

phaseX

The Supercritical Fluids People

Supercritical CO₂ Extraction of Nutraceutical Products

1. Supercritical Fluid Extraction-Current Status

Supercritical fluid extraction, especially with supercritical CO₂, has progressed from its position as solely a laboratory curiosity of the 1960s to today's very large scale commercial operation in the foods and beverages sectors. Coffee and tea are being decaffeinated at more than 150,000 Tons/yr in plants in the US and in Europe, and hops (for flavoring beer) are being extracted at levels of more than 50,000 T/yr in supercritical CO₂ plants in Europe, US, and Asia. Information about long term operation of high pressure supercritical extraction plants, the superior taste characteristics of supercritical CO₂ decaffeinated coffee and tea, higher yield CO₂ extracts from hops, and the markets perception that CO₂ extracts are "better" has motivated the application of supercritical CO₂ to a wide range of botanical and biological substrates, especially to nutraceuticals and essential oils. A cursory examination of the products at nutritional stores and scrutiny of the contents listed on the labels points out the many, many products that contain or consist of supercritical CO₂ extracts; many of the components in the extracts are lipophilic, but supercritical fluid process variants also produce extracts with more polar compounds, such as anti-oxidants, isoflavones, and other glycosides.

Today a score of supercritical CO₂ extraction plants that process spices, essential oils, and nutraceuticals are in operation in many countries throughout the world. The plants process phytosterols, carotenes, xanthophylls, specialty lipids, and anti-oxidants, from botanical, biological, and marine sources.

2. Solubility In Supercritical Fluids

First discovered by two Scottish researchers in 1879, a gas raised to pressure, temperature conditions above its critical point, becomes a solvent with a pressure-dependent dissolving power, the higher the pressure, the higher its dissolving power. In 1955 a seminal paper (by Princeton researchers) articulated industrial process applications for this pressure dependent solvent behavior: A compound could be extracted from a mixture using a gas (i.e., a supercritical fluid), the pressure could be lowered to precipitate and recover the compound, and the gas could then be repressurized and recycled to continue the extraction until it was complete.

It is exactly the process operation described in the 1955 paper that 20 years later was applied to botanical raw materials such as coffee, tea, hops, spices, and still others, using supercritical CO₂ to produce superior products.

Because of its low critical temperature (of 31°C) CO₂ is ideally suited for processing heat sensitive or difficult to concentrate compounds, such as polyunsaturated fatty acids (e.g., GLA, EPA, DHA), carotenoids (β-carotene, lutein, astaxanthin), phytosterols from plant sources, among others.

The extraction process concept is easily explained using solubility data of triglycerides (TG) in supercritical CO₂. Figure 1b gives the solubility data and Figure 1a is a schematic diagram of a supercritical fluid extraction process. Taken together they show how a gas like CO₂ can extract, concentrate, or purify materials while at the same time produce an extract product (or the residual biomass substrate, if that is the product) with no solvent residues.

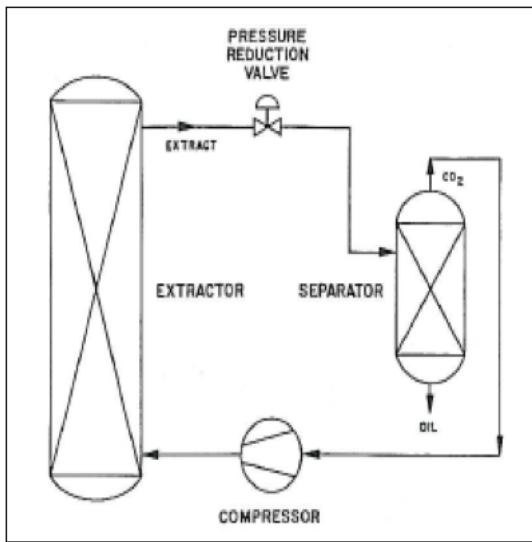


Figure 1a. Extraction Process Schematic

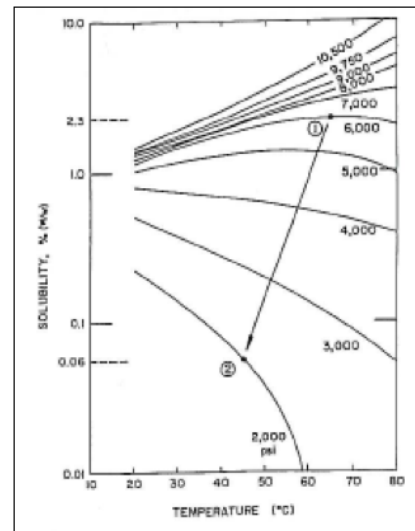


Figure 1b. Solubility of Triglycerides in CO₂

For purposes of explanation assume the extraction vessel in Figure 1a has been charged with a TG-containing substrate, for example, evening primrose seeds containing GLA. Supercritical CO₂ is passed through the (crushed) seeds, and for concreteness of discussion, at 6000psi, 65°C. As the CO₂ passes through the bed; it dissolves GLA until the solubility limit is reached, 2.3%, at Point 1 of Figure 1b. The CO₂ stream, with dissolved GLA, is then expanded through the pressure reduction valve to Point 2, 2000psi, and the directed arrow 1-2 shows the pressure reduction path. (The temperature of the CO₂ drops to 45°C as it flows through the valve.) Importantly, when the CO₂ stream is reduced in pressure, the solubility of GLA is reduced (to 0.06% at Point 2), and the precipitated oil collects in the separator. The CO₂ leaving the separator is recompressed to 6000psi, the temperature adjusted to 65°C, and the extraction continues until all the GLA is extracted from the seeds and has been collected in the separator. (The separator vessel can be drained of its oil contents, periodically, if desired.)

When the vessel is depressurized and the spent charge is removed, no CO₂ remains in the oil-free seeds, and similarly when the extracted GLA is transferred from the separator to a container, no CO₂ remains in the oil. Products such as hops, saw palmetto, astaxanthin, and others are produced in this quite simple-to-operate process that is environmentally conscious and GRAS. Furthermore, because not all components in a botanical substrate will exhibit identical solubility characteristics, the pressure dependent dissolving power of CO₂ can be fine-tuned to separate or concentrate active species that are present in the natural product raw material.

3. Nutraceutical And Natural Extract Products

Even a cursory examination of bottles on the shelves of stores like The Vitamin Shoppe, Whole Foods, GNC, etc., results in the generation of a long list of products containing supercritical CO₂-extracted ingredients: anti-oxidants from tumeric, clove, ginger, sage, oregano; lipids such as gamma linolenic acid (GLA), from evening primrose, docosahexaenoic acid (DHA) and eicosapentaenoic (EPA) acids from marine and algal sources, fatty acids from saw palmetto; carotenoids from algal vegetable, and marine sources; and still other compounds from sources such as valerian, garlic and cinnamon.

It is informative and interesting to relate a positioning statement from one manufacturer's label: "Supercritical means super purity, super potency...". From a technical standpoint the phrase, most probably crafted for its marketing impact, is quite accurate: Because of the selectivity that can be conferred to a supercritical fluid by virtue of pressure tuning, supercritical CO₂ extracts only those components from the botanical raw material that are dissolved at the selected pressure, and various fractions of concentrated (and potent) actives can be collected at different pressure levels. Such concentration cannot be achieved with a single liquid extraction solvent.

Several illustrative examples of materials extracted from botanical and biological substrates with supercritical CO₂ are presented.

a. Concentration of Astaxanthin from Microalgae

Organic solvents, such as acetone, have been used industrially for the extraction of astaxanthin from microalgae. The extract consists of triglycerides and astaxanthin. The maximum concentration of astaxanthin in the extract is limited because acetone cannot separate the carotenoid from the triglycerides. The total lipid content (triglycerides plus astaxanthin) of *Haematococcus pluvialis* varies from about 25% to 45%. With organic solvent extraction a 2.5% astaxanthin, 35% lipid content algae will produce an extract product containing a theoretical maximum of about 7.8% astaxanthin (because acetone extracts the triglycerides and astaxanthin at essentially the same rate). Because the dissolving power of supercritical CO₂ can be tuned by the pressure level, and since triglycerides and astaxanthin do not exhibit identical solubility profiles, triglycerides and astaxanthin can be separated to increase the concentration of astaxanthin in the product.

Figure 1 shows a sample of *H.pluvialis* feedstock, and in the vial a 14% astaxanthin concentrate.



Figure 1. Sample of *H. pluvialis* algae and astaxanthin concentrate

The table gives results from selected plant runs at Phasex. The fourth column compares astaxanthin concentration in the product via acetone extraction.

Astaxanthin Concentration Factors

Astaxanthin Content of Microalgae	Lipid Content of Microalgae	Concentration in Astaxanthin in product	Asta Content of Acetone extract (for comparison)
2.4%	28.4%	14.3%	8.5%
1.9%	26.6%	13.4%	7.1%
2.2%	27.6%	13.5%	8.0%
2.8%	26.3%	16.3%	10.6%
3.9%	33.7%	20.1%	11.6%

b. Concentration of γ -Oryzanol from Rice Bran Oil

The list of anti-oxidants determined to be efficacious in the body is long: γ -oryzanol is among them.

Rice bran oil (extracted with hexane from rice bran and from which the hexane has been evaporated) contains from about 1½ to 2% γ -oryzanol. Supercritical CO₂ is very advantageously applied to this concentration opportunity, and the results are presented in a series of liquid chromatograms. Figure 2 is an HPLC of the rice bran oil feedstock.

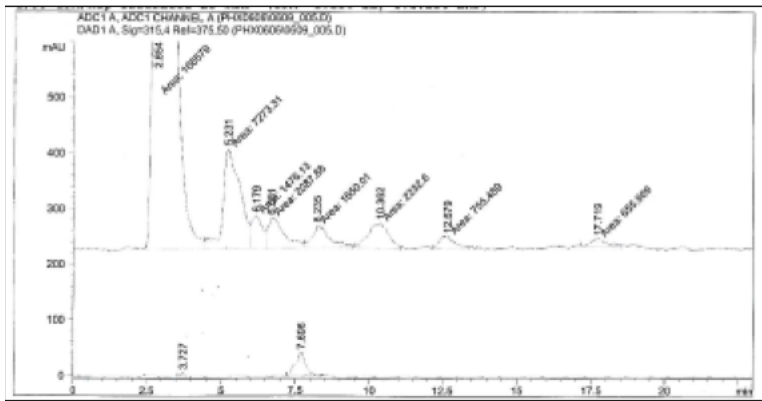


Figure 2. HPLC of Rice Bran Oil Feed

Two analytical detection devices were used to measure γ -oryzanol: UV and ELSD. (ELSD, the top chromatogram in the figure detects total mass; UV, the bottom chromatogram, detects a chromophore; the oil components, viz., triglycerides, free fatty acids, phytosterols, do not possess a chromophore, and thus UV detects only γ -oryzanol. γ -oryzanol elutes at 7.5min.)

In counter-current column operation supercritical CO₂ extracts almost solely the triglycerides and free fatty acids (because at the pressure used the more polar compounds do not dissolve). A chromatogram of the extract is shown in Figure 3, and the UV detector, bottom chromatogram, sees nothing, the ELSD measures the composition to be triglycerides and free fatty acids.

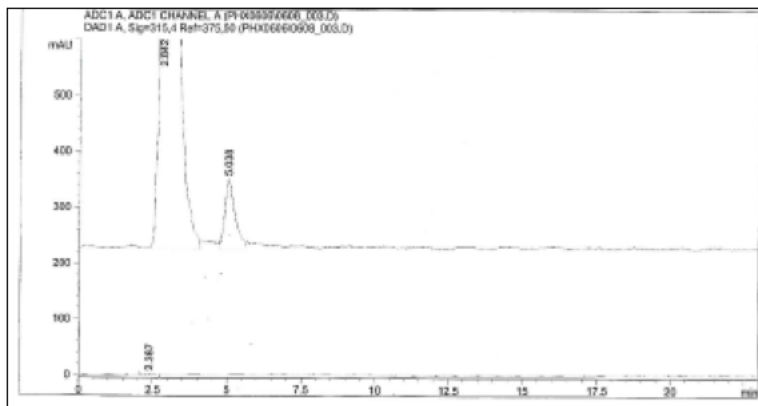


Figure 3. CO₂ Extract of Rice Bran Oil

Figure 4 gives the composition of the product.

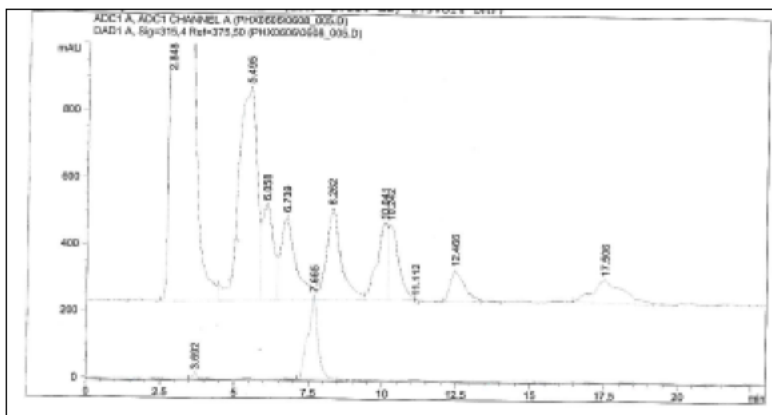


Figure 4. γ -Oryzanol Product

The UV chromatogram (as well as ELSD) shows that γ -oryzanol concentration has been increased 7-fold, from 1.63% in the feed to 11.73% in the product. (Incidentally, and importantly, hexane residues have been stripped from the products during processing in the counter-current column.)

Many more examples could be given where supercritical CO_2 is used to replace organic solvents for extraction or to produce compositions that cannot be obtained with organic solvents. After more than 25 years of proven operation and with increasing emphasis on “green” processing, supercritical CO_2 extraction is being recognized today as “traditional” technology far removed from its former position as a laboratory curiosity.

c. Extraction of Phytosterols from Agricultural Feedstocks

Many agricultural grasses and pollens contain phytosterols in amounts that range from $\frac{1}{2}$ to $1\frac{1}{2}$ percent by weight; if they could be extracted and concentrated economically, these feedstocks represent a vast source of supply of these nutrients.

In this case again extraction with supercritical CO_2 concentrates the phytosterols to a greater degree than an organic solvent can while producing a solvent-free extract and simultaneously a solvent-free spent biomass that can be used in further extraction operations (with aqueous ethanol, for example, for more polar compounds, which themselves can now be concentrated).

Phytosterols concentration factors from selected runs and campaigns in the Toll Processing Plant are given in the table.

Phytosterols Content

Feed	Extract
0.57	7.65
1.93	37.62
1.41	31.84

20-fold concentration of phytosterols is typical.

4. About Phasex Corporation

Phasex Corporation, founded in 1981, is internationally recognized for its development of improved products and superior separations processes using supercritical fluid technology. The company is staffed with a team of problem-solving chemical engineers, chemists, and manufacturing specialists. Phasex offers laboratory feasibility testing and process optimization, product development, toll processing, and licensing for all sectors of industry. Phasex has state-of-the-art facilities for developing supercritical fluid processes from laboratory scale to manufacturing. The company's equipment includes bench scale extraction systems for processing materials from the grams to kilograms level, and two production plants capable of processing liquid and solid feedstocks in multi-ton campaigns. Electrical code rating, Class 1, Division 2 permits organic co-solvents to be used, if required.

Phasex directs the attributes of supercritical fluids to the solution of difficult processing problems for the natural products, pharmaceuticals, polymers, and fine chemicals industries, especially for those products that cannot be processed easily by industry's traditional processes. Currently the Toll Processing Plant extracts phytosterols from pollens, astaxanthin from *H. pluvialis*, and several anti-oxidants and phospholipids are being concentrated from herbal and marine sources.

The complete absence of solvent residues in products is becoming increasingly recognized as an important attribute of supercritical fluids, especially for products for human consumption, and supercritical CO₂ extraction is often referred to in the marketplace as a "solvent-free" process.

5. Closing Remarks

It has been lamented by some that processing with supercritical fluids is not economical, and, although deriving from (failed) applications tested in the 1970s, the general impression still, unfortunately, exists among chemists and chemical engineers that any supercritical fluid process is associated with high costs. However, supercritical CO₂-decaffeinated coffee is being sold competitive with ethyl acetate-decaffeinated coffee, and this fact certainly should contradict the impression that supercritical “anything” is expensive.

The misassociation of high cost with supercritical fluid processes undoubtedly derived from the fate of several widely publicized (but ill-advised) studies in the late 1970s, early 1980s, when their lack of industrial viability was attributed solely to “high processing cost” when, in actuality, there were technical limitations (that were not described). Supercritical fluids are frequently excellent solvents with far ranging applications to many purification problems, but they may, in fact, not be economically viable in every proposed application. The nutraceuticals, food supplements, essential oils applications are continually increasing in size and number because of their technical superiority and because of the positive image these products convey to consumers.

The logo for PhaseX, featuring the word "phaseX" in a bold, lowercase, red sans-serif font.

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