Journal of Zhejiang University SCIENCE A
ISSN 1673-565X (Print); ISSN 1862-1775 (Online)
www.zju.edu.cn/jzus; www.springerlink.com
E-mail: jzus@zju.edu.cn

Enhancement of solubility and mass transfer coefficient of salicylic acid through hydrotropy

S. THENESHKUMAR[1], D. GNANAPRAKASH[1], N. NAGENDRA GANDHI[†‡2]
([1]*Department of Chemical Engineering, St. Peter's Engineering College, Chennai 600054, India*)
([2]*Department of Chemical Engineering, Alagappa College of Technology, Anna University, Chennai 600025, India*)
[†]E-mail: n_nagendra2002@yahoo.com

Received July 6, 2008; Revision accepted Oct. 10, 2008; Crosschecked Apr. 23, 2009

Abstract: This study deals with the effect of hydrotropes on the solubility and mass transfer coefficient of salicylic acid. The solubility and mass transfer studies were performed using the hydrotropes, i.e., sodium acetate, sodium salicylate, citric acid, and urea at concentrations of 0~3.0 mol/L and system temperatures of 303~333 K. It was found that the solubility and mass transfer coefficient of salicylic acid increases with increase in hydrotrope concentration and also with system temperature. All hydrotropes used in this work showed an enhancement in solubility and mass transfer coefficient to different degrees. The maximum enhancement factor values were determined for all hydrotropes used in this study. The highest value was 28.08 for solubility studies and 10.42 for mass transfer studies. The performance of hydrotropes was measured in terms of the Setschenow constant (K_s). The highest value observed was 0.696.

Key words: Hydrotropy, Hydrotropes, Solubilization, Mass transfer coefficient, Separation
doi:10.1631/jzus.A0820516 **Document code:** A **CLC number:** TQ4

INTRODUCTION

Hydrotropes are a class of chemical compounds that cause a several fold increase in the solubility of sparingly soluble solutes under normal conditions. This phenomenon termed hydrotropy is considered as a unique and unprecedented solubilization technique because of the easy recovery of dissolved solute and possible re-use of hydrotrope solutions. This technique also facilitates the separation of close boiling isomers (Huh *et al*., 2005; Barbosa *et al*., 2006; Gaikar and Padalkar, 2008) and non-isomers in mixtures besides increasing the rate of heterogeneous reactions (Laxman and Sharma, 1990; Agarwal and Gaikar, 1992; Raynaud-Lacroze and Tavare, 1993). Neuberg (1916) identified this pioneering technique for very large solubility enhancements for a variety of sparingly soluble organic solutes.

Hydrotropes in general are water-soluble and surface-active compounds that enhance the solubility of organic solutes like acids, esters, alcohols, aldehydes, ketones, hydrocarbons, and fats (Friberg, 1997; Gaikar and Phatak, 1999; Friberg and Blute, 2006; Kim *et al*., 2006). Hydrotropes have been widely used in drug solubilization (Evstigneev *et al*., 2006; Maheshwari and Ajmera, 2006; Maheshwari *et al*., 2006; Sharma and Joshi, 2007), detergent formulation, health care, household applications (Friberg and Brancewicz, 1994; Rigoli *et al*., 2007), and also as an extraction agent for fragrances (Friberg *et al*., 1996; Dandekar *et al*., 2008). Each hydrotrope has a selective ability towards a particular component in the mixture to facilitate easy recovery of the hydrotrope solution by controlled dilution with distilled water (Colonia *et al*., 1998; Mahapatra *et al*., 1988). The solubility enhancement of organic solute is due to the formation of molecular structures in the form of complexes (Badwan *et al*., 1982; Mansur *et al*., 2005; Ooya *et al*., 2005). The previous experimental findings concluded that hydrotropy is a process which

---

[‡] Corresponding author

goes beyond conventional solubilization methods, such as miscibility, co-solvency (Bauduin *et al*., 2005) and the salting-in effect, since the solubilization affected by hydrotropy is higher and more selective compared to other solubilization methods (Balasubramanian *et al*., 1989; Agrawal *et al*., 2004). The effect of hydrotropes on the solubility and mass transfer coefficient of a series of organic esters was studied in our earlier publications (Gandhi *et al*., 1998a; 1998b; Gandhi and Kumar, 2000; Gandhi *et al*., 2000; Meyyappan and Gandhi, 2004; Meyyappan and Gandhi, 2005).

For many binary systems involving a sparingly soluble organic compound, such as salicylic acid, the mass transfer coefficient in the presence of a hydrotrope is probably determined by the difference between the binary diffusivity (solute+solvent) and the diffusivity of the solute in the solution (solute+solvent+hydrotrope). Since salicylic acid serves as a raw material/intermediate for a wide variety of chemicals, drugs, and allied products (Tavare and Gaikar, 1991; Phatak and Gaikar, 1993; Maheshwari, 2006; Souza *et al*., 2006; Cheng and Sabatini, 2007; Ahuja *et al*., 2007; Jain, 2008; Nicoli *et al*., 2008), and the separation of salicylic acid from any liquid mixture is found to be difficult, this hydrotropic technique can be adopted to increase the solubility as well as to separate such mixtures effectively. The hydrotropes used in this work are freely soluble in water, non-reactive and non-toxic.

MATERIALS AND METHODS

All the chemicals used in this work were manufactured by the Aldrich Chemical Co., Milwaukee, USA, with a manufacture's stated purity of 99.9%.

The experimental setup for the determination of solubility values consisted of a thermostatic bath and a separating funnel. Measurement of the solubility of salicylic acid was carried out at temperatures of 303, 313, 323, and 333 K (Vikrant *et al*., 2007). For each solubility test, an excess amount of powdered solid was placed in a separating funnel, and a solution of the hydrotrope (Hodgdon and Kaler, 2007) of known concentration was added. The separating funnel was sealed to avoid evaporation of the solvent at higher temperatures. The hydrotrope solutions of different concentrations were prepared by dilution with distilled water. The separating funnel was immersed in a constant temperature bath fitted with a temperature controller that could control the temperature within ±0.1 °C. 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 the solubility experiments were conducted in duplicate to check their reproducibility. The observed error 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 speed of the impeller in r/min was selected to achieve effective mixing, and was maintained at the same value for all experiments. The vessel used for mass transfer studies had a height of 40 cm and an inner diameter of 15 cm. The turbine impeller had a diameter of 5 cm, width of 1 cm and length of 1.2 cm. It had four blades and rotated at 600 r/min. The baffle had a height of 40 cm, a diameter of 1.5 cm and four baffles arranged at 90° to each other.

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 600, 1200, 1800 or 2400 s and the 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.

RESULTS AND DISCUSSION

Solubility

The solubility of salicylic acid standard in water was 2.14×10^{-2} mol/L at 303 K, compared to "insoluble" as reported in (John, 1987; Perry, 1997). Thus, the solubility value in water is in close agreement with the earlier reported value.

Experimental data on the effect of hydrotropes are plotted in Figs.1a~1d. Sodium acetate was one of the hydrotropes used in this study. The solubility of salicylic acid in water at 303 K in the absence of any hydrotropes was 2.14×10^{-2} mol/L (Fig.1a). A minimum hydrotrope concentration (MHC) (Miguel *et al.*, 2007) of 0.20 mol/L was found to be required to effect a significant increase in the solubility of salicylic acid in water. The solubility of salicylic acid in water did not show any appreciable increase even after the addition of 0.20 mol/L of sodium acetate to the aqueous solution.

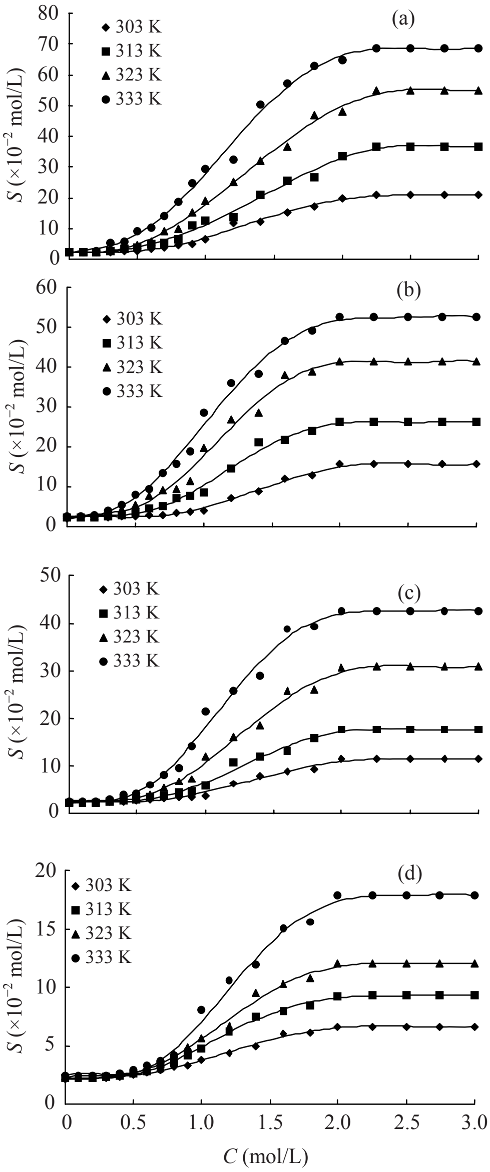

Fig.1 Effect of (a) sodium acetate, (b) sodium salicylate, (c) citric acid, and (d) urea concentration (*C*) on the solubility (*S*) of salicylic acid in water

Therefore, it appears that hydrotropic solubilization is evident only above the MHC (Kumar *et al.*, 2005), irrespective of the system temperature. Hydrotropy does not seem to be operative below the MHC, which may be a characteristic of a particular hydrotrope with respect to each solute. This MHC value assumes greater significance in the context of recovery of hydrotrope solutions. Since hydrotropy appears to operate only at significant concentrations of hydrotrope in water, most hydrotropic solutions release the dissolved salicylic acid on dilution with water below the MHC. Knowledge of MHC values is necessary especially at industrial levels, as it ensures ready recovery of the hydrotrope for re-use.

The solubilization effect varies with the concentration of hydrotrope (Fig.1a). In the present case, a clear increasing trend in the solubility of salicylic acid was observed above the MHC of sodium acetate. This increasing trend was maintained only up to a certain concentration of sodium acetate in the aqueous solution, beyond which there was no appreciable increase in the solubility of salicylic acid. This concentration of sodium acetate (hydrotrope) in the aqueous solution is referred to as the maximum hydrotrope concentration ($C_{\max}$). $C_{\max}$ values of sodium acetate, sodium salicylate, citric acid, and urea with respect to salicylic acid were 2.25, 2.00, 2.00 and 2.00 mol/L, respectively (Table 1). From the analysis of the experimental data, it was observed that a further increase in the hydrotrope concentration beyond $C_{\max}$ did not bring any appreciable increase in the solubility of salicylic acid even at concentrations of up to 3.00 mol/L of sodium acetate in the aqueous solution. Like the MHC values, the $C_{\max}$ values of hydrotropes remained unaltered with an increase in system temperature.

The knowledge of MHC and $C_{\max}$ values of each hydrotrope with respect to a particular solute assumes greater significance in this study, since it indicates the beginning and saturation of the solubilization effect of hydrotropes. The values of MHC and $C_{\max}$ of a hydrotrope with respect to salicylic acid may be useful in determining the recovery of the dissolved salicylic acid and even for calculating the amount that might be recovered from hydrotrope solutions at any concentration between MHC and $C_{\max}$ by simple dilution with distilled water. This is the unique advantage of

Table 1 Minimum hydrotrope concentration (MHC) and maximum hydrotrope concentration (C_{max}) values for hydrotropes

Hydrotrope	MHC (mol/L)	C_{max} (mol/L)
Sodium acetate	0.20	2.25
Sodium salicylate	0.20	2.00
Citric acid	0.30	2.00
Urea	0.40	2.00

the hydrotropic solubilization technique.

In the concentration range of sodium acetate between 0 and 3.00 mol/L, three different regions were obtained using sodium acetate as a hydrotrope. It was inactive below the MHC of 0.20 mol/L, above which an appreciable increase in the solubility of salicylic acid was found up to the C_{max} of 2.25 mol/L, and beyond which there was no further solubilization effect of the hydrotrope. Therefore, sodium acetate was found to be an effective hydrotrope for salicylic acid in the concentration range between 0.20 and 2.25 mol/L. It was also observed that the solubilization effect of sodium acetate was not a linear function of the concentration of the sodium acetate solution. The solubilization effect of sodium acetate increased with an increase in hydrotrope concentration and also with system temperature.

A similar trend was observed in the solubilization effect of other hydrotropes, namely sodium salicylate, citric acid and urea. The MHC values of hydrotropes used in this work ranged between 0.20 and 0.40 mol/L (Table 1) and the C_{max} values between 2.00 and 2.25 mol/L (Table 1). The maximum solubilization enhancement factor (φ_s), which is the ratio of the solubility values in the presence and absence of a hydrotrope, ranges between 3.09 and 28.08. The highest value of φ_s (28.08) was observed in the case of sodium acetate at a system temperature of 333 K (Table 2).

Table 2 Solubility enhancement factor of salicylic acid at different system temperatures

Hydrotrope	φ_s			
	303 K	313 K	323 K	333 K
Sodium acetate	9.74	16.55	23.76	28.08
Sodium salicylate	7.32	11.81	17.91	21.53
Citric acid	5.32	7.96	13.40	17.47
Urea	3.09	4.19	5.25	7.34

φ_s: maximum enhancement factor for solubility

Mass transfer coefficient

A plot of $-\log(1-C_b/C^*)$ vs t was drawn (Fig.2), where C_b is the concentration of salicylic acid at time t and C^* is the equilibrium solubility of salicylic acid at the same hydrotrope concentration. The slope of Fig.2 gives $k_La/2.303$, from which k_La, the mass transfer coefficient was determined. Duplicate runs were made to check the reproducibility. The observed error was <2%.

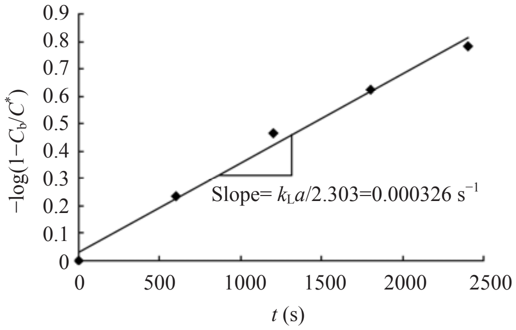

Fig.2 Model plot of $-\log(1-C_b/C^*)$ vs t for sodium acetate hydrotrope at C=0.2 mol/L and $C^*=2.29\times10^{-2}$ mol/L

The mass transfer coefficient for the salicylic acid+water system in the absence of any hydrotrope was determined to be 7.28×10^{-4} s^{-1} at 303 K (Table 3). Table 3 also shows the effect of different hydrotropes on the mass transfer coefficient of salicylic acid at different hydrotrope concentrations. A threshold value of 0.20 mol/L was required for significant enhancement in the mass transfer coefficient of the salicylic acid+water system in the presence of sodium acetate, as observed in the case of solubility determinations. The mass transfer coefficient of the salicylic acid+water system increases with an increase in sodium acetate (hydrotrope) concentration. Beyond a C_{max} value of 2.25 mol/L, there was no appreciable increase in the mass transfer coefficient of salicylic acid, as observed in the case of solubility determinations. The maximum enhancement in the mass transfer coefficient of the salicylic acid+water system in the presence of sodium acetate was found to be 10.42. These observations suggest that an increase in the mass transfer coefficient is found to occur upon increased solubilization. A similar trend in the mass transfer coefficient enhancement (φ_{mtc}) of salicylic acid has been observed for other hydrotropes, namely sodium salicylate, citric acid and urea. The highest value of φ_{mtc} (10.42) was observed in the presence of sodium acetate as hydrotrope at the C_{max} of 2.25 mol/L.

Table 3 Effect of hydrotrope concentration (C) on the mass transfer coefficient (k_La) of salicylic acid

Hydrotrope	C (mol/L)	k_La ($\times10^{-4}$ s^{-1})	E
Sodium acetate	0.00	7.28	–
	0.20*	7.51	1.03
	0.30	9.05	1.24
	0.80	13.37	1.84
	1.40	32.50	4.46
	2.25**	75.88	10.42
	3.00	78.26	10.75
Sodium salicylate	0.00	7.28	–
	0.20*	7.37	1.01
	0.30	8.84	1.21
	0.80	12.48	1.71
	1.40	29.89	4.11
	2.00**	69.70	9.57
	3.00	71.89	9.88
Citric acid	0.00	7.28	–
	0.20	7.32	1.01
	0.30*	7.91	1.09
	0.40	13.18	1.81
	1.00	17.43	2.39
	1.40	25.72	3.53
	2.00**	45.29	6.22
	3.00	47.10	6.47
Urea	0.00	7.28	–
	0.40*	12.55	1.72
	1.20	20.46	2.81
	2.00**	30.17	4.14
	3.00	33.39	4.59

E: enhancement factor for mass transfer coefficient (φ_{mtc}); *MHC: minimum hydrotrope concentration; **C_{max}: maximum hydrotrope concentration

Effectiveness of hydrotropes

The effectiveness factor of each hydrotrope with respect to salicylic acid at different system temperatures was determined by analyzing the experimental solubility data for each case, applying the model suggested by Setschenow and later modified by Gaikar and Sharma (1986) as given by the equation below:

$$\log(S/S_m)=K_s(C_s-C_m),$$

where S and S_m are the solubility values of salicylic acid at any hydrotrope concentration (C_s) and the minimum hydrotrope concentration (C_m) (the same as MHC), respectively. The Setschenow constant (K_s) can be considered to be a measure of the effectiveness of a hydrotrope in any given conditions of hydrotrope concentration and system temperature. The Setschenow constant values of the hydrotropes sodium acetate, sodium salicylate, citric acid and urea, for the salicylic acid+water system at different system temperatures are listed in Table 4. The highest value observed was 0.696, in the case of sodium acetate as the hydrotrope at 333 K.

Table 4 Setschenow constant (K_s) of hydrotropes with respect to salicylic acid at different system temperatures

Hydrotrope	K_s			
	303 K	313 K	323 K	333 K
Sodium acetate	0.468	0.582	0.661	0.696
Sodium salicylate	0.464	0.580	0.660	0.694
Citric acid	0.408	0.511	0.628	0.687
Urea	0.289	0.368	0.424	0.514

CONCLUSION

The solubility of salicylic acid, which is practically insoluble in water, was increased to a maximum value of 28.08 in the presence of sodium acetate as a hydrotrope, 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 salicylic acid. The separation of salicylic acid from any liquid mixture, which was found to be difficult, can be carried out effectively using this technique. The MHC and C_{max} values of the hydrotropes with respect to salicylic acid is used for the recovery of the dissolved salicylic acid and hydrotrope solutions at any hydrotrope concentration between MHC and C_{max} by simple dilution with distilled water. This technique will eliminate the huge cost and energy normally involved in the separation of the solubilized salicylic acid from its solution.

ACKNOWLEDGEMENTS

We thank Ms. R. Meena Suhanya and Ms. R. Jaana Saranya of St. Peter's Engineering College for their help during this work.

References

Agarwal, M., Gaikar, V.G., 1992. Extractive separation using hydrotropes. *Separations Technology*, **2**(2):79-84. [doi:10.1016/0956-9618(92)80010-B]

Agrawal, S., Pancholi, S.S., Jain, N.K., Agrawal, G.P., 2004. Hydrotropic solubilization of nimesulide for parenteral administration. *International Journal of Pharmaceutics*, **274**(1-2):149-155. [doi:10.1016/j.ijpharm.2004.01.012]

Ahuja, N., Katare, O.P., Singh, B., 2007. Studies on dissolution enhancement and mathematical modeling of drug release of a poorly water-soluble carrier. *European Journal of Pharmaceutics and Biopharmaceutics*, **65**:26-38.

Badwan, A.A., Ei-Khordagui, L.K., Salesh, A.M., 1982. The solubility of benzodiazepines in sodium salicylate solutions and proposed mechanism for hydrotropic solubilization. *International Journal of Pharmaceutics*, **13**(1):67-74. [doi:10.1016/0378-5173(82)90143-0]

Balasubramanian, D., Srinivas, V., Gaikar, V.G., Sharma, M., 1989. Aggregation beaviour of hydrotropic compounds in aqueous solutions. *The Journal of Physical Chemistry*, **93**(9):3865-3870. [doi:10.1021/j100346a098]

Barbosa, S., Taboada, P., Castro, E., Mosquera, V., 2006. Influence of SDS and two anionic hydrotropes on the micellized state of the triblock copolymer $E_{71}G_7E_{71}$. *Journal of Colloid and Interface Science*, **296**(2):677-684. [doi:10.1016/j.jcis.2005.09.019]

Bauduin, P., Renoncourt, A., Kopf, A., Touraud, D., Kunz, W., 2005. Unified concept of solubilization in water by hydrotropes and cosolvents. *Langmuir*, **21**(15):6769-6775. [doi:10.1021/la050554l]

Colonia, E.J., Dixit, A.B., Tavare, N.S., 1998**.** Phase relations of *o*- and *p*-chlorobenzoic acids in hydrotrope solutions. *Journal of Chemical & Engineering Data*, **43**(2):220-225. [doi:10.1021/je970182l]

Cheng, H.F., Sabatini, D.A., 2007. Separation of organic compounds from surfactant solution: a review. *Separation Science and Technology*, **42**(3):453-475. [doi:10.1080/01496390601120664]

Dandekar, D.V., Jayaprakasha, G.K., Patil, B.S., 2008. Hydrotropic extraction of bioactive limonin from sour orange (*Citrius aurantium L.*) seeds. *Food Chemistry*, **109**(3):515-520. [doi:10.1016/j.foodchem.2007.12.071]

Evstigneev, M.P., Evstigneev, V.P., Hernandez Santiago, A.A., Davies, D.B., 2006. Effect of a mixture of caffeine and nicotinamide on the solubility of vitamin (B_2) in aqueous solution. *European Journal of Pharmaceutical Sciences*, **28**(1-2):59-66. [doi:10.1016/j.ejps.2005.12.010]

Friberg, S.E., 1997. Hydrotropes. *Surface Physics*, **2**:490-494.

Friberg, S.E., Blute, I., 2006. Hydrotropy. Surfactant Science Series 129 (Liquid Detergents) (2nd Ed.). CRC Press, p.19-38.

Friberg, S.E., Brancewicz, C., 1994. O/W microemulsions and hydrotropes: the coupling action of a hydrotrope. *Langmuir*, **10**(9):2945-2949. [doi:10.1021/la00021a016]

Friberg, S.E., Yang, J., Huang, T., 1996. A reversible extraction process of phenyl ethyl alcohol, a fragrance. *Industrial & Engineering Chemistry Research*, **35**(9):2856-2859. [doi:10.1021/ie950661i]

Gaikar, V.G., Padalkar, V.K., 2008. Characterization of mixed of structural isomers of sodium butyl benzene sulfonate and sodium dodecyl sulphate by SANS, FTIR spectroscopy and NMR spectroscopy. *Journal of Molecular Liquids*, **138**(1-3):155-167. [doi:10.1016/j.molliq.2007.10.001]

Gaikar, V.G., Phatak, P.V., 1999. Selective solubilization of isomers in hydrotrope solution *o*-/*p*-chlorobenzoic acids and *o*-/*p*-nitro anilines. *Separation Science and Technology*, **34**(3):439-459. [doi:10.1081/SS-100100660]

Gaikar, V.G., Sharma, M.M., 1986. Extractive separation with hydrotropes. *Solvent Extraction and Ion Exchange*, **4**(4):839-846. [doi:10.1080/07366298608917896]

Gandhi, N.N., Kumar, D.M., 2000. Effect of hydrotropes on solubility and mass transfer coefficient of amyl acetate. *Bioprocess and Biosystems Engineering*, **23**(1):31-36.

Gandhi, N.N., Kumar, D.M., Sathyamurthy, N., 1998a. Effect of hydrotropes on solubility and mass transfer coefficient of butyl acetate. *Journal of Chemical & Engineering Data*, **43**(5):695-699. [doi:10.1021/je970212k]

Gandhi, N.N., Kumar, D.M., Sathyamurthy, N., 1998b. Effect of hydrotropes on solubility and mass transfer coefficient enhancement of ethyl benzoate. *Journal of Chemical & Engineering Data*, **26**:63-68.

Gandhi, N.N., Kumar, D.M., Sathyamurthy, N., 2000. Effect of hydrotropes on solubility and mass transfer coefficient of butyl acetate. *Journal of Chemical & Engineering Data*, **45**(3):419-423. [doi:10.1021/je970212k]

Hodgdon, T.K., Kaler, E.W., 2007. Hydrotropic solutions. *Current Opinion in Colloid and Interface Science*, **12**(3):121-128. [doi:10.1016/j.cocis.2007.06.004]

Huh, K.M., Lee, S.C., Cho, Y.W., Lee, J., Jeong, J.H., Park, K., 2005. Hydrotropic polymer micelle system for delivery of paclitaxel. *Journal of Controlled Release*, **101**(1-3):59-68. [doi:10.1016/j.jconrel.2004.07.003]

Jain, A.K., 2008. Solubilization of indomethacin using hydrotropes for aqeous injection. *European Journal of Pharmaceutics and Biopharmaceutics*, **68**(3):701-714. [doi:10.1016/j.ejpb.2007.06.013]

John, A.D., 1987. Lange's Handbook of Chemistry. McGraw-Hill, New York, p.7-347.

Kim, T.H., Choi, S.M., Kline, S.R., 2006. Polymerized rodlike nanoparticles with controlled surface charge density. *Langmuir*, **22**(6):2844-2850. [doi:10.1021/la052949a]

Kumar, S., Parveen, N., Kabir-ud-Din., 2005. Additive-induced association in unconventional systems: a case of the hydrotrope. *Journal of Surfactants and Detergents*, **8**(1):109-114. [doi:10.1007/s11743-005-0338-2]

Laxman, M., Sharma, M.M., 1990. Reduction of isophorone with borohydride: change in regio selectivity with hydrotropes. *Synthetic Communications*, **20**(1):111-117. [doi:10.1080/00397919008054621]

Mahapatra, A., Gaikar, V.G., Sharma, M.M., 1988. New strategies in extractive distillation: use of aqueous solution of hydrotropes and organic bases as solvent for organic acids. *Separation Science and Technology*, **23**(4):429-436. [doi:10.1080/01496398808060714]

Maheshwari, R.K., 2006. Novel application of hydrotopic solubilization in the analysis of bulk sample of ketoprofen and salicylic acid. *Asian Journal of Chemistry*, **18**:393-396.

Maheshwari, R.K., Ajmera, A., 2006. A novel application of hydrotopic solubilization in the quantitative analysis of bulk sample of ketoprofen and frusemide. *Asian Journal of Pharmaceutics*, **1**:60-62.

Maheshwari, R.K., Jain, N.K., Chaturvedi, S.C., 2006. Titrimetric analysis of aceclofenac in tablets using hydrotropic solubilization technique. *Indian Drug*, **43**:516-518.

Mansur, C.R.E., Pires, R.V., Gonzalez, G., Lucas, E.F., 2005. Influence of the hydrotrope structure on the physical chemical properties of polyoxide aqueous solutions. *Langmuir*, **21**(7):2696-2703. [doi:10.1021/la048167j]

Meyyappan, N., Gandhi, N.N., 2004. Solubility and mass transfer coefficient enhancement of benzyl acetate in water through hydrotropy. *Journal of Chemical & Engineering Data*, **49**(5):1290-1294. [doi:10.1021/je0342872]

Meyyappan, N., Nagendra, G.N., 2005. Solubility and mass transfer coefficient enhancement of benzyl benzotate in water through hydrotropy. *Journal of Chemical & Engineering Data*, **50**(3):796-800. [doi:10.1021/je049756u]

Neumann, M.G., Schmitt, C.C., Prieto, K.R., Goi, B.E., 2007. The photophysical determination of the minimum hydrotrope concentration of aromatic hydrotropes. *Journal of Colloid and Interface Science*, **315**(2):810-813. [doi:10.1016/j.jcis.2007.07.020]

Neuberg, C., 1916. Hydrotropy. *Biochemische Zeitschrift*, **76**:107-108.

Nicoli, S., Zani, F., Bilzi, S., Bettini, R., Santi, P., 2008. Association of nicotinamide with parabens: effect of solubility, partition and transdermal permeation. *European Journal of Pharmaceutics and Biopharmaceutics*, **69**:613-621.

Ooya, T., Moo, H.K., Saitoh, M., Tamiya, E., Park, K., 2005. Self-assembly of cholesterol-hydrotropic dendrimers conjugates into micelle-like structure: preparation and hydrotropic solubilization of paclitaxel. *Science and Technology of Advanced Materials*, **6**(5):452-456. [doi:10.1016/j.stam.2005.01.006]

Perry, R.H., 1997. Perry's Chemical Engineer's Handbook (7th Ed.). McGraw-Hill, New York, p.2-45.

Phatak, P.V., Gaikar, V.G., 1993. Solubility *o*- and *p*-chlorobenzoic acid in hydrotrope solutions. *Journal of Chemical & Engineering Data*, **38**(2):217-220. [doi:10.1021/je00010a007]

Raynaud-Lacroze, P.O., Tavare, N.S., 1993. Separation of 2-napthol: hydrotropy and precipitation. *Industrial & Engineering Chemistry Research*, **32**(4):685-691. [doi:10.1021/ie00016a015]

Rigoli, I.C., Schmitt, C.C., Neumann, M.G., 2007. The hydrotrope effect on the photopolymerization of styrenesulfonate initiated by Ru complexes. *Journal of Photochemistry and Photobiology A: Chemistry*, **188**(2-3):329-333. [doi:10.1016/j.jphotochem.2006.12. 031]

Sharma, D.K., Joshi, S.B., 2007. Solubility enhancement strategies for poorly water soluble drugs in solid dispersion: a review. *Asian Journal of Pharmaceutics*, **1**:9-14.

Souza, T.P., Zanette, D., Kawanami, A.E., Rezende, L., Ishiki, H.M., Amaral, A.T., 2006. pH at the micellar interface: synthesis of pH probes derived from salicylic acid, acid-base dissociation in sodium dodecyl sulfate micelles, and Poisson-Boltzmann simulation. *Journal of Colloid and Interface Science*, **297**(1):292-302. [doi:10.1016/j.jcis.2005.10.008]

Tavare, N.S., Gaikar, V.G., 1991. Precipitation of salicylic acid: hydrotropy and reaction. *Industrial & Engineering Chemistry Research*, **30**(4):722-728. [doi:10.1021/ie00052a015]

Vikrant, B.W., Prajesh, S.K., Vilas, G.G., 2007. Effect of temperature on aggregation behaviour of aqueous solution of sodium cumene sulfonate. *Journal of Molecular Liquids*, **133**(1-3):68-76. [doi:10.1016/j.molliq.2006.07.006]