
Thermodynamic aggregation behaviour of p-cymene in hydrotropic solution

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Abstract: The paper deals with the thermodynamic properties and aggregation behaviour of p-cymene through hydrotropy. Different hydrotropes namely urea, resorcinol, sodium cumene sulfonate and pyrogallol has been used to study the solubility under a wide range of hydrotrope concentrations (0 to 3.00 mol.kg⁻¹) and different system temperatures (303.15 to 333.15 K). The effectiveness of hydrotrope with respect to the system was measured by Setschenow constant KS and reported for all hydrotropes used in this study. The influence of different system temperatures on thermodynamic properties like standard Gibbs free energy change (ΔG°), standard enthalpy change (ΔH°) and standard entropy change (ΔS°) of solubilisation with respect to p-cymene has been ascertained. The aggregation behaviour between the solute and the hydrotrope and among the hydrotrope molecules have also been studied using step wise association model.

Keywords: hydrotropy; solubilisation; association constant; standard Gibbs free energy change; standard enthalpy change; standard entropy change; association model; FTIR.

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N. Nagendra Gandhi is a Project Mentor. He is a Professor and Head of Chemical Engineering Department, ACT Campus, Anna University, Chennai. He is also the Director of the Institute of Catalysis and Petroleum Technology. His areas of interest include extraction, green technology, hydrotropy,

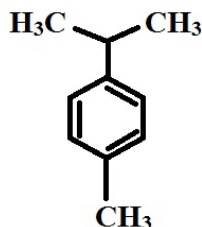
environmental studies, mass transfer, and separation technologies. His findings helped in increasing the solubility of insoluble petroleum and other pharmaceutical compounds notably furfural underwent a major solubility rise.

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1 Introduction

P-cymene (Figure 1) is a transparent liquid, naturally occurring aromatic organic compound. It can be extracted from dipentene on the reactions of dehydrogenation and disproportionate by Raney nickel or Pd/C as catalyst. P-cymene is an intermediate compound mainly used in pharma industries (Selvaraj et al., 2002). Studies on p-cymene and its derivative monoterpenes show that they are effective antioxidant and anticarcinogenic agents. It is also widely used for synthesis of p-cresol (Zhang et al., 2010). Due to growing importance of p-cymene as an intermediate in the production of such styrene's as methyl and alpha four dimethyl styrene's and as an intermediate in the preparation of nitrogenous gasoline additives. However conversion obtained is too low to serve as a suitable basis for commercial development because of its poor solubility. In case of orofacial pain p-cymene is an effective agent (Santana et al., 2011). The phenomenon of increasing the aqueous solubility of substances normally insoluble or sparingly soluble in water by the third compound or additive without surfactant aggregation is termed hydrotropy or hydrotropism (Neuberg, 1916).

Figure 1 Structure of p-cymene



Hydrotropy is the phenomenon of increasing the solubility of water insoluble or sparingly water-soluble organic compounds in aqueous solutions in the presence of hydrotropes. Hydrotropes themselves are highly water-soluble organic salts. The increase in solubility of an organic substance is a strong function of the hydrotrope concentration and depends not only on the nature of hydrotrope but also on the nature of solute (Gnanaprakash et al., 2012). A mere dilution of the hydrotropic solution by water precipitates the solute ensuring a simple solute recovery technique. This technique can be used to separate close boiling mixture (Jenamajayan et al., 2009). Hydrotropy is suggested to be superior to other solubilisation techniques such as co solvency, salting in, micellar solubilisation and miscibility (Nwodo et al., 2013). Hydrotropes are mainly used in drug solubilisation (Maheshwari, 2006; Maheshwari et al., 2008, 2010; Manoj Kumar and Sangeetha, 2016),

detergents, household applications and also extraction agent for fragrances. This technique can also be adopted to separate close boiling azeotropic mixtures. The problem of emulsification (Mckee, 1946) which is normally encountered with conventional surfactant solution is completely not found with hydrotrope solution.

The rate of heterogeneous reactions can be increased by using hydrotropic technique (Varma and Pandit, 2005) as well as for the separation of close boiling liquid mixtures through extractive distillation and liquid-liquid extraction (Balasubramanian et al., 1989; Meyyappan et al., 2005). Hydrotrope has the advantage of certain properties like being independent of pH, non-flammability, highly selective towards a particular compound, the availability of hydrotrope is cheap and it is easily available absence of emulsion makes this technique superior to other solubilisation methods (Thenesh Kumar et al., 2009). Due to the solubilising effect of these hydrotropes, the mass transfer coefficient can also be considerably enhanced (Shimizu and Matubayasi, 2014; Mehta et al., 2016; Nagendra Gandhi and Dharmendra Kumar, 2000; Nagendra Gandhi and Meyyappan, 2004, 2005; Gnanaprakash et al., 2013).

2 Materials and methods

2.1 Samples

All chemicals used in this study were brought from Sisco Research Laboratories Pvt. Ltd., Mumbai. With a manufacturer stated purity of 99 %. Hydrotrope used in this study i.e., urea, pyrogallol, resorcinol, and sodium cumene sulfonates are of analar grade. Double distilled water was used for the preparation of hydrotropic solution.

2.2 Solubility

For each solubility test, about 100 ml of p-cymene was taken in a beaker and 100 ml of a solution of the hydrotrope of known concentration was added. The solution was stirred using magnetic Stirrer fitted with a temperature controller which could control the temperature within ± 0.1 K at a suitable temperature and for a specific time interval. The entire content of the beaker was then transferred to a separating funnel and allowed to stand for some time. The aqueous layer was carefully separated from solute layer and analysed to quantify the concentration using high performance liquid chromatography method (HPLC). C-18 columns packed with silica gel with mobile phase as acetonitrile-water were used. The results were plotted. All the solubility experiments were conducted in duplicate to check the reproducibility. The observed error in the reproducibility was $< 2\%$.

2.3 FTIR analysis

The Infrared spectrum analysis was performed on the samples using a Bruker Vertex 70/70 V. The FTIR spectra were recorded in the wave number ranging from $3,000\text{--}500\text{ cm}^{-1}$.

3 Results and discussion

3.1 Solubility analysis

As per the literature the solubility of *p*-cymene in water at a temperature of 298 K is reported to be $1.74 \times 10^{-4} \text{ mol.kg}^{-1}$. From this data we can infer that *p*-cymene is practically insoluble in water. In this work the solubility of *p*-cymene in water without any addition of hydrotrope is measured at a temperature of 303.15 K and it shows a value of $2.86 \times 10^{-4} \text{ mol.kg}^{-1}$. It was observed that the solubility of *p*-cymene in water has not shown any appreciable increase even after the addition of 0.30 mol.kg^{-1} of urea in the aqueous phase. The concentration of urea was increased above 0.30 mol.kg^{-1} , the solubility of *p*-cymene in water was found to increase significantly till the concentration of 2.00 mol.kg^{-1} beyond which there is no appreciable increase in the solubility of *p*-cymene.

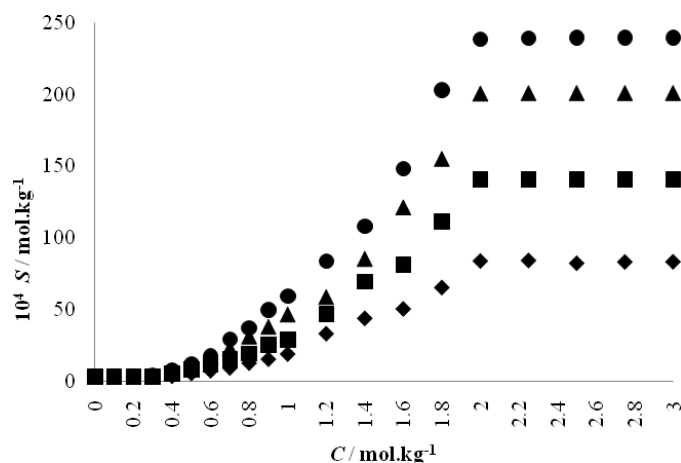
Minimum hydrotrope concentration (MHC): the hydrotropic effect is significant above a MHC that is a characteristic of a given hydrotrope, analogous to the critical micelle concentration (CMC) of a surfactant. However, because hydrotropes have relatively short hydrocarbon chains or hydrophobic groups, their MHCs are usually in the molar range. The solubility of an organic compound in a hydrotrope solution rises almost exponentially immediately above the MHC, but at higher concentrations of the hydrotrope, it might level off to a plateau depending on the nature of the solute. Dilution of the saturated solution with water is usually sufficient to recover the dissolved solute, which separates out as another solid or liquid phase when the hydrotrope concentration drops below its MHC. C_{max} – This increasing trend is maintained only up to a certain concentration of the hydrotrope beyond which there is no appreciable increase in the solubility of the solute. This particular concentration of hydrotrope in the aqueous phase is said to be maximum hydrotrope concentration (C_{max}).

The knowledge of MHC and C_{max} values of each hydrotrope with respect to a particular solute assumes greater significance, since it clearly shows the beginning and saturation of the solubilisation effect of Hydrotropes. However, the effect of hydrotrope was found to be predominant at concentrations close to the C_{max} value of a hydrotrope in most cases. The values of MHC and C_{max} of a hydrotrope with respect to *p*-cymene may be useful in determining the recovery of the dissolved *p*-cymene even to an extent of 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 solubilisation technique.

In Figures 2, 3, 4, 5, three different regions were observed. One is inactive region below MHC, the other one between MHC to C_{max} , shows appreciable increase in the solubility of *p*-cymene and was found to be 2.00 mol.kg^{-1} , beyond which there is no further solubilisation effect of hydrotrope. From Figure 2, urea was found to be an effective hydrotrope in the concentration range between 0.30 to 2.00 mol.kg^{-1} . It has also been observed that the solubilisation effect of urea was not a linear function of the concentration. A similar trend in the solubilising effect of resorcinol (Figure 3), sodium cumene sulfonate (Figure 4) and pyrogallol (Figure 5) were observed at increased system

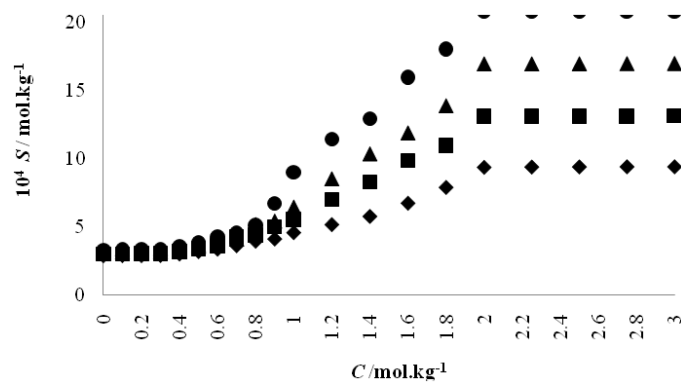
temperatures, viz., 303.15, 313.15, 323.15, 333.15 K with the values of MHC and C_{max} remained unaltered even at higher temperatures. The solubilisation effect of urea increases with increase in hydrotrope concentration and also with system temperature. The maximum enhancement factor values observed for the p-cymene in water system for urea at 303.15 K, 313.15 K, 323.15 K and 333.15 K are 28.82, 46.36, 63.57 and 71.86 respectively.

Figure 2 Effect of urea concentration (C) on the solubility (S) of p-cymene in water at various temperatures



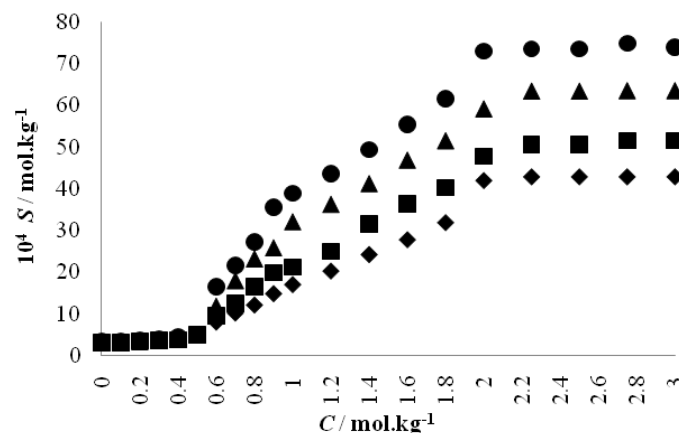
Notes: ◆: 303.15 K; ■: 313.15 K; ▲: 323.15 K; ●: 333.15 K.

Figure 3 Effect of resorcinol concentration (C) on the solubility (S) of p-cymene in water at various temperatures



Notes: ◆: 303.15 K; ■: 313.15 K; ▲: 323.15 K; ●: 333.15 K.

Figure 4 Effect of sodium cumene sulfonate concentration (C) on the solubility (S) of p-cymene in water at various temperatures



Notes: ◆: 303.15 K; ■: 313.15 K; ▲: 323.15 K; ●: 333.15 K.

Figure 5 Effect of pyrogallol concentration (C) on the solubility (S) of p-cymene in water at various temperatures

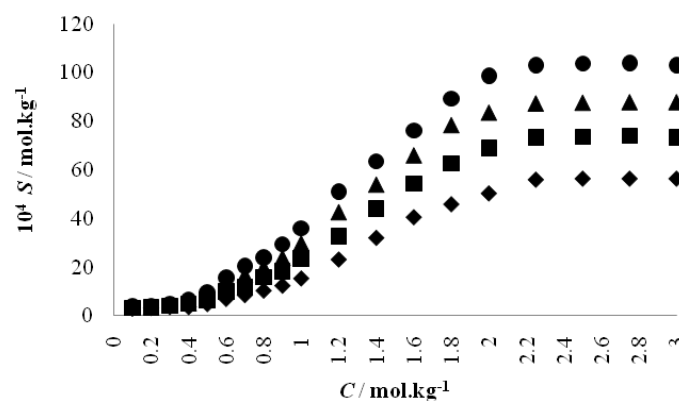


Table 1 MHC and C_{max} values for hydrotropes

Hydrotrope	MHC	C_{max}
	mol.kg ⁻¹	mol.kg ⁻¹
Urea	0.30	2.00
Resorcinol	0.40	2.20
Sodium cumene sulfonate	0.40	1.80
Pyrogallol	0.20	2.00

Table 1 shows the MHC values of hydrotrope used in this work range between 0.30, 0.40 and 0.20 mol.kg⁻¹ which seem to depend on the hydrophilicity of a hydrotrope. The C_{max} values of hydrotropes are 2.00, 2.20, 1.80 mol.kg⁻¹.

Table 2 Maximum solubilisation enhancement factor for p-cymene

<i>Hydrotrope</i>	Φ_s			
	$T = 303.15\text{ K}$	$T = 313.15\text{ K}$	$T = 323.15\text{ K}$	$T = 333.15\text{ K}$
Urea	28.82	46.36	63.57	71.86
Resorcinol	3.21	4.32	5.36	6.25
Sodium cumene sulfonate	14.45	15.78	18.69	21.98
Pyrogallol	16.33	21.92	24.17	24.82

3.2 Enhancement factor (Φ_s)

Enhancement Factor is defined as the ratio of solubility of the system in the presence of hydrotrope to that in the absence of a hydrotrope i.e., the solubility of the system at the maximum concentration of the hydrotrope to the solubility of the system in water.

$$\text{Enhancement factor} = \frac{\text{Solubility value at } C_{\max}}{\text{Solubility value in the absence of hydrotrope}}$$

3.3 Effectiveness of hydrotropes

Experimental data was used to find the effectiveness factor of each hydrotrope with respect to p-cymene at different system temperatures using the model suggested by Setschenow and later modified by Pathak and Gaikar. The equation is given below.

$$\log \left[\frac{S}{S_m} \right] = K_s [C_s - C_m] \quad (1)$$

where S and S_m are the solubility of p-cymene at any hydrotrope concentration C_s and the MHC C_m (same as MHC) respectively. The Setschenow constant K_s can be considered as a measure of the effectiveness of a hydrotrope at any given conditions of hydrotrope concentration and system temperature. The Setschenow constant values of hydrotropes namely resorcinol, urea, sodium cumene sulfonate and pyrogallol for p-cymene – water system at different system temperatures.

The highest value has been observed as 0.99 in the case of urea as hydrotrope at 333.15K from Table 3. This shows that urea is the most effective hydrotrope for p-cymene solubilisation, followed by pyrogallol, sodium cumene sulfonate and resorcinol.

Table 3 Setschenow Constant (K_s) of hydrotropes with respect to p-cymene

<i>Hydrotrope</i>	(K_s)			
	$T = 303.15\text{ K}$	$T = 313.15\text{ K}$	$T = 323.15\text{ K}$	$T = 333.15\text{ K}$
Urea	0.85	0.95	0.96	0.99
Resorcinol	0.30	0.38	0.44	0.48
Sodium cumene sulfonate	0.65	0.70	0.73	0.75
Pyrogallol	0.65	0.72	0.75	0.77

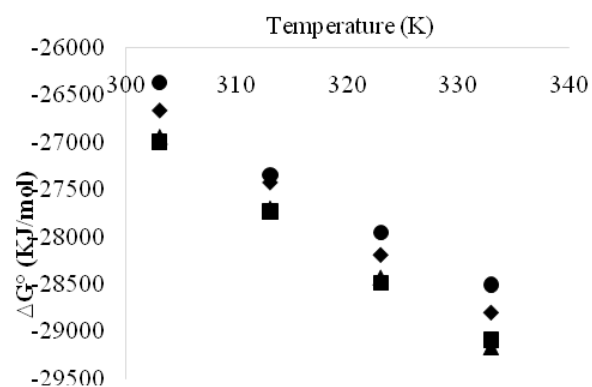
3.4 Aggregation characteristics of hydrotropes

The standard free energy of aggregation per mole of hydrotrope is given by

$$\Delta G^\circ = RT \ln(X_{MHC}) \quad (2)$$

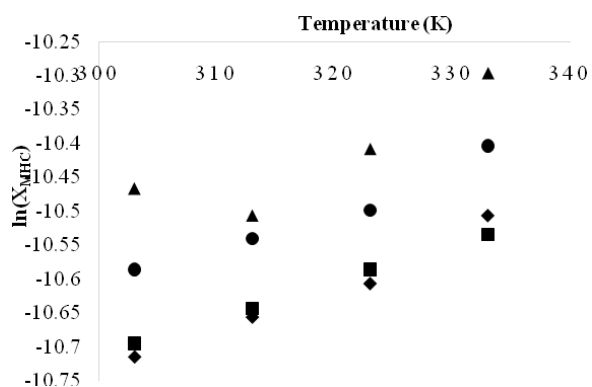
A graph was plotted for ΔG° and different hydrotropes. From Figure 6 it is observed that free energy decreases as the temperature increases which shows the relationship between the standard free energy of both hydrotropes and temperature.

Figure 6 Temperature versus ΔG°



Notes: ◆: urea; ■: resorcinol; ▲: sodium cumene sulfonate; ●: pyrogallol.

Figure 7 Temperature vs $\ln(x_{mhc})$



Notes: ◆: urea; ■: resorcinol; ▲: sodium cumene sulfonate; ●: pyrogallol.

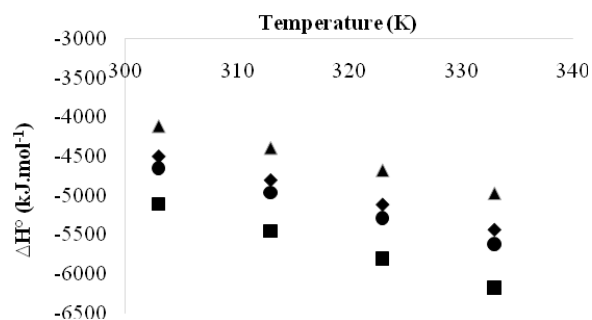
To determine the value of Standard enthalpy change (ΔH°) Van't Hoff equation is used to find out the standard enthalpy of aggregation.

$$\Delta H^\circ = -RT^2 \left(\partial \ln X_{MHC} / \partial T \right) \quad (3)$$

when $\ln X_{MHC}$ values were plotted against temperature, the trend of graph was linear in nature Figure 7. $(\partial \ln X_{MHC} / \partial T)$ values required to calculate can be obtained from the slopes of the plot. Negative value for enthalpy as seen from Figure 8 is calculated using equation (3). Values indicate the aggregation behaviour of hydrotropes to be exothermic in nature. Entropy is a measure of disorderliness or randomness of the system Standard entropy of aggregation was calculated from.

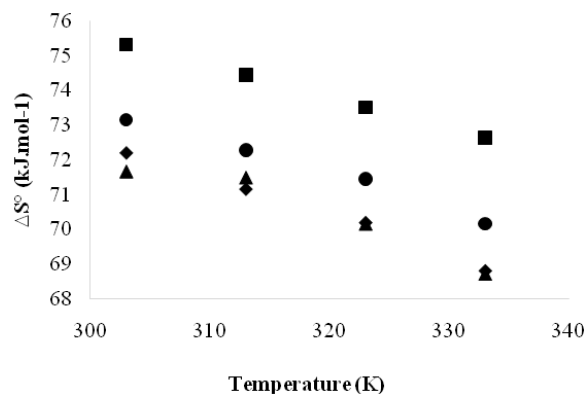
$$\Delta S^\circ = [(\Delta H^\circ - \Delta G^\circ) / T] \quad (4)$$

Figure 8 Temperature versus ΔH°



Notes: ◆: urea; ■: resorcinol; ▲: sodium cumene sulfonate; ●: pyrogallol.

Figure 9 Temperature versus ΔS°



Notes: ◆: urea; ■: resorcinol; ▲: sodium cumene sulfonate; ●: pyrogallol.

Figure 9 shows that the values of standard entropy are positive in magnitude. It can be stated that aggregation of hydrotropes is favoured entropically. The decrease in entropy values with temperature indicates that self-aggregation becomes poor at higher temperature. This may be due to the fact that molecular motion will be higher when temperature increases. The values of decreasing standard free energy, standard entropy and standard enthalpy with increasing temperature for different hydrotropes are seen from Table 4.

Table 4 Change in enthalpy, entropy and free energy for different hydrotropes at T = (303.15 to 333.15) K

Hydrotropes	<i>T</i>	<i>S</i>	ΔG°	ΔH°	ΔS°
	<i>K</i>	$\times 10^{-4} \text{ mol.kg}^{-1}$	kJ.mol^{-1}	kJ.mol^{-1}	kJ.mol^{-1}
Urea	303.15	2.220	-26,993.4	-5,114.11	72.20
	313.15	2.354	-27,731.6	-5,457.25	71.16
	323.15	2.474	-28,484.9	-5,811.52	70.20
	333.15	2.734	-29,089.3	-6,176.94	68.80
Resorcinol	303.15	2.265	-26,943.1	-4,121.82	75.31
	313.15	2.384	-27,698.9	-4,398.38	74.44
	323.15	2.526	-28,428.9	-4,683.91	73.51
	333.15	2.66	-29,165.8	-4,978.43	72.64
Sodium cumene sulfonate	303.15	2.846	-26,367.8	-4,656.13	71.66
	313.15	2.734	-27,342.2	-4,968.54	71.48
	323.15	3.014	-27,951.2	-5,291.09	70.16
	333.15	3.375	-28,506.5	-5,623.78	68.72
Pyrogallol	303.15	2.526	-26,668.6	-4,503.47	73.15
	313.15	2.645	-27,428.8	-4,805.63	72.28
	323.15	2.757	-28,193.9	-5,117.61	71.44
	333.15	3.032	-28,802.9	-5,439.39	70.16

3.5 Stepwise association model

In this study the aggregation behaviour of hydrotrope and the solubilisation of p cymene are explored and Table 5 lists the hydrotrope – solute (K_{hs}), hydrotrope – hydrotrope (K₂) Association constants. Since aggregation of the hydrotrope is a pre-requisite for the solubilisation of a solute, an association model is used. The model attempts to explain the increase in the solubility of a hydrophobic solute in an aqueous solution of a hydrotrope in terms of the associations between hydrotrope–hydrotrope and hydrotrope–solute molecules. Solubilisation of p-cymene in hydrotrope solutions can be studied with the help of association model. According to this model aggregation of the hydrotropes occurs step by step and the solute solubilises through co-aggregation with the hydrotropic aggregates.

Hydrophobic effect plays a significant role in self aggregation of hydrotropes. This effect is influenced by the structure of hydrocarbon and opposed by electrostatic repulsion among the charged head groups this in turn enhances the favourable aggregation of hydrotropes. The association constant for an n-mer of hydrotrope with a monomer is related to the dimerisation constant (K_2 , L/mol), i.e., $K_n = K_2/n$. The total concentration of the hydrotrope (C_s) and the monomer concentration (H_1) can be related by the following Equation (5)

$$C_s - [H_1] \{ 2 \exp^{(K_2[H_1])} - 1 \} \quad (5)$$

Table 5 Hydrotrope –solute (K_{hs}), hydrotrope – hydrotrope (K_2) association constants

<i>Hydrotrope</i>	<i>T</i>	<i>K</i> ₂	<i>K</i> _{hs}
	<i>K</i>	<i>L.mol</i> ⁻¹	<i>L.mol</i> ⁻¹
Urea	303.15	1.740	130.1
	313.15	1.856	135.6
	323.15	1.942	137.3
	333.15	2.256	142.9
Resorcinol	303.15	0.062	32.6
	313.15	0.068	32.8
	323.15	0.069	32.9
	333.15	0.070	33.4
Sodium cumene sulfonate	303.15	0.183	52.1
	313.15	0.186	52.3
	323.15	0.187	52.5
	333.15	0.188	52.7
Pyrogallol	303.15	0.436	83.8
	313.15	0.475	84.2
	323.15	0.510	84.7
	333.15	0.526	85.6

A solute molecule can reside between the hydrotrope molecules and reduce the electrostatic repulsion between the charged groups of the hydrotrope molecules, effectively compacting the aggregate structure and providing geometrical constraint to the incorporation of more solute molecules into the same aggregate. Since most solubility studies with hydrotrope solutions show a sigmoidal nature of the solubility curve with hydrotrope concentration, it is appropriate to assume a finite capacity of a hydrotrope aggregate to solubilise the solute. Considering that the association constant for incorporation of a solute molecule into an *n*-mer of hydrotrope decreases with every new addition of a solute molecule, hydrotrope *n*-mer is assumed to take up a maximum of (*n*-1) solute molecules. The total amount of the solute associated with the hydrotrope aggregates, under the assumption that hydrotrope aggregate-solute association constant decreases with increase in number of solute molecules (*j*) in the co-aggregate ($K_{ni} = K_{hs}/j$), is given by Equation (6).

$$S_T = 2[S_1] \left(\frac{K_{hs}}{K_2} \right) \left(e^{K_2[H_1]} - (1 + K_2[H_1]) \right) \quad (6)$$

The amount of solute associated with the can be related to the total concentration of the hydrotrope which is a measurable quantity. These two equations can be used to estimate the values of the association parameters K_2 and K_{hs} from the solubility data. They characterise the hydrotrope-hydrotrope and hydrotrope-solute associations.

The experimental solubility data of *p*-cymene was fitted into the association model [equations (5) and (6)]. The Equations (5) and (6) are nonlinear and a nonlinear least-squares method has been adopted. Equation (5) can be converted into a polynomial where the monomer concentration (H_1) can be obtained in terms of total hydrotrope concentration (C_s). This concentration can be substituted into equation (6) to estimate the relevant parameters such as K_2 and K_{hs} , which represent the hydrotrope-hydrotrope and hydrotrope-solute associations respectively.

Although the hydrotrope aggregates are formed in aqueous solutions, their aggregation tendency is much weaker than that of solute-hydrotrope co-aggregation. With increase in temperature, the association constants (K_2 and K_{hs}) were also found to increase. It seems that the temperature increase effect a significant change in the aggregate structures, thereby causing more solute to be solubilise in the hydrotrope solutions.

3.6 Characterisation of FTIR spectra

Figures 10, 11, and 12 presents the FTIR spectra of pure *p*-cymene, *p*-cymene and urea below MHC and *p*-cymene and urea at MHC. The FTIR spectra of pure *p*-cymene demonstrated the FTIR peaks at $1,671\text{ cm}^{-1}$ (C = C stretching of alkanes), $1,413\text{ cm}^{-1}$ (C-C stretching of aromatics), $2,939\text{ cm}^{-1}$ (C-H stretching of alkanes), the same peaks were observed in pure *p*-cymene, sample below MHC and sample at MHC. The presence of new peaks in spectra of sample at MHC indicates that are due to aggregation. Furthermore the absence of peak from urea indicates the lack of aggregation in the sample of *p*-cymene and urea below MHC.

Figure 10 FT-IR spectra of pure *p*-cymene

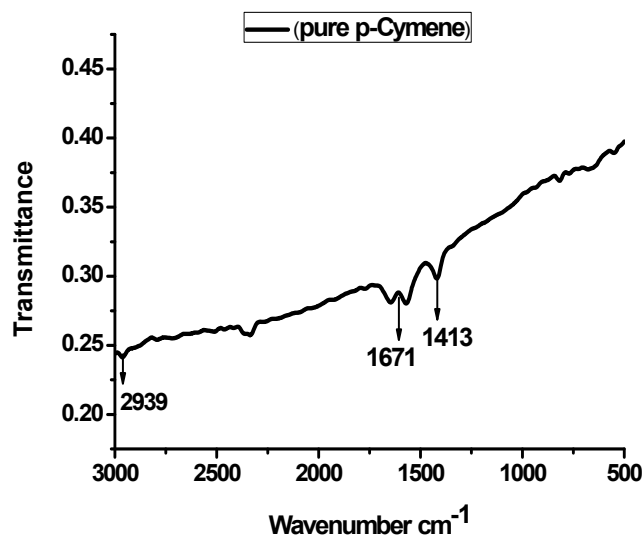
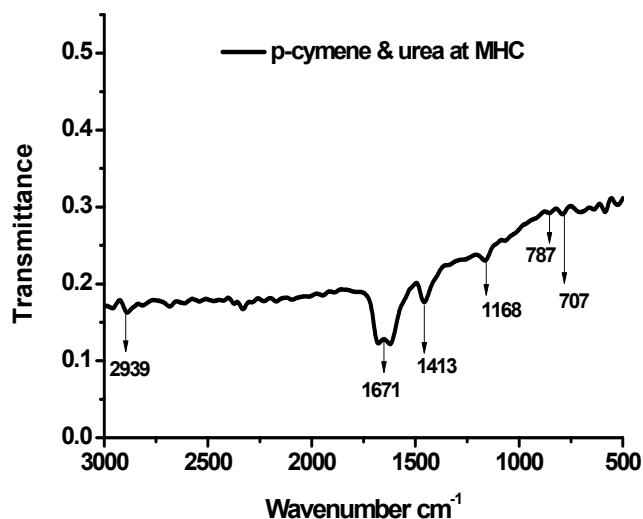
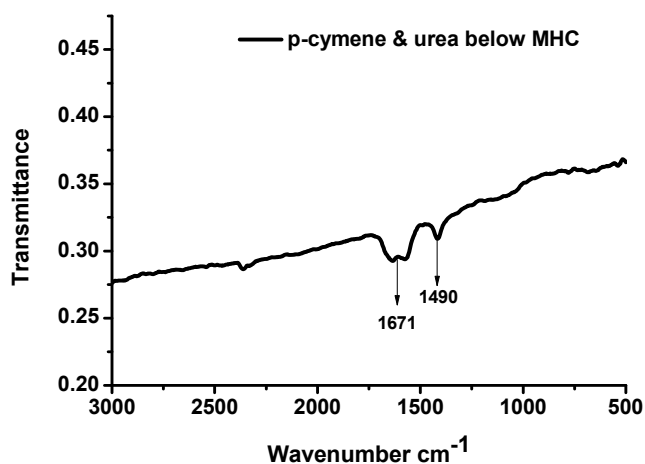


Figure 11 FT-IR spectra of p-cymene and Urea at MHC**Figure 12** FT-IR spectra of p-cymene and Urea below MHC

4 Conclusions

The solubility of p-cymene in double distilled water, urea, resorcinol, sodium cumene sulfonate and pyrogallol was measured and the result obtained manifested that the solubility of p-cymene which is insoluble in water, has been increased by a maximum enhancement factor of 71.86, in the presence of urea as hydrotrope at a temperature of 333.15 K. This would be helpful in increasing the mass transfer coefficient and in turn increase the rate of output of the product synthesised from p-cymene. Solubility value plays an important role to study thermodynamic stability. The thermodynamic properties like standard Gibbs free energy change, standard enthalpy change and standard entropy change indicated that the aggregation process was exothermic and also spontaneous in

nature. The study on association constant suggests that interaction between the hydrotrope and solute molecules increases with the increase in system temperature thereby causing more solute to solubilise. At lower temperature enhancement of solubility is observed due to the effect of hydrotropy, when temperature is increased, solubility has been improved because of mesoscale solubilisation.

References

- Balasubramanian, D., Srinivas, V., Gaikar, V.G. and Sharma, M.M. (1989) 'Aggregation behavior of hydrotropic compounds in aqueous solution', *The Journal of Physical Chemistry*, Vol. 93, No. 9, pp.3865–3870.
- Gnanaprakash, D., Thenesh Kumar, S. and Nagendra Gandhi, N. (2012) 'Enhancement of solubility and mass transfer coefficient of cinnamic acid through hydrotropy', *Asian Journal of Chemistry*, Vol.24, No.8, pp.3582–3586.
- Gnanaprakash, D., Thenesh Kumar, S. and Nagendra Gandhi, N. (2013) 'Enhancement of solubility and mass transfer coefficient of benzoic acid through hydrotropy', *Polish Journal of Chemical Technology*, Vol. 15, No. 1, pp.46–50.
- Jenamayjayan, D., Jayakumar, C. and Nagendra Gandhi, N. (2009) 'Separation of a phenol/ o-chlorophenol mixture through hydrotropy', *Journal of Chemical and Engineering Data*, Vol.54, No. 6, pp.1923–1926.
- Maheshwari, R.K. (2006) 'Application of hydrotropic solubilization in the analysis of aceclofenac', *Asian Journal of Chemistry*, Vol. 18, No. 2, pp. 1572–1574.
- Maheshwari, R.K., Arif, D., Mittal, P., Manchandani, P., Indurkha, A. and Jawade, S.A. (2008) 'A novel method for quantitative determination of aceclofenac in bulk drug and tablets using ibuprofen sodium as a hydrotropic solubilizing agent', *Journal of Applied Chemical Research*, Vol. 5, No. 1, pp.63–68.
- Maheshwari, R.K., Srivastav, V.K., Prajapat, R.P., Jain, A., Kamaria, P and Sahu, S. (2010) 'New spectro photometric estimation of ornidazole tablets employing urea as a hydrotropic solubilizing additive', *Indian Journal of Pharmaceutical Sciences*, Vol.72, No.2, pp.258–261.
- Manoj Kumar, V and Sangeetha, D (2016) 'Disparate practical way of doing solubility enhancement study to improve the bioavailability of poorly soluble drugs', *Journal of Chemical and Pharmaceutical Research*, Vol. 8, No. 1, pp.208–235.
- Mckee, R.H. (1946) 'Use of hydrotropic solutions in industry', *Industrial and Engineering Chemistry*, Vol. 38, No. 4, pp.382–384.
- Mehta, P., Patil, S. and Chavan, B. (2016) 'Quantitative analysis of salicylic acid bulk sample using hydrotropic solubilizing agents', *Asian journal of Pharmaceutical and clinical research*, Vol. 9, No. 1, pp168–169.
- Meyyappan, N. and Nagendra Gandhi, N. (2005) 'Effect of hydrotropes on the solubility and mass transfer coefficient of benzyl benzoate in water', *Journal of Chemical and Engineering Data*, Vol. 50, No. 3, pp.796–800.
- Nagendra Gandhi, N. and Dharmendra Kumar, M. (2000) 'Effect of hydrotropes on solubility and mass transfer coefficient of methyl salicylate', *Journal of Chemical and Engineering Data*, Vol. 45, No. 3, pp.419–423.
- Nagendra Gandhi, N. and Meyyappan, N. (2004) 'Solubility and mass transfer coefficient enhancement of benzyl acetate in water through hydrotropy', *Journal of Chemical and Engineering Data*, Vol. 49, No. 5, pp.1290–1294.
- Nagendra Gandhi, N. and Meyyappan, N. (2005) 'Solubility and mass transfer coefficient enhancement of benzyl benzoate in water through hydrotropy', *Journal of Chemical and Engineering Data*, Vol. 50, No. 3, pp.796–800.
- Neuberg, C. (1916) 'Hydrotropy', *Biochem. Z*, Vol.76, No. 1, pp.107–108.

- Nwodo, N.J., Nnadi, C.O. and Nnadi, K. (2013) 'Development and validation of novel hydrotropic solubilization method for spectrophotometric determination of halofantrine in pure and solid dosage form', *Scholar Academic of pharmacy*, Vol. 2, No. 4, pp.298–303.
- Santana, M.F., Quintans-Junior, L.J., Socrates Cavalcanti, C.H., Makson Oliveria, G.B., Guinmares, A.G., Cunha, E.S., Melo, M.S., Marcio Santos, R.V., Adriano Araujo, A.S. and Bonjardim, L.R. (2011) 'p-cymene reduces orofacial nociceptive response in mice', *Revista Brasileira de Farmacognosia*, Vol. 21, No. 6, pp. 1138–1143.
- Selvaraj, M., Seshadri, K.S., Sinha, P.K., Krishnasamy, V. and Lal, K.B. (2002) 'Comparison of mesoporous A1-MCM-41 molecular sieves in the production of p-cymene for isopropylation of toluene', *Journal of Molecular Catalysis A: Chemical*, Vol. 186, No. 1, pp.173–186.
- Shimizu, S. and Matubayasi, N. (2014) 'Hydrotropy: monomer–micelle equilibrium and minimum hydrotrope concentration', *J. Phys. Chem. B*, Vol. 118, No. 35, pp10515–10524.
- Thenesh Kumar, S., Gnanaprakash, D. and Nagendra Gandhi, N. (2009) 'Enhancement of solubility and mass transfer coefficient of salicylic acid through hydrotropy', *Journal of Zhejiang University Science*, Vol. 10, No. 5, pp.739–745.
- Varma, M.M. and Pandit, J.K. (2005) 'Influence of urea and xylitol on the dissolution rate of flurbiprofen', *Indian Pharmacist*, Vol.4, No. 1, pp. 97–99.
- Zhang, Q.G., Bi, L.W., Zhao, Z.D., Chen, Y.P., Li, D.M., Gu, Y., Wang, J., Chen, Y.X., Bo, C.Y. and Liu, X.Z. (2010) 'Application of ultrasonic spraying in preparation of p-cymene by industrial dipentene dehydrogenation', *Chemical Engineering Journal*, Vol.159, Nos. 1–3, pp.190–194.