# Solubility and Mass Transfer Coefficient Enhancement of Stearic Acid through Hydrotropy

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The effect of various hydrotropes such as sodium salicylate, sodium benzoate, and nicotinamide on the solubility and mass transfer coefficient of stearic acid was investigated under a wide range of hydrotrope concentrations, (0 to 3.0) mol·kg$^{-1}$, and different system temperatures, $T$ = (303 to 333) K. It was found that the solubility and mass transfer coefficient of stearic acid increase with the increase in hydrotrope concentration and also with system temperature. All hydrotropes used in this work showed an enhancement in the solubility and mass transfer coefficient to different degrees. The order of increase in the solubility and mass transfer coefficient of stearic acid with respect to different hydrotropes was found to be sodium salicylate > sodium benzoate > nicotinamide. The maximum enhancement factor value has been determined for both the solubility and the mass transfer coefficient. The effectiveness of hydrotropes was measured in terms of Setschnew constant $K_s$ and reported for all hydrotropes used in this study. In addition the solubility data are also fitted in a polynomial equation as a function of hydrotrope concentration. The solubility data fitted in a polynomial equation give a better fit since the variance is less than 0.6.

## Introduction

The term "hydrotropy" refers to a solubilization process whereby the addition of a large amount of a second solute results in an increase in the aqueous solubility of a poorly soluble compound.[1,2] Hydrotropic agents (or hydrotropes) are compounds that at high concentrations solubilize poorly water-soluble molecules in water.[3] At concentrations higher than a minimum hydrotrope concentration (MHC), hydrotropic agents self-aggregate and form noncovalent assemblies of lowered polarity, that is, nonpolar microdomine, which solubilize hydrophobic solutes.[4]

Stearic acid (octadecanoic acid) is a saturated fatty acid derived from animal and vegetable fats and oils. In different countries, it is mainly produced by the oleochemical (palm oil) industry, and it has been the primary fatty acid commodity for many years.[5] Stearic acid is used in the manufacturing of pharmaceutical products. Recently it has been used in the development of a drug delivery system, because it is considered to be inert, inexpensive, and biocompatible, besides having low toxicity.[6] In addition, stearic acid has been used for a cyclosporine A drug carrier system[7] and for masking the bitter taste of pharmaceutical compounds.[8] Stearic acid is prepared in the form of lipospheres for application as a kind of drug delivery system. Lipospheres can be prepared using supercritical fluid technology which utilizes carbon dioxide as an antisolvent by means of coprecipitation. In deploying the coprecipitation process for the production of lipospheres, stearic acid as a matrix and an active pharmaceutical ingredient (API) should be able to be dissolved in certain organic solvents. This condition implies that for successful production of lipospheres, the solubility of the API and stearic acid must not be infinite.[9]

The self-aggregation of the hydrotropic agent is different from surfactant self-assemblies (i.e., micelles) in that hydrotropes form planar or open-layer structures instead of compact spheroid assemblies.[10] Hydrotropic agents are structurally characterized by having a short, bulky, compact moiety, such as an aromatic ring, while surfactants are characterized by long hydrocarbon chains. In general, hydrotropic agents have a shorter hydrophobic segment, leading to higher water solubility, compared to surfactants. Hydrotropy is considered to be superior to other solubilization methods, such as micellar solubilization, miscibility, cosolvency, and salting-in, because the solvent character is independent of pH, has high selectivity, and does not involve emulsification.[11]

The effect of hydrotropes on the solubility and mass transfer coefficient for a series of organic acids and esters such as salicylic acid, 2-nitrobenzoic acid, butyl acetate, ethyl benzoate, amyl acetate, methyl salicylate, and benzyl acetate was studied in our earlier publications.[12–19] It has been observed that, in many two-phase reaction systems involving a sparingly soluble organic compound like stearic acid, the mass transfer coefficient was found to be very low solely due to the poor solubility of stearic acid in the aqueous phase. Since stearic acid serves as a raw material/intermediate for a wide variety of chemicals and allied products[20–22] and the separation of stearic acid from any liquid mixture seems to be difficult, this hydrotropic technique can be adapted to increase the solubility as well as to separate such mixtures effectively. Data on various aspects of hydrotropic study on the solubility and mass transfer coefficient for stearic acid + water system are reported for the first time.

## Experimental Section

All of the chemicals used in this work were procured from S D Fine-Chem Ltd., Mumbai, with a manufacturer's stated purity of 99 %.

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10.1021/je901041n 
Published on Web 03/16/2010

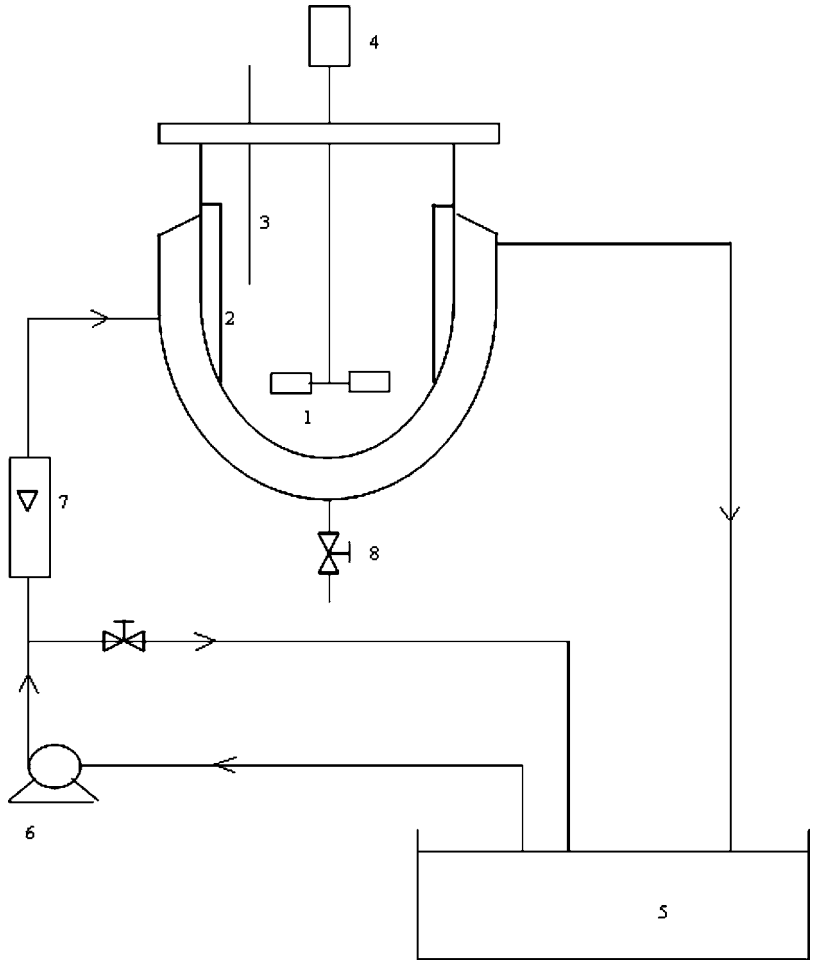


**Figure 1.** Schematic diagram of the experimental setup: 1, agitated vessel; 2, baffle; 3, thermometer; 4, electric motor; 5, water bath; 6, peristatic pump; 7, rotometer; 8, outlet valve.

The experimental setup for the determination of solubility values consisted of a thermostatic bath and a separating funnel. For each solubility test, an excess amount of powdered solid was taken in a separating funnel, and 100 mL of a solution of the hydrotrope of known concentration was added. The separating funnel was immersed in a constant-temperature bath fitted with a temperature controller which could control the temperature within ± 0.1 K. The setup was kept overnight for equilibration. After equilibrium was attained, the solution was filtered from the remaining solid. The concentration of the dissolved organic acid in aqueous hydrotrope solutions was analyzed by titration using standardized NaOH solutions using phenolphthalein as an indicator. All of the solubility experiments were conducted in duplicate to check the reproducibility. The reproducibility was < 2 %.

The experimental setup for the determination of the mass transfer coefficient consisted of a vessel provided with baffles and a turbine impeller run by a motor to agitate the mixture. The schematic diagram of the experimental setup is shown in Figure 1. The vessel used for mass transfer studies is of 40 cm height and of 15 cm inner diameter. The turbine impeller diameter is 5 cm, the width 1 cm, and the length 1.2 cm. It has four blades. The baffle is 40 cm high with a diameter of 1.5 cm. There are about four baffles that rotate at a speed of 600 rpm.

For each run, to measure the mass transfer coefficient, an excess amount of powdered solid was added to the aqueous solution of the hydrotrope of known concentration. The sample was then agitated for a known time of (600, 1200, 1800, and 2400) s. After the end of fixed time $t$, the entire mixture was transferred to a separating funnel. After allowing the sample to stand for some time, the solution was filtered from the remaining solid. The concentration of the solubilized organic acid in aqueous hydrotrope solutions at time $t$ was analyzed in the same way as for solubility determinations. A plot of $-\log[1 - c_b/c^*]$ versus $t$ is drawn, where $c_b$ is the concentration of stearic acid at time $t$ and $c^*$ is the equilibrium solubility of stearic acid at the same hydrotrope concentration. The slope of the graph gives $k_L a/2.303$, from which $k_L a$, the mass transfer coefficient, was determined. Duplicate runs were made to check the reproducibility. The observed difference was < 2 %.

## Results and Discussion

***Solubility.*** The solubility of stearic acid standard in water is $1.20 \cdot 10^{-3}$ mol·kg$^{-1}$ at 303 K, compared to being "insoluble" as reported by John.[23] Thus, the solubility value of stearic acid in water is in excellent agreement with the earlier reported values.[23,24]

Experimental data representing the average of duplicate determinations on the effect of hydrotropes, that is, sodium salicylate, sodium benzoate, and nicotinamide, on the solubility of stearic acid are plotted in Figures 2 to 4. Sodium salicylate is one of the hydrotropes used in this study. The solubility of stearic acid in water at 303 K in the absence of any hydrotrope is $1.20 \cdot 10^{-3}$ mol·kg$^{-1}$ (Figure 2). It has been observed that the solubility of stearic acid in water increases significantly only after the addition of 0.30 mol·kg$^{-1}$ of sodium salicylate in the aqueous solution. This concentration is referred to as the MHC.[25]

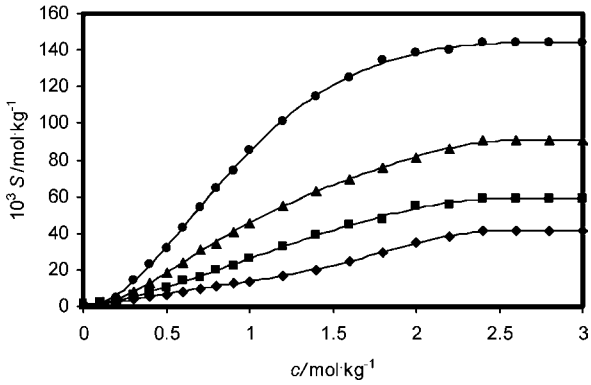


**Figure 2.** Effect of sodium salicylate concentration ($c$) on the solubility ($S$) of stearic acid in water at different temperatures: ♦, $T = 303$ K; ■, $T = 313$ K; ▲, $T = 323$ K; and ●, $T = 333$ K.

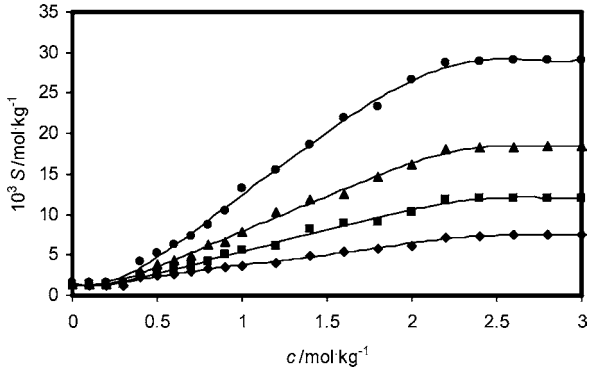


**Figure 3.** Effect of sodium benzoate concentration ($c$) on the solubility ($S$) of stearic acid in water at different temperatures: ♦, $T = 303$ K; ■, $T = 313$ K; ▲, $T = 323$ K; and ●, $T = 333$ K.

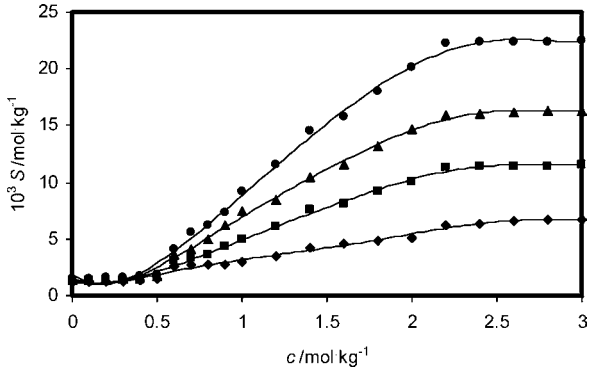


**Figure 4.** Effect of nicotinamide concentration ($c$) on the solubility ($S$) of stearic acid in water at different temperatures: ♦, $T = 303$ K; ■, $T = 313$ K; ▲, $T = 323$ K; and ●, $T = 333$ K.

**Table 1. MHC and $c_{max}$ Values for Hydrotropes**

| hydrotrope | MHC / mol·kg$^{-1}$ | $c_{max}$ / mol·kg$^{-1}$ |
|---|---|---|
| sodium salicylate | 0.30 | 2.40 |
| sodium benzoate | 0.40 | 2.20 |
| nicotinamide | 0.60 | 2.20 |

Therefore, it is evident that hydrotropic solubilization is displayed only above the MHC, irrespective of system temperature. Since hydrotropy appears to operate only at significant concentrations of hydrotrope in water, most hydrotropic solutions release the dissolved stearic acid on the dilution with water below MHC. The knowledge of MHC values is necessary especially at industrial levels, as it ensures ready recovery of the hydrotrope for reuse.

**Table 2. Maximum Solubilization Enhancement Factor ($\varphi_s$) of Stearic Acid**

| | $\varphi_s$[a] | | | |
|---|---|---|---|---|
| hydrotrope | $T = 303$ K | $T = 313$ K | $T = 323$ K | $T = 333$ K |
| sodium salicylate | 34.56 | 45.84 | 66.73 | 95.95 |
| sodium benzoate | 6.21 | 9.36 | 13.61 | 19.41 |
| nicotinamide | 5.62 | 8.97 | 11.99 | 14.99 |

[a] $\varphi_s$ is the maximum enhancement factor for solubility.

**Table 3. Effect of Hydrotrope Concentration ($c$) on the Mass Transfer Coefficient ($k_La$) of Stearic Acid**

| hydrotrope | $c$ / mol·kg$^{-1}$ | $10^4\ k_La$ / s$^{-1}$ | $\varphi_{mtc}$[a] |
|---|---|---|---|
| sodium salicylate | 0.00 | 4.01 | |
| | 0.20 | 4.29 | 1.06 |
| | 0.30[b] | 8.42 | 2.10 |
| | 0.40 | 9.22 | 2.30 |
| | 0.60 | 9.70 | 2.41 |
| | 0.80 | 12.63 | 3.15 |
| | 1.00 | 15.64 | 3.90 |
| | 1.20 | 20.13 | 5.02 |
| | 1.40 | 22.46 | 5.60 |
| | 1.60 | 24.86 | 6.20 |
| | 1.80 | 26.54 | 6.62 |
| | 2.00 | 28.30 | 7.06 |
| | 2.20 | 30.44 | 7.59 |
| | 2.40[c] | 42.11 | 10.50 |
| | 2.60 | 42.35 | 10.56 |
| | 2.80 | 42.79 | 10.67 |
| | 3.00 | 42.19 | 10.77 |
| sodium benzoate | 0.00 | 4.01 | |
| | 0.20 | 4.20 | 1.03 |
| | 0.40[b] | 8.42 | 2.10 |
| | 0.60 | 8.60 | 2.14 |
| | 0.80 | 8.90 | 2.23 |
| | 1.00 | 13.03 | 3.25 |
| | 1.20 | 16.36 | 4.08 |
| | 1.40 | 19.49 | 4.86 |
| | 1.60 | 22.18 | 5.53 |
| | 1.80 | 24.74 | 6.17 |
| | 2.00 | 28.11 | 7.01 |
| | 2.20[c] | 37.97 | 9.47 |
| | 2.40 | 38.18 | 9.52 |
| | 2.60 | 38.54 | 9.61 |
| | 2.80 | 38.74 | 9.66 |
| | 3.00 | 39.07 | 9.74 |
| nicotinamide | 0.00 | 4.01 | |
| | 0.20 | 4.10 | 1.01 |
| | 0.40 | 4.70 | 1.17 |
| | 0.60[b] | 8.30 | 2.07 |
| | 0.80 | 8.78 | 2.19 |
| | 1.00 | 12.43 | 3.10 |
| | 1.20 | 13.79 | 3.44 |
| | 1.40 | 16.84 | 4.02 |
| | 1.60 | 17.44 | 4.35 |
| | 1.80 | 19.25 | 4.80 |
| | 2.00 | 19.85 | 4.95 |
| | 2.20[c] | 27.75 | 6.92 |
| | 2.40 | 28.03 | 6.99 |
| | 2.60 | 28.55 | 7.12 |
| | 2.80 | 28.95 | 7.22 |
| | 3.00 | 29.27 | 7.30 |

[a] $\varphi_{mtc}$ is the enhancement factor for the mass transfer coefficient. [b] MHC is the minimum hydrotrope concentration. [c] $c_{max}$ is the maximum hydrotrope concentration.

The solubilization effect varies with the concentration of hydrotrope (Figure 2). In the present case, a clear increasing trend in the solubility of stearic acid was observed above the MHC of sodium salicylate. This increasing trend is maintained only up to a certain concentration of sodium salicylate in the aqueous solution, beyond which there is no appreciable increase in the solubility of stearic acid. This concentration of sodium

**Table 4. Setschenow Constant ($K_s$) of Hydrotropes with Respect to Stearic Acid**

| | $K_s$ | | | |
|---|---|---|---|---|
| hydrotrope | $T = 303$ K | $T = 313$ K | $T = 323$ K | $T = 333$ K |
| sodium salicylate | 0.598 | 0.658 | 0.717 | 0.778 |
| sodium benzoate | 0.275 | 0.384 | 0.431 | 0.470 |
| nicotinamide | 0.230 | 0.352 | 0.399 | 0.460 |

salicylate (hydrotrope) in the aqueous solution is referred to as the maximum hydrotrope concentration ($c_{max}$). From the analysis of the experimental data, it is observed that a further increase in hydrotrope concentration beyond $c_{max}$ does not bring any appreciable increase in the solubility of stearic acid even up to 3.00 mol·kg$^{-1}$ of sodium salicylate in the aqueous solution.

The saturation of the hydrotropic effect beyond $c_{max}$ may be due to the nonavailability of water molecules to form further aggregates comprising of additional MHC agglomerates. Similar to the MHC values, $c_{max}$ values of hydrotropes also remained unaltered at increased system temperatures. The values of MHC and $c_{max}$ of a hydrotrope with respect to stearic acid may be useful in determining the recovery of the dissolved stearic acid even to an extent of the calculated amount from hydrotrope solutions at any concentration between MHC and $c_{max}$ by simple dilution with distilled water. This is the unique advantage of the hydrotropic solubilization technique.

From the experimental data plotted in Figure 2, it can further be observed that, to achieve the particular solubility of stearic acid, say 24·10$^{-3}$ mol·kg$^{-1}$, the sodium salicylate concentration should be 1.57 mol·kg$^{-1}$ at 303 K, 0.93 mol·kg$^{-1}$ at 313 K, 0.60 mol·kg$^{-1}$ at 323 K, and 0.42 mol·kg$^{-1}$ at 333 K in the aqueous solution. Thus, it can be seen that, as the system temperature increases, the concentration of sodium salicylate required in the aqueous phase to achieve a particular solubility of stearic acid decreases. A similar trend has been observed for other systems also. It has also been observed that the solubilization effect of sodium salicylate was not a linear function of the concentration of the sodium salicylate. The solubilization effect of sodium salicylate increases with the increase in hydrotrope concentration and also with system temperature.[26]

A similar trend has been observed in the solubilization effect of other hydrotropes, namely, sodium benzoate and nicotinamide. It has also been observed that the MHC values of hydrotrope used in this work range between (0.30 and 0.60) mol·kg$^{-1}$ and the $c_{max}$ values of hydrotropes range between (2.20 and 2.40) mol·kg$^{-1}$ (Table 1). The highest value of solubilization enhancement factors $\varphi_s$, which is the ratio of solubility values in the presence and the absence of a hydrotrope, has been observed in the case of sodium salicylate as 95.95 at a system temperature of 333 K (Table 2).

Hydrotropic solubilization has been claimed to be a collective molecular phenomenon, possibly occurring by the intercalation or coaggregation of a solute with the hydrotrope aggregates, and the self-aggregation of hydrotrope molecules in aqueous solutions is considered to be a prerequisite for the enhanced solubility of the solute.[27–29] A hydrotrope, above a MHC, is expected to form organized loose nanoassemblies with distinct hydrophobic regions where the solute can be solubilized. The solute molecules may also take part in the aggregation process of the hydrotrope, thereby forming coaggregates with the hydrotrope molecules in aqueous solutions. The formation of a stable coaggregate depends on the molecular structure as well as the functional group(s) attached to the carbon skeleton of the solute as it would govern the intercalation of the solute between the hydrotrope molecules. The solubilization of a solute is influenced by its hydrophobic part and also the chain length of an alkyl group of a hydrotrope.

***Mass Transfer Coefficient.*** The mass transfer coefficient of the stearic acid + water system in the absence of any hydrotrope was determined as 4.01·10$^{-4}$ s$^{-1}$ at 303 K (Table 3). The effect of different hydrotropes on the mass transfer coefficient of stearic acid at different hydrotrope concentrations is also given in the same table. It can be seen that a threshold value of 0.30 mol·kg$^{-1}$ is required to effect significant enhancement in the mass transfer coefficient of the stearic acid + water system, as observed in the case of solubility determinations. The mass transfer coefficient of the stearic acid + water system increases with the increase in sodium salicylate concentration. The maximum enhancement factor for the mass transfer coefficient of the stearic acid + water system in the presence of sodium salicylate was found to be 10.50 (Table 3). A similar trend in the mass transfer coefficient enhancement ($\varphi_{mtc}$) of stearic acid has been observed for other hydrotropes also, namely, sodium salicylate and nicotinamide. The highest value of $\varphi_{mtc}$ (10.50) has been observed in the presence of sodium salicylate as a hydrotrope at a $c_{max}$ of 2.40 mol·kg$^{-1}$.

***Effectiveness of Hydrotropes.*** The effectiveness factor of each hydrotrope with respect to stearic acid at different system temperatures has been determined by analyzing the experimental solubility data for each case applying the model suggested by

**Table 5. Correlation Constants for Polynomial Equation 2**

| | correlation constants[a] | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| $T$ | $a$ | $b$ | $c$ | $d$ | $e$ | | $g$ | |
| K | kg$^5$·mol$^{-5}$ | kg$^4$·mol$^{-4}$ | kg$^3$·mol$^{-3}$ | kg$^2$·mol$^{-2}$ | kg·mol$^{-1}$ | $f$ | mol·kg$^{-1}$ | $V$ |
| | | | | Sodium Salicylate | | | | |
| 303 | 2.375 | −20.700 | 65.661 | −93.914 | 63.154 | −4.102 | 1.295 | 0.046 |
| 313 | 0.526 | −04.472 | 15.468 | −32.410 | 41.030 | 4.800 | 1.144 | 0.394 |
| 323 | 2.375 | −23.819 | 92.980 | −179.400 | 167.050 | −15.093 | 1.533 | 0.315 |
| 333 | 1.537 | −18.268 | 89.373 | −220.640 | 248.270 | −17.256 | 1.394 | 0.511 |
| | | | | Sodium Benzoate | | | | |
| 303 | 0.335 | −3.089 | 0.663 | −17.166 | 12.879 | −1.032 | 1.167 | 0.026 |
| 313 | 0.339 | −3.203 | 1.573 | −20.702 | 19.162 | −3.092 | 1.344 | 0.067 |
| 323 | 0.638 | −5.819 | 20.226 | −34.698 | 31.005 | −4.877 | 1.426 | 0.117 |
| 333 | 0.699 | −6.236 | 21.739 | −39.939 | 41.158 | −6.592 | 1.575 | 0.201 |
| | | | | Nicotinamide | | | | |
| 303 | 0.256 | −2.557 | 9.637 | −17.179 | 14.673 | −2.916 | 1.262 | 0.043 |
| 313 | 0.286 | −2.685 | 9.880 | −18.903 | 19.892 | −4.999 | 1.453 | 0.056 |
| 323 | 0.400 | −3.861 | 14.793 | −29.663 | 32.150 | −8.554 | 1.656 | 0.095 |
| 333 | 0.405 | −3.796 | 14.368 | −30.049 | 36.146 | −10.089 | 1.868 | 0.177 |

[a] *a*, *b*, *c*, *d*, *e*, *f*, and *g*: correlation constants for polynomial eq 2; *V*: variance in correlation.

Setschenow[30] and later modified by Gaikar and Pathak,[31] as given by the equation

$$\log[S/S_m] = K_s[c_s - c_m] \quad (1)$$

where $S$ and $S_m$ are the solubilities of stearic acid at any hydrotrope concentration $c_s$ and the MHC $c_m$, respectively. The Setschenow constant $K_s$ can be considered as a measure of the effectiveness of a hydrotrope at any given system temperature. The Setschenow constant values of hydrotropes, namely, sodium salicylate, sodium benzoate, and nicotinamide, for the stearic acid + water system at different system temperatures are listed in Table 4. The highest value has been observed as 0.778 in the case of sodium salicylate as a hydrotrope at 333 K.

***Empirical Correlation for Solubility.*** Since the exponential relation may not be valid at lower and higher hydrotrope concentrations, the solubility of stearic acid was correlated empirically into a polynomial equation at different system temperatures $T =$ (303 to 333) K, and the data have been fitted in a polynomial equation of the form

$$S = ac_s^6 + bc_s^5 + cc_s^4 + dc_s^3 + ec_s^2 + fc_s + g \quad (2)$$

which gives a better fit for the solubility data. The values of correlation constants "*a* to *g*" are reported in Table 5 along with the variance of the fit. The solid curves in Figures 2 to 4 are from these polynomial equations.

## Conclusions

The solubility of stearic acid, which is practically insoluble in water, has been increased to a maximum of 95.95 times in the presence of sodium salicylate as a hydrotrope at a temperature of $T = 333$ K with a corresponding increase in the mass transfer coefficient. This would be useful in increasing the rate of output of the desired product made from stearic acid. The recovery of the dissolved stearic acid from hydrotrope solution is ensured at any hydrotrope concentration between MHC and $c_{max}$ by simple dilution with distilled water, which alters the solution properties of hydrotrope aggregates, instantaneously affecting the MHC agglomerates. This also facilitates the reuse of hydrotrope solution, which will eliminate the huge cost and energy normally involved in the separation of the solubilized stearic acid from its solution. The unprecedented increase in the solubilizing effect of hydrotropes is attributed to the formation of organized aggregates of hydrotrope molecules at a particular concentration. The solubility data fitted in a polynomial equation give a better fit since the variance is less than 0.6.

### Supporting Information Available:

Effect of the concentrations of sodium salicylate, sodium benzoate, and nicotinamide on the solubility of stearic acid in water, in Tables 1, 2, and 3, respectively. This material is available free of charge via the Internet at http://pubs.acs.org.

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Received for review December 11, 2009. Accepted March 2, 2010.

JE901041N