SUPERCRITICAL FLUID EXTRACTION AT HIGH PRESSURES (>700 BAR): THEORETICAL CONSIDERATIONS AND PRACTICAL APPLICATIONS

Jerry W. King*

GENESIS – Engineering Research Center
University of Arkansas
700 Research Center Blvd, Fayetteville, AR, 72701, USA

Abstract. Supercritical fluid extraction (SFE) at high pressures (700 bar or greater) has generally not been considered due to the perceived capital high capital equipment costs and limited benefits. Recent reported studies however have indicated that such extracts are enriched in important ingredients that can only be achieved under such conditions. This presentation will first theoretically correlate these observed enhancements with the physicochemical properties of the extraction fluid and the target solute(s) providing a rationalization as to the observed extraction enhancement based on solubility considerations. Literature results from both supercritical fluid extraction and chromatography indicate that distinct solubility maxima are achieved between 650 – 1000 bar pressure and that mole fraction solubility exhibit a parabolic dependence on extraction pressure. The decreasing difference in the cohesive energy densities as reflected by the relative solubility parameter differences between the solvent (fluid) and solute accounts for the solubility enhancement particularly when applied to bioactive solutes present at low concentrations in the target matrix. These optimized observed extraction results which are solute dependent occur at fluid reduced extraction densities between 2.00 – 2.50 which correspond to solute solubility parameters between 17.0 – 21.0 MPa$^{1/2}$. For solutes contained at low concentrations in lipid mixtures, a benefit may still arise at higher extraction pressures (>1000 bar) and with solutes having ~700 MPa cohesive energy densities. Extraction of solutes present at low levels in lipid mixtures, pigments from natural products, spice extractives containing capsanthin or piperine, etc. using higher pressures result in extracts that are multi-folded with respect to their target bioactive constituents. Polymers such as polyethylene glycols (PEGs) can be dissolved or co-extracted at these higher pressures along with the bioactive constituents to potentially yield an encapsulated extract for food or nutraceutical use. The application of this principle in terms of extraction plant cost and the value of the resultant extract will conclude the presentation.

Keywords: carotenoids, solubility maxima, solubility parameter theory, supercritical extraction, ultrahigh pressure

1. Introduction

Optimization of the conditions for supercritical fluid extraction (SFE) is critical to obtaining extracts which contain the desired compounds, particularly when extracting physiologically-active ingredients intended for use in the food and nutraceutical industrial sectors. Approaches utilizing supercritical fluid media have ranged from so-called "total or exhaustive" extraction to fractionation and enriched (folded) extracts enhanced with respect to specific "target" compounds. Historically, most SFEs have been conducted in the pressure regime of 100-450 bar (10-45 MPa) due to the attendant cost of the required high pressure processing equipment [1]. However SFE done at any set of chosen conditions of pressure and temperature discriminates with respect to components contained within the food or natural matrix – even exhaustive extraction using the above cited pressure range may enrich or deplete certain components contained in the starting material [2].

Recently the use of higher extraction pressures has been advocated, i.e., even pressures beyond 700 bar (70MPa), a pressure limit often advocated for the rapid extraction of seed oils and lipid mixtures [3]. Using higher extraction pressures, i.e., ultrahigh pressure SFE, has permitted the enhanced recovery of certain components within a natural product matrix that are marginally-soluble in SC-CO_2 at lower extraction pressures. For example, in the extraction of pigment moieties from some plant matter, it has been shown that a higher extraction yield of polar pigments like xanthophylls (such as lutein) relative to carotenoids (beta-carotene) can be accomplished. For these compounds exhibiting marginal solubility in SC-CO2, the application of ultrahigh extraction pressures has provided not only a better recovery from the natural product matrix, but perhaps a more authentic extract that is comparable to that obtained using organic solvents.

There is limited information in the literature on the extraction of natural products or solute solubility studies in this ultrahigh pressure range however some guidance is to be gleaned from the ancient studies of Stahl [4], Giddings and coworkers [5,6] and Friedrich et al in the area of oil seed extraction [7]. These studies were done at an "analytical" scale and are basic research. For example, the classic work of the Giddings group and Stahl team confirmed the solubility of various types of more polar and higher molecular weight solutes in SC-CO_2 and similar fluids, at high pressures up to 2000 bar (200MPa), but at very low solute solubility levels. Although this might seem insignificant from a processing point of view, one should consider the importance that these small amounts of compounds in natural product matrices can confer properties on the extract, such as their organoleptic, color, and antioxidant properties.

SFEs done at lower pressures, i.e., 100-450 bar can compromise the extraction of all of the components which occur in a natural product. For this reason, higher extraction pressures are being employed with SFE to obtain extracts enhanced, or folded, with respect to important ingredients. There are numerous examples of foodstuffs and natural products extracted on a laboratory scale up to 700 bar. Some examples from the industrial literature are: algae oil + pigments (750 bar), argun nuts (700 bar), chamomile (750 bar), caraway (700 bar), celandine root (700 bar), chili pepper (700 bar) cocoa polyphenols as well as press cake (700 bar), coriander (850 bar), dill seed (700 bar), earth almond (700 bar), evening primrose oil (700 bar), lecithin de-oiling (700 bar), hops (700 bar), marjoram (700 bar), oregano (750 bar), red paprika (750 bar), roasted peanuts (700 bar), rosemary (800 bar), roasted sesame oil (700 bar), thyme (750 bar), tomato peels (750 bar), and turmeric (800 bar).

Knez in conjunction with Uhde [8] report a slight increase in the maximum yield from sage at 1300 bar and 100 C with a S/F of approximately 60. A two-stage separator train was used with the first separator being held at 150-250 bar between 40 – 80^oC. This allowed a higher extraction with respect to the carnosolic acid content in the extract than could be obtained using a single vessel separator. Similarly for the extraction of rosemary at 1000 or 1500 bars, 60-80^oC, and S/F's = 20-60 (mass). A 10-folded extract with respect to carnoslic acid content could be obtained by using precipitation conditions between 100-300 bar and 40-60^oC when optimizing operation of the two vessel separator train; the other major bioactive components in rosemary were not changed. The terminal separator containing the odoriferous components, while the initial separator on a mass basis contained less mass of the total extract relative to the second separator vessel – but this is dependent on the collection temperature used with each separator vessel.

Extraction of carotenoids and their oxygenated analogues is faster at higher extraction pressures at an equivalent temperature. The more polar the natural pigment moiety is the more compromised its extraction into SC-CO_2 as demonstrated by Favati et al [9] as well as others. Using freeze-dried alfalfa leaf protein concentrate (LPC) as a test case, Favati et al demonstrated that 300 bar and 40^oC were sufficient for removal of 95% of the beta-carotene from the LPC; faster extractions being realized at even higher pressures. Lutein on the other hand, even at 700 bar and 40^oC. could only be recovered at ~ 70% level. In this study, solubility parameters for SC-CO_2 at 40^o C were estimated to be 5.57H (100 bar), 7.92H (300 bar), 8.66H (500 bar), and 9.12H (700 bar) (1H = 1 Hildebrand unit = 1 $cc^{3/2}/mole^{1/2}$, approx. 1H = 2.0455 $MPa^{1/2}$). The solubility parameters for beta-carotene and lutein are 8.71H and 10.0H, respectively, which rationalizes the lower extraction of the oxygenated lutein moiety with respect to the nearly complete recovery of beta-carotene as extraction pressure is increased. This trend has been confirmed in similar studies involving pigments, such as those of Steinhagen of Uhde [10] who reported mixed carotenoid extractions between 700 – 1500 bar at 40 – 60^oC using a 2 – separator train at a S/F = 40.

An enhanced yield of paprika "color" can also be affected at 750 bar and 65^oC in 20 minutes extraction time [11]. Nagy et al also reported on coriander extraction from 500 – 850 bar – the yield of extract and time of extraction being improved as extract pressure is increased. Based on a 10 wt. % yield of coriander extract – at 500 bar one needs about 75 kg CO_2 / kg-feed while at 850 bar only 26 kg-CO_2/ kg-feed is required. This means at the same specific mass flow rate that the extraction time at 850 bar is 1/3 that required at 500 bar. Similarly, Luetge et al [12] also studied the SFE of nut kernels at 40^oC over the pressure range of 300 – 1500 bar and demonstrated a decreasing S/F with increasing extraction pressure. At the maximum nut oil yield, an S/F ~ 80 was required at 300 bar, while at 1500 bar the S/F was 20. This has implications for the processing costs – at least a one-fourth reduction in cost can be realized in going from an extraction pressure of 300 to 1500 bar. We have also observed the same trends in extracting cottonseed oil in SC-CO_2 at 820 bar and 80^oC vs. 544 bar and 50^oC, where a reduction from 7 to 2 extractor bed volumes, and a much quicker extraction, resulted from conducting the extraction at the higher pressure.

It is obvious from the above that the application of higher pressures at the appropriate temperature can lead to higher solute solubilities and faster extractions when performing SFE. The question examined in this paper is how solute solubility trends with pressure - based on the solute's molecular structure - can influence the relative selectivity of solutes within the target matrix as higher level of pressure is applied. We note of particular significance, the occurrence of solubility maxima for many solutes, and their relative magnitudes can influence extraction behavior and final results while performing SFE at ultrahigh pressures. The prediction of what pressure these solubility maxima will occur, and their fundamental dependence on a solute's molecular structure, i.e., solubility parameter (δ) is the subject of this paper.

2. Theoretical and Experimental Approach

Space limitations in these proceedings do not permit a thorough discussion of the theoretical approach that is being evoked to rationalize SFE results obtained by applying ultrahigh extraction pressures. We use here advances in solubility parameter theory [13] to explain the extraction enhancement and selectivity which occurs at pressures beyond 700 bar (70 $MPa^{1/2}$). As suggested by Giddings [6], the solubility parameter of a critical fluid can be calculated using Equation 1 as:

$$\delta_{fluid} = 1.25(P_C)^{\frac{1}{2}}\left(\frac{\rho_{r,fluid}}{\rho_{r,liquid}}\right) \tag{1}$$

where δ_{fluid} = solubility parameter of the fluid at a specific pressure and temperature
P_c = critical pressure of the fluid
$P_{\text{r, fluid}}$ = reduced density of the fluid at a specified P_c and T_c
$P_{\text{r, liquid}}$ = reduced density of the fluid under liquid conditions (~2.6 – 3.1)

The δ_{fluid} at any pressure and temperature can be calculated using a plot or equation relating reduced thermodynamic variables as well as the P_c of the subject fluid.

Solute solubility parameters, δ or δ_o, can be obtained by several methods or sources. In this study, the group contribution method of Fedors [14] has been employed. In addition, three-dimensional solubility parameters (HSP's) as defined by Equation 2 below:

$$\delta_T^2 = \left(\frac{E_d}{V_m}\right) + \left(\frac{E_p}{V_m}\right) + \left(\frac{E_h}{V_m}\right) = \underbrace{\delta_d^2 + \delta_p^2 + \delta_h^2}_{\text{HSP's}} \tag{2}$$

where the total δ_T^2 is equal to sum of the squares of the component solubility parameters, δ_d, δ_p, and δ_h representing the dispersion (d), polar (p), and hydrogen bonding (h) internal energy contributions, respectively, and V_m is the molar volume of the fluid at the designated pressure and temperature - have also been utilized.

The condition for maximum solubility between a solute and a solvent (fluid) is given in Equation 3 below:

$$\delta_{\text{fluid}} = \delta_o \tag{3}$$

and the condition for miscibility between the solute and the fluid is approximated by Equation 4 as:

$$(\delta_{\text{fluid}} - \delta_{\text{o}}) \sim 2.5\ \text{cal}^{1/2}/\text{cc}^{3/2} \text{ or } 5.11\ \text{MPa}^{1/2} \tag{4}$$

The temperature correction for the δ postulated by Jayasri and Yaseen [15], given in Equation 5, is calculated as follows:

$$\frac{\delta}{\delta_{ref}} = \left(\frac{1-T_r}{1-T_{r,ref}}\right)^{0.34} \tag{5}$$

where δ_{ref} is a reference solubility parameter at a reference reduced temperature, T_{ref},

The temperature dependence for the three-dimensional solubility parameters: δ_d, δ_p, and δ_h are provided by Equations 6, 7, and 8, respectively:

$$\frac{\delta_{d,ref}}{\delta_d} = \left(\frac{V_{ref}}{V}\right)^{-1.25} \text{(6)};\ \frac{\delta_{p,ref}}{\delta_p} = \left(\frac{V_{ref}}{V}\right)^{-0.5} \text{(7)};\ \frac{\delta_{h,ref}}{\delta_h} = \exp\left[-1.32*10^{-3}\left(T_{ref} - T\right) - \ln\left(\frac{V_{ref}}{V}\right)^{0.5}\right] \text{(8)}$$

where V_{ref} is the molar volume at the reference reduced temperature, T_{ref}, and V is the molar volume at the particular temperature of extraction. Equations 6, 7, and 8 can be applied to both solute and solvent (fluid). It is assumed that the effect of pressure on the solute molar volume is negligible, although this can be corrected for if P-V-T data is available for the solute [16].

For the figures taken from the Bowman thesis [17], the following equations apply:

$$\ln I = V_o/RT\left(2\delta_o\delta_{fluid} - \delta_{fluid}^2\right) \tag{9}$$

and I = solubility enhancement factor

Solubility measurements made in supercritical fluids over a large range of pressure have been shown to be correlated by a parabolic equation, Equation 10 as:

$$\log x_2 = a\delta_{fluid}^2 + b\delta_{fluid} + c \tag{10}$$

where x_2 = mole fraction of the solute in the fluid phase , and a, b, and c are least square fit parameters for the parabolic equation.

If we equate Equations 9 and 10, then we can obtain the solute solubility parameter, δ_o, from the least square fit parameters, a and b, as:

$$\delta_o = -b/2a \tag{11}$$

As noted in the Results and Discussion section, solute solubility parameters can also be obtained using inverse gas chromatography (IGC) experiments as described in our previous studies [18], where the solubility parameter of solute is obtained either from the slope or intercept of the following equation, Equation 12, as:

$$\left(\frac{\delta_1^2}{RT} - \frac{X}{V_1}\right) = (2\delta_2/RT)\delta_1 - \left(\frac{\delta_2^2}{RT} + X_s/V_1\right) \tag{12}$$

and δ_1 = solubility parameter of the injection probe solvent, $\delta_2 = \delta_o$, R is the gas constant in appropriate units, and V_1 = molar volume of the probe solute corrected for temperature, and X_s = entropic contribution to the interaction parameter.

3. Results and Discussion

As commented in the Introduction section, SFE using higher extraction pressures potentially can result in a more authentic extract containing enrichment of key ingredients, but an understanding of how to optimize the process is needed. Table 1 lists the solubility parameters calculated by the group contribution approach for several classes of compounds found in many seed oils. This list is not exhaustive but shows in general that the solubility parameter for long-chained fatty acids can span over 1-1.5 $MPa^{1/2}$ or more between individual acids found in seed oil mixtures. Minor components such as sterols, tend on the average δ's that are higher than the fatty acids, making them somewhat more difficult to extract and separate during SFE. Relative to these two groups, the ubiquinones on the principle are slightly less polar requiring less pressurization of the CO_2 to reach the condition where $\delta_{fluid\,=}\,\delta_o$. Carotenoids and xanthophylls on the other hand require even higher pressures for their optimal extraction, but note that between members of this solute class, their δ's differ depending on their molecular structure features such as polarity and alkyl chain length, and particularly the presence of the hydroxyl moiety. Phospholipids as a general lipid class tend to have even higher δ's and experience has shown that even at 700 bar, they have limited solubility in SC-CO_2 [19]. Hence knowledge of a compound's solubility parameter can provide useful information as to their relative extractability into SC-CO_2.

However there is some risk in using the group contribution method of calculating solubility parameters based on the assumption that one compound present in the matrix is representative of a like mixture of these compounds in the matrix to be extracted. The use of three dimensional δ's provides a somewhat improved accuracy that is equivalent to a compound's δ determined by traditional solubility studies [20]. We have found that for natural product mixtures, such as oilseeds, wax esters etc., that a convenient way of determining the δ of the mixture is to employ inverse gas chromatography (IGC) [21,22]. Our experience has shown that IGC δ's tend to more accurately reflect the overall cohesional energy density of natural product mixture as well as providing information on its temperature dependence. Examples of the δ's of such mixtures are shown in Table 2, and in general tend to be somewhat lower than using a δ for a specific component in the mixture via the group contribution approach. The solubility parameter calculated for the principle component found in jojoba oil (the C_{42} ester) by the Fedors method is all most 2 $cal^{1/2}/cc^{3/2}$ greater than the values listed in Table 2, but more accurately reflects the lower extraction pressures required relative to those utilized for the optimal SFE of soybean oil. These δ's determined over an extended temperature range can be extrapolated to lower temperatures, but caution should utilized if the mixture undergoes a phase change at lower extraction temperatures. The range of values listed from the independent study of Adamska et al [23] for polyethylene glycol polymers (PEGs), also known commercially as Carbowaxes, provide a rationalization and quantitative explanation as to the need for higher extraction pressures when using SFE. More will be noted on this later.

Examples of how solubility parameter can be used to rationalize and design optimal extraction conditions for the SFE of natural product mixtures are shown in Figures 1,2, and 3. Figure 1 is a graph showing the δ trends for CO_2 under pressure as a function of temperature up to 100 MPa (1000 bar), as well as the δ's of components commonly found in spices as calculated by a 3-dimensional group contribution method [24]. As previously noted, $\delta_{fluid\,=}\,\delta_o$ is the condition of optimal extraction of a given target solute, however solubility parameter theory predicts that under the criterion, $(\delta_{fluid} - \delta_o) \sim 2.5\ cal^{1/2}/cc^{3/2}$ or $5.11\ MPa^{1/2}$, that miscibility and hence partial solubilization of the target solute will occur at lower pressures. Note that by applying this criterion in Figure 1 to the solutes, β-carotene and lutein, one can expect to see a substantial extraction of β-carotene into CO_2 between 10-30 MPa which is what we have experienced in practice [9]. Similarly, lutein can be extracted at low levels in a natural product matrix, but requires higher pressures for both miscibility and solubility in SC-CO_2 (30 MPa). However what is most interesting with regard to both β-carotene and lutein, is their extractability improves with pressure, and can be optimized at pressures exceeding 60 MPa, where the δ for CO_2 is approaching and overlapping with the miscibility limit for these solutes.

Table 1. Solubility parameter of some lipid components present in seed oils.

Compound (Type)	Solubility parameter @ 25°C ($MPa^{1/2}$)
Fatty Acids	
Stearic Acid	18.66
Oleic Acid	18.74
Palmitic Acid	18.79
Linoleic Acid	18.82
Arachidonic Acid	18.85
Cervonic Acid	18.88
Linolenic Acid	18.90
Caprylic Acid	19.76
Sterols	
β-Sitosterol	19.4
Stigmasterol	19.5
Cholesterol	19.7
Ubiquinones	
Coenzyme Q10	17.90
Coenzyme Q6	17.94
Pigments	
β-carotene	18.15
Lutein Stearate Diester	18.5
Lutein Stearate Monoester	19.37
Lutein	20.51

Table 2. Solute solubility parameters determined by inverse gas chromatography (IGC) [18, 23]

Solute(s)	δ (Temperature Range)*
Soybean Oil	7.9 – 6.9 (58.7 – 123.4°C)
Jojoba Oil	6.8 – 5.6 (58.5 – 144.7°C)
Soybean Oil Methyl Esters	8.03 – 7.39 (49.9 – 85.1°C)
Glycerol	16.7 – 15.9 (51.5 – 110.6°C)
Polyethylene Glycol 2000 (Carbowax)	9.33 – 8.77 (85 – 105°C)

*δ in units of $cal^{1/2}/cc^{3/2}$

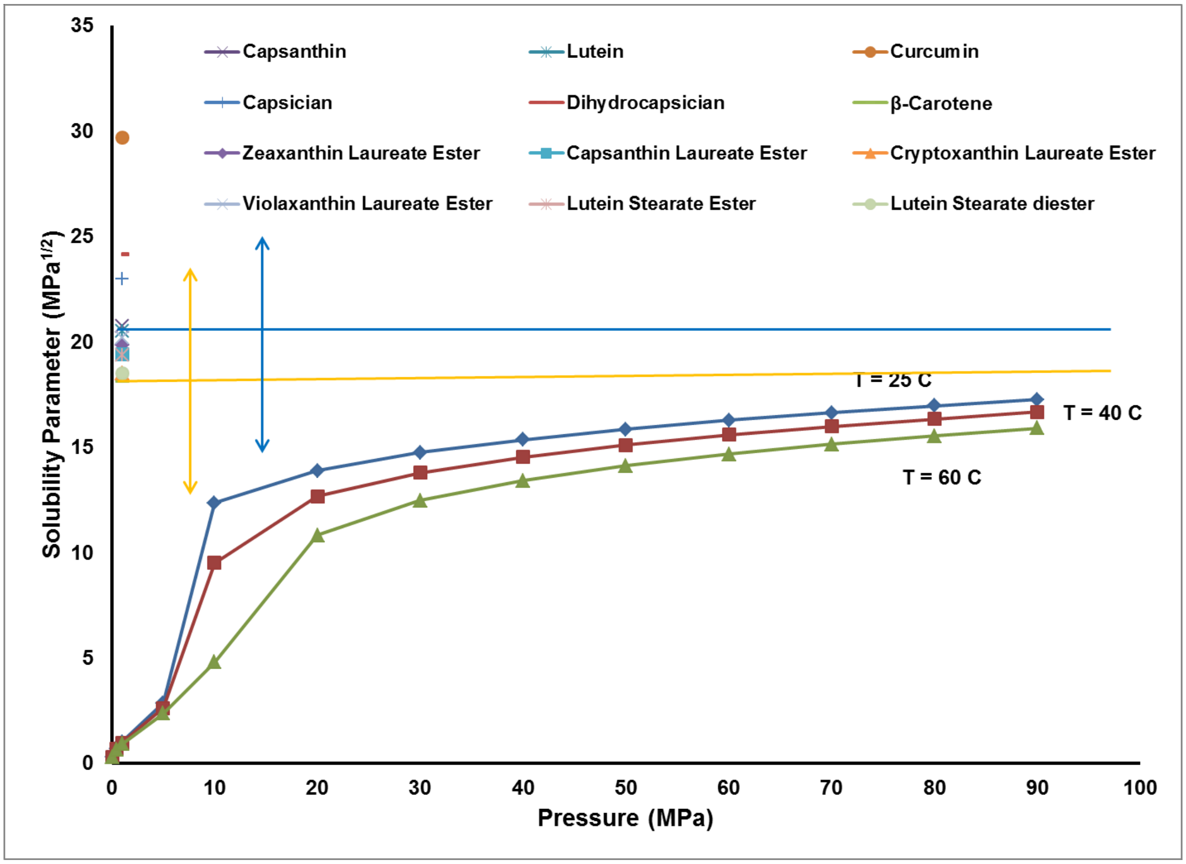


Figure 1. Solubility parameter of carbon dioxide as a function of temperature relative to the computed solubility parameters for various components found in spices (vertical axis) such as pigments and pigment esters.

Similarly, the SFE of astaxanthin, a high value pigment commercially derived from algae propagation [25, 26], can be optimized using a similar approach and rationalization. As shown below in Figure 2, astaxanthin extract is composed of astaxanthin containing two hydroxyl groups on the terminus of molecular structure (A), however the predominant species in naturally-occurring astaxanthin are the long chained alkyl esters (C_{14} and C_{16} – chain length esters). The presence of these less polar ester compounds in astaxanthin promotes their solubility in SC-CO_2 as shown in Figure 3. Here the respective solubility parameters have been plotted for the astaxanthin moieties (no temperature correction has been applied) as well as the temperature-pressure trends for CO_2. It can be seen based on the solubility parameter analogy (Figure 3), that as the δ for CO_2 approaches that of the astaxanthin moieties at lower temperatures and higher pressures, that miscibility and improved extractability of these components should be realized. Based on the trends depicted in Figure 3,

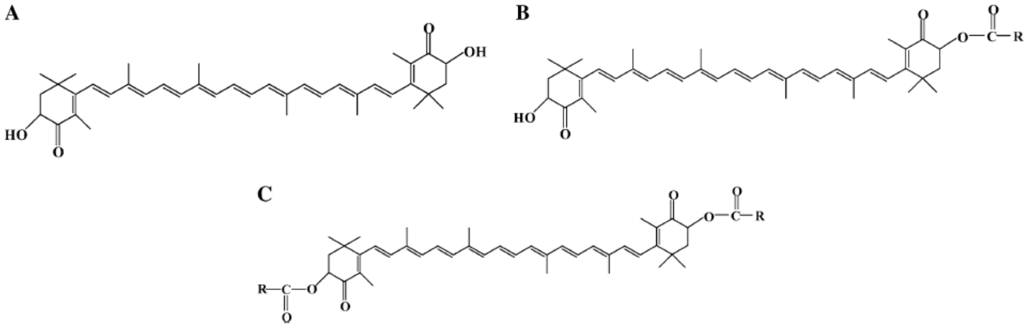


Figure 2. Structures of astaxanthin (A), astaxanthin monesters (B) and diesters (C). R, unsaturated or unsaturated alkyl chains.

solubilization of the principal component found in algae-produced astaxanthin (astaxanthin monopalmitate), should begin at about 50 MPa since the range of miscibility for the monoester spans from 15 – 25 $MPa^{1/2}$ based on the criterion stated in Equation 4. Further, this situation should only improve at higher extraction pressures as the solubility parameter for SC-CO_2 approaches that for the constituents found in astaxanthin extract at a pressure of 100 MPa or higher as shown below.

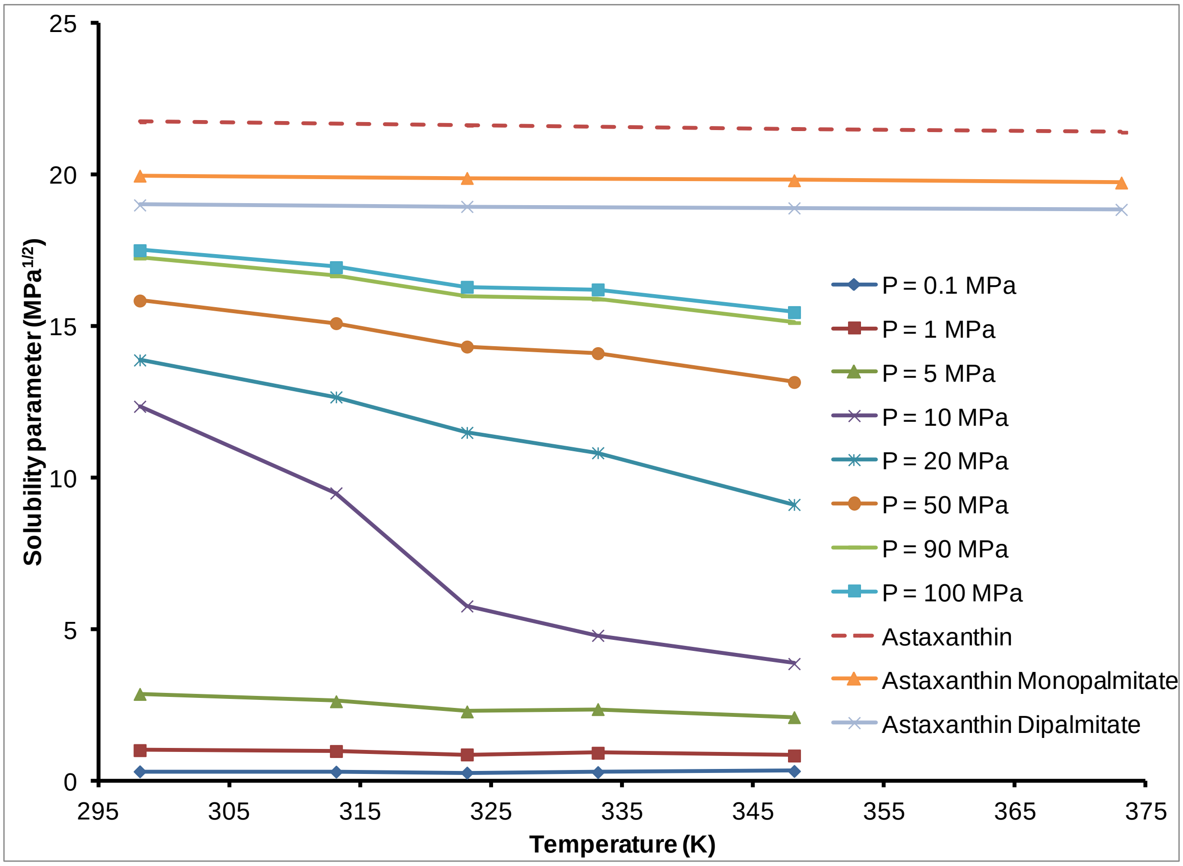


Figure 3. Comparison of solubility parameters of astaxanthin palmitate esters with that of SC-CO_2 as a function of temperature (here R_1 and R_2 are the palmitic acid groups).

This begs the question than, can we predict with reasonable certainty what might be the optimal pressure range for extracting target solutes? It has been known for some time that certain supercritical fluid-solute systems exhibited solubility maxima [27, 28], but to date little use has been made of the phenomena, and modeling of these solubility trends largely ignored. Actually the occurrence of solubility maxima in supercritical fluid systems is quite widespread, and in Table 3 we have cited a number of systems based on a survey of solubility studies in SC-CO_2 [29] and well known SC-CO_2 - lipid systems [30]. The criterion in citing these systems is based on the distinct occurrence of solubility maxima based on both mole and weight fraction solubility variance with pressure as a function of temperature, or systems where it was obvious that a maxima was being approached. The list in Table 3 is not all inclusive, but shows a number of SC-CO_2 – solute systems of varying chemical type in which solubility maxima varying between 185 to over 2000 bar. What would be welcomed is a way of predicting the approximate occurrence of these maxima perhaps based on the consideration of solute molecular structure. This then would allow for the optimization of solute solubility in SC-CO_2 and similar fluids as a function of pressure and temperature.

It is instructive to examine a few systems that have been studied over an extensive pressure range to forecast what possibilities exist by extending the pressure range for SFE. In this regard, the work of Czubryt et al [6] is acknowledged in Figure 4 where the solute solubility trend for four diverse solutes is plotted as a function or pressure up to 2000 bar at 40°C in SC-CO_2. Here for example, the solubility of stearic acid and

Table 3. Solutes which exhibit solubility maxima in supercritical carbon dioxide [29]

Acenaphthene (350 bar>)
Adamantane (~600 – 700 bar)
Aesculetin (~1500 bar)
Ametryne (~240 bar)
1-Amino-2-ethylanthraquinone (~300 bar>)
Aniseed Essential Oil (~100 bar)
1, 4-Bis(hexadecylamino)anthraquinone (~800 bar)
1, 4-Bis(octadecylamino)anthraquinone (600 - 800 bar)
1, 4-Bis(octylamino)anthraquinone (~800bar)
Rac-Boc-Piperazine (~200 bar>)
n-Butanol (~600 bar)
Capsaicin (~400 bar>)
Carbonyl-πcyclopentadienyl(tris (4-trimethylsilylphenyl)phosphine)cobalt (185 bar)
β-carotene (~500 bar>)
Castor Oil (~535 bar)
C.I. Disperse Black (~275 bar)
C.I. Disperse Blue 79:1 (~275 bar)
C.I. Disperse Brown (300 bar)
C.I. Disperse Red 60 (1000 bar>)
C.I. Disperse Red 137 (~300 bar)
Cyclotrimethylenetrinitraamine (~450bar)
Dotriacontane (>250 bar)
Ethyl Palmitate (>160 bar)
Fluorene (~450 bar)
Glycine (~1750 bar)
Heptacosane (~230 bar)
Hexacosane (~270 bar)
Hexamethylbenzene (>380 bar)
1-Hydroxy-2-(methoxymethyl)anthraquinone (~350 bar)
Imipramine Hydrochloride (~450 bar)
Iron tris(acetylacetonate) ((350 bar>)
Jojoba Oil (~580-600 bar)
6-Methylcoumarin (~200 bar)
Naphthalene (~300 bar)
m-Nitrophenol (~450bar>)
Octacosane (~280bar>)
L-Phenylalanine (~2000 bar>)
Prometryne (~250bar)
p-Quinone (~350 bar>)
Soybean Oil (~1250 bar)
Squalane (650-700 bar)
Lipid Oil Systems
Soybean Oil (~1000 bar)
Sitosterol (~820 - 850 bar)
Jojoba Oil (~600 - 630 bar)
Soybean Oil (~900 bar)
Cottonseed Oil (~820 – 1000 bar>)
Beta – Carotene (680 – 920 bar)

1-octadecanol in SC-CO_2 increases up to approximately 300 bar and then decreases as higher extraction pressures are applied. This shows that the maximum solubility for 1-octadecanol and stearic acid would be realized ~300 bar, while solubility maxima for the polyethylene glycol polymers (Carbowaxes) occur around 2000 bar. Note that the respective maxima in Figure 4 occur at fluid densities ranging from ~0.9 – 1.3 g/cc corresponding to δ's from ~7.5 to 11 $cal/^{2/}cc^{3/2}$. Hence the application of pressure will discriminate between these four solutes in SC-CO_2 on the basis of pressure, and actually fluid density. It is therefore suggested that if you wanted to prepare a PEG polymer complex containing stearic acid, one way would be to precipitate them from SC-CO_2 at say a pressure of 1000 bar. Figure 4 illustrates the advantage of going to higher extraction pressures to remove higher MW compounds, even although there are chemical structure dissimilarities in the four cited solutes shown in Figure 4. Hence, by selecting the appropriate extraction pressure as well as letdown receiver pressure, one can produce an extract that contains both an active ingredient and polymeric matrix.

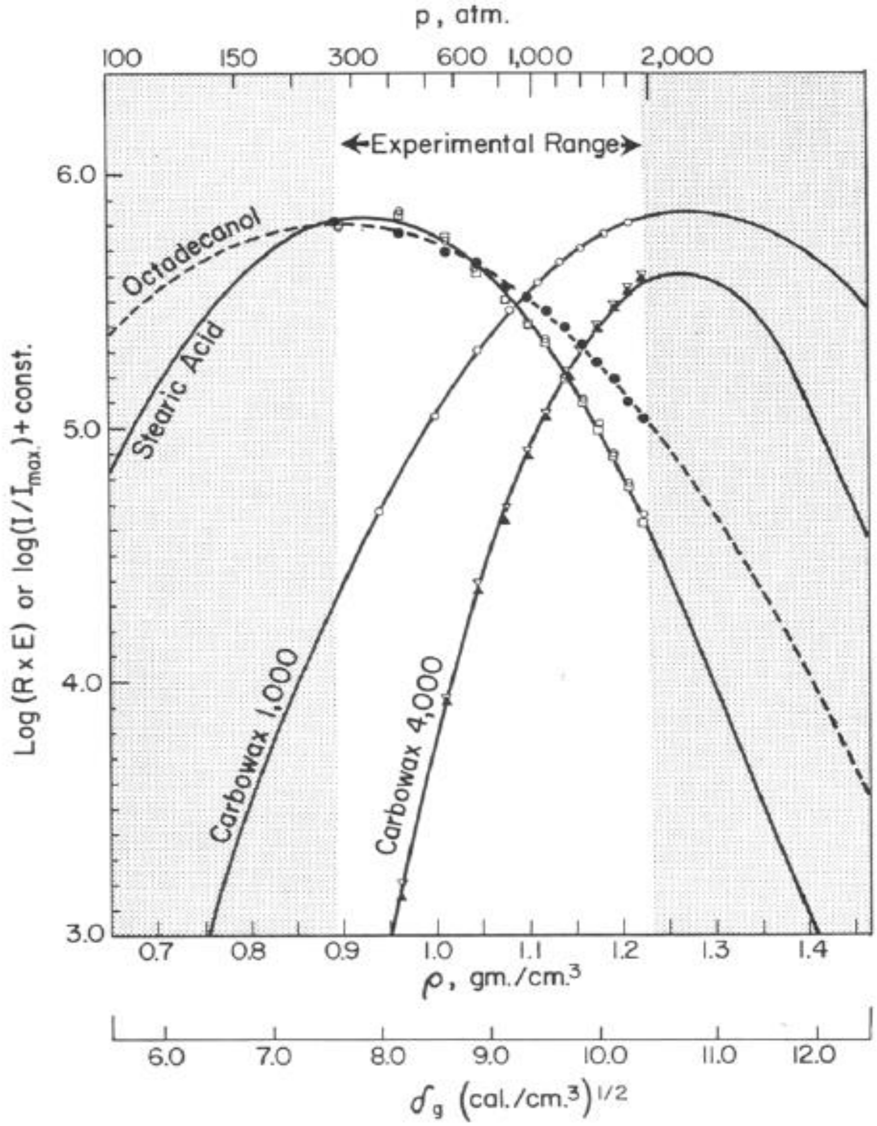


Figure 4. Relative solubility of the designated solute in CO_2 ($X_2/X_{2,max}$) at 40°C as a function of carbon dioxide density (ρ), solubility parameter (δ) and pressure (P).

Hence the occurrence of solubility maxima in SC-CO_2 for different solutes is to be expected, but the high pressure extraction condition that is optimal for one solute and may not be so for another. This is borne out by the β-carotene solubility measurements and correlations of Kraske et al [31] involving three supercritical fluids including SC-CO_2. They found that indeed β-carotene reaches an solubility maxima, depending on the temperature, between 70 – 90 MPa (700-900 bar) which is in approximate agreement with the trends shown in Figure 4. The occurrence of these solubility maxima have been verified by others for a variety of solute – supercritical fluid systems and is a general phenomenon based on solubility parameter theory. Many engineering-based solubility correlations which have been offered in the literature do not take this trend into account and only correlate solubility trends over a very limited range of pressures-temperatures for solute solubility in a supercritical fluid. It should however be recognized that the supercritical fluid does not have to be at a density to yield a solubility parameter that is equal to the target solute(s) to dissolve some of the target solute – the solute's solubility in SC-CO_2 will just be below the maxima solubility it could have in the SC-CO_2.

In general extractions for specific compounds and mixtures of compounds occur more rapidly as the extraction pressure increases at a constant temperature due to their increased solvency in SC-CO_2, but again this is compound specific, and in fact it is well known, that for the extraction of a mixture of compounds, some of the target solutes will reach a solubility maximum in SC-CO_2 at which their solubility in the compressed fluid decreases with further application of pressure. This solubility trend is somewhat parabolic in nature, and has been modeled some years ago against experimental solubility data by Bowman [17] in unpublished thesis results. Bowman studied 19 binary systems consisting of 13 solute types in 5 different fluids, and Figures 5 and 6 are typical of the data trends.

Shown below in Figure 5 is the logarithm of the absolute solubility for diethylstilbesterol dipalmitate in both SC-CO_2 and fluoroform (HCF_3) at fluid solubility parameters ranging from 5 – 12 $cal^{1/2}/cc^{3/2}$. Distinct solubility maxima are apparent and the solubility trends can be fitted to a least squares parabolic distribution. Note as remarked above, that the compound's solubility in the two different supercritical fluids starts to decrease at a certain value of the fluid δ (and pressure), corresponding to a "salting out" of the solute from the supercritical fluid medium

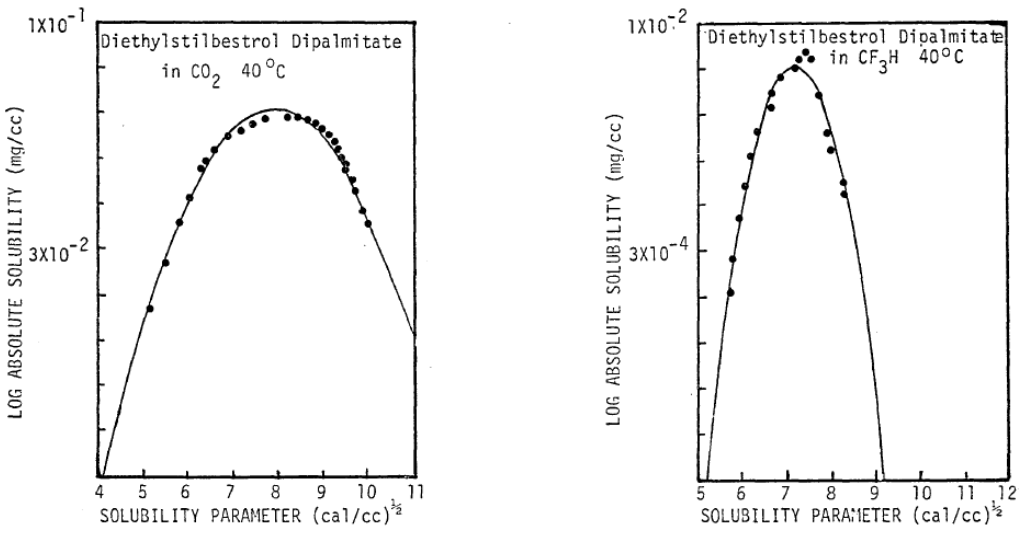
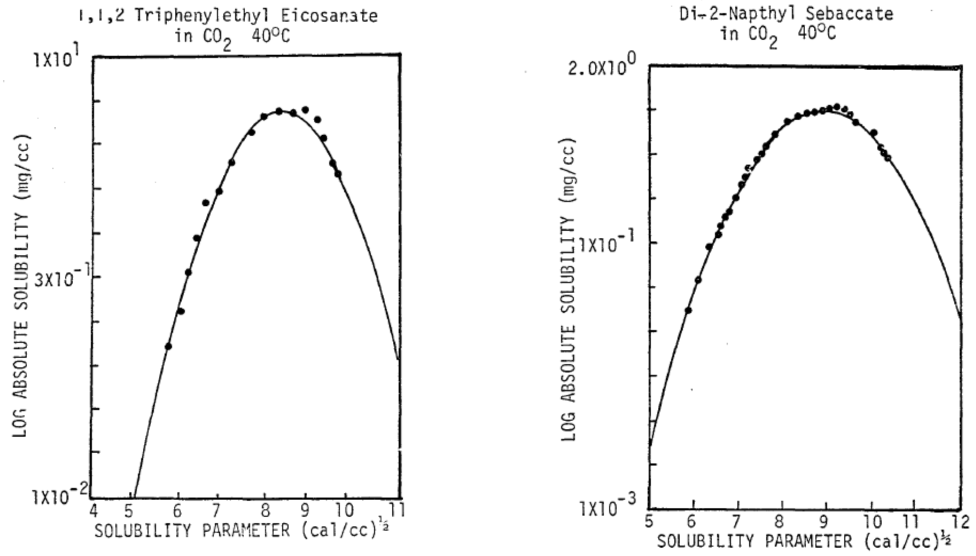

(a) (b)

Figure 5. Log of the absolute solubility (mg/cc) vs. fluid solubility parameter for diethylstilbestrol dipalmitate at 40°C in carbon dioxide (a) and 1,1-diphenyl-1-adamantanecarboxylate in fluoroform (b).

Similar trends are noted in Figure 6 for two different solutes in SC-CO_2 at 40°C. The interesting question is how does the occurrence of a solubility maxima at a certain value for the δ of the fluid correspond to the δ_o of the extracted solute? This can be ascertained by employing the two equations given in the Theoretical and Experimental Approach section, namely by equating the coefficients in Equations 9 and 10 to yield Equation 11, from which δ_o can be determined. These values are tabulated in Table 4 as well as δ_o computed from the group contribution of Small [32] used by Bowman [17]. For the 10 listed solutes, the overall agreement between the experimental values from the fluid-solute solubility experiments, δ_o and the calculated values of δo, is quite satisfying.


(a)

(b)

Figure 6. Log of the absolute solubility (mg/cc) vs. fluid solubility parameter for 1,1,2 - triphenylethyl eicosanate (a) and di-2-napthyl sebacate (b) at 40°C in carbon dioxide.

Table 4. Solute solubility parameters – theory vs. experimental and solute solubility in SC-CO2 @ 40°C

Solute	**Solute δ_o (Theory)**	**Solute δ_o (Exp.)**	**Solubility (mg/cc)**
Ethyl 330	8.76	8.72	0.39 +/- 0.05
Diethylstilbesterol Dipalmitate	8.77	8.00	0.022 +/- 0.001
1,1-Diphenylethyl Adamantanecarboxylate	8.20	8.53	2.66 +/- 0.05
1,1,2-Triphenylethyl Eicosnate	8.42	8.37	5.20 +/- 0.07
Di-2-Naphthyl Sebecate	8.76	8.92	1.19 +/- 0.05
Polystyrene (MW=2030)	9.1	8.64	0.068 +/- 005
1,3,5-Triphenylbenzene	10.7	10.1	0.551 +/- 0.005
Anthracene	9.90	10.2	4.4 +/- 0.5
2,3 – Benzanthracene	9.90	9.4	0.32 +/- 0.001
Pentacene	9.90	9.96	0.000274 +/- 0.00001

Note the wide variation in the magnitude of the absolute solubilities for the solutes at solubility maxima as shown in the last column of Table 4. These are a number of magnitudes lower than the solubility that many of these solutes exhibit in an optimal liquid solvent medium as determined by Bowman [17], and other investigators, when comparing solute solubility in supercritical fluid media with optimal liquid solvents for the same solute(s).

4. Concluding Remarks

The case for employing ultrahigh pressure SFE is beginning to emerge from the research laboratory utilizing small scale extraction equipment. Typical 1000 bar or greater-rated extraction equipment has been scaled at 5-10 liter with respect to extraction vessel size, and even larger pilot plant equipment is present in Germany, Slovenia, South Korea, Poland, Russia, China, Italy, Austria and Taiwan. The Valensa Corporation in the United States currently produces a “Deep Extract” platform of products using higher pressure SFE to achieve a more “complete natural extract”. Products that are offered include an enhanced sawtooth palmetto berry folded product, as well as enhanced astaxanthin-containing marine extracts.

References

[1] M. Meireles, Extracting Bioactive Compounds from Food Products, CRC Press, Boca Raton, FL, 2009.p. 388-401.
[2] J. King, K. Srinivas, D. Zhang, Advances in critical fluid processing. In: Alternatives to Conventional Food Processing, A. Proctor (ed.)., Royal Society of Chemistry, Cambridge, UK, 2010.
[3] J. King, Supercritical fluid processing of nutritionally functional lipids - Chapter 6. In: C. Akoh and O. Lai (eds.). Healthful Lipids. AOCS Press, Champaign, IL, 2005, pp. 99-126.
[4] E. Stahl, K. Quirin, D. Gerard, Dense Gases for Extraction and Refining. Springer-Verlag, Berlin, 1988.
[5] J. Giddings, M. Myers, J. King. Dense gas chromatography at pressures to 2000 atmospheres. J. Chromatogr. Sci. 7 (1969) 276-283.
[6] J. Czubyrt, M. Myers, J. Giddings, Solubility phenomena in dense carbon dioxide ags in the range of 270-1900 atmospheres. J. Phys. Chem. 74 (1968) 4260-4266.
[7] G. List, J. Friedrich, J. King, Supercritical CO_2 extraction and processing of oilseeds. Oil Mill Gazetteer 95 (6):28-34. 1989.
[8] C. Luetge, M. Bork, Z. Knez, M. Kreiner, Ultra high pressure dense gas extraction and fractionation, In Proceedings 5th Int. Symp. High Pressure Process Technol. Chem. Eng., Segovia, Spain (2007).
[9] F. Favati, J. King, J. Friedrich, K. Eskins, Supercritical CO_2 extraction of carotene and lutein from leaf protein concentrates. J. Food Sci. 53 (1988) 1532-1536.
[10] C. Luetge, V. Steinhagen, M. Bork, Z. Knez, Supercritical carbon dioxide extraction of plant materials at ultrahigh pressure. Proceedings of the 9th International Symposium on Supercritical Fluids (ISSF-2009), Arcachon, France, 2009.
[11] B. Nagy, B. Simándi, E. Lack, Modeling of Supercritical Fluid Extraction of Plant Materials,, Proceedings of the 12th European Meeting on Supercritical Fluids, Graz, Austria, May 9-12, 2010, 465.
[12] C. Luetge, M. Bork, Z, Knez, M. Hrncic, M. Kraine. Ultra high pressure dense gas extraction and fractionation. In: Z Knez, M. Cocero. 5th International Symposium on High Pressure Process Technology and Chemical Engineering, Segovia, Spain, 2007European Federation of Chemical Engineering, 2007, pp. 1-4.
[13] K. Srinivas, K., J. King, J. Monrad, L. Howard, C. Hansen, Optimization of subcritical fluid extraction of bioactive compounds using Hansen solubility parameters. J. Food Sci., 74, (2009) E342-E354.
[14] R. Fedors, A method for estimating both the solubility parameters and molar volumes of liquids. Polym. Eng. Sci., 14 (1974) 147-154.
[15] A. Jayasari, M. Yaseen, Nomograms for solubility parameter. J. Coatings Technol., 52, (1980) 41-45.
[16] L. Williams, J. Rubin, H. Edwards, Calculation of Hansen solubility parameters for a range of pressure and temperature conditions, including the supercritical fluid region. Ind. Eng. Chem. 43 (2004) 4967-4972.
[17] L. Bowman, Jr., Dense gas chromatographic studies, Ph.D. Thesis, University of Utah, 1976.
[18] J. Vincent, K. Srinivas, K, J King,. Characterization of the solvent properties of glycerol using inverse gas chromatography and solubility parameters. J. Am. Oil Chemists’ Soc., 89 (2012), 1585-1597.
[19] L. Montanari, L. J. King, G. List, K Rennick,, Selective extraction of phospholipid mixtures by supercritical carbon dioxide and cosolvents. J. Food Sci., 61 (1996) 1230-1233, 1253.
[20] C. Hansen and A. Beerbower, Solubility Parameters, In Kirk-Othmer Encyclopedia of Chemical Technology, Suppl. Vol., Wiley-Interscience, New York, 1971.; also, L. Williams, Hansen Solubility Parameters: A User’s Handbook, CRC Press, Boca Raton, FL, 2007, p. 190.
[21] J. King, Determination of the solubility parameter of soybean oil by inverse gas chromatography. Lebensmittel

Wissenschaft Technol. 28 (1995) 190-195.

[22] K. Srinivas, T. Potts, J. King, Characterization of the solvent properties of methyl soyate using by inverse gas chromatography and solubility parameters. Green Chem. 11, (2009) 1581-1588.

[23] K. Adamska, A. Voelkel, Hansen solubility parameters for polyethylene glycols by inverse gas chromatography. J. Chromatogr. A 1132 (2006) 260-267.

[24] K. Srinivas, J. King, Supercritical carbon dioxide and subcritical water: complimentary agents in the processing of functional foods. In Functional Food Product Development, J. Smith and Edward Charter (eds.), Wiley-Blackwell, Oxford, UK, 2010, pp. 39-78.

[25] F. Miao, F., D. Lu, D., Y. Li, M. Zeng, Characterization of astaxanthin esters in Haematococcus pluvalis by liquid chromatography-atmospheric pressure chemical ionization mass spectrometry. Anal. Biochem. 352 (2006) 176-181.

[26] A. Guedes, H. Amaro, F. Malcata, Microalgae as sources of carotenoids, Mar. Drugs, 9 (2011) 625-644.

[27] J. Friedrich Supercritical CO2 extraction of lipids from lipid-containing materials. U.S. Patent 4,466,923, 1984.

[28] K. Quirin, Solubility behavior of fatty oils in compressed carbon dioxide in the pressure range up to 2,600 bar. Fette-Seifen Anstrichmittel 84 (1982) 460-468.

[29] R. Gupta, J. Shin, Solubility in Supercritical Carbon Dioxide, CRC Press, Boca Raton, FL, 2007.

[30] E. Stahl, K. Quirin, D. Gerard, Solubilities of soybean oil, jojoba oil, and cuticular wax in dense carbon dioxide. Fette-Seifen Anstrichmittel 85 (1983) 458-463.

[31] T. Kraska, K. Leonhard, D. Tuma, G. Schneider, Correlation of the solubility of low volatile organic compounds in near- and supercritical fluids. Part I: applications to adamantine and β-carotene. J. Supercrit. Fluids 23 (2002) 209-224. [32] P. Small, Some factors affecting the solubility of polymers, J. Appl. Chem. 3 (1953) 71-80.