Supercritical Fluid Applications: Industrial Developments and Economic Issues

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After 2 decades of development of extraction/fractionation processes mainly dedicated to natural products, many "new" applications of supercritical fluids are now either under investigation or already at commercial scale in various areas.

Extraction (SFE). Many large-scale units are operated worldwide for extraction of solid natural materials, mainly for food ingredients and phytopharmaceuticals. Residual organic solvent (or other impurities) can also be removed from final active compounds or high-grade polymers at large scale. As special cases of extraction, ceramics binder removal, or liquid carbon dioxide cleaning for halogenated solvents substitution for both textile dry wash and metal degreasing, can be cited.

Fractionation (SFF). Industrial applications are designed to take profit of the very high selectivity of supercritical fluids with attractive costs related to continuous operation: polymer fractionation (specialty lubricants, pharmaceuticals, etc.), aromas production from fermented and distilled beverages, polyunsaturated fatty acids, active compounds from fermentation broth, pollution abatement on aqueous streams, etc.

Preparative-Scale Supercritical Fluid Chromatography (PSFC). Industrial development is now restricted to purification of polyunsaturated fatty acids and enantiomers.

Impregnation. The great diffusivity of supercritical fluids permits one to reach a homogeneous distribution of active compounds in various porous matrixes: drugs in patches or medical devices, preservatives in wood, desacidification and reinforcement agents in books, aromas in food products, concrete carbonation for mechanical properties improvement, etc. Similarly, supercritical fluid *dyeing of textiles*, especially polyesters, is considered to substitute classical aqueous dyeing with related water pollution.

Particle Design. Extended efforts are pursued by many pharmaceutical companies, based on different processes using supercritical fluids, for the manufacture of new *drug delivery systems* (micro/nanoparticles, complex microspheres/capsules, coated tablets and beads, etc.). On the other hand, polymer powders "engineering" is also considered for specialty products; meanwhile, a very large-scale production unit of paints is operated in the U.S. (combination of reaction and atomization in supercritical carbon dioxide) and large-scale applications of supercritical fluid dispersion are currently used in numerous industrial *painting* facilities (UNICARB process).

Aerogel Drying. The manufacture of high-efficiency insulation material or special porous materials (catalyst, porous supports, specialty glass, etc.) is envisaged at large scale, from both inorganic (mainly silica) and organic sol−gel polymers.

In the long term, supercritical fluids will be very widely used as *reaction* media, because their tunable properties are highly attractive and they permit one to reduce the diffusion limitations of the reaction kinetics. Some *biological* applications might also provide solutions to drastic problems related to cell lysis, sterilization, and virus inactivation.

On the other hand, applications for *pollution abatement* are also subjected to an increasing interest because CO_2 is a "green" solvent and permits one to design environmentally-friendly processes with both pollutants recovery and recycle: industrial wastes, contaminated soils, polluted water streams, volatile organic compound (VOC) reduction. Moreover, supercritical (or subcritical) *water* appears as a unique medium for highly hazardous materials destruction.

In this paper, I will first present the status of industrial applications of supercritical fluids and the future trends that can be foreseen at present time. Then, I will give some economic data, based on the know-how gathered by SEPAREX during these last 15 years of working on many supercritical fluids applications and manufacturing more than 70 plants at pilot scale or industrial scale.

Present Status of Industrial Applications of Supercritical Fluids[1−9]

German Supremacy in SFE/SFF... The supercritical fluid technology was German at the origin, with the first large-scale applications in food industries (coffee decaffeination and hops resins extraction), supported by a vigorous R&D effort mainly oriented on natural products[1] and by the well-known experience of the high-pressure chemical engineering German industry. Without competitors in the 1980s, the German companies extended their activities to new areas (tea decaffeination), including smaller volume applications in food (aromas, colorants, and diet lipids) and pharmaceutical and cosmetic active principles, and offered toll processing either as a complementary activity to better amortize their investment in increasing the operation time, especially for plants dedicated to seasonal vegetables, or as a full-time activity.

...Now Competed by New Operators. Until now, only very large plants dedicated to coffee decaffeination and hops extraction were built in the U.S.; meanwhile, several flexible medium-capacity plants were built in France and Italy, for SFE/SFF toll processing of food ingredients and pharmaceutical and cosmetic active principles. Other small-size plants are also operated for

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specialty product manufacture, such as, for example, bone delipidation leading to a porous material used for grafts on humans. Medium-capacity units are now under construction or consideration for toll processing in the U.S., and another one is operating in Canada. Moreover, it seems that the situation is now moving fast in Asia, with construction of several SFE/SFF units in China and South Korea for phytopharmaceuticals preparation and in India for spices and aromas extraction on site of large agricultural productions.

...and Development of Other Processes. On the other hand, this technology is also developing in other areas: preparative supercritical fluid chromatography is applied for polyunsaturated fatty acids purification on a large scale in Spain and in England, while one of the world largest plants using supercritical fluids is now under operation in the U.S. for paint manufacture, combining polymer reticulation, mixing with pigments, and particle atomization.[7] Supercritical fluid dispersion is currently used in numerous industrial painting facilities (UNICARB process), with a claimed reduction of VOC emission of up to 60%. Moreover, chemical reactions[5,8,9] are presently operated in supercritical fluid media: of course, the well-known classical ethylene polymerization but also very promising applications as butene hydration and especially hydrogenation that can be operated without mass-transfer limitations at extremely high rates. Several supercritical water oxidation (SCWO) units for dangerous waste destruction[5,8,9] are also on-stream or under construction.

Future Trends of Industrial Development

At the present time, it is clear that the most important markets are related to *natural product processing* for "classical" applications in food and nutraceutical/pharmaceutical/cosmetic industries. For these areas, SFE is known to lead to higher prices than organic solvent extraction that is presently widely used, explaining that the CO_2-extracts market is still limited and restricted to some niches; on the other hand, SFF has not yet become widespread despite more acceptable prices. However, new attractive opportunities have been appearing in various domains beyond natural products processing and extraction/fractionation processes. The following considerations are to be taken into account to foresee what will happen soon:

(i) Regulations Issues. In a growing number of countries, most organic solvents are banned for food products extraction or authorized with extremely low residual concentrations; similarly, pesticide removal from natural stuffs is of growing interest, as it is already operated on ginseng. Moreover, in the long term, the regulations will ease SFE/SFF development in relation with several issues: work ambiance control, ozone depletion, VOC release control, and residual concentration in the final product for consumer and environmental protection.

(ii) Quality Considerations. SFE/SFF are being developed for the preparation of high-value products such as food supplements and nutraceuticals, for which the "natural" character of the preparation mode has a high marketing value. It is the same for phytopharmaceuticals that are subjected to a real expansion both in the Western countries for consumers eager to move from "chemicals" to "naturals" and also on the Pacific rim where the Chinese tradition is very strong and is moving to preparations including CO_2 extracts. Moreover, it is to be noticed that supercritical fluid treatments lead to the elimination of pests often present in tropical natural raw materials, even if the products cannot be considered as sterilized according to common standards but only decontaminated.

(iii) Innovative Products. "New" food ingredients that are not at all comparable with those obtained from classical solvent extraction or distillation can be manufactured, but they need acceptance by the users that their manufacture is often long and sometimes costly. The pharmaceutical industry is paying great attention to *drug delivery systems* that are opening new therapeutic routes for many major drugs related to widespread diseases (asthma, diabetes, cancer, etc.). In other areas, several products like aerogels and high-quality ceramics are now moving to the market.

(iv) Innovative Processes. Innovation is required for solving many environmental problems, like VOC emission reduction, and supercritical processes are often considered as a "radical" solution that permits one to eliminate organic solvents, and particularly chlorinated solvents or CFC, such as those for painting, metal degreasing, or textile cleaning or dyeing. On the other hand, "green" chemistry will drastically develop in the next decades, using supercritical fluid (mainly carbon dioxide and water) as reaction media and/or separation agents.

The supercritical fluid development in the various fields of application can be evaluated as follows:[1-5,7-9]

(A) Flavors/fragrances extracted with supercritical carbon dioxide are of higher organoleptic quality, generally closer to natural stuffs; moreover, the absence of any organic solvent residue is very favorable. However, it would be a mistake to consider this domain as extremely promising in the short term, because experience showed that most final users are not ready to pay a supplement to substitute their classical product by a high-grade one processed with CO_2; moreover, surprisingly, they are reluctant to incorporate a "better" component in their compositions because they should have to reconsider them. This is the reason that the CO_2-extracts market is yet restricted to some niches: high-grade flavors or fragrances (like vanilla), fractions of extracts impossible to obtain easily by classical processes (like pepper, paprika, and ginger) or fractions without banned solvents (like aromas from rum, cognac, whisky, etc.). Nevertheless, it seems that things are now changing, and future business in the flavors and fragrances domain seems much brighter than expected a few years ago.

(B) Food ingredients are also extracted or refined by supercritical fluid processes: colorants (desodorization of natural colorants, orange color from the pot marigold flower, carotenoids from palm oil, shellfish, or carrots, etc.), antioxidant preservatives (deodorization of rosemary extract), texture agents (lecithin purification), and low-fat products (egg-yolk powder).

(C) Nutraceuticals can be extracted from various natural sources: SFE of medicinal plants (*Serenoa repens* or *Pygeum africanum* for prostates adenoma cure, chamomile extract, etc.), or SFF of oils, constitute, an increasing market to substitute extracts obtained with organic solvents and to propose new high-quality products; some raw materials are treated for elimination of pesticides (ginseng) or for desodorization/purification (fish oil). There is no doubt that the so fast increasing nutraceutical market is opening large possibilities to

SFE, and possibly SFF applications, with the problem of cost being much less sensitive than for food or perfumery products.

(D) Pharmaceutical/cosmetic active principles also offer many opportunities because they can be extracted, fractionated, and purified from either natural or synthetic sources; numerous examples can be cited: SFE of active molecules from natural products, and SFE for elimination of residual solvents (synthetic drugs), of monomers (polymeric patches or implants and cosmetic laquers), or of other toxic pollutants. However, the more promising applications seem to be the manufacture of new drug delivery systems based on particle design: nano- or microparticles for improving the bioavailability of poorly soluble molecules, microspheres or microcapsules for sustained-release drugs, microparticles for inhalation, etc.

(E) Chemical industries also offer a very wide range of applications to supercritical fluids processes, especially for separation and purification of specialty chemicals using SFE, SFF, or chromatographic processes and possibly soon for synthesis in these media, with the requirement of moving to a “green” chemistry![8]

(F) Material treatment using supercritical fluids appears as one of the most promising areas for development in many industries: polymer purification and expansion, porous material (polymer, wood, paper, etc.) impregnation, particle design especially for paint manufacture and delivery systems (pesticides, preservatives, drugs, etc.), aerogel drying for high-performance insulation materials, coatings and surface treatment, ceramics binder removal, and carbon fiber/carbon alloys preparation, etc. Surface treatment is also receiving great attention in order to avoid organic solvents: metal degreasing and dry cleaning (for which hundreds of machines are planned to be marketed in the next years), textile dyeing, coating applications, etc.

(G) Pollution abatement is also a potentially wide field for pollutant extraction or concentration by SFE/SFF (industrial wastes, soil remediation, polluted waters, etc.). However, very innovative technologies are yet to be developed to reach “acceptable” costs, even if this technology permits one to recycle valuable products at the difference with most other processes. Moreover, it is not yet clear if SCWO will really become a competitive process vis-à-vis classical incineration because drastic technical problems related to corrosion and plugging need to be solved.

Economic Issues

Most companies believe that supercritical fluid technology is too expensive because of very high investment costs in comparison with classical low-pressure equipment and, even if it leads to high-quality products, should be restricted to high-added-value products. Yet, this is far from true when very large volumes of materials are treated, as in the case of coffee/tea and hops processing, paint manufacture, soil remediation, and waste treatment!

High Investment Costs Growing Slowly with Capacity Increase... Reliable cost estimation of supercritical fluid equipment is not presently available from published sources, and figures can drastically change according to the type of equipment, instrumentation automation, etc. Here we will present the data we have gathered from our own experience of building

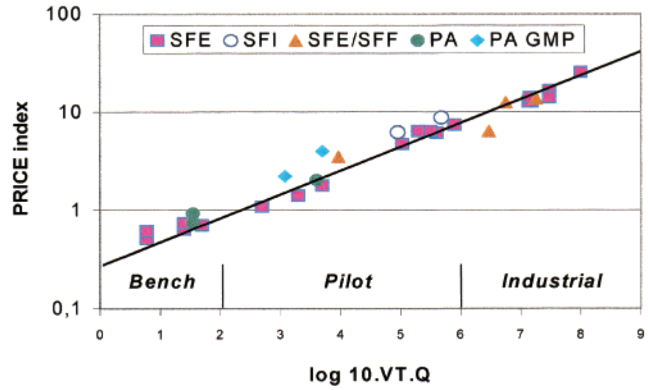

Figure 1. SF unit prices.

pilot- and industrial-scale SFE/SFF, online SFE/impregnation (SFI), and particle atomization (PA) units.

The data are related to SF equipment consisting of the following:

(1) Extractors and/or column, reactors, atomizing chambers, etc., of the total net volume V_T (L).

(2) Separation steps with an automatic extract withdrawal system.

(3) One liquid CO_2 reservoir.

(4) One CO_2 pump delivering a variable flow rate from 30% to 100% of the design flow rate Q ($kg{\cdot}h^{-1}$), at the service pressure.

(5) Several heat exchangers: condenser, subcooler, and heaters.

(6) All related piping, valves, instruments, and utility services required for a reliable and safe operation in automatic mode, to minimize manpower and maintenance costs.

The observed costs of such units, delivered on a turnkey basis, are reported on Figure 1, where, surprisingly, all prices (here represented by a dimensionless price index PI on a logarithmic scale) are near to a straight line with a slope of 0.24 versus the log of product of total volume V_T by the design flow rate Q:

$$PI = A(10V_TQ)^{0.24} \tag{1}$$

As for similar units, the solvent flow rate Q is proportional to the total extractors (+ column) volume V_T, this demonstrates that the cost of a SF unit roughly increases as the square root of the capacity. In fact, this confirms a feeling that has been shared for a long time; although this correlation is only based on our own experience and shall be considered with caution, it is surprising that it applies on such a large range of capacities, from the bench scale (0.5-L autoclave) to the industrial scale (500-L autoclave); but, it certainly underestimates prices of the small bench-scale equipment (0.2-L autoclave) and overestimates the price of much larger units, like those for hops or coffee/tea processing, that are probably much less costly than predicted by this rule. On the other hand, a significant price increase appears when special requirements are needed, such as, for example, for combination of extraction and extract impregnation (SFI) or for a unit built according to GMP requirements, as shown on Figure 1.

This shows that capital amortization sharply decreases when capacity increases, what is a strong incentive to use large capacity multi-products units in “time-sharing” rather than operating small capacity units dedicated to only one product. Obviously, this is clearly not possible when drastic requirement are imposed, especially for processing pharmaceuticals in compliance with GMP rules; moreover, such units must be built according to a drastic quality assurance plan and are generally priced much more than food-grade units, from 30 to 100%, depending on the size, as shown on Figure 1 for five particle atomization (PA) units: three built without and two with these requirements.

...But Low Operating Costs. The most important operating cost of SFE is often manpower, except for very large units (coffee, tea, hops, etc.), because raw and spent material handling cannot be totally automated; generally, two persons are required when the unit is running; however, when long-duration batches are required, it is possible to avoid manpower operation during the night, leading to important savings. The manpower cost is lower for SFF because it can be operated on continuous mode without permanent survey. Anyway, optimization of the unit design must take into account the manpower cost depending on local considerations and batch duration.

Cleaning is one of the most important time-consuming operations that is frequently underestimated during cost estimation on a large-scale flexible (multipurpose) unit. It is extremely important to consider the cleaning issue at the very beginning of any SF equipment design, especially—but not only—for those dedicated to food or pharmaceutical products: This shall influence many choices so as to avoid piping/instruments dead ends and all zones that could not be swept easily by the process fluids. For example, we developed very low volume multitubing/multiinstrument connections and very low volume high-speed separators in the form of cyclonic chambers. Moreover, adequate parts must be installed to permit an easy rinsing of the whole unit with liquid solvent: The ports locations must be carefully determined so that a total drainage is rapidly completed.

The variable costs gather energy and fluids (carbon dioxide and cosolvent when required). On small- and medium-scale units, energy is not so expensive, especially when heat is supplied by steam available on site or hot water heated by fuel or gas; electrical heating is the most flexible but should be limited to small-scale units. Regarding CO_2 consumption of SFE units, it is mainly due to extractor depressurization at the end of the extraction cycle: At first, the fluid is recycled until the pressure reaches the CO_2 reservoir pressure ($\sim$45 bar); then the fluid is vented to the atmosphere, leading to a loss of a mass (in kg of CO_2) approximately equal to 120 V (V in m^3). In areas where CO_2 is expensive and for very large scale units ($V_T > 1$ m^3), it may be valuable to use a recompression unit to recover this carbon dioxide and recycle it. Regarding SFF, CO_2 consumption is mainly related to entrainment in extract and raffinate; according to SEPAREX technology, both streams are depressurized step by step with recycling of CO_2 after a first depressurization step at $\sim$50 bar; this dramatically reduces CO_2 consumption that can be evaluated at $\sim$0.1 kg/kg of feed processed in the unit. It is to be noticed that, for both SFE and SFF, the variable costs are significantly increased when a cosolvent is required, because of cosolvent losses and cosolvent recovery from spent material or raffinate and extracts.

Maintenance cost shall not be underestimated! Industrial production on high-pressure equipment requires a high reliability with drastic safety requirements because hazards must be eliminated: This requires a *preventative* maintenance because many parts must be inspected and changed periodically; moreover, a rigorous operation plan must be enforced to eliminate any risk of deterioration of the basic parts, and safety sensors must be continuously logged. Preventative maintenance and inspection first concern the high-pressure pump(s) (check valves and membrane(s) are highly sensitive to abrasion or perforation by solids), autoclave closure systems and gaskets (to prevent solvent leakage), and baskets (external gaskets to avoid solvent bypass; sintered disks to detect deformation prior to rupture due to plugging). Of course, pressure vessels must be inspected and submitted to pressure tests according to official standards. Moreover, the main process valves must be often checked because they are the key to safe operation during autoclave opening for raw material change. Sensors must be recalibrated periodically, in comparison with traceable reference sensors, and data logging validated.

Finally, I would stress the fact that maintenance is eased when a great attention is paid to a few “details”: Raw material granulometry is a basic requirement for reliable operation of SFE, because the presence of fine particles may plug the basket sintered disks that will subsequently deform or even rupture, causing powder entrainment throughout the plant; on the other hand, a performant extract–solvent separation is necessary to avoid entrainment of some fraction of extract (or powder in PA units) through the fluid recycle loop; finally, an efficient cleaning should be frequently operated to eliminate cumulative deposition in the piping and instruments.

Conclusion

Although extensive R&D investigations have been carried out worldwide for more than 25 years, it is disappointing that supercritical fluid applications have still been limited to few areas and it is not certain that development will rocket soon. However, this should not lead one to give up the numerous opportunities coming up now, from food ingredients and nutraceuticals to pharmaceuticals, from biological applications and pollution abatement to new materials manufacture. As for many new technologies, probably too optimistic forecasts and uncontrolled technical announcements have rendered potential users rather skeptical after having been promised so attractive solutions...far from economic feasibility! May I repeat once more that supercritical fluid processes are not always the best answers but should be considered as alternatives among others, with their own advantages and limitations.

For me, it is false both to underestimate the final operating cost—as promised by some inexperienced workers on the field—and to overestimate it because this high-pressure technology continues to appear “exotic” to many engineers. As demonstrated here before, large-capacity plants, with optimized design and operation, lead to prices that are very often, and surprisingly for many people, of the same order of magnitude as those related to “classical” processes submitted to similar constraints in terms of environmental and consumer protection. Moreover, there are also cases where supercritical fluids permit one to make products or operations that cannot be realized by any other means.

Whatever will be the difficulties and delays, I am confident that the global trend to “green” technologies is creating favorable conditions to move to supercritical fluid solvents and reaction media.

Thousands of documents may be cited! We just cite a few basic references to help the reader to enter the field.

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