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RESEARCH PAPER

Solubilization of (+)-Limonene by Anionic/Cationic Mixed Surfactant Systems

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ABSTRACT

The combined effects of sodium *n*-octyl sulfate (SOS) and cetyltrimethylammonium bromide (CTAB) on the solubilization of (+)-limonene in aqueous solution were studied using a headspace gas chromatography technique. The findings showed the mixing of SOS and CTAB resulted in positive synergistic effects on the solubility of (+)-limonene. The positive synergistic effects are explained from the perspective of the phase behavior of this mixed surfactant system.

Key Words: Solubilization; (+)-Limonene; Mixtures of surfactants.

INTRODUCTION

The solubility of insoluble substances in aqueous solution can be increased significantly by the addition of a surfactant. Surfactants used for solubilization in practical applications almost always consist of mixtures of surface active agents.[1] The solubilizing ability of mixed surfactants is much greater or less than the solubilizing ability of each individual surfactant alone. It will be important to clarify if a pronounced synergistic effect for solubilization actually does occur in certain types of mixed surfactant systems, because this is interesting not only for practical applications, such as pharmaceutical products, but also in academic research. There have not been many studies concerning solubilization of insoluble substances using mixed surfactant systems, although many studies have been published about the individual single surfactant system.[2]

Herein, we report the synergistic effects by the mixtures of oppositely charged surfactants [sodium *n*-octyl sulfate (SOS) and cetyltrimethylammonium bromide (CTAB)] on the solubilization of an insoluble substance [(+)-limonene] in aqueous solution using the static headspace gas chromatography technique.[3,4] This technique is very attractive for analysis

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of volatile insoluble substances dissolved in aqueous solutions.

EXPERIMENTAL

Materials

The SOS and CTAB, used as solubilizers, and (+)-limonene, used as the insoluble substance, were obtained from Kanto Chemical Co., Inc. and were used without further purification. The water used in the present study was water for injection JP (Japanese Pharmacopoeia, Otsuka Pharmacy Co., Ltd.).

Sample Preparation

Sample solutions (5 g) containing various concentrations of (+)-limonene and surfactants in water were prepared into 13.4 mL headspace vials and sealed using silicone septa and aluminum foil. The total concentrations of SOS and CTAB were 0.1 mol/L. The vials were then thermostatted at 25 ± 0.1°C and shaken overnight before analysis.

Gas Chromatographic Analysis

After equilibrium was established, 200 μL of (+)-limonene vapor from the above solution was drawn from the vial using a gas-tight syringe. This sample was then analyzed by gas chromatography (GC; GC-14B, Shimadzu Co., Tokyo, Japan) with a flame-ionization detector using a 1 m × 3 mm i.d. glass column packed with PEG-20M. The temperature of detection was 250°C, and the column oven temperature was 105°C. Nitrogen was used as the carrier gas (flow rate, 30 mL/min). The area of each peak was measured using a Shimadzu Chromatopac C-R6A integrator.

RESULTS AND DISCUSSION

Activity (a_L) of the (+)-limonene in the solution was defined by Eq. (1),[5]

$$a_L = \frac{A_L}{A_L^0} \tag{1}$$

where A_L and A_L^0 are the integrated GC peak areas obtained from the headspace of the (+)-limonene in the solution and its pure state, respectively. The partial vapor pressure of the (+)-limonene (P_L) is then obtained by multiplying the activity calculated in Eq. (1) with the vapor pressure of the pure (+)-limonene [P_L^0, 186.7 Pa[6]] at 25°C.

$$P_L = a_L \cdot P_L^0 \tag{2}$$

Figure 1 shows the experimental curves of the relative peak area (A_L/A_L^0) as a function of (+)-limonene fed in the SOS/CTAB mixed systems composed of various SOS mole fractions ($X_{\mathrm{SOS}} = 0$, 0.3, 0.7, and 1.0) as an example. When the activity of (+)-limonene in solution reached about 1, the relative peak area did not change any further, despite the increasing amounts of (+)-limonene fed into the system. This phenomenon has been used to determine the solubility of a substance with significant volatility (i.e., the point of attaining a plateau on the curve can be looked on as the solubility of substance in solution).[3] In general, it was suggested that the amount of substance in the vapor over the solution will be extremely small. However, this amount should not be overlooked for highly volatile substances, such as (+)-limonene, used in this study, because the actual quantity in the solution after equilibrium differs widely from the quantity added initially. We calculated the number of moles of (+)-limonene in the vapor from the partial vapor pressure of the (+)-limonene calculated

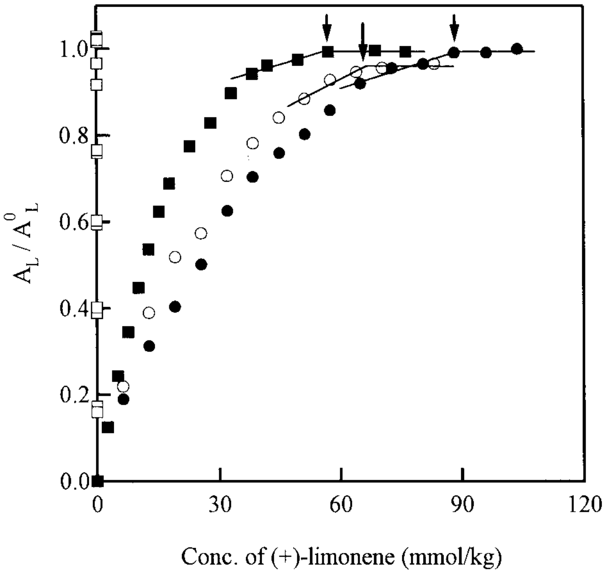

Figure 1. Relative peak area as a function of the amount of (+)-limonene fed in SOS/CTAB mixed solutions. ○, $X_{\mathrm{SOS}} = 0$; ●, $X_{\mathrm{SOS}} = 0.3$; ■, $X_{\mathrm{SOS}} = 0.7$; □, $X_{\mathrm{SOS}} = 1.0$.

in Eq. (2) and the ideal gas equation, and then determined the actual (+)-limonene concentration in the solution by subtracting the number of moles in the vapor from the total amount of (+)-limonene added to the vial. These corrected (+)-limonene concentrations in the solution were used as values for the x axis in Fig. 1.

The phase solubility diagrams of (+)-limonene in the mixed surfactant solutions and those in the individual single SOS and CTAB solutions are shown in Fig. 2. It is preferable to estimate the synergistic solubilization effects on the solubility of insoluble substance using an additivity mixing rule.[7] In the mixed systems (closed circle), the relation between the solubility of (+)-limonene and the mole fraction of SOS is depicted. In the individual single surfactant systems of SOS (open square) and CTAB (open circle), these concentrations correspond to the concentrations in the SOS/CTAB mixed solutions. Moreover, the dashed line in the figure represents the calculated solubility (S_{cal}) of (+)-limonene in the mixed surfactant solutions based on the additivity mixing rule [Eq. (3)] using the solubility of (+)-limonene in the individual single surfactants.[7]

$$S_{\mathrm{cal}} = SP_{\mathrm{SOS}} \times [\mathrm{SOS}_t] + SP_{\mathrm{CTAB}} \times [\mathrm{CTAB}_t] + S_w \tag{3}$$

where SP_{SOS} and SP_{CTAB} are the moles of the (+)-limonene solubilized per unit mole of SOS and CTAB, respectively. $[\mathrm{SOS}_t]$ and $[\mathrm{CTAB}_t]$ are the total concentrations of SOS and CTAB in the mixed surfactant solutions, respectively, and S_W is the solubility of (+)-limonene in water.

The results in Fig. 2 show that the experimental solubility of (+)-limonene in the mixed surfactant solutions is clearly larger than the calculated solubility (S_{cal}) in all X_{SOS}.

To determine the synergistic effects of the mixture of SOS and CTAB on the solubility of (+)-limonene, the differential ratio (R) between the experimental and the calculated solubility of (+)-limonene was evaluated according to the following equation[7]:

$$R = \frac{S_{\mathrm{exp}} - S_{\mathrm{cal}}}{S_{\mathrm{cal}}} \tag{4}$$

where S_{exp} is the experimental solubility of (+)-limonene in a mixed surfactant solution. When R is equal to zero, this implies that there is no synergistic effect on the solubilization. The R values, as a function of X_{SOS} in the mixed surfactant solutions, are plotted in Fig. 3. It was shown that the R values were positive in all X_{SOS} and became maximum in the region from approximately $X_{\mathrm{SOS}} = 0.7$ to approximately $X_{\mathrm{SOS}} = 0.8$. The solution properties of the mixed surfactant system are often superior in applications to the properties of the individual single surfactants, because mixing of surfactants leads to the formation of a variety of microstructures, including a novel equilibrium vesicle phase.[7] The phase behaviors of mixtures of SOS and CTAB in aqueous solution have been studied in detail by Brasher et al.[8] These phase behaviors are shown in Fig. 3. The relation between solubilizing ability and phase behavior in the SOS/CTAB mixed solutions was examined. As a result, it became clear that the positive synergistic effects for the solubilization of (+)-limonene by the mixture of SOS and CTAB is particularly large in the single-phase vesicle region and in the two-phase vesicle/lamellar region.

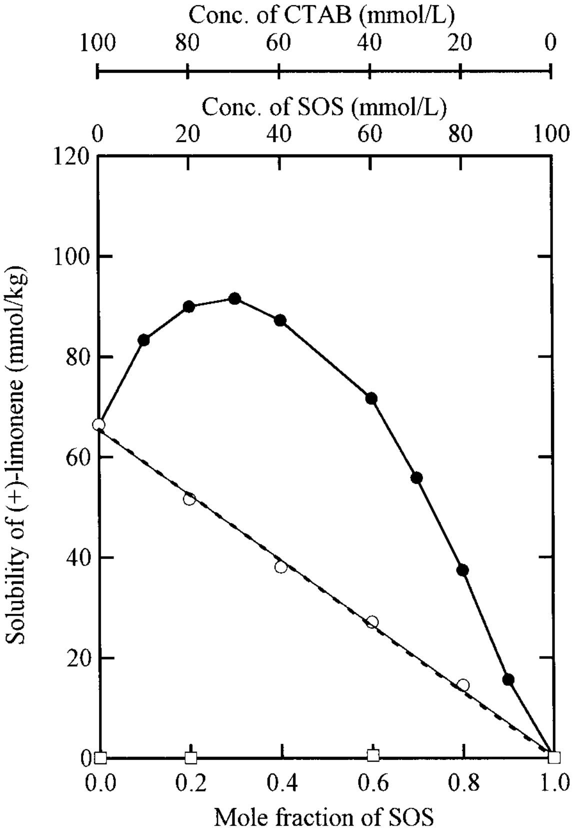

Figure 2. Phase solubility diagram of (+)-limonene in SOS/CTAB mixed solutions, and individual single SOS and CTAB solutions. ----, S_{cal} ; ●, SOS/CTAB; □, SOS; ○, CTAB.

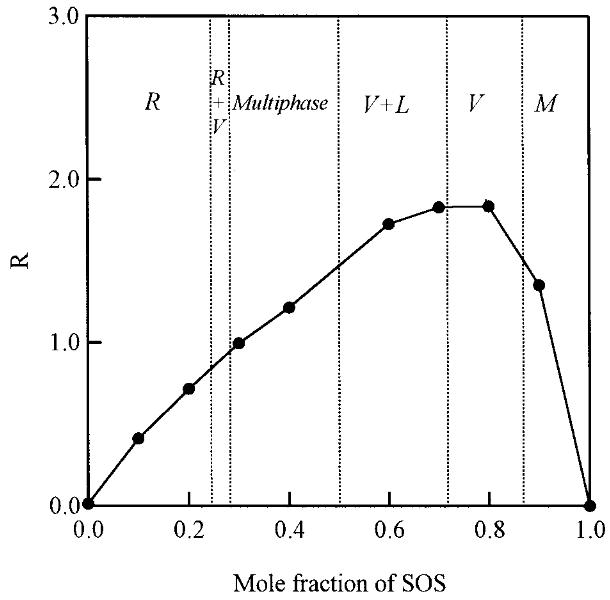

Figure 3. *R* values as a function of the mole fraction of SOS in SOS/CTAB mixed solutions. R, rodlike micelle region; V, vesicle region; L, lamellar phase region; M, spherical micelle region.

CONCLUSIONS

It was clear that the mixture of SOS and CTAB showed positive synergistic effects for the solubilization of (+)-limonene because of the formation of a variety of microstructures, such as vesicle and lamellar, which are not observed by the individual single surfactants. In many practical applications, one of the most important problems of solubilization is how to solubilize the great number of insoluble substances with a small amount of surfactant. Knowledge of the experimental findings of the present study becomes a fundamental guide in the selection of surfactants in practical use in the pharmaceutical field, cosmetic field, and so forth.

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