Review

Application of supercritical and subcritical fluids in food processing

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Abstract

Using high pressure as a processing tool can overcome the legal limitations for solvent residues and restrictions on the use of conventional solvents in chemical processes. Additionally, particulate products can also be achieved by means of supercritical fluid (SCF) processing. This contribution will give a limited overview of applications of subcritical fluid and SCF and will present the energy savings compared with conventional production methods. Considering these qualities, SCFs could certainly be applied as a replacement for conventional solvents in extractive and non-extractive processes, as a nontoxic, inexpensive, non-flammable, and non-polluting solvent. Many applications, such as high pressure sterilization, jet-cutting, thin film deposition for microelectronics, and the separation of value-added products from fermentation broths in the biotechnology field, have been developed on an industrial scale to produce marketable food products.

Key words: separation; fractionation; extraction; value-added products; green solvents.

Introduction

In recent times, the design of new products with certain characteristics or the design of environmentally friendly processes has presented a challenge for engineers. Most commonly, the industrial technologies for producing different products were operated at atmospheric pressure. On Earth, this pressure ranges from 0.25 bar, on the highest mountain, up to almost 1000 bar at the bottom of the ocean. Nowadays, the demand for new products has increased, and it has thus become necessary to find ways to shift technological processes towards high pressure. The pressures used in high-pressure industrial processes range from 50 bar (in particle formation processes) to over 200 000 bar (conversion of graphite to diamond) (Knez, 2016).

Research in supercritical extraction technology started about two decades ago. Meanwhile, several hundred supercritical extraction plants have been designed to operate at extremely high pressures (up to 2000 bar) worldwide. Typical applications, operated by means of supercritical fluids (SCFs), are the extraction of hop constituents, decaffeination of tea and coffee, and the separation of lecithin from oil, all of which are high-pressure processes, which are performed on a large industrial scale. Several smaller industrial units are also in operation for extraction of spices for the food industry and natural substances for use in cosmetics (Luetge et al., 2007).

Using SCFs in numerous processes may lead to the production of completely new products with certain characteristics having a very low impact on the environment, such as low energy consumption during the process, along with health and safety benefits. The use of most supercritical (SC) fluids in industrial processes can replace far more damaging conventional solvents. The most important SCFs, such as SC CO₂ and SC H₂O, are nontoxic, non-flammable, non-carcinogenic, non-mutagenic, and also thermodynamically stable. Other advantages of SCFs include health and safety (Knez, 2016).

Typical thermophysical properties of SCFs are low viscosity, high diffusivity, density, and the dielectric constant of SCF, which can easily be changed by varying the operating pressure and/or temperature.

SCF can be used as solvents for precipitation and micronization (PGSS®, RESS, etc.), as a reaction medium, as a mobile phase for chromatography (supercritical fluid chromatography—SFC), and so on. However, the most commonly investigated process where SCFs
are used as solvent media is the supercritical fluid extraction (SFE) process (Oman et al., 2013).

The unique thermodynamic and fluid dynamic properties of different gases used as dense fluids, e.g. subcritical fluid or SCFs, can also be used for integrated extraction and in situ formulation, like impregnation of solid particles, for formation of solid powdery emulsions, particle coating, etc.

The relatively new use of high pressure as a tool may lead to the production of completely new products with special characteristics that are impossible to obtain in any conventional way. Additional advantages of high-pressure processes are their low environmental impact, economic feasibility, and sustainability for certain high-value products (e.g. in the food or pharma industries), or for special products that could not be produced at ambient pressures (e.g. polymers).

We could summarize that extraction of substances from solids or liquids and their integrated formulation in products with specific properties form one of the very promising applications of SCFs, and several laboratory-scale as well as industrial-scale applications, including fundamental data for design of high pressure processes, will be presented.

SCFs as Solvent Media in Supercritical Extraction Process

The advantage of using SCF for isolation of natural substances has been reported and explained in the literature. However, one of the most important advantages of using SCFs as extraction media is selective extraction of compounds or fractionation of total extracts (Lack et al., 2001; Knez et al., 2010). An enormous influence on the economy of the process is also exerted by mass transfer, which is usually described as extraction yield vs. extraction time, or as the solvent-to-feed ratio (S/F = mass of SC solvent/to solid material) (Reverchon and De Marco, 2006; Knez, 2016).

SFE is a separation process where solid or liquid matter is processed with SCF in order to obtain soluble compounds from the mixtures. SCF offers a variety of applications, owing to its specific properties, which can be relatively easily adjusted by changing pressure and temperature. A fluid above critical temperature has gas-like properties, which can be relatively easily adjusted by changes in the operating pressure and/or temperature. The relatively new use of high pressure as a tool may lead to the production of completely new products with special characteristics that are impossible to obtain in any conventional way. Additional advantages of high-pressure processes are their low environmental impact, economic feasibility, and sustainability for certain high-value products (e.g. in the food or pharma industries), or for special products that could not be produced at ambient pressures (e.g. polymers).

The most common solvent used as a SCF is carbon dioxide (CO₂). When polar components are extracted and supercritical CO₂ (SC–CO₂) is used as a solvent, a polar modifier or cosolvent is mixed with SC–CO₂ to enhance solubility. Examples of such a modifier are methanol, ethanol, etc. When a modifier is added, it is not only solubility but also viscosity and density that are increased. Because of the increase in density and viscosity, the diffusivity in the mobile phase decreases; hence, mass transfer is reduced. To obtain the highest yields possible, the process needs to be optimized. First, the influence of process parameters on the extraction has to be studied. Depending on the results, the optimal operating parameters are chosen. One way to determine the optimal parameters is by the use of response surface methodology (RSM). This method uses the multiple regression model (a polynomial second-order equation), from which optimum parameters are selected. This model is described in the work of Wang et al., where optimization with RSM for SFE of essential oils from Cypersus rotundus is described (Wang et al., 2012). Last but not least, the extraction rates depend on the morphology of the material and the location of the solute in the plant material. If the desired solute is on the surface of the material, extraction rates are usually high. However, when the desired compounds lie deeper in the material, it takes more time to extract them. In those cases, mass transfer depends on particle shape and size, as well as on the porosity of the solid material. If the structure of the material is more complex and the desired compounds are deeper inside, greater resistance to diffusion is expected (Gorbaty and Bondarenko, 1998; Reverchon and De Marco, 2006; Diaz and Brignole, 2009; Pereira and Meireles, 2010). Therefore, the preparation of a sample is very important for SFE of natural matter (Weathers et al., 1999; Lang and Wai, 2001). Usually, a material has to be mechanically pretreated—i.e. mechanically processed by grinding, milling, and cutting—to reduce mean particle size. As mentioned in this section, smaller particles provide faster extraction, owing to lower diffusion paths and less diffusion resistance (Oman et al., 2013).

One of the major process benefits of using SCFs as extraction media is derived from the thermophysical properties of SCFs: high diffusivity, low viscosity, density, and the dielectric constant of SCF, which can be fine-tuned by changes in the operating pressure and/or temperature.

The motivation for using high pressure in a large range of high-pressure technologies and processes is based on its chemical, physicochemical, physico(bio)chemical, physicohydrodynamic, and physicohydraulic effects (Bertucco and Vetter, 2001).

Solubility and Phase Equilibrium

Natural compounds in the presence of SCF

Determination of solubility data

Since high solubility of the relevant compound in the supercritical solvent is essential for economy in the extraction process, practical analysis will verify whether extraction using SCF is a suitable technique for isolation of the target compound. Several parameters influencing solubility, mass transfer of target compounds in the SCF, and consequently extraction yield have to be considered. Extract quality depends on pressure and temperature, which can seriously influence the composition of the final extracts (Rizvi et al., 1986; Brennecke and Eckert, 1989; Bharath et al., 1992; Knez et al., 2010). In addition, the pressure drop effect has to be evaluated and taken into account when optimizing parameters to obtain the best ratio between yield and solvent amount and extraction time (Capuzzo et al., 2013). The highest possible loading of SC solvent should be achieved in the extraction step of the processes, whereas in the separation step of the process, the solubility of the solute in the solvent should be the lowest (McHugh and Krukonis, 1990).

A detailed literature review shows that many research articles published in past years report phase behaviour of various natural substances, including antioxidants, pharmaceuticals, colouring
matters, pesticides, spices, aromas, and constituents of essential and vegetable oils in CO₂ (Stahl et al., 1981; Reverchon, 1997; Brunner, 2005; Del Valle et al., 2005; Reverchon and De Marco, 2006), whereas only a few articles deal with the phase equilibria of compounds in alternative SCFs, in particular SF₆ and several refrigerants, such as difluoroethane (HFC-32), pentfluoroethane (HFC-125), 1,1,1,2-tetrafluoroethane (HFC-134a), 1,1,1,2-trifluoroethane (HFC-143a), 1,1-difluoroethane (HFC-152a), 1,1,1,2,3,3,3-heptafluoropropane (HFC-227ea), CHF₃, and CH₂F₂ (Mertoglan et al., 1996; Roth, 1996; Tuma and Schneider, 1999; Diefenbacher and Türk, 2001; Park et al., 2002; Chapoy et al., 2005), but there were no data reporting phase equilibria in argon.

Choosing argon as a solvent is reasonable, given its inactivity, low thermal conductivity, and easy accessibility. Furthermore, its critical point (Table 1) is achieved at low temperature and relatively low pressure, which is important in case of thermolabile components (Drake et al., 1990).

Up to now, argon has been used as a protective atmosphere for certain foodstuffs, notably fruits and vegetables to prevent deterioration of food. Its inert nature is also employed to advantage in medicine and laboratory analyses for quality control, in electronics as a carrier gas for reactive molecules, and as an inert gas to protect semiconductors against impurities. It is also used to create an inert protective atmosphere between the liquid metal and surrounding air in metallurgy and welding. Since it does not react with the filament, even at high temperatures, argon is used as an inert atmosphere in incandescent light bulbs, to create blue light in neon-type lamps, and also as a filler for windows with double glazing (Haynes, 2014). The physicochemical properties of argon are provided in Table 1.

The phase equilibrium of substances in the presence of dense gases has been discussed in the literature for ternary and multicomponent mixtures (McHugh and Krukonis, 1990; Sadus, 2012; Brunner, 2013). As established above, extraction yield, which influences the economy of the process, is dependent on the solubility of compounds in phases present in the system. Mass and heat transfer are motivated by the difference from the equilibrium state at given conditions of the state. Even a binary system of a substance in a solvent near its critical conditions can exhibit unexpected behaviour, especially in the case of mixture components with differing molecular size and shape, structure, and polarity. Phase behaviour can be presented by P-T and P-x projections of P-T-x space diagrams.

Phase behaviour

In systems solid-SCF, where the normal melting temperature of the solid is higher than the T⁰ of the SCF, two possible types of phase behaviour exist. The simplest one is typical of mixtures whose components are chemically similar. The critical mixture curve runs continuously between the critical points of both components in the mixture. The solid-liquid-gas (SLG) line is continuous and begins at the normal melting point of the heavy component, bends back toward the lower temperatures, as the pressure is increased, and ends at a temperature usually well below the critical temperature of the lighter component. The melting point of the pure solid normally increases as the hydrostatic pressure is increased. However, when the solid is in presence of dense gas, which is well soluble in melting of the heavy component, the melting point of the solid decreases with increasing pressure, owing to increasing the solubility.

The second type of solid-SCF phase behaviour is typical of systems where the solid and SCF differ considerably in molecular size, shape, and/or polarity and can be interpreted as type III fluid phase behaviour (De Loos, 2006), according to the classification by van Konynenburg and Scott (Van Konynenburg and Scott, 1980). In this type of system, the light gas is not very soluble in the heavy liquid, even at high pressures. Therefore, the melting point depression of the solid is relatively small. The SLG curve is no longer continuous; three-phase SLG equilibrium is represented by the two branches of the SLG line in the P-T diagram. The high-temperature branch of the SLG line starts at the normal melting point of the solid and intersects the critical-mixture curve at the upper critical end point. The low-temperature branch of the SLG line intersects the critical-mixture curve at the lower critical end point. At these two points, the liquid and gas phases merge into a single fluid phase in the presence of excess solid. Only solid-gas equilibria exist between these two branches of the SLG line. Possible phase behaviour for type III systems with interference of the solid phase is presented in detail by De Loos (De Loos, 2006).

**Table 1** Physicochemical properties of argon (National Institute of Standards and Technology, 2017).

| Properties | Value |
|------------|------|
| Tₙ (°C)   | −189.36 |
| Tₚ (°C)   | −183.85 |
| Tᶜ (°C)   | −122.3 |
| Pₑ (bar)  | 48.98 |
| ρₑ (kg/m³) | 537.7 |
| ρₑ (at 1.013 bar and 15°C) (kg/m³) | 1.67 |
| ρₑ (at 1.013 bar and 21°C) (kg/m³) | 1.38 |
| Dipole moment (Debye) | 0 |

**Extraction Processes**

Applications for extraction using SCFs are numerous. In the literature, several overviews can be found (Stahl et al., 1981; Gardner, 1993; Lack and Seidlitz, 1993; Moyler, 1993; Lack and Simandi, 2001; Reverchon and De Marco, 2006; Eltringham and Catchpole, 2007; Martinez et al., 2007; Mendes, 2007; Brunner, 2013). At the same time, on the internet pages of the equipment producers (Uhde HPT, Natex, Sitec, Nova Swiss, Waters Corporation), references are given.

From these data, it can be seen that the highest capacities are installed for coffee and tea decaffeination. The second largest application is for the extraction of hop (Knez, 2016). The extraction of spices for production of oleo-resins and the extraction of bioactive material from plants are two very diverse applications of SC for extraction. One of the most noticeable applications is the extraction of oil from degumming residue to obtain highly concentrated and very pure lecithin. Applications of liquid/subcritical fluid extraction or SFE are numerous and have been used for separation of ethanol from water, separation of aromas from various alcoholic beverages, separation of components from citrus oils, and for purification of tocopherols. In the future, a further limitation on the use of organic solvents and new applications will be the method of processing during sustainable production.
changing the process parameters. The limitation on further application of extracts obtained by high pressure technology lies in the price of the product, which in comparison with conventionally obtained products, is relatively high. The legal limitations on solvent residues and solvents (for products meant to be used in human applications) and isolation/fractionation of special components from total extracts, in combination with various formulation and sterilisation processes (controlled release, for example) will increase the use of dense gases for extraction applications.

There are fewer industrial units for separation of components from liquid mixtures using SCFs. A literature search shows some laboratory-scale studies on extractions in systems of liquid/supercritical fluid. Several data on binary systems of liquid/SCF can be found, but there are less data on systems involving liquid/liquid/supercritical fluid.

In our manuscript, the fundamentals (phase equilibrium data for some systems liquid/SCF), along with design and applications of processes for the extraction of components from liquid mixtures, will be presented.

As in all extraction processes, in supercritical extraction of solid and liquid mixtures, the solubility of a single component or mixture of components in SCF is the basic data for designing separation processes. The components or mixture of compounds to be extracted needs to be soluble in SCF/dense gas. As is known from thermodynamics, the solubility of compounds in SCF/dense gases is based on the density of SCF/dense gas, which is dependent on the pressure and temperature of SCF. Another very important parameter that influences the solubility of compounds in SCF is the dielectric constant of SCF, which is influenced by the temperature and/or pressure of SCF. A general flow sheet of the extraction process is presented in Figure 1.

In the extraction step, the solubility of the compound or mixture of the compound has to be the highest, whereas in the separation step, the solubility of the compound in SCF has to be the lowest. Therefore, the phase equilibrium data are the most important data for the design of operating pressures and temperatures for SCF at an extraction plant. Based on the phase equilibrium data, the theoretical mass of SCF necessary for separation of the compound from the solid or liquid mixture can be calculated.

Design process parameters have a very important influence on the investment cost for a high-pressure plant and consequently on the economy of the process.

Besides, as mentioned above, the solubility data for a solute in SCF mass transfer also exert an enormous influence on the economy of the extraction process. Mass transfer models usually describe extraction yield vs. extraction time, but a better presentation for the design of extraction apparatuses is yield vs. S/F mass of SC solvent (to solid material). In Figure 2, typical extraction curves for isolation of a substance from solids is presented.

There are fewer industrial units for separation of components from liquid mixtures using SCFs. Extraction of liquid mixtures with SCFs is comparable to liquid-liquid extraction, where compressed gas is used instead of an organic solvent. In liquid-SCF extraction processes, the pressure plays an important role. In changing pressure and/or temperature, the physicochemical properties of the SCF, like density, viscosity, surface tension, and dielectric constant, are changed. Selective extraction of components or fractionation of total extracts is possible by using different gases for isolation/fractionation of components and/or changing the process parameters. Another advantage is that, depending on the feed material, the density difference between the two counter-current flowing phases can be adjusted.

One of the most important advantages of using SCFs is simple solvent regeneration. In comparison with liquid-liquid extraction, solvent regeneration includes, in most cases, a necessary re-extraction or distillation step, which is energy-consuming and therefore cost intensive. Heat treatment of the extract or the raffinate phase may cause degradation of heat sensitive substances. For an extraction plant where SCFs are used, solvent regeneration is achieved by changing the pressure and/or temperature after the extraction step, thus changing the density and consequently the solvent power of the gas, which can later be easily recycled after separation of the solute. Compared with extraction of solids with SCF, liquids could be continuously introduced in and withdrawn from the high pressure extraction unit. This gives the benefit of higher throughputs in continuously operating counter-current processes.

A literature search shows some laboratory scale studies on extractions in systems using liquid/supercritical fluid. Several data on binary systems of liquid/SCF can be found, but there is less data on systems using liquid/liquid/supercritical fluid, which are necessary for the design of extraction processes of liquid mixtures with SCFs (Knez, 2016).
As in conventional continuous liquid–liquid extraction, in liquid/sub- or supercritical solvents extraction, several modes of operation are available. Single stage extraction is the simplest one and is used for systems where separation factors for the solute are high. Multistage separation is necessary when the separation factor between components is in the order of 1–10. Different modes of operation for multistage processes are used, such as multistage cross-flow, where relatively low loading of solvent with extract is obtained at each stage.

In multistage counter-current extraction, high loading of solvent with extracts is also possible, along with different geometry of the apparatus.

The design of counter-current liquid/subcritical fluid extraction or SFE can be modelled by using typical, commonly used, basic equations: mass balance, energy balance, equilibrium distribution coefficients, and mass transfer rate equations.

In the design of multistage liquid/subcritical fluid or SFE, determination of number of theoretical stages/transfer units, as well as the size and type of a separation device with respect to separation performance, and design of a solvent cycle is necessary.

Based on the above facts and experimental data, the costs of separation using a liquid/sub- or supercritical process need to be determined.

The costs per ton of the feed are influenced by throughput and mode of operation (batch processing has higher operating costs, whereas the process costs are lower in continuous mode) and range from approximately 60 €/kg feed at a throughput of cca. 200 tons per year in batch processing, down to approximately 0.06 €/kg feed at a throughput of cca. 60 000 tons per year for a continuous process. It is reported that common estimation methods yield results with an error of ±30%, whereas even after the project has been completed, costs are difficult to determine any closer than 5% (Brunner, 2010).

Other applications

From an economic point of view, technologies involving elevated pressures require high investment costs for high-pressure equipment. Because of this, it is reasonable to apply SFE for the separation of components with high-added values, such as nutraceuticals.

Table 2. Range of materials encapsulated using PGSS™ in the past 7 years.

| Material                                                                 | Solvent | Reference                          |
|-------------------------------------------------------------------------|---------|------------------------------------|
| acai® pharmaceutical substance                                          | CO₂     | (Bogorodski et al., 2015)          |
| α-Lipoic acid/hydrogenated colza oil                                     | CO₂     | (Mishima et al., 2016)             |
| BCS II API                                                              | CO₂     | (Pestieau et al., 2014)            |
| β-Carotene                                                              | CO₂     | (De Paz et al., 2012)              |
| CO₂ as solute, co-solute or co-solvent in particle formation processes  | CO₂     | (Nunes and Duarte, 2011)           |
| Coenzyme Q(10) (CoQ(10))                                                | water   | (Hu et al., 2011)                  |
| Curcumin                                                                | CO₂     | (São Pedro et al., 2016)           |
| Curcuminoids                                                            | CO₂     | (Perko et al., 2015)               |
| Cydia pomonella granulovirus (CpGV)                                     | CO₂     | (Pemsel et al., 2010)              |
| Elderberry juice                                                        | CO₂     | (Bánovgýi et al., 2016)            |
| Epigallocatechin gallate (EGCG) solid formulations                      | CO₂     | (Gonçalves et al., 2016)           |
| Fenofibrate                                                             | CO₂     | (Pestieau et al., 2015)            |
| Fucoidan and astaxanthin                                                | CO₂     | (Kwon et al., 2011)                |
| Hybrid carriers containing a glyceryl monostearate (Lumulse (R) GMS-K), a waxy triglyceride (Cutina (R) HR), silanized TiO₂, and various active agents | CO₂     | (García-González et al., 2010)     |
| Hydrogenated canola oil                                                 | CO₂     | (Cifci and Temelli, 2016)          |
| Hydrogenated castor oil                                                 | water   | (Hana et al., 2012)                |
| Ibuprofen                                                               | CO₂     | (Chen et al., 2013)                |
| Lavandin essential oil                                                  | CO₂     | (Varona et al., 2013)              |
| Lavandin essential oil                                                  | CO₂     | (Varona et al., 2010)              |
| Lavandin essential oil in liposomes, soy lecithin particles             | water   | (Varona et al., 2011)              |
| Limonene in modified starch                                             | CO₂     | (Machado et al., 2016)             |
| Lipid/PEG particles                                                     | CO₂     | (Vezzù et al., 2010)               |
| Liposomal microencapsulation                                            | CO₂     | (Tsai and Ruzvi, 2016)             |
| Microparticles from anhydrous milk fat (AMP) and a diacylglycerol-based modified milk fat (D-AMP) | CO₂     | (Lubary et al., 2011)              |
| Nano-sized drugs                                                        | CO₂     | (Sheh et al., 2012)                |
| Pea protein                                                             | CO₂     | (Do Carmo et al., 2016)            |
| PEGylated biodegradable polyesters                                       | CO₂     | (Perrinelli et al., 2016)          |
| perfluorocarbon (PFC) gases                                             | CO₂     | (Rodríguez-Rojo et al., 2013)      |
| Poly(d,l-lactic acid) (PDLLA) and poly(ethylene glycol) (PEG)           | CO₂     | (Kelly et al., 2012)               |
| Poly(ethylene oxide) (PEO) 6000                                          | water   | (Pham et al., 2012)                |
| Polybutylene terephthalate (PBT)                                        | CO₂     | (Pollak et al., 2011)              |
| Polymers                                                                | CO₂     | (Knez et al., 2011)                |
| Polymers                                                                | CO₂     | (Sauceau et al., 2011)             |
| Resveratrol                                                             | CO₂     | (Rodríguez Blanco, 2013)           |
| Resveratrol on lecithin and β-glucans                                   | CO₂     | (Salgado et al., 2015)             |
| Soy-bean lecithin—pluronic L64® encapsulated quercetin particles in nanometric scale | CO₂     | (Lévas et al., 2016)               |
| Spherical PEG particles                                                 | CO₂     | (Martin et al., 2010)              |
| Tristearate                                                             | CO₂     | (Mandžuka et al., 2010)            |

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**Reference**

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Brunner, 2010

Cifci and Temelli, 2016

Hana et al., 2012

Chen et al., 2013

Varona et al., 2013

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Machado et al., 2016

Vezzù et al., 2010

Tsai and Ruzvi, 2016

Lubary et al., 2011

Sheh et al., 2012

Do Carmo et al., 2016

Perrinelli et al., 2016

Rodríguez-Rojo et al., 2013

Kelly et al., 2012

Pham et al., 2012

Pollak et al., 2011

Knez et al., 2011

Sauceau et al., 2011

Rodríguez Blanco, 2013

Salgado et al., 2015

Lévas et al., 2016

Martin et al., 2010

Mandžuka et al., 2010

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For a comprehensive list of references, please consult the full article.
pharmaceuticals, food additives, or components with a high feed-to-solvent (F/S) extraction ratio.

A ‘green’ revolution as one part of necessary sustainable development can also use high pressure as a tool. The main impetus for this conversion is driven, on the one hand, by concern for the environment in reducing the usage of solvents and energy. On the other hand, increasing consumer demand for new and natural products sees high pressure as a tool to design and produce natural products with completely new characteristics.

In recent times, there has been greater emphasis on the recovery of high value-added products by using sustainable technologies. One of the ways to achieve this is the application of subcritical fluid and SCF. Some applications of PGSS™ process on different types of material are presented in Table 2. Some applications of supercritical fluid extraction (SFE) for separation of flavonoids and other phenolic compounds from plants, with CO₂ as a solvent are given in Table 3.

**Conclusion**

SCF-based technologies offer important advantages over organic solvent technology, such as ecological friendliness and ease of product fractionation.

There are fewer industrial units for separation of components from liquid mixtures using subcritical fluid or SCF. The main advantages of using SCF for isolation of natural products include solvent-free products, no co-products, and low temperatures in the separation process. In addition, the processes can easily be linked with direct micronization and crystallization from SC-CO₂ by fluid expansion (Knez, 2016). Besides the commonly used gas, carbon dioxide, for sub- or supercritical extraction, other sub- or supercritical solvents are being used. Sub- and supercritical CO₂ and supercritical H₂O are non-carcinogenic, non-toxic, non-mutagenic, non-flammable, and thermodynamically stable. In addition, CO₂ does not usually oxidize substrates and products, allowing the process to be operated at low temperatures. At the moment, water is the cheapest solvent and fractionation of substances is under way.

With regard to contemporary issues, future research will be focused towards utilization of the many valuable compounds present in natural materials. These can be of economic importance in the food industry and are known for their beneficial health effects. Technologists will be encouraged to develop new processes and soft technologies for preserving the beneficial characteristics of these compounds. Hence, future research efforts should be oriented to developing methods for isolation and identifying new compounds and preserving them after minimal processing and storage of various nutritional products, pharmaceuticals, cosmetics, and other materials. Recent demand has tended towards implementation of extraction and formulation processes that enable the transition to ‘green’ technologies, without further use of environmentally and health-hazardous organic solvents. Furthermore, according to a basic concept of bio refineries, the SFE process allows extraction of very pure, high-value product from materials which otherwise would be considered by-products or waste and sold cheaply, or simply disposed of. Such processing concepts promote reuse of residues from the food industry. A possible solution to the low bioavailability of the relevant compounds could be represented by nano-formulation. However, in the field of material processing, comprising particle size reduction and foam formation, in-depth research is still needed to obtain the necessary data for designing and optimizing the technologies.

| Compound(s) | Plant | Reference |
|-------------|-------|-----------|
| Anthocyanin | Raspberry | (Laroze et al., 2010) |
| Blueberry | Cranberry | Elderberry |
| Apigennin | Chamomile | Olive | Spearment | Shiyacha |
| Arteoilln C | Brazilian propolis | Spearnt | Olive | Pine tree | Berries | Marigold |
| Catechin | | | | | (Hamburger et al., 2004) |
| Coumarins | Rice | Dodder | Wormwood | Emburana | Sweet grass |
| Gallic acid | Rice | Macela | Barbados nut | Soybean | Wild cherry | Grape | Sour cherry |
| Genistein | Soybean | Wild cherry | (Serra et al., 2010) |
| Isocoumarin | Corianter | (Chen et al., 2009b) |
| Kämpferol | Tea | Rooibos | Black currant | (Liu et al., 2009) |
| Lignan | Five-flavor berry | (Sovova et al., 2007) |
| Myricetin | Crowberry | Tea | Rooibos | (Ligot et al., 2008) |
| Quercetin | Onion | Grape | (Ligot et al., 2005) |
| Polyphenols | Cocoa | (Lanzott, 2006) |
| Rutin | Tea | Rooibos | Tea | Crowberry | (Laaksonen et al., 2011) |
| Resveratrol | Grape | Hop | (Yu et al., 2005) |
| Tannin | Canola | Stonebreaker | (Markon et al., 2010) |
| Vitexin | Maypop | (Moraes et al., 1997) |
| Wogonin | Pigeon pea | (Giannuzzo et al., 2003) |

**Table 3. Some applications of supercritical fluid extraction (SFE) for separation of flavonoids and other phenolic compounds from plants, with CO₂ as a solvent.**

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Conflict of interest statement
None declared.

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