

Apparent Solubility of Natural Products Extracted with Near-Critical Carbon Dioxide

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ABSTRACT

The apparent solubility controls the initial stage of supercritical fluid extraction of natural products, which is most important for the process economics. Based on the literature, data on CO₂ apparent solubility of volatile substances from different matrices as leaves, flowers, rhizomes and seeds were collected and compared with their thermodynamic solubility. The adsorption isotherm derived by del Valle and Urrego as a modification of the isotherm proposed by Perrut *et al.* is universal enough to interpret these data as well as the apparent solubility of vegetable oils from seeds, for which it was originally proposed. When the apparent solubility of minor extract components in CO₂ is compared with their thermodynamic solubility, their fraction in the extracted mixture should be taken into account.

Keywords: Supercritical Fluid Extraction; Solubility; Adsorption Isotherm; Vegetable Oils; Volatile Compounds

1. Introduction

Supercritical fluid extraction (SFE) is a green separation process yielding products free of any traces of organic solvents and, as such, it is applied to manufacture hops extract, caffeine-free coffee beans, extracts from spices and medicinal plants, and other products. Supercritical solvent of choice for this purpose is carbon dioxide, which is non-flammable, non-explosive, non-toxic, and inert. Another advantage with respect to thermolabile substances is its low critical temperature, 31.2°C. The range of extraction conditions is sometimes extended below the critical temperature to liquid CO₂.

The SFE is carried out in high-pressure equipment at pressures higher than the critical pressure of CO₂, which is 7.14 MPa. The investment cost of a plant for SFE is therefore substantially higher than the cost of a plant for conventional extraction with organic solvents.

The CO₂ extracts compete in the market with products of conventional extraction and it is not always possible to make the production cost comparable, though the operation cost of SFE is lower. Both extraction conditions (extraction temperature, pressure, solvent flow rate and time of extraction) and pretreatment of extracted plant should be optimized to minimize the production cost. The fluid leaving the extractor under optimum conditions is usually a saturated solution of extract in supercritical CO₂, or almost saturated solution [1]. Thus, the concentration of saturated solution in equilibrium with extracted plant, called apparent solubility, is an important quantity con-

trolling the extraction kinetics and affecting the production cost.

The term “apparent” is used to distinguish the equilibrium fluid phase concentration established when the plant material to be extracted is contacted with supercritical CO₂ for sufficient time from the thermodynamic solubility of extract in the solvent, in the absence of plant matrix. The apparent solubility can be estimated from published data on the kinetics of SFE from different plants, provided that the solvent residence time was sufficient for saturation.

The apparent and thermodynamic solubilities are usually identical for vegetable oils extracted from seeds [2]. The apparent solubility of volatile substances, however, is often much lower than their thermodynamic solubility in CO₂. Rodrigues *et al.* [3] determined the apparent solubility of extracts from three aromatic plants and found that the apparent solubility of clove oil was by one or two orders higher than the apparent solubility of ginger and eucalyptus oils. Sovová *et al.* [4] made experiments and thermodynamic modeling for a model system representing the partition of volatile substances between CO₂ and vegetable oil during their SFE from seeds. Recently, del Valle and Urrego [5] published a study where different aspects of SFE from plants are discussed. With respect to the apparent solubility in CO₂, they modified previously published relationships for adsorption isotherms of vegetable oils extracted from seeds and obtained a very good description of experimental data. Further, they proposed a simple and rational explanation for

the low apparent solubility of volatile compounds: when the initial extract content in the plant is low (as it is usually in the case of volatile compounds), its concentration in CO₂ filling the void space in the extraction bed is much lower than its thermodynamic solubility, even if it is all dissolved immediately.

The aim of this work was to collect more literature data on the apparent solubility of CO₂ extracts from plants in order to check these hypotheses on the effect of plant matrix on extraction kinetics.

2. Apparent Solubility of Vegetable Oils from Seeds

2.1. Combined Equilibrium Relationship

Experimental data on SFE kinetics are usually obtained by determining the amount of extract at certain time intervals. Extraction yield, e , is calculated as the mass of extract over the mass of plant that was placed into the extractor (the feed). The extraction yield is plotted against the extraction time, t , or against the solvent-to-feed ratio, q , which is equal to the mass of passed carbon dioxide over the feed. The experimental points are connected by cumulative extraction curve (**Figure 1**). In the plot $e = e(q)$, the slope of the cumulative curve is equal to the concentration of extract in the solution flowing out of the extractor.

When the plant material is mechanically pretreated by milling, grinding, cutting or other method, a part of soluble substances is released and is freely accessible on the surface of obtained plant particles that form the extraction bed. As supercritical fluids exhibit very good transport properties, the mass transfer from particle surface to bulk fluid is quick. When several minutes of static extraction precede opening the valve at extractor outlet at $t = 0$, equilibrium is established and the apparent solubility can be read from the initial slope of cumulative extraction curve. It is, however, necessary to check that the

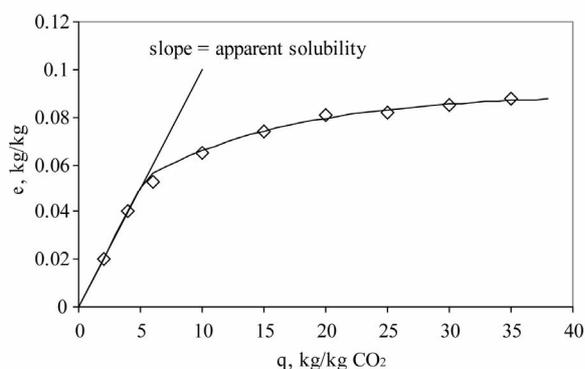


Figure 1. Experimental data and typical cumulative extraction curve. The initial slope equals the apparent solubility for sufficient residence times.

solution was saturated. This can be done by evaluating two extraction runs carried out at different solvent residence times, it means at different solvent flow rate-to-feed ratios. If the solution was saturated in both cases, the slopes of the two extraction curves $e = e(q)$ are equal. The content of extractable substances in the plant can be estimated as the asymptote of extraction curve at large times. To obtain from extraction curve more information on kinetic parameters, mathematical models including mass balance of extracted substances in the solid and fluid phases, relationships for mass transfer rates in the particles and in the fluid phase, and a relationship for phase equilibrium are necessary.

It was repeatedly confirmed that the apparent solubility of vegetable oils extracted from seeds with dense CO₂ is equal to their thermodynamic solubility in CO₂, which is similar for all vegetable oils consisting of triacylglycerols of fatty acids, most of which contain 18 C atoms. As the solubility was correlated with temperature and CO₂ density [6-8], the apparent solubility of vegetable oils can be predicted according to these correlations. The fact that plant matrix does not affect the initial extraction rate of oils from seeds is connected with high content of oils in seeds, which is measured in tens of percent. When, however, the initial content of oil in seed was reduced by preceding extraction, the equilibrium apparent solubility of oil from depleted seeds was lower than the thermodynamic solubility and decreased with decreasing oil content (**Figure 2**).

The effect of seed matrix on the solubility of sunflower oil in CO₂ was observed and modelled by Perrut *et al.* [10]. The initial slope of extraction curve was equal to the thermodynamic solubility of oil and, after a part of oil was extracted, the extraction continued at a slower rate, with a lower slope of extraction curve. Such a decrease is normally attributed to mass transfer resistance

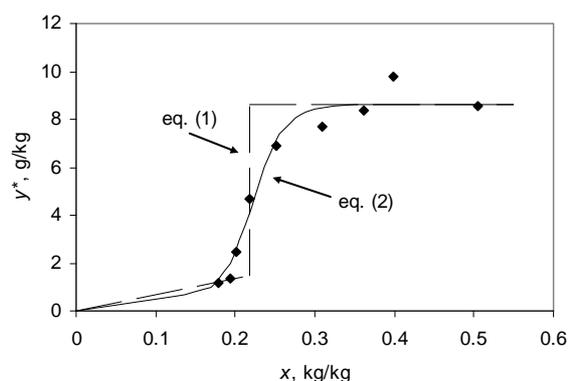


Figure 2. Equilibrium solubility of oil extracted with CO₂ at 40°C and 35 MPa from canola seeds in dependence on the oil concentration in seeds. The experimental data [9] are redrawn according to ref. [5]. Coefficients of Equation (1): $y_0 = 8.6$ g/kg, $x_t = 0.22$ kg/kg, $K = 6.8$ g/kg. Coefficients of Equation (2): $y_0 = 8.6$ g/kg, $x_t = 0.23$ kg/kg, $K = 5.0$ g/kg, $n = 12.5$.

in the seed particles after the easily accessible oil from particle surface has been exhausted. In this case, however, the solution flowing out of the extractor was still saturated because the extraction curves $e = e(q)$ measured for different residence times overlapped after the decrease in extraction rate as well as in their first section. Perrut *et al.* therefore proposed equilibrium function in the following form:

$$y^* = y_0 \text{ for } x \geq x_t, y^* = Kx \text{ for } x < x_t, Kx_t < y_0 \quad (1)$$

where y^* is the equilibrium fluid phase concentration, y_0 is the thermodynamic solubility, x is the solid phase concentration, x_t is the minimum solid phase concentration at which the seed matrix does not affect the apparent solubility, and K is the partition coefficient for oil interacting with seed matrix. Perrut *et al.* were aware that real equilibrium curve is smooth but simplified it to this form in order to minimize the number of adjustable coefficients. Using Equation (1) in a model for SFE, Sovová [11] derived the condition under which the overall extraction curve does not exhibit the second decreased slope corresponding to the apparent solubility of oil interacting with matrix, though this interaction does exist: the initial concentration of oil in the seed matrix, x_0 , must fulfill the inequality $Kx_0 > y_0$.

It is relatively easy to ensure saturation of the solution flowing out of the extractor when a free solute is dissolved. When the solute interacts with matrix, the local driving force of the extraction is lower and much larger residence time is necessary to achieve the saturation. Thus, the apparent solubility read directly from the second slope of extraction curves could be underestimated in the case of solute interacting with matrix, though the initial slope measured for the free solute gives a correct value of solubility, y_0 . To obtain correct value of partition coefficient K , solution of a complete model for SFE where both equilibrium and mass transfer relationships are included should be compared with experimental extraction curve.

A smooth variant of the equilibrium function was recently published by del Valle and Urrego [5]:

$$y^* = Kx + \frac{x^n}{x_t^n + x^n} (y_0 - Kx) \quad (2)$$

Equation (2) reduces to Equation (1) for high values of exponent n . Numerical integration of SFE model equations is substantially easier when the equilibrium is described by this smooth equilibrium curve instead of the broken curve, Equation (1). Besides, the smooth curve fits well the available equilibrium data (**Figure 2**).

2.2. Summary

Though the thermodynamic solubility of oil in CO_2 is usually a sufficient equilibrium characteristic to model

the whole extraction curve, it should be borne in mind that after a part of oil has been extracted, the rest is bound to matrix and its equilibrium fluid phase solubility is therefore lower and monotonously decreases in the further course of extraction. Equations (1) and (2) closely describe these changes.

3. Apparent Solubility of Volatile Substances in CO_2

3.1. Thermodynamic Solubility of Terpenes, Essential Oils and CO_2 Extracts

The content of volatile substances in plants and herbs is usually a few per cent or less and therefore it is expected that the solute-matrix interaction plays in their SFE a more important role than in the SFE of vegetable oils from seeds. While the vegetable oils are regarded in SFE as one compound because the solubility of individual oil triglycerides in CO_2 is similar and therefore no fractionation of extract occurs, the SFE of volatile substances from aromatic plants takes place simultaneously with extraction of non-volatile substances. Different groups of extract components have different solubility and therefore fractionation in time is observed, and both initial composition and asymptotic yield are pressure and temperature dependent. Despite of this, for the sake of simplicity, the extracts will be regarded as one compound in the estimation of apparent solubility.

Similarly to the techniques used to produce essential oils (steam distillation or hydrodistillation, and pressing in the case of citrus oils), the SFE is a separation technique that isolates from plant materials volatile substances, mostly terpenoids: monoterpenes (MT) and oxygenated monoterpenes (OMT), sesquiterpenes (ST) and oxygenated sesquiterpenes (OST). Besides, the extracted oleoresin contains non-volatile substances like fatty oil, cuticular waxes, higher terpenoids, alkaloids and other minor components. The volatiles-to-non-volatiles ratio in the extract is controlled by extraction conditions; the fraction of non-volatile substances increases with increasing extraction time and with increasing pressure.

The differences in thermodynamic solubility of terpenoids, essential oils and CO_2 extracts are evident in **Figure 3**.

Monoterpenes are represented by α -pinene, oxygenated monoterpenes by *cis*-verbenol, and sesquiterpenes by α -humulene. The solubility of bergamot oil, where the percentage of MT and OMT is almost equal, is depicted in the plot between the solubilities of the two classes of terpenoids. The following solubilities of CO_2 extracts from three plants were measured in the team of Prof. Meireles. Clove oil was extracted with liquid CO_2 at 25°C and 15 MPa from clove buds, rich in essential oil. Its major components are eugenol, eugenol acetate (both

OMT) and β -caryophyllene (ST) and, correspondingly, its solubility in CO₂ is slightly lower than the solubility of OMT in **Figure 3**. Very probably, its solubility is similar to the solubility of essential oil from clove buds. Nevertheless, in contrast to vapor-liquid equilibrium at temperatures 40°C and more, the system clove buds extract + CO₂ exhibits two liquid phases in equilibrium with a vapor phase at temperatures 30°C and 35°C. The solubility of vetiver grass oil is much lower. Its volatile fraction consists of ST and OST, and though the solubility of OST in CO₂ is expected to be lower than that of ST, this difference cannot be large enough to explain the low solubility of the vetiver grass oil. The more probable reason is the presence of cuticular waxes and other non-volatile compounds, all of them less soluble in CO₂ than the volatile fraction, as the vetiver grass oil was extracted with supercritical CO₂ at 40°C and 20 MPa, under the conditions where the solubility of cuticular waxes is not negligible. The lowest solubility in CO₂ exhibits the fennel extract, extracted from seeds with dense CO₂ at 30°C and 25 MPa, under the conditions when fatty oil is relatively well soluble. Thus, the fraction of fatty oil components in fennel extract is high and strongly affects its solubility in CO₂.

3.2. Desorption from Plant Matrix

The apparent solubility listed in **Table 1** was calculated from the first slope (or, where indicated, from the second slope) of cumulative extraction curves of SFE carried out at 40°C, published in the literature. Their values at 9 - 10 MPa are much lower than the solubility of free extracts shown in **Figure 3** and therefore we assume that these extract are adsorbed on plant matrix, as suggested already by Goto *et al.* [27].

It is evident in **Figure 4** where the data from **Table 1**

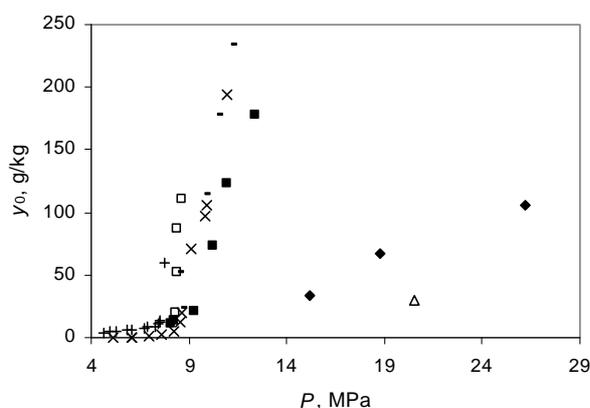


Figure 3. Thermodynamic solubility in CO₂ at 40°C. (+) α -pinene [12], (x) *cis*-verbenol [12], (-) α -humulene [13], (□) essential oil: bergamot [14], (■) CO₂ extract: clove buds [15], (◆) CO₂ extract: vetiver grass [16], (△) CO₂ extract: fennel seed [17].

are plotted that no significant increase of apparent solubility with increasing pressure occurs. Thus, the generally recommended low pressures (9 - 10 MPa) for SFE of volatile substances at 40°C are substantiated not only because the coextraction of less soluble compounds is reduced but also because the kinetics would not be markedly enhanced at higher pressures.

Similar apparent solubilities were evaluated from literature data at 50°C (not shown here).

3.3. Washing Out of Free Solute

All extraction curves were checked for the phenomenon described in detail by del Valle and Urrego [5] and in-

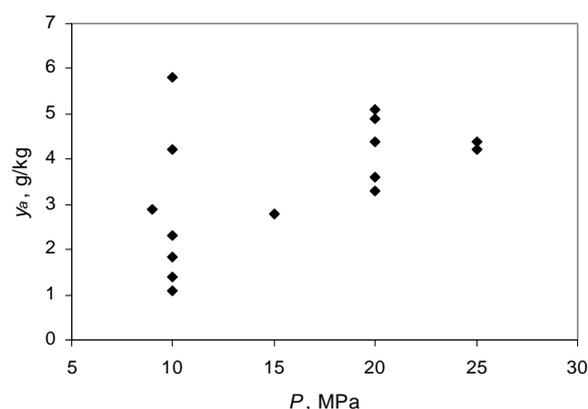


Figure 4. Apparent solubility of extracts adsorbed on plant matrix, reported in **Table 1**.

Table 1. Apparent solubility (y_a) of volatiles extracted from plants with CO₂ at 40°C.

Plant	Substrate	Pressure, MPa	y_a , g/kg	Ref.
Chamomile	flowers	10	1.8	[18]
Chamomile	flowers	20	5.1	[18]
Chamomile	flowers	10	1.1	[19]
Chamomile	flowers	25	4.4	[19]
Clove ^a	buds	10	2.3	[20]
<i>Cordia verbenacea</i>	leaves	20	3.3	[21]
Ginger	rhizome	15	2.8	[22]
Ginger	rhizome	25	4.2	[22]
Orange ^a	peel	20	3.6	[23]
Orange ^a	peel	20	4.4	[23]
Peppermint	leaves	10	1.4	[24]
Peppermint	leaves	9	2.9	[25]
Peppermint	leaves	10	5.8	[25]
St. John's Wort	aerial part	10	4.2	[26]
St. John's Wort	aerial part	20	4.9	[26]

^aSecond slope.

cluded in the model for SFE [11] as “Case C”, when all free solute dissolves in the solvent before the solvent starts flowing out of the extractor and then it is quickly washed out. It occurs when the content of free solute in the plant is not sufficient to saturate the solution. The cumulative extraction curve should show a break to slower extraction of the solute bound to matrix at the time equal to the residence time. When the mass of plant in the extractor is N , the mass of the solvent in the void space is M , the mass flow rate is F and the content of free solute on the surface of plant particles is x_1 , the initial fluid phase concentration will be $y_a = x_1 N / M$, the residence time is $t_r = M / F$ and the corresponding solvent-to-feed ratio is $q_1 = M / N$.

All extraction curves on which the data in **Table 1** are based were inspected for the early break at t_r or q_1 , which was observed for the substrates with the highest contents of volatile substances: clove buds [20] containing 15% of extract, which apparent solubility in CO_2 according to the first slope was 180 mg/g, and orange peels of two sorts, one with 11.1% orange oil and $y_a = 40$ mg/g and the other one with 5.5% orange oil and $y_a = 30$ mg/g [23]. All other plants contained less than 5% extract.

3.4. Partition between Fatty Oil and CO_2

The apparent solubility of volatile substances extracted from seeds should be considered separately because they are distributed between the vapor phase and oil in the seeds, which is insoluble at lower pressures and is coextracted at higher pressures. The apparent solubility of volatile substances from seeds at 40°C and 8 - 12 MPa was shown to be directly proportional to the volatile oil-to-fatty oil ratio in the seed and to increase with increasing pressure [28]. As **Figure 5** shows, the apparent solubility evaluated from the first slopes of extraction curves of fennel and nutmeg oils follows this trend.

3.5. Summary

The apparent solubility of mixtures of volatile substances is lower than their thermodynamic solubility in CO_2 . One

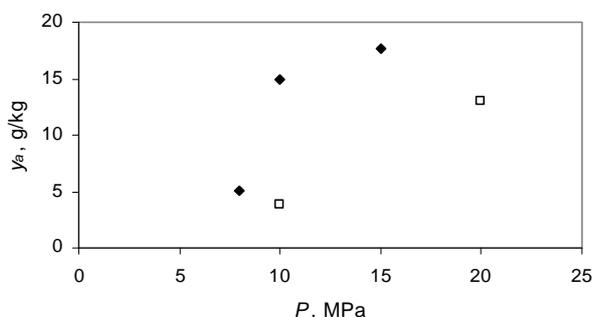


Figure 5. Apparent solubility of extracts from seeds in CO_2 at 40°C : (◆) fennel seed [29], (□) nutmeg [30].

reason for it is the effect of coextracted non-volatile substances and the other reason is the interaction of extracted substances with plant matrix. Only when the content of volatile substances in the plant is high, as in clove buds and citrus fruit peels, a part of extract is freely washed out.

4. Extraction Behavior of Minor Extract Components

4.1. Apparent Partition Coefficient

Extracts from botanical materials are always mixtures of compounds but as long as the major components are of similar solubility, the extracted oleoresin is treated as one substance in the analysis of extraction kinetics. When, however, kinetics of SFE of a minor component is examined and the apparent solubility of this compound is compared with its thermodynamic solubility in CO_2 , large discrepancies are observed, particularly when its content in the plant is by orders of magnitude lower than the content of oleoresin. Such discrepancies were listed by del Valle and Urrego [5] in a table comparing the apparent and thermodynamic solubilities of different carotenoids extracted from tomato skin, carrots, red pepper, and annatto seeds, purine alkaloids from maté tea leaves, and other examples. As Saldana *et al.* [31] concluded, pure-component solubility data do not enable a direct prediction of extraction kinetics of these substances from natural products.

The apparent solubility of minor components should be considered in respect to their content in the mixture extracted from the herb or plant. Thus, when the content of oleoresin in the plant is initially x_{ol} and the content of the minor component, a part of the oleoresin, is x_m , the apparent solubility calculated from the first slope of cumulative extraction curve for the minor component should be multiplied by x_{ol}/x_m before it is compared with thermodynamic solubility measured for pure substance. Such procedure was applied by Shen *et al.* [32] who determined the apparent solubility of major and minor components of oleoresin extracted with CO_2 from rice bran and used for the corrected quantities term “apparent partition coefficients”.

The conversion of apparent solubility to apparent partition coefficient is illustrated in **Table 2** on the values measured for maté tea leaves [31]. The contents of extractible minor components caffeine, theobromine and theophylline in the leaves were 4.3, 0.35 and 0.047 mg per g of dry maté leaves, respectively, and the oleoresin content in dry leaves is estimated by us according to another paper on SFE of maté leaves [33] to 20 mg/g. The apparent partition coefficient of caffeine is still lower than its thermodynamic solubility but the other two purine alkaloids exhibit higher apparent partition coeffi-

cients than is their thermodynamic solubility, indicating entrainer effects of co-extracted substances.

The second set of literature data used to compare the apparent partition coefficient with thermodynamic solubility concerns the SFE of capsaicinoids from Jalapeno pepper (*Capsicum annuum*) [34]. The results are shown in **Table 3**. The contents of oleoresin and capsaicinoids in dry jalapeno pepper were 102.2 and 0.24 mg/g, respectively. The high value of apparent partition coefficient indicates that the extracted oil acts as entrainer of capsaicinoids.

4.2. Summary

It should be taken into account in the analysis of SFE kinetics of individual extract components that the solvent capacity is partially occupied by the other mixture components and therefore the apparent partition coefficient should be used instead of the apparent solubility.

5. Conclusions

The equilibrium relationship expressing behavior of both free solute and solute interacting with matrix, published by Perrut *et al.* [9] and modified by del Valle and Urrego [5], was confirmed to be applicable to different solutes and different plant matrixes.

The apparent solubility of vegetable oils extracted from seeds is usually equal to their thermodynamic solubility. The apparent solubility of volatile fraction of extracted oleoresin is lower than its thermodynamic solubility due to the co-extracted non-volatile substances and due to the interaction with matrix (adsorption on the leaf, flower, bud, peel or rhizome matrices and absorption in the fatty oil in seeds). When the content of volatile-rich

Table 2. Apparent partition coefficients in SFE of maté tea leaves at 25.5 MPa and 70°C [5,31].

Solute	Thermodynamic solubility, g/kg	Apparent solubility, g/kg	x_{ol}/x_m	Apparent partition coefficient, g/kg
Caffeine	2.05	0.094	4.7	0.44
Theobromine	0.007	0.0044	57.1	0.25
Theophylline	0.014	0.00013	426	0.55

Table 3. Apparent partition coefficients of capsaicinoids extracted with CO₂ from jalapeno pepper [34].

$P, \text{MPa}/T, ^\circ\text{C}$	Thermodynamic solubility, mg/g	Apparent solubility, g/kg	x_{ol}/x_m	Apparent partition coefficient, g/kg
12/40	0.52 ^a	0.008	426	3.41
32/40	2.11 ^b	0.036	426	15.3

^aData from ref. [35]; ^bExtrapolated from ref. [35].

extract in peels or buds was higher than 5%, washing out of a free part of extract was observed.

The solubility of minor extract components, when considered separately, is better characterized by the apparent partition coefficients than by the apparent solubility. To calculate the partition coefficients, global yield should be determined in addition to the yield of target minor components.

6. Acknowledgements

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