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Solid-Liquid Extraction of Taxane Compounds from Yew Needle

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Abstract: Solid-liquid extraction of the taxane compounds in yew needles is carried out with methanol. The concentration of each component in the raffinate is estimated from the observed concentration in the extract and material balance equations with a solvent-permeation model that solvent permeates the solid. The obtained distribution coefficient is found to be independent of the particle size. It suggests a possibility that the extract is in equilibrium with the liquid solution in the raffinate. Based on the experimental results, the effect of operating conditions on separation performance of countercurrent-multistage extraction is studied by using the ideal stage calculation.

Keywords: Solid-liquid extraction, distribution coefficient, taxane compound, Yew needle, simulation

INTRODUCTION

Taxol (1) is a diterpene amide that has antitumor activity (2), and works on breast and ovarian cancers effectively. Thus, it has been sold as an anticancer drug, and its sales figures in the world reach about one and one-half billion dollars in the year 2000.

Taxol is contained in the yew trees such as *Taxus brevifolia* (1), *Taxus cuspidata*, and so on (3), and extracted from the trees to produce the anticancer

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drug. At the same time, the drug is synthesized in the industrial processes with 10-diacetylbaccatin III and diacetylbaccatin III (4, 5) that are also obtained from the yew trees. However, the price of taxol is still higher at 1000 yen/mg, because the taxane content of the yew trees is very low (6). In order to reduce the cost of taxol, many studies on the total synthesis (7, 8) and semisynthesis (9, 10) of taxol have been made, but the developed processes have not been applied to the commercial plants yet because of complexity of the chemical structure (11). This may indicate that it is essential to improve the separation process to extract the taxane compounds efficiently from the yew trees and to purify them.

The yew trees have more than 300 kinds of taxane compounds (12). However, many of them have not been analyzed on biological and/or physiological activities yet, so that they are considered as unnecessary materials in separation of the taxane compounds from the yew trees. Meanwhile, among the identified and analyzed taxane compounds, cepharomanine and taxines B can be applied to the taxol synthesis (9, 13), but cinnamyl taxane neither has the biological activity nor is it used as a raw material for the taxol synthesis (14). Thus, cinnamyl taxane is necessary to separate from mixtures of the taxane compounds. So far, there have been many studies on separating taxol and the taxane compounds, but many of them were focused on purification of the target substance by HPLC (15–18). Of course, that separation method with HPLC is indispensable for purification, but the solid-liquid extraction (19) to separate the taxane compounds from the yew trees and liquid-liquid extraction to refine the taxane compounds are also important to use those substances as much as possible. Particularly, since the taxane compounds are contained inside the botanical cells, there is a possibility that the concentration in the extract liquid is in equilibrium with that in the liquid solution in the cell. The studies on the extraction mechanism between liquid and solid with the internal structure are necessary to improve the solid-liquid extraction process, but it has not been elucidated sufficiently (20).

In the literature, the bark of yew trees was used as a solid feed for the solid-liquid extraction, because the taxane compounds abound in the bark among the parts of yew tree (21). However, use of the live bark is not recommended from the viewpoints of the growing rate of yew trees and protection of environment. Instead, the yew needles are more preferable because they are regenerative (19). In the present study, the dry needles of *Taxus cuspidata* are used as a solid feed, and the proper solvent for extracting the total amount of solutes is examined. Then, the distribution coefficient and selectivity of taxane compounds are measured, and the extraction mechanism in the solid-liquid extraction is discussed. Finally, the ideal stage calculation of the solid-liquid extraction is carried out based on the experimental results, and the operating conditions on separation performance of the solid-liquid extraction process are discussed.

CHARACTERIZATION OF YEW NEEDLE

Preparation of Fine Particles of the Yew Needle

The dry needles of *Taxus cuspidata* are ground in order to extract the taxane compounds efficiently in the solid-liquid extraction. The obtained particles are classified into four groups in size, and the Feret diameters of any four hundred particles in each group are measured to determine the average particle size. The obtained particle sizes, d_p, are 32, 250, 537, and 915 μm.

Total Amount of Target Solutes in the Yew Needle

Table 1 summarizes the identified taxane compounds contained in the yew needle with the maximum absorption wavelength. As shown in the table, some of the taxane compounds have UV absorption at the same wavelength. Since the taxane compounds with UV absorption at a given wavelength cannot be distinguished by a UV spectrophotometer, the compounds with UV absorption at the same wavelength are considered as one target solute to be extracted from the yew needle. For convenience, those target solutes are named as component A, B and C in order of wavelength.

In general, it is very difficult to measure the concentration of solutes in the raffinate (solid phase) directly in the solid-liquid extraction. However, if the amounts of solutes in the solid feed are given, the amounts of solutes in the raffinate can be determined from the concentration in the extract (liquid phase) and material balance equations. Thus, the total amounts of components in the yew needle are measured by repeating single extraction until the concentration in the extract becomes negligible small. In the first single extraction, 50 mg of the yew needle powder is soaked in 50 ml of methanol in a 100 ml of Erlenmeyer flask, and it is shook by a thermoshaker at 298 K for 24 to 168 hours, of which time is changed with the particle size. During the experiments, the yew needle powder is well dispersed and the volume of

Table 1. Typical taxane compounds

Taxane compound	$\lambda_{\max}$ (μm)	Component	$\sum_{k=1}^{n}$ (ABS$_{ik}$)
Taxines B	210	A	13.22 ($\sigma = 0.24$)
Taxol	227	B	7.20 ($\sigma = 0.18$)
10-deacetylbaccatin III	227		
Deacetylbaccatin III	227		
Cepharomanine	227		
Cinnamyl taxane	280	C	4.03 ($\sigma = 0.15$)

the solvent does not change apparently. Then, the raffinate is separated from the solution, and the absorbance of each component in the extract, $[ABS_i]$, is measured by a UV spectrophotometer. Meanwhile the raffinate is dried to prepare the feed solid for the next extraction. Subsequently, the same procedure is repeated. To confirm reproducibility of the experimental data, three crosscurrent extraction runs are carried out with the same experimental conditions. The experimental conditions are summarized in Table 2 (Experiment 1).

The amount of each component in the entire amount of the extract is the maximum amount that can be extracted from the solid under a given operating condition, and it could represent the total amount of the component in the yew needles. In the present study, the total amount of the component in the yew needles is assumed constant and independent of solvents. Then, assuming that the concentration of each component in the extract is proportional to the absorbance of the component, the total amount of component i in the yew needles, Fx_i^{total}, is evaluated by the following equations that are obtained from the material balance equations.

$$Fx_i^{\text{total}} = E\sum_{k=1}^{n} y_{ik} = Ek_i\sum_{k=1}^{n}[ABS_{ik}] \tag{1}$$

$$y_{ik} = k_i[ABS_{ik}] \tag{2}$$

where F and E are the weight of the yew needle and the extract, respectively, and n is the stage number of the crosscurrent extraction.

The experimental results show that the absorbance of each component at the seventh stage is less than a ten-thousandth of that at the first stage. The sum of the absorbance for seven stages is listed in Table 1 with the standard deviation for each component. Meanwhile, the values of k_i in Eq. (1) cannot be determined in the present study, because each component is a mixture and not all the chemical species are identified so that a calibration curve is not obtained. Therefore, the variables of $x_{ij}/x_i^{\text{total}}$ and $y_{ij}/x_i^{\text{total}}$ are introduced to evaluate the concentration in the raffinate and extract, of which the details are shown in the latter section.

Table 2. Experimental conditions

	Experiment 1	Experiment 2	Experiment 3
Volume of solvent [ml]	50	50	500
Weight of feed solid [mg]	50	50	500
Diameter of solid [μm]	32, 250, 537	32	32, 250, 537
Temperature [K]	298	298	298
Solvent	Methanol	See Table 3	Methanol

Water Content of Yew Needle

The moisture content of the dry yew needles is measured by using a Carl-Fischer moisture analyzer with the different weights of particles. The observed moisture content is proportional to the weight of the solid particles, and the mass fraction of water obtained is about 0.06.

SELECTION OF SUITABLE SOLVENT FOR EXTRACTION OF SOLUTES FROM THE YEW NEEDLE

In order to determine a suitable solvent to extract the taxane compounds from the yew needles, experiments of single extraction are carried out with various solvents. In the experiments, the yew needle powder of 32 μm particle (50 mg) is soaked in 50 ml of solvent in a 100 ml of Erlenmeyer flask, and it is shook by a thermo-shaker at 298 K for 24 hours, in which the yew needle powder is dispersed and the volume change of the solution is not observed apparently. Then, the raffinate is separated from the solution, and the concentration of each component in the extract is measured by a UV spectrophotometer (Experiment 2). The experimental conditions are summarized in Table 2. The solvents examined are water, six alcohols, five hydrocarbons, three nitriles and four ethers, and are summarized in Table 3.

To calculate the distribution coefficient and selectivity, the simplest model that solvents are impermeable to the solid is applied with the following assumptions. In what follows, the basic equations for crosscurrent extraction are shown, because they can be applied for single extraction as well as crosscurrent extraction.

1. The solvent does not permeate the solid.
2. The concentration in the raffinate is in equilibrium with that in the extract.
3. The amount of each component in the extract, $E_j y_{ij}$, is very small compared with the amount of feed, F.
4. The concentration of component i in the raffinate at the last stage n is negligible.

Table 3. Solvent used in Experiment 2

Group	Material
Water	Water
Alcohol	Methanol, ethanol, *n*-propanol, 1-butanol, 1-hexanol, 1-decanol
Ester	Ethylformate, ethylacetate, ethylpropyrate, ethylbutyrate
Nitrile	Acetnitrile, propiononitrile, hexanitrile
Hydrocarbon	Heptane, hexane, pentane, octane, decane

Under the assumptions, the amounts of the extract and raffinate at the j stage, E_j and R_j are constant respectively. Thus, if they are represented by E and R, the material balance equations for the component i at each stage are expressed by

$$\begin{aligned} Fx_i^{\text{total}} &= Ey_{i1} + Rx_{i1} \quad (i = 1, C; \quad j = 1) \\ Rx_{ij-1} &= Ey_{ij} + Rx_{ij} \quad (i = 1, C; \quad j = 2, n) \end{aligned} \tag{3}$$

By combining Eq. (2) with Eq. (3), the following equation is obtained.

$$\begin{aligned} Fx_{ij} &= \left(Fx_i^{\text{total}} - E \sum_{k=1}^{j} y_{ik} \right) \\ &= Ek_i \left(\sum_{k=1}^{n} [ABS_{ik}] - \sum_{k=1}^{j} [ABS_{ik}] \right) \end{aligned} \tag{4}$$

Here the variables, $x_{ij}/x_i^{\text{total}}$ and $y_{ij}/x_i^{\text{total}}$ are introduced because the value of k_i is not obtained in the present study. They are expressed by using $[ABS_{ij}]$ as follows.

$$\frac{y_{ij}}{x_i^{\text{total}}} = \frac{F[ABS_{ij}]}{E \sum_{k=1}^{n} [ABS_{ik}]} \tag{5}$$

$$\frac{x_{ij}}{x_i^{\text{total}}} = \frac{\sum_{k=1}^{n} [ABS_{ik}] - \sum_{k=1}^{j} [ABS_{ik}]}{\sum_{k=1}^{n} [ABS_{ik}]} \tag{6}$$

The distribution coefficient, m_{ij}, and selectivity, β_{iC}, at the stage j are defined by,

$$m_{ij} = \frac{y_{ij}}{x_{ij}} \tag{7}$$

$$\beta_{iC} = \frac{m_{ij}}{m_{Cj}} \tag{8}$$

In order to evaluate the concentration in the extract and raffinate, the distribution coefficient and selectivity, the values of $\sum_{k=1}^{n} [ABS_{ik}]$ shown in Table 1 are assumed independent of the solvents, because the relative values of the distribution coefficient and selectivity are only necessary to compare separation performance of the solvents. Fig. 1 shows the distribution coefficient of each component calculated by Eq. (7) with $j = 1$. The abscissa of the figure is the number of carbons in solvent, G, and the distribution coefficient obtained by water is plotted at $G = 0$ as an alcohol having no carbon. The distribution coefficient of each component obtained by a given alcohol takes a similar value without respect to the components. Furthermore, the coefficient has the maximum value at $G = 1$ (methanol), and decreases with increase in number of carbons in solvent. Similar tendency is observed for the solvents of ether and nitrile.

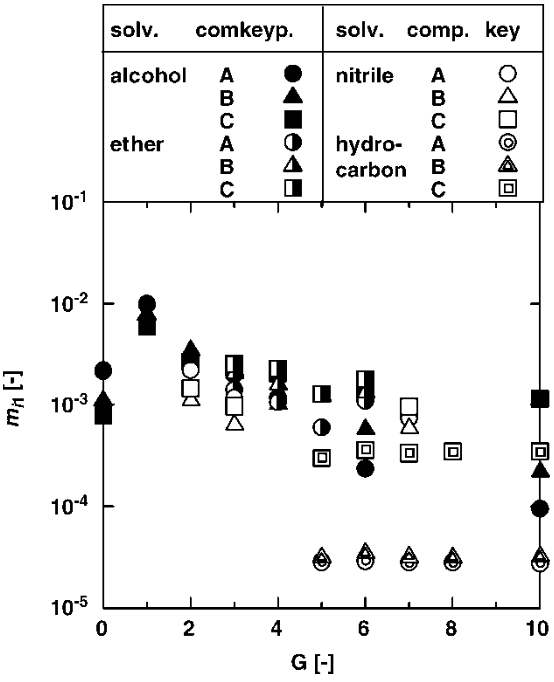

Figure 1. Distribution coefficients with different solvents.

Meanwhile, the distribution coefficients of each component obtained by hydrocarbon have almost the same values independently of the carbon numbers in solvent, but the distribution coefficient of component C is higher than that of components A and B. Those results indicate that methanol is a proper solvent to extract all components from the yew needles with the smallest amount of solvent.

Figure 2 shows the selectivities of components A and B to the component C, β_{AC} and β_{BC} calculated by Eq. (8) with $j = 1$. The abscissa of the figure is the number of carbons in solvent. In the cases of alcohol, nitrile and ester, the selectivities of both components have maximum values at $G = 0$ (water), and decrease with increase in carbon number of solvent. Meanwhile, the selectivities of both components obtained by hydrocarbons take constant values independent of the carbon numbers, and have the lower values than those by the other solvents. Those results indicate that the polar solvent such as water or methanol is proper to extract the components A and B selectively, and nonpolar solvent such as hydrocarbon is proper to extract the component C selectively. Therefore, the following conclusion is obtained that all the components are separated from the yew needles by the solid-liquid extraction with methanol and that the components A and B are separated from the component C by the liquid-liquid extraction with the liquid mixture of water and hydrocarbon.

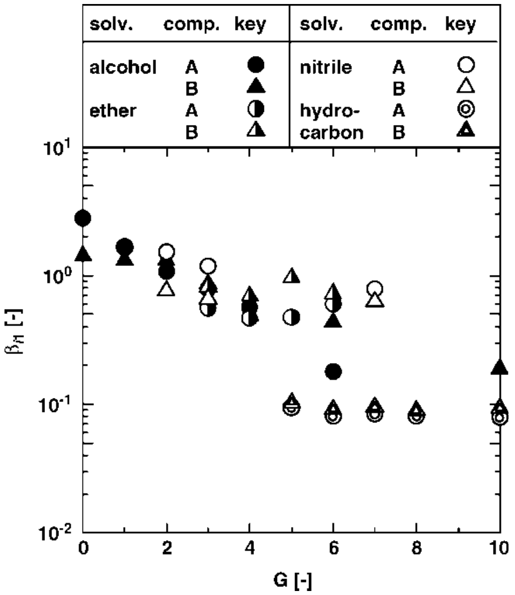

Figure 2. Separation factors with different solvents.

AMOUNT OF SOLUTION IN THE RAFFINATE IN SOLID-LIQUID EXTRACTION

The botanical cell, the essential element of the yew needle, is composed of nucleus, cytoplasm, and cell membrane. If solvent can permeate the dried cytoplasm through the cell membrane, there is a possibility that the liquid solution is formed with solutes in the solid, and the concentration of the solution in the solid phase affects the concentration in the external liquid that surrounds the solid.

The amount of solution in the raffinate, R^*, can be determined from the weight of the raffinate that has no liquid on the surface. To estimate the value of R^*, the single extraction runs are carried out with methanol for 24 to 168 hours, of which the time is different with the particle size. Then, the raffinate is separated from the solution, and the weight of the wet raffinate, W, is measured at a given time interval, while the wet raffinate is dried under the constant temperature and humidity. Those measurements are carried out with different particle in size. The experimental conditions are summarized in Table 2 (Experiment 3).

Figure 3(a) shows an example of the drying rate, $v = dW/dt$, which is measured by the particles of 250 μm. The drying rate is almost constant in the first drying period, and begins to decrease at $v = 5 \times 10^{-4}$ g/s. The same onset values, at which the drying rate started to decrease, are obtained

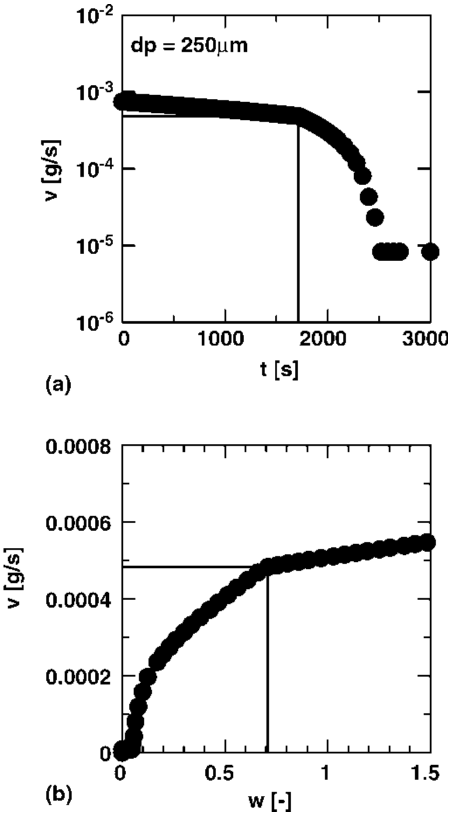

Figure 3. Drying curve for the raffinate.

by the drying experiments with the different particles in size. This may suggest that solvent attached on the raffinate surface evaporates in the first drying period, and diffuses in the solid and seeps out of the solid in the second drying period.

The drying rates are plotted against the solvent content in Fig. 3(b). The solvent content, w, is defined by:

$$w = \frac{W - W_\infty}{W_\infty} \tag{9}$$

where W_∞ is the weight of raffinate corresponding to the equilibrium solvent content, and is determined from the weight of raffinate at 24 hours later in the drying experiments. The solvent content at $v = 5 \times 10^{-4}$ g/s, w_c, which represents the critical solvent content, is 0.68 for the particles of 250 μm from Fig. 3(b). Similarly, $w_c = 0.35$ and $w_c = 0.70$ are obtained for the 32 μm- and 573 μm particles, respectively. The amount of solution in the raffinate,

R^*, is calculated with the observed values of w_c by:

$$R^* = w_c W_\infty \tag{10}$$

The reason why the value of w_c is dependent on the particle size is not clear, but it might be due to difference in the number of cells in a solid particle. Since it takes 24, 48, and 168 hours to achieve phase equilibrium in solid-liquid extraction for 32, 250, and 537 μm particles, the solvent may penetrate deep into the solid. Reversely, the second drying period starts 20, 30, and 35 minutes later in drying. Thus, the solvent deep in the solid could not arrive at the surface because of lower rate of diffusion, so that more amount of solvent might remain in the solid, as the particle size is bigger.

DISTRIBUTION CURVE AND DISTRIBUTION COEFFICIENT

In order to measure the distribution coefficient and selectivity of each component, the experiments of crosscurrent extraction are carried out with methanol for the different particles in size, and the concentration of each component in the extract phase is analyzed by a UV spectrophotometer at each stage (Experiment 1). The experiments are carried out in the way described in the previous section. To confirm reproducibility of the experimental data, three extraction runs are carried out at the same experimental conditions. The experimental conditions of Experiment 1 are summarized in Table 2.

To evaluate the concentration of the raffinate based on the experimental fact that the solvent permeates the raffinate (solid phase), the concentration of solution in the raffinate is assumed to be in equilibrium with that in the extract (the solvent permeation model). Under the assumption, the material balance equations in crosscurrent extraction are expressed as follows.

$$\begin{aligned} Fx_i^{\text{total}} &= E_1^* y_{i1} + R_1^* x_{i1}^* \quad (i = 1, C; \quad j = 1) \\ R_{j-1}^* x_{ij-1}^* &= E_j^* y_{ij} + R_j^* x_{ij}^* \quad (i = 1, C; \quad j = 2, n) \end{aligned} \tag{11}$$

where E_j^* and R_j^* are the amounts of the extract and solution in the raffinate at the stage j, and x_{ij}^* is the concentration of component i in the solution in the raffinate. Furthermore, the following assumptions are made.

1. The amount of solution in the raffinate at each stage, R_j^* is constant, that is,

$$R_j^* = R^* \tag{12}$$

2. The amount of each component in the extract, $E_j^* y_{ij}$, is very small compared with the amount of feed, F.
3. The concentration of component i in the liquid solution in the raffinate at the final stage n is negligible small.

From the assumptions (1) and (2), the amount of extract at each stage becomes constant, that is, $E_j^* = E^*$, and is calculated from the following equation with R^*.

$$E^* = S - R^* \tag{13}$$

By combining those equations with Eq. (11), the following equation is obtained.

$$x_{ij}^* = \frac{1}{R^*}\left(Fx_i^{\mathrm{total}} - E^* \sum_{k=1}^{j} y_{ik}\right) \tag{14}$$

Thus the value of $x_{ij}^*/x_i^{\mathrm{total}}$ can be calculated from the following equation by using the values of $y_{ij}/x_i^{\mathrm{total}}$, R^* and E^*.

$$\frac{x_{ij}^*}{x_i^{\mathrm{total}}} = \frac{1}{R^*}\left(F - E^* \sum_{k=1}^{j} \frac{y_{ik}}{x_i^{\mathrm{total}}}\right) \tag{15}$$

The distribution coefficient, m_{ij}^*, at the stage j is defined by

$$m_{ij}^* = \frac{y_{ij}}{x_{ij}^*} \tag{16}$$

Figures 4(a), 4(b), and 4(c) show the distribution curves of components A, B, and C, respectively. The ordinate is the concentration in the raffinate calculated by Eq. (15), and the subscript j that represents the stage number is omitted from the symbols x. The parameter in the figure is the particle size, d_p The figures show that the concentration of component A in the raffinate increases with increase in the concentration of the component in the extract, and the distribution curves are well correlated without respect to the particle size. Figures 5(a), 5(b), and 5(c) show the distribution coefficients of components A, B and C, respectively. The distribution coefficients are almost constant in the low concentration region of $y_{ij}/x_i^{\mathrm{total}}$, and the difference in the distribution coefficients between the particle sizes is small. Furthermore, the concentration of the solution in the raffinate is not equal to that in the extract, and it is one hundred to one thousand times as much as that in the extract. In order to confirm the possibility of higher concentration of the solution in the raffinate, the solid that is obtained by drying the extract liquid is dissolved in the solvent, and the concentration of the solution is measured. The concentration of the solution obtained is much higher than the concentration in the solution in the raffinate. Therefore, it is reasonable to consider that concentration in the extract is in equilibrium with that in the solution in the raffinate.

Meanwhile, solvent is often assumed not to permeate the solid phase in solid-liquid extraction. Thus, the distribution curves and distribution coefficients are calculated based on that assumption mentioned above. The distribution curve of component A is shown in Fig. 6(a). The ordinate is the

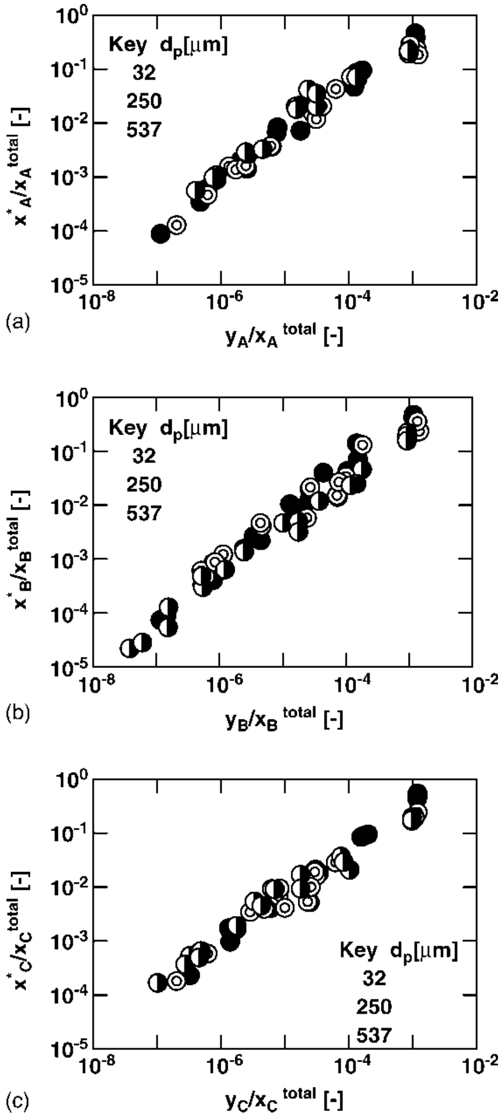

Figure 4. Distribution curves of each component based on the liquid concentrations in the raffinate.

concentrations in the raffinate calculated by Eq. (6). The parameter in the figure is the particle size, d_p. The concentration of component A in the raffinate increases with increase in the concentration of the component in the extract. The figure also shows that the concentration in the raffinate seems to increase with increase in the particle size. Figures 6(b) and 6(c) show the

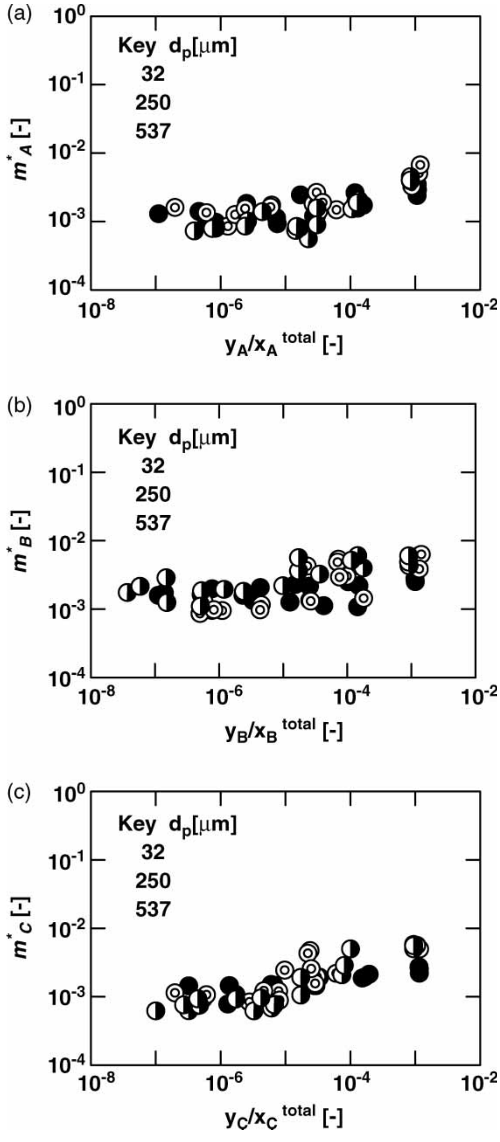

Figure 5. Distribution coefficients of each component based on the liquid concentrations in the raffinate.

distribution curves of components B and C, respectively. As is similar to the component A, the concentration in the raffinate increases with increase in the concentration in the extract. Similarly, the concentrations of both components are affected by the particle size, and the concentrations obtained by the particle of 32 μm are smaller than those by other particle sizes are.

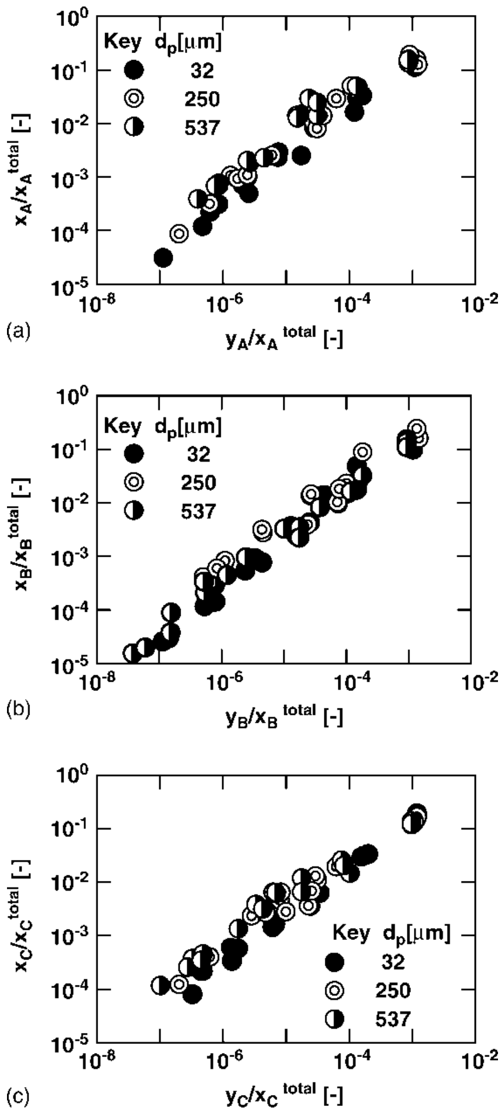

Figure 6. Distribution curves of each component.

Figures 7(a), 7(b), and 7(c) show the distribution coefficients of components A, B, and C calculated by Eq. (7), respectively. The distribution coefficients of all the components slightly increase with increase of the concentration in the extract. Furthermore, those values are somewhat different with the particle size, and the distribution coefficients obtained by 32 μm-particle show the larger values compared with those by the particles

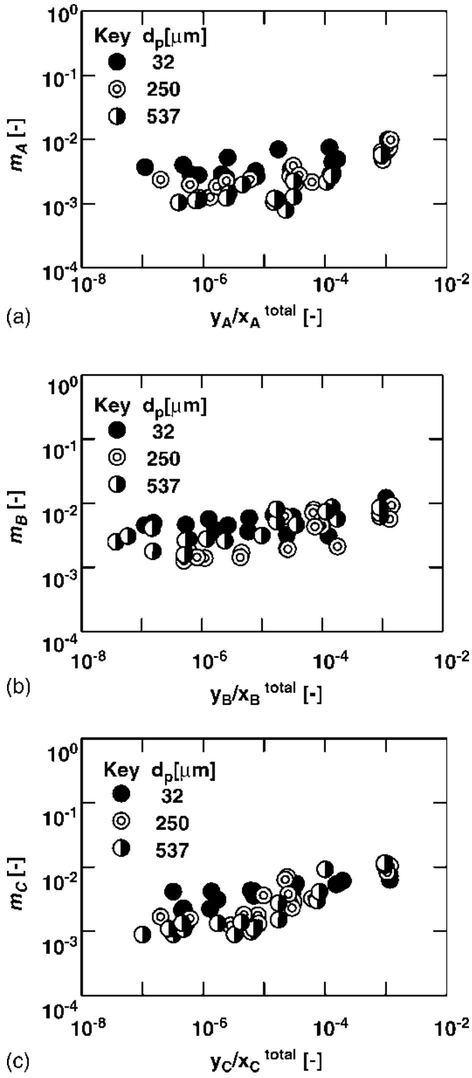

Figure 7. Distribution coefficients of each component.

with other diameters. In other words, the distribution coefficient of each component seems dependent on the particle size.

This is due to the model that solvent is impermeable to the solid, because other assumptions are not related to the particle size. Since the solutes are hard to move in the solid freely, only the concentration of solutes near the solid surface may contribute to phase equilibrium with the liquid phase. If the concentrations of solutes in the solid become larger as the particle size becomes larger, the size dependency on distribution coefficient and selectivity may appear. Those considerations indicate a possibility that solvent permeates the cell.

IDEAL STAGE CALCULATION FOR EXTRACTION OF SOLUTES FROM THE YEW NEEDLE

In general, the countercurrent multistage extraction is usually more effective than the crosscurrent extraction. In order to study the effect of operating conditions on the number of stages in the countercurrent multistage extraction and determine the optimum operating conditions with the optimum number of stages, simulation of countercurrent multistage extraction for yew needle is made under the model that solvent permeates the solid.

Basic Equations for Simulation of Countercurrent Multistage Extraction

In the countercurrent multistage extraction with *n* stage, the material balance equation for component *i* at each stage is expressed as follows.

$$\begin{aligned} &Fx_i^{\text{total}} + E_2^* y_{i2}^* = R_1^* x_{i1}^* + E_1^* y_{i1}^* \\ &R_{j-1}^* x_{ij-1}^* + E_{j+1}^* y_{ij+1}^* = R_j^* x_{ij}^* + E_j^* y_{ij}^* \\ &R_{n-1}^* x_{in-1}^* = E_n^* y_{in}^* + R_n^* x_{in}^* \end{aligned} \tag{17}$$

Here, the following assumptions are made.

1. The amount of solution in the raffinate is constant at all the stage, that is,

$$R_1^* = R_2^* = \cdots = R_n^* = R^* \tag{18}$$

2. The concentrations of solutes in the extract are very low and the flow rate of extract is constant at all the stages, that is,

$$E_1^* = E_2^* = \cdots = E_n^* = E^* \tag{19}$$

3. The solution in the raffinate is in equilibrium with the extract liquid, and the distribution coefficient of each component is constant.

$$y_{ij}^* = m_{ij}^* x_{ij}^* \tag{20}$$

$$m_{i1}^* = m_{i2}^* = \cdots = m_{in}^* = m_i^* \tag{21}$$

From the experimental results, the amount of solution in the raffinate, R^*, is given by wF, and E^* is expressed by the following equation.

$$E^* = S - R^* = S - wF \tag{22}$$

Therefore, Eq. (17) is reduced as follows.

$$\frac{wx^*_{ij-1}}{x_i^{\text{total}}} + \left(\frac{S}{F} - w\right)\frac{y^*_{ij+1}}{x_i^{\text{total}}} = \frac{wx^*_{ij}}{x_i^{\text{total}}} + \left(\frac{S}{F} - w\right)\frac{y^*_{ij}}{x_i^{\text{total}}} \tag{23}$$

$$\frac{wx^*_{ij-1}}{x_i^{\text{total}}} = 1 \quad \text{at } j = 1 \tag{24}$$

$$\frac{y^*_{ij+1}}{x_i^{\text{total}}} = 0 \quad \text{at } j = n \tag{25}$$

Simulation of countercurrent multistage extraction is carried out with the values of S/F and the number of stages as parameters. The simulation conditions are summarized in Table 4.

Calculation Results

Figure 8 shows the concentration profiles in the countercurrent multistage solid-liquid extraction with 20 stages. The parameter in the figure is the solvent-to-feed ratio, E/F. As shown in the figure, the amount of solvent 300 times as much as feed is necessary to extract 99.9% of the target solutes from the yew needle. Figure 9 shows the solute concentration in the raffinate at the last stage in the countercurrent-multistage extraction with 5, 10, and 20 stages. The abscissa is the solvent-to-feed ratio. As shown in the figures, the solute concentration in the raffinate at the last stage increases with increase of the flow rate of the solvent, and $E/F = 800$ is required for 5-stage extraction process, $E/F = 400$ for 10-stage process and $E/F = 300$ for 20-stage process.

Table 4. Simulation conditions for countercurrent multiple extraction

Parameter	Unit	Values
$y_{i,n+1}$	(−)	0
n	(stage)	5, 10, 20
F	(kg/h)	100
E/F	(−)	100, 300, 400, 500, 800, 1000
m_A	(−)	0.00164
m_B	(−)	0.00191
m_C	(−)	0.00157

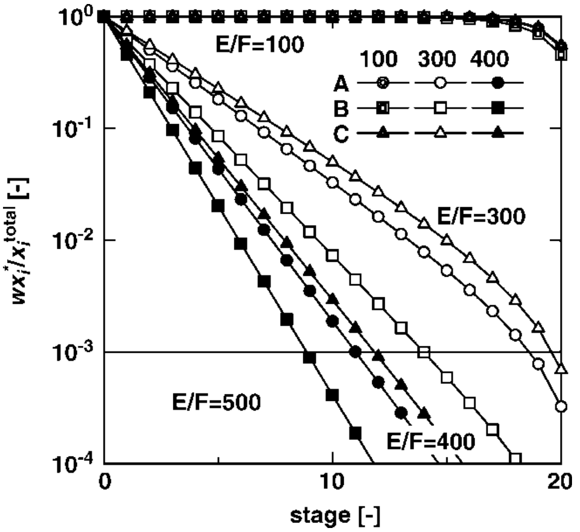

Figure 8. Concentration profiles of the solutes in the raffinate in countercurrent multistage extraction process with different E/F.

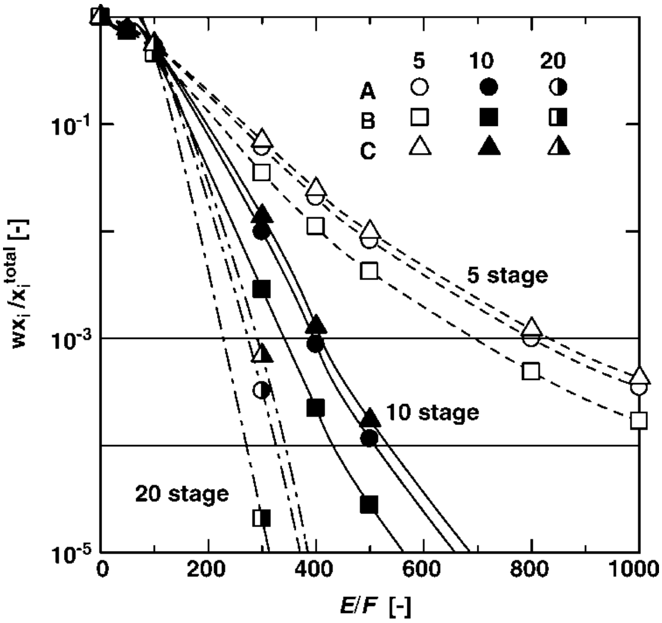

Figure 9. Effect of E/F on the concentration of solutes in the raffinate at the last stage in countercurrent multiple extraction process.

CONCLUSION

In order to examine the proper solvent for solid-liquid extraction of the taxane compounds from the yew needle, the single extraction experiments are carried out with various solvents. The solvents examined are water, six alcohols, five hydrocarbons, three nitriles, and four ethers. Among the solvents, methanol gives the largest distribution coefficients for all the components. Thus, methanol is selected as the proper solvent for the solid-liquid extraction. In the data reduction of the experiments, the value of Fx_i^{total}, which is measured by methanol, is assumed independent of solvents. However, since the solvent permeates the raffinate, the value of Fx_i^{total} could be different with solvents. Thus, it will be separately examined by a further study.

The experiments of crosscurrent extraction are carried out to measure the distribution coefficients of solutes in the yew needle with methanol. The distribution coefficient of each component is calculated based on the solvent-permeation model, and it shows independency of the particle size. Meanwhile, the distribution coefficient is calculated based on the model that solvent does not permeate the solid. The calculated distribution coefficient and selectivity show dependence on the particle size and concentration.

Based on the extraction equilibrium model that solvent permeates the raffinate, simulation of the countercurrent-multistage-extraction is carried out for separation of the taxane compounds from the yew needles with methanol. The results show that 99.9% of solutes are extracted from the yew needles with E/F = 300 in 20-stage extraction process.

SYMBOLS

$ABS_{i,j}$	Absorbance of component i at the stage j in UV spectra (−)
d_p	Particle diameter (m)
E_j	Amount of the extract phase at the stage j (g)
F	Amount of feed (g)
G	Carbon number of solvent (−)
k_i	Proportional constant of the component i (−)
m_i	Distribution coefficient of the component i (−)
n	Stage number (−)
R_j	Amount of the raffinate at the stage j (g)
$R^*{}_j$	Amount of liquid solution in the raffinate at the stage j (g)
S_j	Amount of solvent at the stage j (g)
T	Temperature (K)
t	Time (h)
V	Volume of solvent (l)
v	Drying rate (g s^{-1})
W	Weight of the wetted raffinate (g)
W_∞	Equilibrium solvent content (g)

w	Solvent content (−)
$x_{i,j}$	Mass fraction of component i at the stage j in the raffinate (−)
x_i^{total}	Mass fraction of component i in the solid feed (−)
$x^*_{i,j}$	Mass fraction of component i at the stage j in the liquid solution in the raffinate (−)
$y_{i,j}$	Mass fraction of component i at the stage j in the extract phase (−)

Greek Letters

$\beta_{\mathrm{i,C}}$	Selectivity of component i for solid-liquid extraction (−)
ηi	Yield of component i for solid-liquid extraction (−)

Subscripts

A	Components including Taxines B
B	Components including Taxol and 10-deacetylbaccatin
C	Components including Cinnamyl taxanes
i	Component
j, k, n	Stage

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