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SUPERCRITICAL FLUID TECHNOLOGY

Potential in The Fine Chemicals and Pharmaceutical Industry

by

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** Please note: All Tables and Figures at end of Text.*

Introduction

Separations are essential operations in many a process for the manufacturing of fine chemicals and pharmaceuticals; its prime function is to meet specifications of raw materials, intermediates and end-products, by-products and effluents.

The vision which directs efforts for improvement of the chemical manufacturing can be characterised as with *"Zero-Loss Operations"*.

"Loss" not only refers to material loss, as results from less-than-perfect selectivity of chemical conversions, but also to thermodynamic loss. Minimization of this energy loss is important with regards to energy use.

A transformation with minimized energy loss saves non-renewable energy resources and limits emissions of carbon dioxide.

In particular those separations which are thermally driven can be targeted as major areas for continuous improvement. These separations are distillation, extraction and absorption; all require heat input for recovering of products and solvents/absorbents.

Especially in the fine chemicals and pharmaceutical industry, materials to be processed can be sensitive to heat; desired specifications might deteriorate as a result of these thermal treatments. It is therefore desired to limit exposure time, or avoid thermal burdens at all.

Separation processes which could meet those requirements are therefore much desired; the use of Supercritical Fluids may contribute here on a significant scale.

I believe the SCF technology offers new and exciting opportunities, not as a substitute for, and competing with existing technologies, but specifically in those areas where the typical properties of SCF-s can be uniquely applied, thereby offering new product or product modifications which cannot be made otherwise.

This requires the renewed focus for the SCF technology, which has become apparent during the last years. In this workshop I shall stress those new SCF-typical applications.

The supercritical state of a fluid is determined by its temperature; at a temperature above the Critical Temperature (T_C) the fluid is supercritical. The second condition is set by the fluid pressure; strictly speaking a fluid is supercritical only at pressures above its critical pressure (P_C).

This so-called Critical Point (CP) represents the end of the saturated vapour pressure curve in the P-T diagram.

The area of interest for SCF technology is basically located slightly above the CP; in this range largest changes in fluid properties occur with relatively minor variations of T and P.

As an illustration Table 1 present critical data of some selected compounds. The choice of CO_2 as a prime SC fluid is partly due to its critical temperature, which is slightly higher than room temperature. As can be seen there exist several other components with T_C values around the ambient level; this broadens the application of SCF technology since the choice of fluids is not strictly limited to CO_2.

Other arguments for choosing CO_2 for food and pharmaceutical applications is its non-toxic, non-flavour, non-flammable and environmental-friendly character; CO_2 is readily available and is a natural product. Low concentrations of CO_2 that might remain in the products in general do not cause harm when consumed by humans or animals. This is not the case for some of the other SCF-s. Specifications suggested for CO_2 are listed in Table 2.

As said, the physical properties of SCF-s vary readily with only minor changes in pressure or temperature. This is illustrated in Figures 2 and 3 which show that density, viscosity and self-diffusivity changes dramatically when passing through the critical pressure, at a temperature slightly above T_C. These properties are important for separation processes because of the same affect rate of mass-transfer and solvent-character of CO_2.

SCF-s hold an intermediary position between pure liquid and pure gaseous state; depending on the pressure and temperature of the SCF the fluid has *"liquid-like"* densities, which favours solubility of solutes, but is more *"gas-like"* for diffusivity and viscosity. This favours the use of SCF as an extraction agent with excellent transport properties.

The attraction of SCF-s in separation is principally due to its ability of increasing the volatility of substances at temperatures far below its normal boiling point or its temperature where unwanted thermal deterioration may occur.

Figure 4 illustrates this volatility (or solubility) enhancement for sitosterol in SC CO_2. The solubility of CO_2 for sitosterol can be tuned by adjusting pressure and or temperature.

Sitosterol dissolved to saturation in CO_2 at 500 bar and 80 C precipitates from this SC solution when the temperature is lowered at constant pressure or when the pressure is lowered while maintaining 80 C.

Sitosterol can thus be extracted from a matrix and recovered from solution by adjusting pressure and or temperature.

Solubility characteristics differ for particular components with temperature and pressure and this provides the basis for extraction selectivity; by adjusting pressure and temperature one component might be volatilized more strongly over the other component and hence preferentially extracted.

Alternatively one component might precipitate from solution preferentially over the other component and hence be recovered in enriched concentration.

This provides the means for fractionative extraction.

SCF Extraction Processes

Application of SCF-s has traditionally been focussed on its use as solvent for extracting valuable components from solid matrixes. To my knowledge the largest single application which has reached commercial practice is the production of decaffeinated coffee beans.

The incentive was to replace chlorinated solvents which were considered environmentally unfriendly (destruction of atmospheric ozone) and to avoid traces of solvents in the extracted beans; same are not suited for human consumption and may affect the coffee flavour adversely.

Maxwell House Coffee Co. (General Food Corporation) opened a SC CO_2 caffeine extraction plant in 1990 in Houston, with a capacity of 50 million lbs/year of beans; a 60 million lbs/year extraction plant was already in operation in Germany. Green beans, before roasting are contacted at 90-100 C with SC CO_2 of 4000 psig; removal of caffeine reaches 97%. A flow of SC CO_2 is passed through a charge of beans, placed in a pressure vessel.

The caffeine-loaded CO_2 leaving the pressure vessel is contacted with water in a pressure absorber; here caffeine dissolves in water and the caffeine-free CO_2 is returned to the extractor. The extraction process however is more complicated than explained here; the humidity of SC CO_2 and of the beans play crucial role. Humid CO_2 extracts only the desired caffeine and leaves aroma substances retained in the beans.

But by careful control of the system's humidity caffeine can be selectively extracted and the extract has a quality superior over caffeine extracted with water/methylene chloride.

Batch VS Continuous Operations

Extraction of coffee beans and hops is a batch operation; the extractor is cleaned, charged with material and pressurized before the extraction starts. At the end of the extraction the extractor is depressurized, and the extracted material is taken out. Special quick-closure systems have been designed which enable fast extractor (dis-) charging; systems which allow beans to be fed continuously into a pressurized extractor, without damaging of beans, do not exist.

However, solids feeding systems operating continuously will be needed in order to make SCF technology attractive for larger-scale applications such as vegetable seed extractions. Work in progress is based on an extruder which crushes the seeds and forms thus a gas-tight plug. This plug is continuously forwarded into the pressurized extractor. A problem to be solved exist at the outlet of the extractor where solids must be taken out without loss of compressed gases.

Since the seeds need to be broken anyway in order to bring about intensive contact between solvent and seeds, the extruder technique might be useful for this application.

SCF Solubility Enhancement

Although the solubility of solutes in SCF-s are enhanced with pressure, SCF-s remain poor solvents; solubilities commonly do not exceed several % wt, but are in many cases less than 1% wt. To increase this one adds so-called entrainers; these are components which dissolve more readily in the SCF and enhance the solubility of the solute to be extracted.

Examples are the lower alcohols, aceton, alkanes, etc. which are effective entrainers for SC CO_2. Entrainers often effect also the selectivity of extractions.

This entertainer effect explains also why solubilities of single components in SCF-s can be different from solubilities of the same components but now present as mixture. The presence of one solute modifies the solvent properties of the SCF, so that solubility of a second component is markedly effected.

Presence of entrainers complicates the separation process, since the entrainer-solute mixture, which is recovered from the SCF, needs further separation.

Extraction of Liquids

- **Batch Extraction**

  Autoclave is charged with liquid

  SCF is passed through liquid

  Extract is recovered from solution by change of temperature and/or pressure

  Enables fractionation of extract