 has a zero dipole moment, it has a large quadrupole moment and it is a charge separated molecule with partial charges on both the carbon (positive) and oxygen (negative). Therefore, CO_2 can behave as either an electron acceptor or an electron donar, that is analgous to behave as a Lewis acid or Lewis base [14]. Due to such properties, the solvent features of CO_2 differ greatly from other solvent of short alkyl chain hydrocarbons, which consist of same solubility parameters to CO_2 [15]. Furthermore, CO_2 is a compound available in nature, and it is found in mineral water and it also represents a part of the cycle of life. The variation of viscosity and diffusivity for CO_2, at selected pressures and temperatures are shown in figure (2a) and figure (2b)[16]. As CO_2 is more selective, by change the pressure and temperature, it is also simply removed by realizing the pressure thus, its use requires one recompression step and one purification step only instead of many separation steps, hence the energy require for the organic solvent in the conventional methods. Therefore, it is considered that the process is consuming less energy, furthermore, waste plant material can be recycled simply, which is difficult to be done to the plant material that soaked in organic solvent in case of traditional extrac-tion. Additionally, thermally labile constituents can be extracted with supercritical CO_2 as no high temperature separation steps are needed [17].

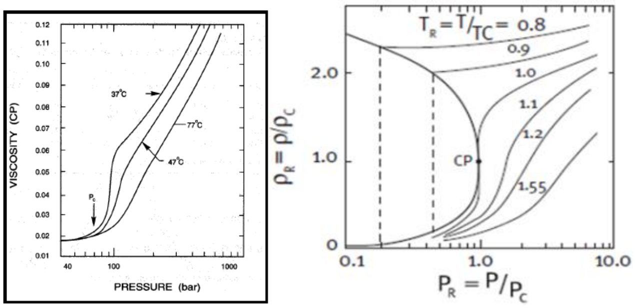

Figure 2 (a) Viscosity of Carbon Dioxide in the Supercritical State [16] (b) Densityvs. pressure diagram for carbon dioxide [16].

The use of supercritical carbon dioxide minimizes the energy required as compare with distillation since it has ability to vapor-ize non-volatile components at moderate temperatures and this explain the superiority of supercritical carbon dioxide to obtain a better yield and to maintain the native composition that available in the genuine plant [18]. Additionally the presence of pressure in the equipment does not allow for oxygen to enter during the ex-traction process, hence oxidation reaction does not occur. The benefits in using supercritical fluid are huge of a safety, health and environmental nature. The employment of supercritical CO_2 for the extraction of vegetable matrices has been reported as a green extraction solution aiming at the replacement of conven-tional organic solvents [19, 20]. Furthermore, the impossibility regarding the availability of organic solvent residues in the ex-tract for human consumption. However, it is reported in some application that the obtained extracts are more acceptable to taste panels comparing to the extracts got in another methods which may be due to the closeness to which the extracted flavor resem-bles that in the original plant. However, there are some ad-vantages for the uses of CO_2 as a green solvent. It is a poor sol-vent for compounds which possess high polarity[21, 22]. It is generally used in its supercritical state (above Tc = 31ºC and Pc = 7.38 MPa), that means CO_2 should be applied under pressure which may need to costly instrument [22, 23]. Supercritical fluids often by themselves are not convenient for the extraction of more polar components such as polyphenols. This problem can be solved by the use of an entertainer (also known as moderators, co-solvents or modifiers which lead to enhance the solubility of polar solutes in the supercritical fluids [24] by introducing strong or molecular interaction in the solvation shell of the solute [25]. However, using an organic modifier results an additional purifi-cation step in order to remove any remaining of the solvent (e.g methanol) especially if the wanted product is required for con-sumption purposes [26]. Thus it becomes clear that the extraction selectivity get improved by using the modifiers. Water and short chain alcohols such as methanol and ethanol are affected and often the popular co-solvents acceptable in the field of industrial. Adding a little amount of such polar modifiers to the bulk carbon dioxide can increase the solubility of polar and non-volatile solutes in supercritical carbon dioxide.

2.3 Modifiers

Modifiers which also named as co-solvents and entertainers are needed to enhance the solubility of substances in the supercritical fluid mixture. The use of modifiers result in increasing the cost of operating process, in addition to increasing the difficulties related with the collecting of components as well as reducing the selectivity of extraction. Some examples of modifiers like methanol, ethanol and acetone. Methanol is the major modifier applied for supercritical fluid extraction applying carbon dioxide. However, it is slightly appropriate for extracting natural products for medicinal uses due to its toxicity, but when improving a process for extracting the natural products methanol has a benefit for exploring system dynamic [27]. Additionally, modifier lead to reduce the crossover pressure for a system. The crossover pressure is known as the boundary between density effects and vapour pressure effects on solubility [15]. Rising the temperature at a constant pressure result in reduce the solvent density, which lead to reduce the solubility of solute. In other hand the volatility of the solute will increase resulting in rise the solubility of solute. At a pressure more than the crossover pressure, rising the temperature cause rising the solubility because of dominating the effects of volatility. However, at a pressure less than the crossover pressure, rising temperature result in reduces solubility, because of density effects dominating [16].

Methanol is one of the preferred modifier, since it is highly miscible with CO_2 , it's highly percentages give it ability to attack the bonding between solutes and plant matrices, reducing the mass transfer resistance for extractions. It was concluded that the co-solvent has been taken a significant role in the interaction with the solute / matrix to simplify solute desorption from the matrix and prohibit reabsorption by increasing the solutes solubility in the supercritical fluid [28]. Modifier can be introduced into a system by three familiar ways sequential addition, pre-mixed fluids and direct spiking on the surfaces of solid. It was reported that direct spiking on the surfaces of solid is the simplest, most reproducible, and most economical method, furthermore this method lead to static stage where the co-solvent is given time to modify the surface of the solid. This modification result in decreasing the time required for successful extraction to the given quantity of the plant sample. Sequential addition of $\mathbf{CO_2}$ and modifier is suitable when the system has limited solubility, whereas premixed fluids seem to be poor method, because of the change in modifier concentration over time, due to shifting the equilibrium of pre-mixed fluid in the cylinder or tank [29]. Entertainers raise the solubility of polar solutes in supercritical fluids by introducing stronger molecular interaction in the salvation shell of the solute. However, this mean further purification step may be needed to eliminate any residual solvent (e.g. methanol) if the final product is prepared for consuming [25].

2.4 Supercritical Fluid Extraction Process

The system consists of a pump for CO_2 , another pump if a modifier is used, a pressure cell to contain the sample, which help to maintain the pressure in the system and a vessel to collect the sample. The liquid is pumped to the area of heating in which it is converted to supercritical conditions, after that it passes into the vessel of extraction, and it quickly diffuses into the solid matrix and dissolves the plant sample to be extracted. The dissolved sample is pushed from the extraction cell into a separator at lower pressure, and the extracted sample set out. CO_2 then cooled, compressed again and recycled, or discharged to atmosphere [30].

Table 2 Supercritical Fluid Extraction Process (SFE)

S.No	Name	Description
1	Pumps	Carbon dioxide is generally pumped as a liquid below 5ºC (41ºF) and a pressure of nearly 50 bar. The solvent is pumped as a liquid because, if it was pumped as a supercritical fluid much of the pump stroke would be used up in compressing the fluid, instead of pumping it. For small scale extractions (up to a few grams / minute), reciprocating CO_2 pumps or syringe pumps are often used, whereas diaphragm pumps are most commonly used for large scale extractions. The pump heads will generally need cooling and the CO_2 will be cooled before introducing to the pump [30].
2	Pressure Vessels	They may range from simple tubing to more advanced purpose built vessels with fast release fittings. The pressure needed is about 74bar at least, and most extractions are performed at under 350 bar. But, sometimes higher pressures may be required, like in case of extraction of vegetable oils, in which 800 bar pressure are sometimes needed for perfect miscibility of the two phases [31]. The vessel has to be equipped with a means of heating. It can be keep inside an oven for small vessel, or an oil or electrically heated jacket for larger vessels. It is necessary to take care in case of using rubber seals on the vessel, since it is possible that CO_2 dissolve in such rubber leading to swelling, and the rubber will tear on depressurization [30].
3	Pressure maintenance	The pressure in the system should be kept from the pump right through the pressure vessel. In a small system (up to about 10 ml/min) a simple restrictor can be applied. This can be either a capillary tube cut to length or a needle valve which can be regulated, to keep the pressure at variety of flow rates. In larger systems a back pressure regulator will be utilized, that preserve upstream of the regulator by means of a spring, compressed air, or electrically driven valve. Whatever is applied, heating is necessary to provide since adiabatic expansion of the CO_2 results in considerable cooling. This may cause a problem if water or another extracted material is found in the sample, since this may freeze in the restrictor or valve resulting in blockages [30].
4	Collection	The supercritical solvent is passed into a vessel at lower pressure than the extraction vessel. The density and dissolving power of supercritical fluids differ sharply with pressure so the solubility in the lower density CO_2 is much lower, and the material precipitates for collection. The soluble material can be fractionated by applying a series of vessels at decreasing pressure. It is possible to recycle CO_2 or depressurized to atmospheric pressure and dismissed for analytical SFE, the pressure is often turned away to atmosphere, and now gaseous carbon dioxide bubbled through a solvent to enclose the precipitated constituents [30].
5	Heating and Cooling	The fluid is cooled before pumping to preserve liquid conditions, and then heated after pressurization. The fluid is diffused into the separator so the heat should be supported to inhibit immoderate cooling. For small system of extractions, like for analytical purposes, it is generally enough to pre-heat the fluid in a length of tubing within the oven where the extraction cell is kept. The restrictor can be heated either electrically or by using hair dryer. However, for larger scales, the energy needed for every step of the extraction operation can be calculated applying the thermodynamic characteristics of the supercritical fluid [32]. Fig.3 represents the schematic diagram of SFE apparatus

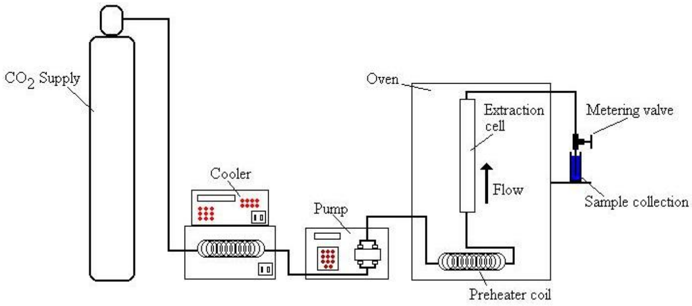

Figure 3 Schematic diagram of SFE apparatus

3. Advantage and Disadvantages of SFE

3.1. Advantages

Near liquid densities increase the probability of interactions between the carbon dioxide and the substrate as occur in liquid solvent. The gas like diffusivity of supercritical fluids is typically one to two orders of magnitude greater than liquids, which lead to exceptional mass transfer properties. Furthermore, near zero surface tension and low viscosities like gases, enable supercritical fluids to penetrate simply through a micro porous matrix material to extract the preferred constituents. The synergistic combination of density, viscosity, surface tension, diffusivity, pressure and temperature dependence resulting in unusual extraction capabilities of supercritical fluids. Another strong side of SFE is the ability to exactly control which components in a complex matrix are extracted and which ones are left behind. This is achieved through exact control of several key parameters like temperatures, pressures, flow rates and processing times. Yields from SFE are generally much greater than those of extractions conducted by extraction techniques, product purity is high, and decomposition of compounds never happens since relatively moderate temperature is applied. Characteristics of a supercritical fluid can be modified by changing the pressure and temperature, allowing selective extraction. Substituting the traditional organic solvents with SCF in performing the extraction is an important advancement in solving pollution problem. Supercritical fluid extraction enable for separation of waste components and decreasing the recycling of the solvent. In addition to that super critical fluid extraction process found to be highly effectiveness with high extraction rates also. Extraction is considered to be a diffusion-based process, in which the solvent is needed to diffuse into the matrix and the extracted material to diffuse out of the matrix into the solvent. SFE is a substitute technique to liquid extraction utilizing solvents like hexane of dichloromethane. Generally some residual solvent remain in the extract and the matrix since they can be recovered simply from the extract because of its volatility. There will be no mischievous residue and no environmental pollution [33]. On the other hand, Carbon dioxide can bring out easily by decreasing the pressure and often without resulting of any trail, so it is environmentally amiable. A supercritical fluid are not of high cost, not active and have no toxicity, therefore they can be quickly eliminated after the completion of extraction by giving them a chance to evaporate into the atmosphere [34].

The process in conventional liquid- liquid extraction include recovery of the consumed extraction solvent which is often conducted using distillation which may lead to consume of more energy. However in case of supercritical fluid solvent, lowering the pressure of the mixture is useful in the separation of the solute from the mixture and the supercritical solvent can be recycled by compression it again. Furthermore, supercritical fluids show usually zero surface tension, which cause facile penetration into micro porous materials. As a result of that, the extraction process can be done often more likely with supercritical fluids (solvents) due to their advantageous combination of physicochemical properties.

3.2. Disadvantage of SFE

The need for high pressures increases the cost compared to conventional liquid extraction. Therefore SFE will be only applied where there will be significant advantages. Carbon dioxide is non-polar, and has somewhat limited dissolving power, so it cannot always be applied as a solvent on its own, especially for polar solutes. The use of modifiers enhances the range of materials which can be extracted. Food grade modifier like ethanol can often be applied and can further be helpful for the collection of the extracted material, but decrease some of the benefits of using a solvent which is gaseous at room temperature.

4. Employment of SFE in herbal medicines extraction

Plants denoted as a considerable source of chemical ingredients that are used as natural medication for some diseases for periods of times. Bioactive compounds are natural non nutrient components of plant food biosynthesized as secondary metabolites [53]. Bioactive plants are usually specified in plant foods like vegetables, grains, fruits, coffee, tea and non-food plants like herbs, aromatics, spices and sometimes in plant waste materials from factories [51]. These valuable compounds can be extracted from several parts of plants like seeds ،roots, leaves, stems, buds ،tubers, flowers and fruits [54]. Several studies have been emphasized that these bioactive constituents showed significant biological activities like anti-microbial, anti-oxidant, anti-septic [55,56], antibacterial,anti-fungal [57], anti-viral, anti- inflammatory [54], anti-tumor [58], anti-obesity, anti- cholinesterase, phagocytotic, and a lot of therapeutic effects [59,60]. Supercritical CO_2 extraction has been considered as the best modernistic technology to extract bioactive components effectively and safely. During SFE, the choice of working conditions affected by the target components to be extracted. Moreover, the parameters including pressure, temperature, extraction time, particle size and co-solvent concentration are the most memorable and have to be taken into account for effective extraction. Plants natural bioactive compounds can be classified into three main categories which called phenolics alkaloids and terpenoids [53,61,62].

4.1. Phenolic Compounds

Phenolic compounds or phenols are secondary natural metabolites which present in the plant kingdom [64]. About 8000 classes of phenols are known such as flavonoids, stilbenes, lignans, resveratrol, and gallic acid [62]. Many researchers have confirmed that consuming of phenols can play a definite role in human health by controlling metabolism, weight, inveterate diseases, and cell reproduction due to their anti-oxidant effect and free radical scavenging properties [61]. Flavonoids cosidered as the most famous bioactive copmpounds among phenolics class. Flavonoids are familiar for their anti-oxidant and chelating features which supply indispensable health benefits including the control and forbidding of cancer, cardiovascular diseases, and chronic inflammatory conditions [65]. Now a days, SFE reported as the efficient technology for the extraction of phenolic compounds from several plants and it was informed that applying a temperature of 60◦C , a pressure of 200 bar, and using 5% ethanol as the co-solvent are the desirable parameters for the extraction process of phenols[51].

4.2.Alkaloids

Alkaloids are secondary plant metabolites consist in their structure of carbon, hydrogen, nitrogen, and at times oxygen. They are alkaline in nature due to the presence of nitrogen atom. Every plant species involve a few alkaloids, but the most familiar alkaloids are morphine, codeine, caffeine, nicotine, cocaine, and vinblastine [61]. Some alkaloids show considerable bioactivities that have produced to their utilization as pharmaceuticals. On the other side, some research studies emphasized that the increase consuming of some alkaloids like caffeine which present in different sorts of plant like coffee beans, cocoa beans, mate leaves and tea leaves causes several diseases to human like insomnia, nervousness and irritability [63]. As a result of that it was needful to exclude caffeine, and supercritical CO_2 has been considered as a successful recent method to extract and exclude caffeine from coffee, tea, and other species [60]. Additionally, variety of scientific researchers exhibited that SC- CO_2 extraction is the rapid and operative technique to extract alkaloids [51].

4.3 Terpenes or Terpenoids

Terpenoids are the most notable groups of secondary metabolites. Their chemical structure formed by head to tail rearrangement of two or more isoprene molecules. Isoprene is a basic structure of the terpenoids, made of a branched five-carbon unit synthesized from acetyl-CoA or 3-phosphoglycerate [66]. Many terpenoids have been extracted using SC- CO_2 and they exhibit wide applications in different fields. According to many studies on terpenoids extraction with SC- CO_2 , it was emphasized that the temperature around 40◦C and the pressure of 250 bar are the suitable parameters for achieving the highest yield, but using of different co-solvents was not considered [51]. Carotenoids are a famous type of tetraterpene plant pigments; they are accountable for the yellow-red colors of different plant organs. Carotenoids are amongst the most remarkable bioactive components which can reinforce human health due to their pro-vitamin A activity, anti-cancer activities, and anti-oxidant power [67, 68]. Carotenoids from different vegetables matrices like carrots, pumpkins, tomatoes, peach, sweet potato, apricot, yellow, red and green peppers, have been effectively extracted by supercritical carbon dioxide [67]. Essential oils formed of terpenes or terpenoids and they are used to manufacture medicines. Essential oils have abundant valuable biological activities like anti-inflammatory, anti-oxidant, anti-fungal and anti-bacterial [69]. The anti-microbial activity of essential oils can be linked with their capability to break through the bacteria cell wall and frustrate its functional properties [70]. Essential oils have been extracted efficiently using supercritical CO_2 from variety sorts of herbs and it was reported that moderate pressures (90–120 bar) and temperatures (35–50◦C) are desired to dissolve the essential oil ingredients during extraction [69, 51].

5. Novel applications of supercritical fluid extraction

5.1. Reactions in Supercritical media

Polymerizing of supercritical ethylene leads to the formation of polyethylene. The process of radical polymerization required 1200-3000 bars of ethylene pressure and (150-300)ºC in order to form an enough high molecular weight of polyethylene organic peroxide or oxygen were applied as initiators [35]. The salvation power of a supercritical fluid can be modified by the changes in its pressure and this feature was used in the fractionation purpose of polymers like ethylene-based co-polymers, poly-siloxane and poly-ethylene [36]. Furthermore, the features of supercritical fluids can be applied in the separation of the product from the catalyst or the reactants by minimize the reaction mixture pressure. The enzymes were reported as active compounds in supercritical Carbon dioxide in 1980 [37], [38].

5.2. Application in environmental field

Supercritical carbon dioxide extraction has play important role in the remediation of contaminated soil since ten years. The researchers [39-45] , have extracted on a bench scale PAHs like benzo[a]- anthracene, benzo [a]- pyrene, naphthalene, fluoranthene, perylene, diesel oil containing C_{13}- C_{22} hydrocarbons, PCBs, Chlorophenols like 2- Chlorophenol, 2,4,6 – trichlorophenol, dioxins and furans from spiked and real by several factors such as the type of soil, conditions of extraction and contaminant type sand is considered to be the best matrix of extraction but mud is considered to be a difficult matrix.

5.3. Application in production of particles

Supercritical fluids can be applied as particle formation media [46], [47]. Supercritical fluids were used to make particles by two techniques. Fine particles of compounds that are soluble in a supercritical fluid were used to make particles by two techniques. Fine particles of substances that are soluble in a supercritical solvent were made from rapid expansion from supercritical solutions (RESS). In the RESS method start with dissolving the substance in a supercritical solvent then the pressure is decreased quickly in a specifically designed nozzle which resulted in super saturation of the substance in the supercritical solvent thus small particles with a narrow particle size distribution is formed.

5.4. Application in Food Processing

Supercritical fluid method has many applications in industry. The most familiar and widely applied in food processing in which carbon dioxide is the preferred and convenient solvent due to its critical temperature is relatively not high which allows thermally labile food constituents to extract without degradation. Furthermore, it is non-toxic, not-corrosive, and inexpensive, and no any harmful residue is left after completion of the extraction processes. Semi-batch extraction is conducted since the food materials which have to be extracted are usually solid. Many applications were conducted in industry using supercritical carbon dioxide like extraction of caffeine from green moist coffee beans and to produce natural products, pharmaceutical and especial chemicals [36].

5.5. Separation in continuously operated columns

Relatively non-polar compounds which dissolve in toluene, freons, hexane and chlorinated solvents can be separated by applying supercritical fluid chromatography (SFC) with pure carbon dioxide eluent. Ion-ion interactions between silica and eluted compounds do not happen practically. Compounds which consist of primary or secondary amine groups are fractionated selectively with SFC. Generally such compounds are very difficult to extract them by using HPLC-Silica system because of several peak tailing. SFC method leads to rise the separation rates since the molecular diffusion in supercritical fluids relatively high. Furthermore SFC need low energy to recycle pressurized CO_2 which result in minimize the cost of process. The purification of syclosporin by industrial-scale supercritical fluid chromatography plant is given by A. altonen et.al. [48]. There is one method for carbon dioxide by utilizing the acidic property, then the use of it as a solvent to extract weakly basic organics such as pyridine from an aqueous solution [49]. Many others potential applications still undergo development which involve the regeneration of activated Carbon, the swelling of polymer and the separation of hydrocarbon and oil mixtures [36].

6. Conclusion

Supercritical fluids and especially supercritical carbon dioxide have considered as green solvents for majority of naturally occurring components regarding the manufacture of food and other pharmaceutical products. Carbon dioxide has attainable critical conditions that enable high stability of the extraction performance. Additionally, it prohibits the degradation of thermal compounds and it can be removed simply from the extracted constituents by depressurizing the system and controlling the pressure and temperature. Furthermore, supercritical fluid extraction technology possesses evident features compared to traditional solvent extraction processes. Supercritical fluids have the ability to penetrate into the materials compared to the liquid solvents due to their high diffusivity as well as low viscosity and surface tension. Consequently, they lead to fast mass transfer and extraction. Also, their high density results in high solvent power compared to gases. In supercritical fluid extraction, the capabilities of the solvents are dictated by temperature and pressure parameters as they affect solvent properties including density, viscosity and diffusivity. The temperature and pressure of the supercritical fluids can be modified to specifically dissolute the desired analytes. It is hoped that this study would serve as background knowledge for further studies related to SFE, since it may give proper basic concepts for the researchers who are working in this filed and interested in understanding this recent area of the research.

Data Availability

No data were used to support this study.

Conflicts of Interest

The authors declare that they have no conficts of interest.

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