

# Solubility of butylated hydroxytoluene (BHT) in aqueous and alcohol solutions from 293.15 to 313.15 K

Shipra Baluja<sup>1,\*</sup>, Kapil Bhesaniya<sup>1</sup>, Rahul Bhalodia<sup>1</sup>, Sumitra Chanda<sup>2</sup>

<sup>1</sup>Physical Chemical Laboratory, Department of Chemistry, Saurashtra University, Rajkot, India

<sup>2</sup>Bio-Science Department, Saurashtra University, Rajkot - 360 005, India

\*E-mail address: shipra\_baluja@rediffmail.com

## ABSTRACT

The solubility of Butylated hydroxyl toluene in aqueous and alcohol solutions were determined at different temperatures (293.15 to 313.15) K. Using Van't Hoff and Gibb's equations, some thermodynamic functions such as Gibbs energy, enthalpy and entropy of dissolution, and of mixing of Butylated hydroxyl toluene in aqueous and alcohol solutions, were evaluated from solubility data. The solubility was greater in butanol and minimum in water. The enthalpies, entropy and Gibb's energy of dissolution were positive for all solvents.

**Keywords:** Butylated hydroxytoluene (BHT); Average deviation; Relative deviation; Gibbs energy

## 1. INTRODUCTION

Butylated hydroxytoluene (BHT) [IUPAC: 2,6-di-tert-butyl-4-methylphenol] (Fig. 1) is a lipophilic phenol, primarily used as an antioxidant [1-2] food additive as well as in cosmetics, pharmaceuticals, jet fuels, rubber, petroleum products, and embalming fluid [3-5]. It behaves as a synthetic analogue of vitamin E [6], primarily acting as a terminating agent that suppressed auto oxidation.

These applications prompted us to study the solubility of BHT in different solvents such as methanol, ethanol, propanol, butanol and water. The study is done at different temperatures (293.15 to 313.15 K).

The data may be useful for the design process of pharmaceutical dosage form. Further, the study of temperature dependence solubility data provides the explanation of molecular mechanisms involved in the respective drug dissolution process.

## 2. EXPERIMENTAL

### 2. 1. Materials

BHT, a white powder with a purity of 99.6 mass %, was purchased from Himedia Pvt. Ltd. All the solvents, methanol, ethanol, propanol, butanol and water were analytical grade

reagents and were purified by fractional distillation. Their purities were checked by SHIMADZU GC-MS (Model No QP-2010) and were found to be greater than 99.85 %. Melting point of BHT was determined by DSC and was found to be in agreement with the reported value [7].

## 2. 2. Equipments

Mettler Toledo AB204-S, electronic balance was used with an accuracy of  $\pm 0.1$  mg. The UV spectrophotometer of Shimadzu make was used for concentration determination.

## 2. 3. Solubility measurement

An excess mass of BHT was added to a known mass of solvent in stoppered glass flasks. The solid-liquid mixtures were placed on an ultrasonic bath for about 15 minutes and were stirred in a mechanical shaker for one hour. The samples were then allowed to stand in water bath kept at appropriate temperature with  $\pm 0.05$  K. All samples were maintained at least for 48 hours to reach the equilibrium. This equilibrium time was established by quantifying the BHT concentration to obtain a constant value. After this time, the supernatant solutions were filtered (at isothermal conditions) to insure ensure that they are free of particulate matter before sampling. The concentrations were determined by measuring the absorbance after appropriate dilution and interpolation from previously constructed UV-spectrophotometric calibration curves. All the measurements were repeated at least three times.

## 3. RESULTS AND DISCUSSIONS

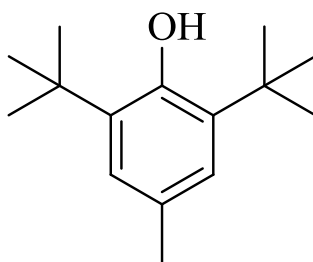
Tables 1 and 2 summarize the physicochemical properties of Butylated hydroxytoluene (BHT) and of studied solvents respectively.

**Table 1.** Physical Data for the selected solvents.

Solvent	Molar mass ( $\text{g}\cdot\text{mol}^{-1}$ )	Boiling point ( $^{\circ}\text{C}$ )	Dielectric constant	Dipole moment
Water	18	100	80	-
Methanol	32	64.6	33	1.70
Ethanol	46	79	24.55	1.69D
Propanol	60	97	20	1.68D
Butanol	74	117.6	18	1.63D

**Table 2.** Physicochemical Data of BHT.

Molar mass (g·mol <sup>-1</sup> )	Melting point (K)	$\Delta H_{fus}$ (kJ·mol <sup>-1</sup> )	$\Delta S_{fus}$ (J·mol <sup>-1</sup> )
220.35	344.15	19.87	57.7365

**2,6-di-tert-butyl-4-methylphenol****Figure 1.** Molecular structure of BHT.

### 3. 1. Ideal and experimental solubility of BHT

The ideal solubility of a crystalline solute in a liquid solvent can be calculated by the following equation:

$$\ln x_2^{id} = -\frac{\Delta H_{fus}(T_{fus} - T)}{RT_{fus}T} + \left(\frac{\Delta C_p}{R}\right) \left[ \frac{(T_{fus} - T)}{T} + \ln\left(\frac{T}{T_{fus}}\right) \right] \quad (1)$$

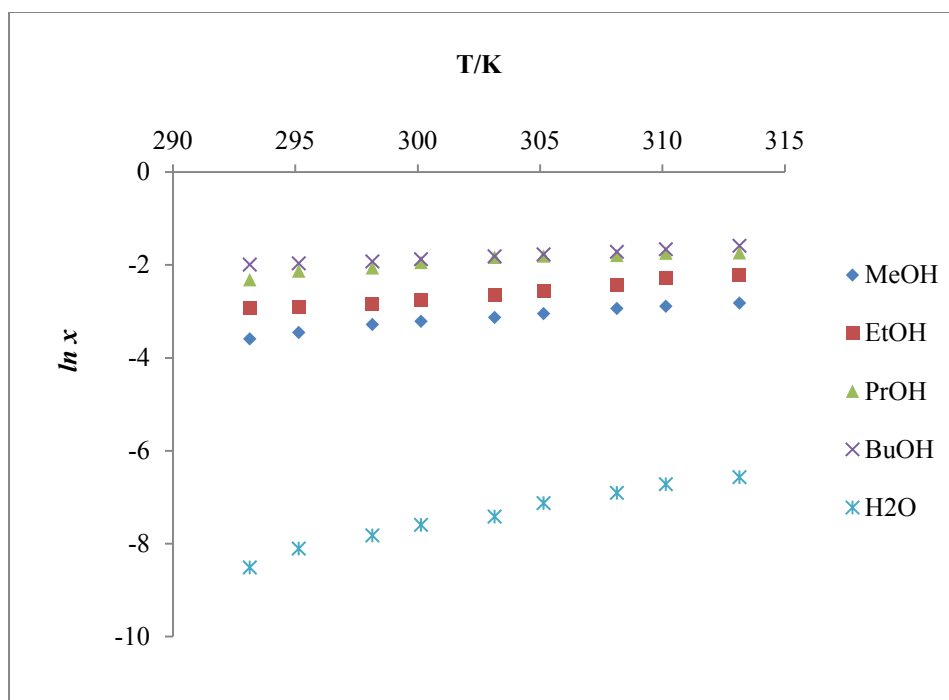
where  $x_2^{id}$  is the ideal solubility of solute as mole fraction,  $\Delta H_{fus}$  is the molar enthalpy of fusion of the pure solute,  $T_{fus}$  is the absolute melting point,  $T$  is the absolute solution temperature,  $R$  is the gas constant (8.314 J mol<sup>-1</sup> K<sup>-1</sup>) and  $\Delta C_p$  is the difference between the molar heat capacity of the crystalline form and the molar heat capacity of the hypothetical super cooled liquid form, both at solution temperature [8].  $\Delta C_p$  can't be easily determined so it is assumed that  $\Delta C_p$  is approximately equal to entropy of fusion  $\Delta S_{fus}$  [9].

The ideal solubilities of BHT at different temperatures are given in Table 3 whereas experimental solubilities of BHT in water and alcohol solutions at different temperatures (293.15 to 313.15 K) are summarized in Table 4. The variation of solubility with temperature is also shown in Figure 2. It is observed that solubility increases linearly with increase in temperature. Further, solubility is higher in butanol and minimum in water. This suggests that solubility increases with increase in  $-CH_2$  group. Further, the minimum solubility of water suggests that BHT structure leads to water association which is not favorable for solubility of BHT in water whereas butanol could form maximum hydrogen bonding with BHT which causes increase in solubility.

**Table 3.** Ideal Solubilities ( $x_2^{id}$ ) of BHT at different temperatures.

Temp. (K)	293.15	295.15	298.15	303.15	305.15	208.17	210.15	313.15
$x_2^{id}$	0.3283	0.3441	0.3692	0.3868	0.4144	0.4338	0.4856	0.5192

$x_2^{id}$  = Ideal solubility of solute (BHT).

**Figure 2.** Solubility  $x$  of BHT as a function of temperature.

The mole fraction solubility  $x$  of BHT was also correlated as a function of temperature by the modified Apelblat equation [10-11]

$$\ln x = A + B (T/K) \quad (2)$$

where  $x$  is the mass fraction solubility of BHT;  $T$  is the absolute temperature and  $A$  and  $B$  are the coefficients in equation (2). The values of these coefficients are given in Table 5. The calculated solubilities  $x_{ci}$  are also reported in Table 4. Further, absolute average deviations ( $AAD$ ) and root-mean-square deviations ( $rmsd$ ), calculated by equations (3) and (4) are listed in Table 5.

$$AAD = \frac{1}{N} \sum_i^N \frac{x_i - x_{ci}}{x_i} \quad (3)$$

$$rmsd = \left[ \sum_{i=1}^N \frac{(x_{ci} - x_i)^2}{N-1} \right]^{1/2} \quad (4)$$

**Table 4.** Experimental Mole Fraction Solubilities ( $x$ ), Calculated Mole Fraction Solubilities ( $x_{ci}$ ) and relative deviation ( $RD$ ) of BHT in different solvents.

$T/K$	$10^{-2} x$	$10^{-2} x_{ci}$	100 RD	$10^{-2} x$	$10^{-2} x_{ci}$	100 RD
Methanol				Ethanol		
293.15	$2.75 \pm 0.02$	$3.18 \pm 0.01$	-0.36	$5.31 \pm 0.03$	$5.06 \pm 0.02$	-1.60
295.15	$3.16 \pm 0.02$	$3.40 \pm 0.01$	2.12	$5.52 \pm 0.02$	$5.47 \pm 0.01$	-0.36
298.15	$3.76 \pm 0.01$	$3.76 \pm 0.01$	-0.02	$5.83 \pm 0.01$	$6.13 \pm 0.01$	1.75
300.15	$4.01 \pm 0.03$	$4.02 \pm 0.02$	0.06	$6.32 \pm 0.04$	$6.62 \pm 0.02$	1.64
303.15	$4.37 \pm 0.01$	$4.44 \pm 0.01$	0.49	$7.05 \pm 0.05$	$7.43 \pm 0.03$	1.93
305.15	$4.75 \pm 0.02$	$4.75 \pm 0.02$	0.02	$7.77 \pm 0.06$	$8.02 \pm 0.02$	1.22
308.15	$5.30 \pm 0.04$	$5.26 \pm 0.02$	-0.31	$8.83 \pm 0.02$	$8.99 \pm 0.03$	0.75
310.15	$5.57 \pm 0.03$	$5.62 \pm 0.01$	0.31	$10.10 \pm 0.03$	$9.71 \pm 0.01$	-1.75
313.15	$5.95 \pm 0.04$	$6.22 \pm 0.03$	1.54	$10.95 \pm 0.06$	$10.89 \pm 0.02$	-0.23
Propanol				Butanol		
293.15	$9.85 \pm 0.05$	$10.98 \pm 0.03$	4.70	$13.58 \pm 0.03$	$13.42 \pm 0.02$	-0.62
295.15	$11.87 \pm 0.04$	$11.61 \pm 0.02$	-1.07	$14.02 \pm 0.02$	$13.98 \pm 0.02$	-0.17
298.15	$12.69 \pm 0.06$	$12.61 \pm 0.03$	-0.35	$14.64 \pm 0.03$	$14.87 \pm 0.01$	0.79
300.15	$14.27 \pm 0.04$	$13.33 \pm 0.02$	-3.54	$15.31 \pm 0.05$	$15.49 \pm 0.03$	0.61
303.15	$16.01 \pm 0.03$	$14.48 \pm 0.02$	-5.53	$16.27 \pm 0.01$	$16.47 \pm 0.01$	0.67
305.15	$16.36 \pm 0.02$	$15.30 \pm 0.02$	-3.74	$16.98 \pm 0.04$	$17.16 \pm 0.02$	0.60
308.15	$16.64 \pm 0.04$	$16.61 \pm 0.03$	-0.08	$18.00 \pm 0.03$	$18.25 \pm 0.02$	0.78
310.15	$17.50 \pm 0.02$	$17.56 \pm 0.01$	0.17	$19.01 \pm 0.03$	$19.02 \pm 0.01$	0.01
313.15	$17.62 \pm 0.04$	$19.08 \pm 0.01$	4.56	$20.49 \pm 0.04$	$20.22 \pm 0.01$	-0.84
Water						
293.15	$0.02 \pm 0.00$	$0.02 \pm 0.00$	2.57			
295.15	$0.03 \pm 0.00$	$0.03 \pm 0.00$	-0.06			
298.15	$0.04 \pm 0.00$	$0.04 \pm 0.01$	-1.68			
300.15	$0.05 \pm 0.01$	$0.05 \pm 0.01$	-1.39			
303.15	$0.06 \pm 0.01$	$0.06 \pm 0.01$	-0.34			
305.15	$0.08 \pm 0.01$	$0.08 \pm 0.01$	-0.77			
308.15	$0.10 \pm 0.00$	$0.10 \pm 0.01$	-0.44			
310.15	$0.12 \pm 0.01$	$0.12 \pm 0.01$	0.32			
313.15	$0.14 \pm 0.02$	$0.16 \pm 0.01$	1.97			

$x_{ci}$  = Calculated solubility of solute (BHT).

where  $N$  is the number of experimental points and  $x_{ci}$  is the solubility calculated by equation (2). The relative deviations ( $RD$ ) between the experimental and calculated values of solubilities are also calculated by equation (5) and are given in Table 4.

$$Relative\ Deviation = \left( \frac{x - x_{ci}}{x} \right) \quad (5)$$

Further, the activity coefficient  $\gamma$  for BHT in different solvents were also calculated as  $x_2^{id} / x$  and is reported in Table 6. It is observed that activity coefficient is minimum for butanol and maximum for water. This trend is similar to solubility of BHT in the studied solvents.

**Table 5.** Constants A and B of equation 2, Absolute Average Deviation ( $AAD$ ), and root mean Square Deviation ( $rmsd$ ) of BHT in different solvents.

Solvents	A	B	$10^{-5}$ rmsd	100 AAD
Methanol	-13.27	0.0335	1.2655	0.4297
Ethanol	-14.21	0.03873	.5965	0.3738
Propanol	-10.30	0.00276	70.200	-0.5413
Butanol	-8.02	0.0205	2.8761	0.2046
Water	-35.71	0.0935	0.0045	0.0194

**Table 6.** The activity coefficient for BHT in different solvents at different temperatures.

Temp. (K)	Activity coefficient				
	Methanol	Ethanol	Propanol	Butanol	Water
293.15	11.93793	6.182546	3.332926	2.417476	1641.466
295.13	10.89133	6.234895	2.899462	2.454823	1147.221
298.15	9.819304	6.332862	2.909423	2.521898	923.0146
300.15	9.644678	6.119487	2.710242	2.526137	773.5032
305.15	9.482994	5.878111	2.588425	2.547061	690.678
305.13	9.131989	5.582619	2.651403	2.55459	542.2118
308.15	8.759692	5.257799	2.790046	2.579243	464.2637
310.15	8.718079	4.807891	2.77484	2.555639	404.6642
313.15	8.725521	4.741265	2.946473	2.533765	370.8346

### 3. 2. Thermodynamic functions of dissolution

From the experimental solubility data, some thermodynamic parameters such as heat of solution ( $\Delta H_{sol}$ ), Gibbs energies of dissolution ( $G_{sol}$ ) and enthalpy of dissolution ( $\Delta H_{sol}$ ) were also evaluated. The heat of solution ( $\Delta H_{sol}$ ) can be calculated using Von't Hoff equation [12]. i.e. from the slope of the plot of  $\ln x$  verses  $1/T$ , if the solubility is low as in case of water. However, in more recent treatments, the mean harmonic temperature,  $T_{hm}$  has been introduced in Van't Hoff equation. The mean harmonic temperature,  $T_{hm}$  is calculated as [13-14]

$$T_{hm} = \frac{n}{\sum_1^n \left( \frac{1}{T} \right)} \quad (6)$$

where n is the number of tested temperatures. In the present case, the  $T_{hm}$  value obtained is 302.79 K. Thus, the modified van't Hoff equation can be written as:

$$\left( \frac{\partial \ln x}{\partial \left( \frac{1}{T} - \frac{1}{302.79K} \right)} \right) = - \frac{\Delta H_{sol}}{R} \quad (7)$$

From the slopes of the plots of  $\ln x$  against  $[(1/T)-(1/T_{hm})]$ ,  $\Delta H_{sol}$  values for all the solvents were evaluated. Further, the standard Gibbs energies of the dissolution process ( $\Delta G_{sol}$ ) were also calculated using following relation:

$$\Delta G_{sol} = -RT_{hm} \cdot \text{Intercept} \quad (8)$$

Using these  $\Delta H_{sol}$  and  $\Delta G_{sol}$  values, the standard entropies of solutions ( $\Delta S_{sol}$ ) were obtained from the equation

$$\Delta S_{sol} = \left( \frac{\Delta H_{sol} - \Delta G_{sol}}{T_{hm}} \right) \quad (9)$$

These thermodynamic values for different solvents are summarized in Table 7. As evident from Table 7, all the thermodynamic parameters are positive for the selected solvents. The enthalpy of solution is maximum in water. Among alcohols, it is maximum for methanol and minimum for butanol. The same is true for entropy and Gibb's energy of the dissolution values. The positive  $\Delta G_{sol}$  suggests that the dissolution process is not spontaneous. This is explained by the experimental solubilities (Table 4), which is much less in comparison to the ideal solubility of BHT (Table 3). The positive enthalpy suggests that the dissolution process is endothermic.

The values of thermodynamic functions calculated from ideal solubility are also reported in Table 7. In this case, Gibb's energy of dissolution is negative which is due to higher ideal solubility of BHT. However, enthalpy and entropy values are positive. In order to

compare the relative contributions to the dissolution process from enthalpy  $\% \zeta_H$  and from entropy  $\% \zeta_S$ , following equations were used:

$$\% \zeta_H = 100 \frac{|\Delta H_{sol}|}{|\Delta H_{sol}| + |T \Delta S_{sol}|} \quad (10)$$

$$\% \zeta_{TS} = 100 \frac{|T \Delta S_{sol}|}{|\Delta H_{sol}| + |T \Delta S_{sol}|} \quad (11)$$

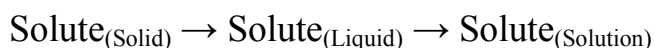
**Table 7.** Thermodynamic functions of experimental and ideal solubilities of BHT.

Solvent	$\Delta G$ (KJ/mole)	$\Delta H$ (KJ/mole)	$\Delta S$ (J/mole)	$\% \zeta_H$	$\% \zeta_S$
Methanol	7.9348	29.7176	68.6341	58.0153	41.9847
Ethanol	6.5931	28.1156	74.3834	56.3847	43.6153
Propanol	4.8586	21.2007	53.9718	56.4724	43.5285
Butanol	4.5615	15.6054	36.4736	58.5593	41.4407
Water	18.6866	72.3235	177.1420	57.4185	42.5815
$x_2^{id}$	-1.0472	7.2389	27.3663	46.6273	53.3727

The values are reported in Table 7. It is clear from these values that the main contributor to the standard Gibb's energy of the dissolution process is enthalpy for all the solvents. However, the respective contributions are reverse with respect to their ideal solubilities.

### 3. 3. Thermodynamic functions of mixing

The dissolution process can be represented by the hypothetical stages:



where fusion and mixing are the respective partial processes towards the drug dissolution process at  $T_{hm}$ . This approximation allows one to calculate the partial thermodynamic contributions to the dissolution process by the following equations:

$$\Delta H_{sol} = \Delta H_{fus}^{302.79} + \Delta H_{mix.} \quad (12)$$

$$\Delta S_{sol} = \Delta S_{fus}^{302.79} + \Delta S_{mix.} \quad (13)$$

where  $\Delta H_{fus}^{302.79}$  and  $\Delta S_{fus}^{302.79}$  represent the thermodynamic functions of the fusion process at the harmonic temperature (302.79K). The  $\Delta H_{fus}^{302.79}$  values were calculated as:



$$\Delta H_{fus}^{302.79} = \Delta H_{fus} - \Delta C_p (T_{fus} - T_{hm}) \quad (14)$$

$\Delta C_p$  is replaced by  $\Delta S_{fus}$  and value of  $\Delta H_{fus}^{302.79}$  was found to be 17.4820 KJ/mole which is quite different from enthalpy value calculated for the ideal dissolution process (Table 5). Similarly, entropy of fusion  $\Delta S_{fus}^{302.79}$  was found to be 57.7365 J/mole which is quite different from that calculated for the ideal dissolution process (Table 7).

So,  $\Delta H_{mix}$  values were evaluated from equation (12) using both  $\Delta H_{fus}^{302.79} = 17.4820$  KJ/mole as well as  $\Delta H_{sol}^{id}$  (given in Table 7). Similarly,  $\Delta S_{mix}$  values were also evaluated from equation (13) using both  $\Delta S_{fus}^{302.79} = 57.7365$  J/mole as well as  $\Delta S_{sol}^{id}$  (given in Table 7). All these values are given in Table 8.

**Table 8.** Thermodynamic functions relative to mixing process.

Solvent	Methanol	Ethanol	Propanol	Butanol	Water
$\Delta H_{mix}$	11.2345 (21.4787)	11.6336 (21.8767)	3.7187 (13.9618)	-1.8766 (8.3665)	54.8415 (65.0846)
$\Delta S_{mix}$	10.8977 (41.2678)	16.6469 (47.0171)	-3.7647 (26.6055)	-21.2629 (9.1073)	119.4056 (149.7757)
$\Delta G_{mix}$	7.9348 (8.9832)	6.5931 (7.6404)	4.8586 (5.9059)	4.5616 (5.6089)	18.6866 (19.7340)

\*Values in parenthesis are those calculated using ideal dissolution values.

By analyzing the partial contribution by ideal solution (related to solute fusion process) and mixing processes to the enthalpy and entropy of solution, it is found that both  $\Delta H_{fus}^{302.79}$  and  $\Delta S_{fus}^{302.79}$  are positive. However, the contribution of the thermodynamic functions relative to the mixing process towards the solution process is varying. If values calculated from  $\Delta H_{fus}^{302.79}$  and  $\Delta S_{fus}^{302.79}$  are considered,  $\Delta H_{mix}$  value is negative for butanol where as  $\Delta S_{mix}$  values are negative for both propanol and butanol and if these values given in parenthesis are compared for different solvents, again  $\Delta H_{mix}$  value is minimum for butanol and  $\Delta S_{mix}$  values are minimum for both propanol and butanol. However, these values are positive. Interestingly, there is not much difference in  $\Delta G_{mix}$  values evaluated by both ways. These values are positive for all the selected solvents and minimum for propanol and butanol.

The net variation in  $\Delta H_{mix}$  values is due to contribution of various kinds of interactions. The enthalpy of cavity formation is endothermic because energy must be supplied to overcome the cohesive forces of the solvent which is generally hydrogen bonding as in case of water. This causes a decrease of solubility. The enthalpy of solute-solvent interaction is exothermic due to various types of interactions. The structure of solvent molecules around non polar groups of solute contributes to a decrease in the net enthalpy of mixing as observed for alcohols.

Further, the minimum solubility of water suggests that BHT structure leads to water association which is not favorable for solubility of BHT in water whereas butanol could form maximum hydrogen bonding with BHT which causes increase in solubility. Thus, it is concluded that solubility of BHT is maximum in butanol and minimum in water. The

dissolution process of BHT in the studied solvents is endothermic in nature and is not spontaneous.

#### 4. CONCLUSION

The solubility of BHT increases with increasing CH<sub>2</sub> group in alcohols and increases with increase in dielectric constant in selected primary alcohols. Further, solubility is higher in butanol and minimum in water. Further, the minimum solubility of water suggests that BHT structure leads to water association which is not favorable for solubility of BHT in water whereas butanol could form maximum hydrogen bonding with BHT which causes increase in solubility. The dissolution process of BHT in the studied solvents is endothermic in nature and is not spontaneous.

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#### Nomenclature

$C$	concentration ( $\text{mol}\cdot\text{L}^{-1}$ )
$T$	absolute temperature (K)
$x_2^{id}$	ideal solubility of solute
$\Delta H_{fus}$	molar enthalpy of fusion of the pure solute
$T_{fus}$	absolute melting point of solute
$R$	universal gas constant ( $J\cdot\text{mol}^{-1}\cdot\text{K}^{-1}$ )
$\Delta C_p$	difference between the molar heat capacity of the crystalline form and the molar heat capacity of the hypothetical super cooled liquid form
$\Delta S_{fus}$	entropy of fusion
$x$	mass fraction solubility
$x_{ci}$	calculated mass fraction solubility
$\gamma$	activity coefficient
$\Delta H_{sol}$	heat of solution
$G_{sol}$	Gibbs energies of dissolution
$\Delta S_{sol}$	entropies of solutions
$T_{hm}$	harmonic temperature

#### Greek symbol

$\gamma$	activity coefficient
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#### Abbreviation

BHT	Butylated hydroxytoluene
AAD	absolute average deviations
rmsd	root-mean-square deviations
RD	relative deviations

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