Thermodynamic Studies of Molecular Interactions in Aqueous α-Cyclodextrin Solutions: Application of McMillan−Mayer and Kirkwood−Buff Theories

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Osmotic vapor pressure and density measurements were made for aqueous α-cyclodextrin (α-CD) solutions in the temperature range between 293.15 and 313.15 K. The experimental osmotic coefficient data were used to determine the corresponding activity coefficients and the excess Gibbs free energy of solutions. Further, the activity data obtained at different temperatures along with the enthalpies of dissolution (reported in the literature) were processed to obtain the excess enthalpy and excess entropy values for the solution process. The partial molar entropies of water and of α-cyclodextrin were calculated at different temperatures and also at different concentrations of α-CD. Using the partial molar volume data at infinite dilution, the solute−solvent cluster integrals were evaluated which yielded information about solute−solvent interactions. The application of McMillan−Mayer theory of solutions was made to obtain osmotic second and third virial coefficients which were decomposed into attractive and repulsive contributions to solute−solute interactions. The second and third osmotic virial coefficients are positive and show minimum at 303.15 K. The Kirkwood−Buff (KB) integrals G_{ij}, defined by the equation $G_{ij} = \int_0^\infty (g_{ij} - 1)4\pi r^2 \, dr$, have been evaluated using the experimental osmotic coefficient (and hence activity coefficient) and partial molar volume data. The limiting values of KB integrals, G_{ij}^0 are compared with molecular interaction parameters (solute−solute i.e., osmotic second virial coefficient) obtained using McMillan−Mayer theory of solutions. We found an excellent agreement between the two approaches.

1. Introduction

In contrast to proteins, polysaccharides are an often neglected class of biopolymers. However, since these are of universal importance in living matter, many studies have been undertaken.[1−4] The hydration of simple carbohydrate molecules in water is well understood. According to Franks,[5] hydration effects due to solute−solvent hydrogen bonding would be highly orientation dependent, and therefore the conformation of the solute molecule might be one of the factors determining hydration effects. Thermodynamic methods provide a useful means of specifying "binding" in the macroscopic sense, i.e. in terms of changes in free energy and enthalpy. Using the concept of the semi-ideal solution, Robinson and Stokes[6] have suggested that the observed concentration dependence of thermodynamic quantities for aqueous simple carbohydrate systems is due to the solute−water interactions in terms of a series of hydration equilibria. Kozak et al.[7] analyzed the activity data for carbohydrates in water by applying Flory−Huggins lattice model and the McMillan−Mayer theory of solutions and discussed the importance of pair and triplet interactions. It has been stated that solution behavior is dominated by solvation rather than solute association and the effects depend on the solute size and binding sites.

In recent years, the chemistry of cyclic oligosaccharide compounds has been progressing steeply due to their ability to form inclusion complexes with a large variety of organic and inorganic compounds in different solvents (including water) and in solid form.[8] For this reason, they are of interest both in basic chemistry and biochemistry and in many applied areas. Cyclodextrins (CDs) possess hydrophobic cavities that provide an enormous host potential for molecular encapsulation. The well-defined chemical structure, availability of different cavity sizes, low toxicity and pharmacological activity, and the protection of the encapsulated molecule from biodegradation make them efficient drug carriers. The glucose units turn their primary and secondary hydroxyl groups toward the exterior ends of the molecule, making the molecule hydrophilic, as a whole. However, the interior surface of the cone, i.e., the cavity, normally considered as the site of the guest molecules, is largely hydrophobic.[9]

There are several experimental and theoretical studies concerned with properties of CDs in water.[10−13] Linert et al.[10] have discussed the solute−solvent interactions between cyclodextrins and water by employing Monte Carlo simulation studies. They proposed that α-CD does not build up a large hydration cloud having higher entropy compared to *β*-CD. A formation of α-cyclodextrin hexahydrate in solution phase has been considered on the basis of the semiempirical PM3 method and density functional theory (DFT) by Nascimento, Jr. et al.[11,12] who explained their results in terms of the presence of a water dimer inside the cavity and a tetramer outside the cavity. The possibility of the presence of α-CD dimeric species in water has been reported, and accordingly, a double inclusion complexation with the guest molecules (water and other molecules) is discussed. Such type of solute−solute association may lead to enhancement of the encapsulating capacity of the α-CD and might be viewed as a model for enzymatically controlled bioreactions. It is amply evident from these studies that encapsulation of water molecules, the H-bonding interactions with available α-CD sites, and the solute−solute association

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tendency must be governing the exhibited thermodynamic properties such as free energy, heat, and entropy changes occurring due to the solvation of α-CD in aqueous medium. Our recent thermodynamic studies on activities of β-cyclodextrin (α-1,4 linkages of seven glucopyranose units) in water at 298.15 K have revealed that in the solubility range (1.85 g per 100 mL of water) both hydrophobic interactions as well as hydrophobic hydration processes are operative.[13] In infinitely dilute solution hydrophobic hydration and at finite concentrations of β-CD, the additional hydrophobic interactions determine the overall thermodynamic properties of solutions.

A recent molecular dynamic (MD) computer simulation and diffusion coefficient studies of β-CD in water have been interpreted in terms of a rigid macrocyclic structure strongly affecting the surrounding water structure ordering that causes a lowering of configurational entropy and hence minimizing the solubility.[14] The Monte Carlo simulation results of α-CD in aqueous solutions have been explained in terms of the greater flexibility of the solute molecules and the interaction of water molecules in the cavity of α-CD as well as the hydrophobic effect.[15] Compared to β-CD, the α-1,4 linkage of six glucopyranose unit compound, i.e., α-cyclodextrin (α-CD), is much more soluble in water (14.5 g per 100 mL of water) and is known for more flexibility in forming inclusion compounds (cavity diameter 4.7−5.3 Å).[9] Therefore, in view of examining the effects due to size, interacting sites, and hydrophobicity we have made measurements of osmotic coefficient and densities of aqueous α-CD solutions (0.01−0.1 mol kg^{-1}) at 293.15−313.15 K. The data are used to obtain the activity of the solvent and the activity coefficients of the components using appropriate methodology. The free energy change (ΔG_{mix}) data are processed to evaluate the heat of mixing and entropy of mixing as well as excess properties as a function of α-CD concentration. The further analysis is made by applying two exact theories of solutions, i.e., McMillan−Mayer[16] and Kirkwood−Buff,[17] to obtain the solute virial coefficient. The results are presented in the following pages and discussed in terms of solute−solvent, solute−solute, and conformational change interactions.

2. Experimental Section

α-Cyclodextrin (98% pure) procured from Lancaster, London, was used without further purification. The amount of water of hydration in the supplied sample was estimated using the thermogravimetric analysis (model: thermal analyzer, TG-DTA-DSC, TA Inc. SDT-2790) and microprocessor-controlled automatic Karl Fischer Titrator (mode: TKF-55, Chemito from M/S Toshniwal Company) analysis. The number of water molecules per molecule of cyclodextrin was found to be 6.24. Our results of TGA agree excellently with those reported in detail by V. Berbenni et al.[18] These authors have found total of 6.44 water molecules involved in the formation of α-CD hydrate in solid form. According to them 2.44 water molecules (released at comparatively high temperature, from ∼420 to 543 K) are held inside the α-CD cavity, whereas the other four water molecules get removed earlier at comparatively low temperature. We observed that the 4.64 water molecules get removed in two stages at 329 K (1.9 water molecules) and 355 K (2.74 water molecules) while the remaining 1.6 water molecules get lost at the temperature up to 420 K. At this stage, it is difficult for us to decide about the number of water molecules inside the α-CD cavity in view of the recent report on α-CD dimer,[12] but most probably the order is about 1.6 to 2. The value of 6.24 water molecules is confirmed by the Karl Fischer titration technique (6.22 water molecules per molecule of α-CD). The salt NaCl of AR grade (BDH) was dried under vacuum at 393 K for 24 h before use. All the solutions were prepared using doubly quartz distilled water on molality basis and were converted to molarity scale whenever required using density data. The density measurements of aqueous solutions of α-cyclodextrin were made using Anton Paar digital densitometer (DMA 60/602) in the temperature range between 293.15 and 313.15 K. The uncertainty in the density data was found to be $\pm 5 \times 10^{-3}$ kg m^{-3}. The osmotic coefficients of aqueous α-cyclodextrin solutions were measured using KNAUER K-7000 vapor pressure osmometer having temperature control of ±0.001 K. The uncertainty in the osmotic coefficient data was found to be $\pm 1 \times 10^{-3}$. The details about the density and osmotic pressure measurements were reported earlier.[19] For each temperature only freshly prepared solutions were used to avoid bacterial (microbial) effects.

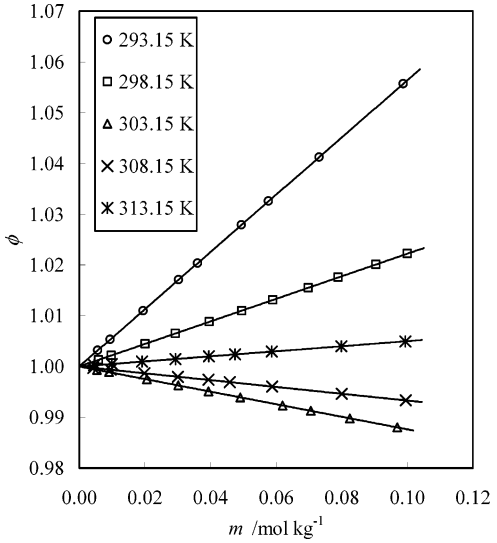

Figure 1. Variation of osmotic coefficient (ϕ) as a function of concentration of α-CD (mol kg^{-1}) at temperatures from 293.15 to 313.15 K.

3. Results and Discussion

The osmotic coefficient (ϕ) values were determined for aqueous α-CD solution in the temperature range between 293.15 and 313.15 K and in the concentration range of 0.01−0.1 mol kg^{-1}. It is found that in the studied low concentration range the osmotic coefficient (ϕ) can be expressed adequately by $\phi = 1 + K_{T,P}m$ at all temperatures ($K_{T,P}$ is a temperature- and pressure-dependent constant). Using the data of osmotic coefficient the water activity (a_w) values have been estimated using the eq 1

$$\phi = -\left[\ln a_w / \left(\frac{x_2}{x_1}\right)\right] \tag{1}$$

where x_1 and x_2 are the mole fraction of water and of α-CD, respectively, in the aqueous solution of α-CD. The variation of osmotic coefficient (ϕ) as a function of concentration of α-CD at different temperatures is shown in Figure 1, and the data are collected in Table 1.

The osmotic coefficient (ϕ) measurement at 298.15 K for aqueous α-CD solutions have been reported by Miyajima et al.;[20] however, our data are in disagreement with the trends obtained by them. The ϕ values reported by these authors are less than unity and decrease with increase in α-CD concentration. In our case the ϕ values increase with concentration at 293.15, 298.15, and 313.15 K, while ϕ decreases at 303.15 and

TABLE 1: Water Activity, Osmotic Coefficient, and Activity Coefficient Data for Aqueous α-CD Solutions at Different Temperatures

m/mol kg^{-1}	ϕ	a_W	γ_1	γ_2	ΔG^E/J mol^{-1}	h	m/mol kg^{-1}	ϕ	a_W	γ_1	γ_2	ΔG^E/Jmol^{-1}	h
293.15 K							308.15 K						
0.00560	1.0032	0.99990	1.00000	1.0063	0.001	39.8	0.00425	0.9997	0.99992	1.00000	0.9994	0.000	
0.00942	1.0053	0.99983	1.00000	1.0107	0.002	36.5	0.00961	0.9994	0.99983	1.00000	0.9987	0.000	
0.01953	1.0110	0.99964	1.00000	1.0223	0.010	33.8	0.01993	0.9987	0.99964	1.00000	0.9973	−0.001	
0.03035	1.0171	0.99944	0.99999	1.0348	0.023	32.8	0.03012	0.9980	0.99946	1.00000	0.9960	−0.002	
0.03603	1.0203	0.99934	0.99999	1.0415	0.033	32.5	0.03936	0.9974	0.99929	1.00000	0.9947	−0.004	
0.04946	1.0279	0.99908	0.99997	1.0574	0.061	31.9	0.04588	0.9969	0.99918	1.00000	0.9939	−0.006	
0.05771	1.0326	0.99893	0.99997	1.0673	0.084	31.6	0.05875	0.9961	0.99895	1.00000	0.9921	−0.009	
0.07314	1.0413	0.99863	0.99994	1.0860	0.134	31.2	0.08001	0.9946	0.99857	1.00001	0.9893	−0.017	
0.09882	1.0557	0.99812	0.99990	1.1179	0.245	30.6	0.09946	0.9933	0.99822	1.00001	0.9867	−0.026	
298.15 K							313.15 K						
0.00593	1.0013	0.99989	1.00000	1.0026	0.000	20.5	0.00449	1.0002	0.99992	1.00000	1.0004	0.000	13.4
0.00976	1.0022	0.99982	1.00000	1.0043	0.001	17.5	0.00996	1.0005	0.99982	1.00000	1.0010	0.000	7.9
0.02012	1.0045	0.99964	1.00000	1.0090	0.004	15.0	0.01912	1.0010	0.99966	1.00000	1.0019	0.001	5.7
0.02929	1.0065	0.99947	1.00000	1.0131	0.009	14.3	0.02927	1.0015	0.99947	1.00000	1.0029	0.002	4.8
0.03960	1.0088	0.99928	0.99999	1.0178	0.016	13.9	0.03949	1.0020	0.99929	1.00000	1.0040	0.004	4.4
0.04958	1.0110	0.99910	0.99999	1.0223	0.025	13.6	0.04744	1.0024	0.99914	1.00000	1.0048	0.006	4.2
0.05901	1.0131	0.99892	0.99999	1.0266	0.036	13.4	0.05870	1.0029	0.99894	1.00000	1.0059	0.010	4.0
0.06982	1.0155	0.99872	0.99998	1.0315	0.050	13.3	0.07991	1.0040	0.99856	0.99999	1.0080	0.018	3.8
0.07890	1.0175	0.99855	0.99997	1.0357	0.064	13.2	0.09940	1.0050	0.99820	0.99999	1.0100	0.027	3.7
0.09044	1.0201	0.99834	0.99997	1.0410	0.084	13.1							
0.10004	1.0222	0.99816	0.99996	1.0455	0.103	13.0							
303.15 K													
0.00543	0.9993	0.99990	1.00000	0.9987	0.000								
0.00911	0.9989	0.99984	1.00000	0.9978	0.000								
0.02062	0.9974	0.99963	1.00000	0.9949	−0.002								
0.03015	0.9963	0.99946	1.00000	0.9926	−0.005								
0.03941	0.9951	0.99929	1.00000	0.9903	−0.008								
0.04907	0.9939	0.99912	1.00000	0.9879	−0.013								
0.06197	0.9923	0.99889	1.00001	0.9848	−0.020								
0.07052	0.9913	0.99874	1.00001	0.9827	−0.026								
0.08244	0.9898	0.99853	1.00001	0.9798	−0.035								
0.09687	0.9880	0.99828	1.00002	0.9763	−0.049								

308.15 K. The disagreement may be because of the fact that these authors used dried (which becomes activated)[18] samples, and there may be kinetics of water absorption involved. Also, due to the solubility limits of α-CD in aqueous medium, the highest possible concentration at 298.15 K is found to be 0.149 mol kg^{-1}; however, these authors have reported the data up to 0.18 mol kg^{-1}. In the present work, we took care in handling the appropriate α-CD sample, knowing the exact composition, i.e. water content, and used a better measuring technique including the standardization with NaCl of the same concentration range. In general, the variation of ϕ as a function of concentration in aqueous nonelectrolyte solutions depends on the temperature of measurements and the nature of solute. For example, aqueous solutions of simple carbohydrates,[6,21,22] 18-crown-16,[19] and β-CD[13] at 298.15 K show an increase in ϕ with concentration ($K_{T,P}$ in the equation $\phi = 1 + K_{T,P}m$ is positive), while solutes such as urea and substituted urea and electrolytes show a decrease in ϕ with concentration[23,24] ($K_{T,P}$ is negative). It has also been shown that in aqueous solutions of *n*-propanol, the activity coefficient of the solvent shows negative deviation from Raoult's law at low temperatures, whereas the same exhibit positive deviation at higher temperatures.[25,26] These aspects will be taken up later in the discussion of activity and activity coefficients.

The water activity was used to obtain the solvent activity coefficient (γ_1). The hydration number (h) of α-CD in aqueous solutions were estimated using the water activity and following Robinson and Stokes[6] method as

$$a_w = \frac{1 - 0.018hm}{1 - 0.018(h-1)m} \qquad (2)$$

The values of hydration number (h) of α-CD in aqueous solutions are also included in the Table 1. The meaning of the hydration number itself is very vague. For the purpose of calculation, it is necessary to consider a definite number of fixed water molecules, but this has to be considered as representing some sort of average interaction of α-CD molecule as well as that of cavity of α-CD with all the water molecules it perturbs. Therefore, the hydration number indicates the sum of cavity molecules (if occupied) as well as the peripherally affected water molecules. The activity coefficients of α-CD (γ_2) in aqueous α-CD solutions at different concentrations and in the studied temperature range were estimated using the osmotic coefficient data and eq 3

$$\ln \gamma_2 = (\phi - 1) + \int_0^m (\phi - 1) \mathrm{d} \ln m \qquad (3)$$

where m is the molality of α-CD in aqueous solutions of α-CD. It is seen from Table 1 that the solvent activity coefficient (γ_1) is close to unity at all studied temperatures. The solute activity coefficient (γ_2) values are greater than unity at lower temperatures and less than unity at 303.15 and 308.15 K.

The activity coefficient data for both components in aqueous α-CD solutions have been used to obtain the excess Gibbs free energy change (ΔG^E) of solution. The data of water activity, activity coefficient, and excess free energy change of aqueous α-CD solutions are given in Table 1 at different temperatures, and their variation with the concentration of α-CD is shown in Figures2 and 3.

Using our activity coefficient data at different temperatures and the limiting partial molar enthalpies of dissolution reported in the literature,[27,28] the excess enthalpy, excess entropy, and partial molar entropies were calculated at different temperatures. For these calculations, the data were processed in the following way. For this part of data processing the activity coefficient and free energy data obtained experimentally, for different

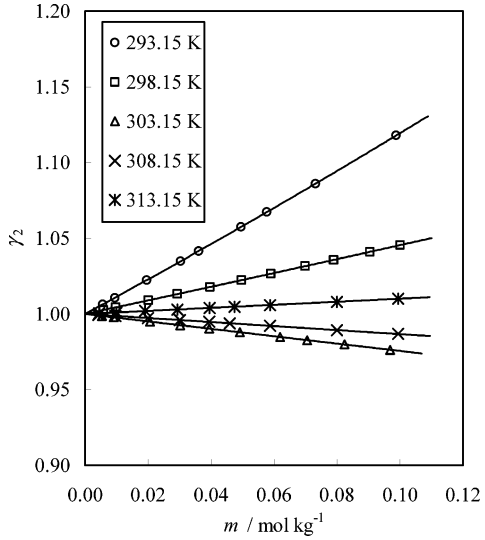

Figure 2. Variation of activity coefficient of α-CD (γ_2) as a function of concentration of α-CD (mol kg^{-1}) at different temperatures.

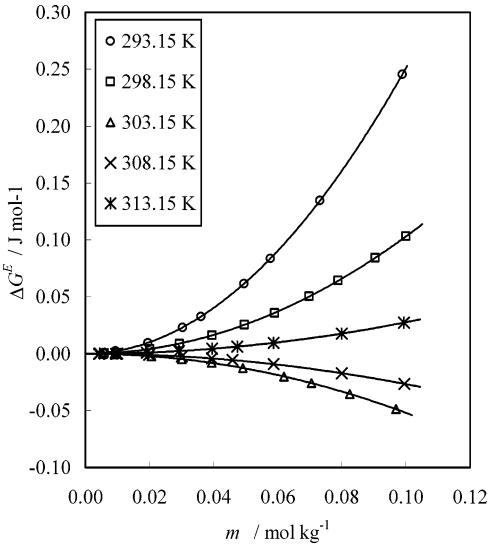

Figure 3. Variation of excess free energy change (ΔG^{E}) as a function of concentration of α-CD (mol kg^{-1}) at different temperatures.

concentrations prepared separately at each of the temperatures, were fitted for the concentration range 0.01−0.1 mol kg^{-1} at all studied temperatures for the sake of comparison between different temperatures. First of all, the activity values of solute and solvent were processed to determine the relative partial molar heat content change due to the transfer of 1 mole of a single component from a solution of one composition to that of another composition using the equation[29]

$$\frac{\partial\left(\ln\frac{a''}{a'}\right)}{\partial T} = -\frac{(\bar{L}'' - \bar{L}')}{RT^2} \tag{4}$$

where $\bar{L}''$ and $\bar{L}'$ are the relative partial molar heat content of solute (or solvent) at the two different activities a'' and a' of solute (or solvent), respectively, at the given temperature. These values were utilized to determine the total heat change due to transfer of 1 mole of solution from one (higher) composition to that of another (lower) composition, i.e. heat of dilution (ΔH_{D}), and hence the corresponding relative apparent molar heat content (ϕ_{L}) of the solute at different temperatures.

$$\Delta H_{\mathrm{D}} = -n_2\phi_L \tag{5}$$

From these values relative partial molar heat content of solute ($\bar{L}_2$) and solvent ($\bar{L}_1$) were calculated at different concentrations for each of the studied temperatures.

$$n_1\bar{L}_1 + n_2\bar{L}_2 = n_2\phi_L \tag{6}$$

$$\bar{L}_2 = \phi_L + n_2\left(\frac{\partial\phi_L}{\partial n_2}\right)_{T,P,n_1} \tag{7}$$

and

$$\bar{L}_1 = -\frac{n_2^2}{n_1}\left(\frac{\partial\phi_L}{\partial n_2}\right)_{T,P,n_1} \tag{8}$$

These values were further combined with differential heat of solution at infinite dilution ($-L_2$)[27,28] obtained from the literature to calculate the excess enthalpy (ΔH^{E}) of solution at different temperatures.

$$\left(\frac{\Delta H^{\mathrm{E}}}{n_1 + n_2}\right) = x_2(\phi_L - L_2) \tag{9}$$

The excess Gibbs free energy (ΔG^{E}) of solution and the Gibbs free energy of mixing (ΔG_{mix}) obtained experimentally were combined with the excess enthalpy (ΔH^{E}) of solution to calculate the excess entropy ($T\Delta S^{\mathrm{E}}$) and the entropy of mixing ($T\Delta S_{\mathrm{mix}}$) of solution and the corresponding partial molar entropies of solute ($\bar{S}_2 - S_2^0$) and solvent ($\bar{S}_1 - S_1^0$) using eqs 10−12.

$$\Delta G_{\mathrm{mix}} = \Delta H_{\mathrm{mix}} - T\Delta S_{\mathrm{mix}} \tag{10}$$

$$(\bar{S}_1 - S_1^0) = \frac{\bar{L}_1}{T} - R\ln a_1 \tag{11}$$

$$(\bar{S}_2 - S_2^0) = \frac{(\bar{L}_2 - L_2)}{T} - R\ln a_2 \tag{12}$$

where S_1^0 is molar entropy of the pure liquid water and $S_2^0$is the molar entropy of the solute in a hypothetical ideal solution of unit mole fraction. The excess partial molar entropies of the solvent $(\bar{S}_1 - S_1^0)^E$ and solute $(\bar{S}_2 - S_2^0)^E$ were further evaluated using equations

$$(\bar{S}_1 - S_1^0)^E = \frac{\bar{L}_1}{T} - R\ln\gamma_1 \tag{13}$$

$$(\bar{S}_2 - S_2^0)^E = \frac{(\bar{L}_2 - L_2)}{T} - R\ln\gamma_2 \tag{14}$$

The values of the parameters ΔG^{E}, ΔH^{E}, $T\Delta S^{\mathrm{E}}$, $(\bar{S}_1 - S_1^0)^E$, and $(\bar{S}_2 - S_2^0)^E$ are collected in Table 2 for the studied concentrations of α-CD in water at different temperatures. For the sake of illustration, we have shown in Figures 4 and 5 the data of ΔG_{mix}, ΔH_{mix}, and $T\Delta S_{\mathrm{mix}}$ as well as ΔG^{E}, ΔH^{E}, and $T\Delta S^{\mathrm{E}}$ as functions of α-CD concentration at 298.15 K. The free energy, enthalpy, and entropy changes for solution process are all negative at all temperatures. The free energy solution data at 298.15 K and the heat of mixing data for α-CD are available in the literature (respectively: ΔG_{s} as −4.72 kJ mol^{-1} and ΔH_{s} as −62.69 kJ mol^{-1})[10,30] from solubility and calorimetry measurements. Our data described above at 0.1 mol kg^{-1} concentration of α-CD based on the change in enthalpy per mole of solution agree well with literature[30] if the data is converted

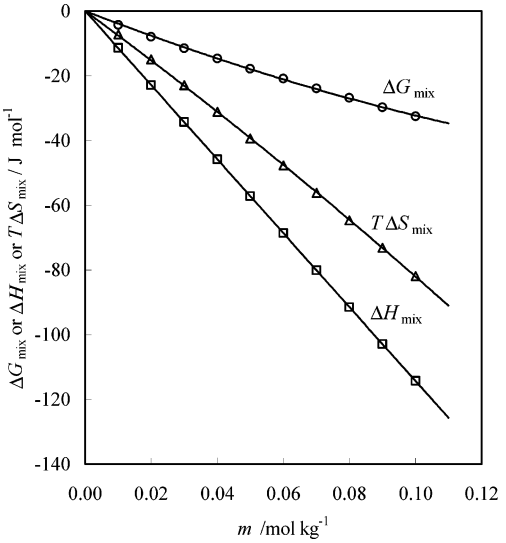

Figure 4. Thermodynamic mixing properties (ΔG_{mix}, ΔH_{mix}, and $T\Delta S_{mix}$) of α-CD in water as a function of concentration at 298.15 K.

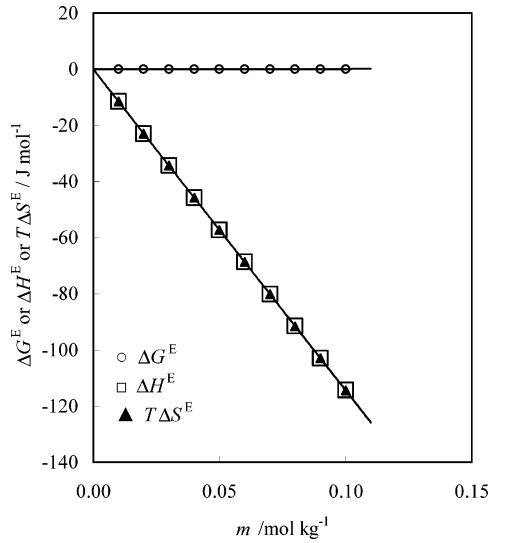

Figure 5. Excess thermodynamic functions (ΔG^E, ΔH^E, and $T\Delta S^E$) of α-CD in water as a function of concentration at 298.15 K.

to per mole of α-CD i.e., solute (−63.56 kJ mol^{-1}), and the details are given in Supporting Information.

The excess free energy changes (ΔG^E) are slightly positive at lower temperatures but very close to zero at higher temperatures. The concentration dependence of ΔG^E is negligibly small. Hence, ΔH^E and $T\Delta S^E$ are strongly concentration dependent, exhibiting compensation behavior at all studied temperatures as shown in Figure 6. If we compare these excess thermodynamic quantities with other macrocyclic ligands in water such as 18-crown-6 (18C6), it is apparent that the extent of nonideality (ΔG^E) is very much less for the α-CD−water system. In the case of 18C6 in water, such a behavior is attributed to the H-bond formation between the oxygen atoms of 18C6 and water molecules, and the peripheral hydration. Thus, it is obvious that the small nonideality in aqueous α-CD solutions based on excess thermodynamic quantities indicates that the dissolution of α-CD in water results from the H-bond formation with oxygen atoms of the hydroxyl group orienting at the outer surface of the α-CD molecule without having many water structural changes because the compensation temperature[31] is almost the same as that of experimental temperature.

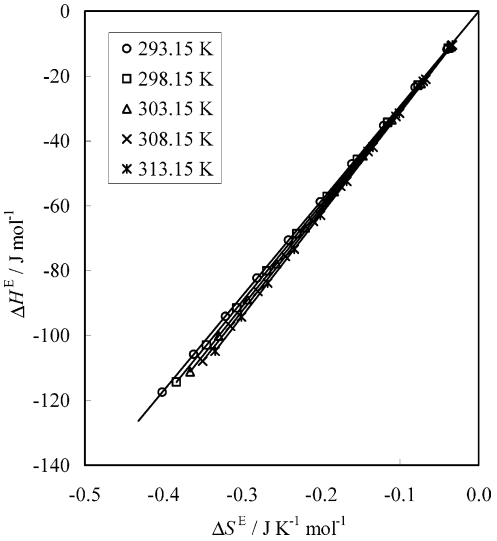

Figure 6. Enthalpy−entropy compensation plots for aqueous α-CD solutions at different temperatures.

The partial excess entropy values for water are almost zero, indicating that the structure of water remains unaffected by the addition of α-CD. Although the viscosity *B* coefficient studies[20] indicate that α-CD is a structure-making solute, it is not being revealed in thermodynamic properties. Alternatively, this may be interpreted in the following way. Warner[32] pointed out the correlation between the next nearest neighbor oxygen distances in a hypothetical ice lattice at 298.15 K (4.75 Å) and distances between oxygen atoms in many organic compounds, suggesting that such an organic molecule could be accommodated in water without the necessity for undue modification of the hydrogen-bonded solvent water structure. As regards to α-CD, the equatorial −OH groups would fit this particular hydration structure.

It has been suggested that in the helix forms of many biopolymers,[33] for example, DNA and collagen, the polar groups capable of hydrogen bonding are separated by an integral number of water repeat units, so that temperature-dependent hydration structures could easily arise and help to stabilize the helix.

Our results of calculating the hydration number using the activity data reveal that the helical structure of α-CD is stabilized by 32−33 water molecules at 293.15 K and 13−14 water molecules at 298.15 K, while 4−5 water molecules are involved in hydration at 313.15 K. Thus, the thermal effect on the conformational motion of α-CD and the interaction of −OH of α-CD with water molecules govern the pattern of hydration. It has been suggested that α-CD has a round structure with a ring of hydrogen bonds between the O(2)H and O(3)H groups. When water is the guest, this structure is somewhat collapsed, two of the O(3)−H−O(2) bridges are opened, and one glucose unit is rotated inward to allow formation of a O(6)−H_2O hydrogen bond.[9] This rotation causes steric strain within the macrocycle having higher energy. We attribute such a conformational change to the corresponding changes in free energy as a function of temperature assisted by the thermal energy (at 303.15 and 308.15 K).

We have a very important result concerning the partial molar excess entropies of α-CD which reveals that there is large decrease of entropy for α-CD molecule in water; the effect is nearly concentration independent as shown in Figure 7. Considering the concentration range (0.01−0.1 mol kg^{-1}) the effect of hydrophobic interaction is not noticeable as it is expected to

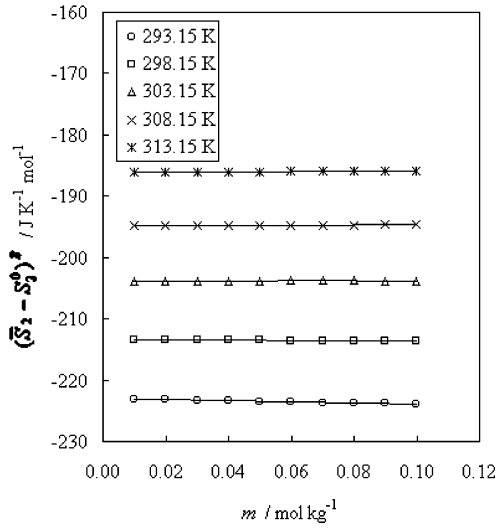

Figure 7. Partial molar excess entropy $(\bar{S}_2 - S_2^0)^E$of α-CD in water at different temperatures.

be increased with an increase in concentration. However, it is definitely not a decreasing function.

We find that the $(\bar{S}_2 - S_2{}^0)^E$ increase from −223.1 to −185.9 J K^{-1} mol^{-1} between the temperature range of 293.15−313.15 K. Thus, α-CD adopts a conformation in water of which entropy increases with rise in temperature or alternatively indicating the presence of hydrophobic interactions between two or more α-CD molecules in the presence of water. This interpretation is in harmony with the concepts of hydrophobic interaction and water structural effects.

The apparent molar and partial molar volumes of solute (α-CD) and water were obtained from the density data using the standard equations. The concentration variation of $\bar{V}_2$ is very small, and the linear extrapolation method is used to compute $\bar{V}_2{}^0$, i.e. partial molar volume at infinite dilution. The data of $\bar{V}_2{}^0$ at different temperatures are collected in Table 3.

3.1. Application of McMillan−Mayer Theory. The solute−solvent cluster integral b_{11}^0 is related to the partial molecular volume of the solute at infinite dilution by[34]

$$b_{11}^0 = -v_2^0 + kT\kappa_T \tag{15}$$

where k is the Boltzmann constant, T is the absolute temperature, and κ_T is the isothermal compressibility coefficient of the pure solvent. The values for solute−solvent interaction NB_{11}^{*0} (where $B_{11}^{*0} = -b_{11}^0$) for aqueous α-CD solutions calculated using eq 15 are given in Table 3. The solute−solvent cluster integral in the above equation is related to the potential of mean force, ω^{11}, between one molecule of solute and one of solvent in the pure solvent by the expression

$$b_{11}^0 = -4\pi\int_0^\infty [1 - \exp(-\omega^{11}/kT)]r^2\,\mathrm{d}r \tag{16}$$

where r is the distance between the centers of the molecules. It was shown that this integral could be split into attractive and repulsive parts as

$$B_{11}^{*0} = 4\pi\int_0^R [1 - \exp(-\omega^{11}/kT)]r^2\,\mathrm{d}r + \int_R^\infty [1 - \exp(-\omega^{11}/kT)]r^2\,\mathrm{d}r \tag{17}$$

$$= S + \Phi^A \tag{18}$$

where R is the distance of closest approach of the two molecules, S is the repulsive, and Φ^A is the attractive contribution. If the form of potential ω^{11} is known, then the integration could be performed to yield B_{11}^{*0}. The simplest potential function regards the molecules as rigid spheres. For two hard spheres of diameters R_1 and R_2,

$$S = \frac{\pi}{6}(R_1 + R_2)^3 \tag{19}$$

The water molecule can be considered to be a sphere of diameter 0.304 nm and α-CD molecule of diameter 1.46 nm. However, consideration of a water molecule as a hard sphere is an approximation and is studied here only to examine the trends, because the interactions in general cannot be justified if large structural changes occur in the solvent. The data of attractive and repulsive contributions to the solute−solvent interactions in water for α-CD at different temperatures are given in Table 3.

According to the McMillan−Mayer theory of solution[16] the osmotic pressure π is given by

$$\frac{\pi}{kT} = n + B_2^* n^2 + B_3^* n^3 + \ldots \tag{20}$$

where n is the number density. The osmotic second and third virial coefficients, B_2^* and B_3^*, were calculated from experimental activity data and the partial molar volume of solute and solvent by[7]

$$B_2^* = \frac{1}{N}\left[(\bar{V}_2{}^0 - V_1{}^0) + V_1{}^0\left(\frac{1}{2} - B\right)\right] \tag{21}$$

$$B_3^* = \frac{1}{N^2}\left[(b/V_1{}^0) + g + (V_1{}^0 - \bar{V}_2{}^0)^2 - V_1{}^0(1 - 2B)(V_1{}^0 - \bar{V}_2{}^0) + (V_1{}^0)^2\left(\frac{1}{3} - C\right)\right] \tag{22}$$

where $V_1{}^0$ and $\bar{V}_2{}^0$ are the partial molar volumes of solvent and solute, respectively, at infinite dilution, B, C, b, and g are the coefficients in the following equations

$$\ln \gamma_1 = Bx_2{}^2 + Cx_2{}^3 + \ldots.. \tag{23}$$

$$\bar{V}_1 = V_1{}^0 + aC_2 + bC_2{}^2 \tag{24}$$

$$\bar{V}_2 = \bar{V}_2{}^0 + gC_2 + hC_2{}^2 \tag{25}$$

The coefficients B and C in eq 23 are related to the solute size, solute−solvent association, solute−solute interaction effects, etc., and the B coefficient in eq 23 is related to the osmotic coefficient constant $K_{T,P}$ by[7]

$$B = -\left[K_{T,\mathrm{P}}\frac{1000}{M_1} + \frac{1}{2}\right]$$

The sign and magnitude of B and C are of special importance in understanding the thermodynamic behavior of solutions. In eqs 24 and 25, $\bar{V}_1$ and $\bar{V}_2$ are the partial molar volumes of solvent and solute, respectively, at concentration C_2. The coefficients a, b, g, and h have been evaluated using the density data of aqueous α-CD solutions determined at different temperatures. It has been shown that the coefficient B is positive for aliphatic alcohols, amines, ketones, and acids, indicating the existence of pairwise solute−solute attractions sufficiently large to overcome the solute size and hydration effects.[7] In the case of α-cyclodextrin, this is true only at 303.15 and 308.15 K, while

TABLE 2: Excess Thermodynamic Data for Aqueous α-CD Solutions at Different Temperatures

m/ mol kg^{-1}	ΔG^E/ J mol^{-1}	ΔH^E/ J mol^{-1}	$T\Delta S^E$/ J mol^{-1}	$(\bar{S}_1 - \bar{S}_1^0)^E$/ J K^{-1} mol^{-1}	$(\bar{S}_2 - \bar{S}_2^0)^E$/ J K^{-1} mol^{-1}	m/ mol kg^{-1}	ΔG^E/ J mol^{-1}	ΔH^E/ J mol^{-1}	$T\Delta S^E$/ J mol^{-1}	$(\bar{S}_1 - \bar{S}_1^0)^E$/ J K^{-1} mol^{-1}	$(\bar{S}_2 - \bar{S}_2^0)$/ J K^{-1} mol^{-1}
			293.15 K						308.15 K		
0.01	0.003	−11.8	−11.8	0.000	−223.1	0.01	0.000	−10.8	−10.8	0.000	−194.8
0.02	0.010	−23.5	−23.6	0.000	−223.2	0.02	−0.001	−21.6	−21.6	0.000	−194.8
0.03	0.023	−35.3	−35.3	0.000	−223.2	0.03	−0.002	−32.4	−32.4	0.000	−194.8
0.04	0.040	−47.1	−47.1	0.000	−223.3	0.04	−0.004	−43.2	−43.2	0.000	−194.7
0.05	0.063	−58.8	−58.9	0.000	−223.4	0.05	−0.007	−54.0	−54.0	0.000	−194.7
0.06	0.090	−70.6	−70.7	0.000	−223.5	0.06	−0.010	−64.8	−64.8	0.000	−194.7
0.07	0.123	−82.3	−82.4	0.000	−223.6	0.07	−0.013	−75.6	−75.6	0.000	−194.7
0.08	0.161	−94.1	−94.2	0.001	−223.7	0.08	−0.017	−86.4	−86.4	0.000	−194.7
0.09	0.203	−105.8	−106.0	0.001	−223.8	0.09	−0.022	−97.2	−97.1	0.000	−194.7
0.10	0.251	−117.5	−117.8	0.001	−223.9	0.10	−0.027	−107.9	−107.9	0.000	−194.7
			298.15 K						313.15 K		
0.01	0.001	−11.5	−11.5	0.000	−213.4	0.01	0.000	−10.5	−10.5	0.000	−186.0
0.02	0.004	−22.9	−22.9	0.000	−213.4	0.02	0.001	−21.0	−21.0	0.000	−186.0
0.03	0.009	−34.3	−34.4	0.000	−213.4	0.03	0.002	−31.5	−31.5	0.000	−186.0
0.04	0.017	−45.8	−45.8	0.000	−213.5	0.04	0.004	−41.9	−42.0	0.000	−186.0
0.05	0.026	−57.2	−57.2	0.000	−213.5	0.05	0.007	−52.4	−52.4	0.000	−186.0
0.06	0.037	−68.6	−68.7	0.000	−213.5	0.06	0.010	−62.9	−62.9	0.000	−186.0
0.07	0.051	−80.1	−80.1	0.000	−213.6	0.07	0.014	−73.4	−73.4	0.000	−186.0
0.08	0.066	−91.5	−91.6	0.000	−213.6	0.08	0.018	−83.8	−83.9	0.000	−186.0
0.09	0.084	−102.9	−103.0	0.000	−213.7	0.09	0.022	−94.3	−94.3	0.000	−185.9
0.10	0.103	−114.3	−114.4	0.000	−213.7	0.10	0.028	−104.8	−104.8	0.000	−185.9
			303.15 K								
0.01	−0.001	−11.1	−11.1	0.000	−203.9						
0.02	−0.002	−22.3	−22.3	0.000	−203.8						
0.03	−0.005	−33.4	−33.4	0.000	−203.8						
0.04	−0.008	−44.5	−44.5	0.000	−203.8						
0.05	−0.013	−55.6	−55.6	0.000	−203.8						
0.06	−0.019	−66.7	−66.7	0.000	−203.8						
0.07	−0.025	−77.8	−77.8	0.000	−203.8						
0.08	−0.033	−89.0	−88.9	0.000	−203.8						
0.09	−0.042	−100.1	−100.0	0.000	−203.8						
0.10	−0.052	−111.1	−111.1	0.000	−203.8						

TABLE 3: Attractive and Repulsive Contributions to Solute−Solvent Interaction Coefficients

T/ K	$10^{-3} \times \bar{V}_2^0$/ mm^3 mol^{-1}	$10^{-3} \times RTk$/ mm^3 mol^{-1}	$10^{-3} \times NB_{11}^{*0}$/ mm^3 mol^{-1}	$10^{-3} \times NS$/ mm^3 mol^{-1}	$10^{-3} \times (-N\Phi^A)$/ mm^3 mol^{-1}
293.15	604.0	1.12	602.9	1731	1128.1
298.15	607.5	1.12	606.4	1731	1124.7
303.15	608.2	1.13	607.1	1731	1124.0
308.15	610.3	1.14	609.2	1731	1121.9
313.15	612.1	1.15	610.9	1731	1120.1

at other studied temperatures, this coefficient has negative values, indicating that hydration effects are predominant at these temperatures as compared to solute−solute attraction. The temperature dependence of B coefficient shows that it goes through a maximum at 303.15 K, and the slope dB/dT is positive in the temperature range of 293.15−303.15 K, whereas it becomes negative in the temperature range of 303.15−313.15K. The osmotic second and third virial coefficients can be decomposed into repulsive and attractive components as[7]

$$R_{2\min} = f(4V_2^0) \tag{26}$$

$$A_{2\min} = R_{2\min} - NB_2^* \tag{27}$$

$$R_{3\min} = 10(V_2^0)^2 \tag{28}$$

$$A_{3\min} = R_{3\min} - N^2B_3^* \tag{29}$$

where f is the factor which is the measure of the ellipticity of the molecule. For spherical molecules f is unity. In aqueous medium α-CD is assumed to be spherical. The values of osmotic second and third virial coefficients as well as the minimum attractive and repulsive contributions to the solute−solute interactions are given in Table 4. The data when processed according to the McMillan−Mayer theory of solutions indicate the presence of an attractive contribution to the solute−solvent interaction coefficient ($-N\Phi^A$) which marginally increases with an increase in temperature, while the same for the solute−solute interaction goes through a maximum at 303.15 K. These are indicative of temperature-dependent solute−solvent as well as solute−solute interactions.

The NB_2^* goes through a minimum at 303.15 K, meaning that along with the hydration effect, a conformation change along with hydrophobic interaction is operative in the solution process. The second virial coefficients obtained through another type of equation, i.e., plotting the data of Π/cRT against c (c is concentration in g/cm^3) yield almost similar values giving good credence to our data and analysis.

It has been shown that the value of $A_{2\min}$ is related to −H bonding sites available for solute molecule. Seen in this light, the value for $A_{2\min}$ for α-CD is in accordance with the data of sucrose and cellobiose as it contains 30 −H bonding sites.[37] However, the same appears to be too high for β-CD, although it has 35 −H bonding sites which are involved in intramolecular bonding due to unique conformation. No explanation is offered for $A_{3\min}$ and $R_{3\min}$ as the data may not be of sufficient accuracy.

3.2. Application of Kirkwood−Buff Theory. The activity data have been subjected to the analysis in terms of the Kirkwood−Buff (KB) theory[17] in order to gain the information in depth on molecular interactions and to compare them with the results of McMillan−Mayer theory. The KB theory is an exact theory of solutions which does not involve the assumption of pairwise additivity of the total potential energy and is applicable to both spherical as well as nonspherical molecules.

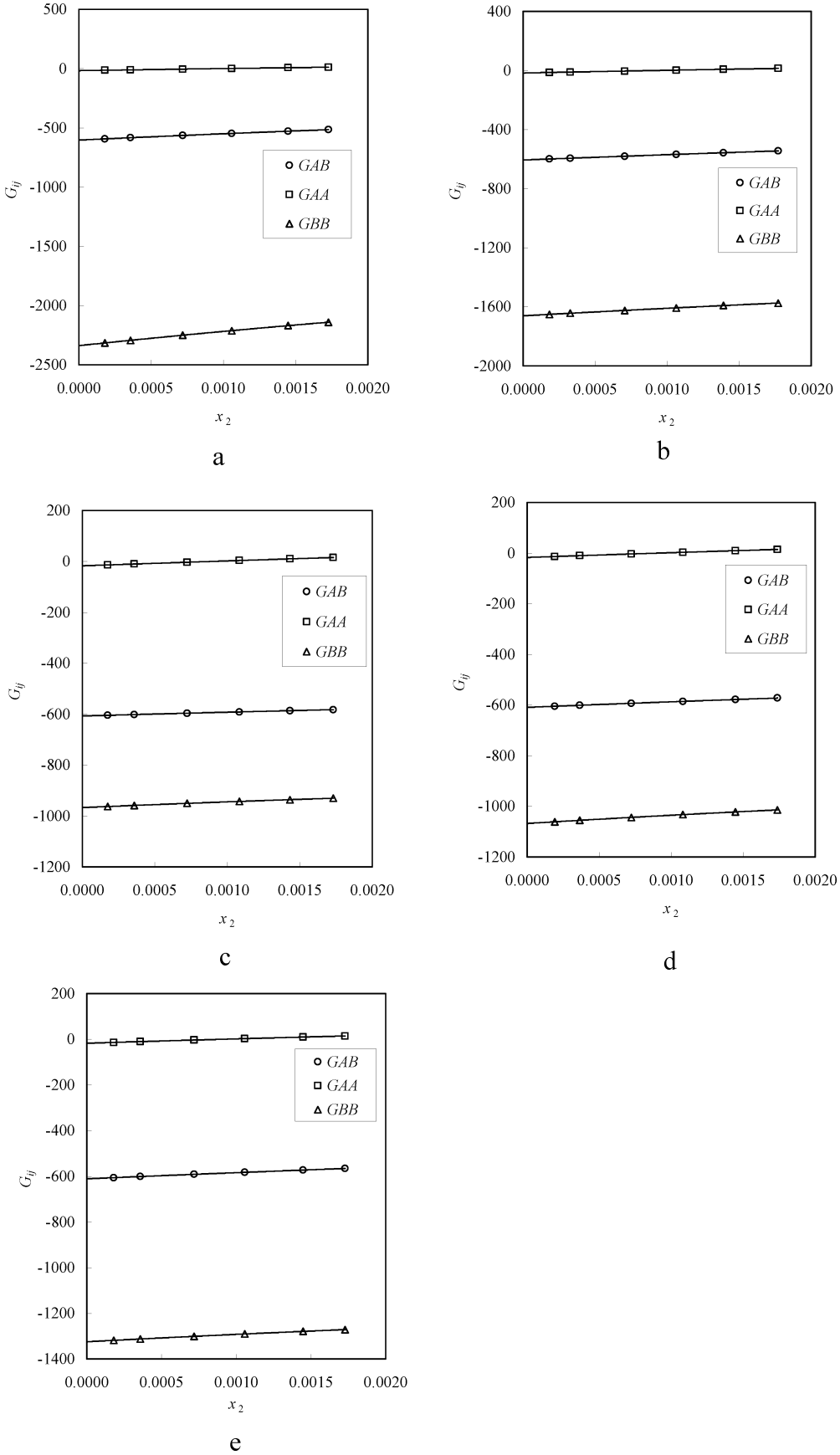

Figure 8. KB integrals for aqueous α-CD solutions at 293.15 K (a), 298.15 K (b), 303.15 K (c), 308.15 K (d), and 313.15 K (e).

The theory gives a recipe for computing some thermodynamic quantities from integrals over the pair correlation functions in multicomponent systems as originally formulated. The relevant thermodynamic quantities are the partial molar volume, isothermal compressibility, and derivatives of chemical potential with respect to concentration. Kirkwood−Buff theory links the thermodynamic properties to Kirkwood−Buff integrals G_{ij} defined by equation

TABLE 4: Attractive and Repulsive Contributions to Solute−Solute Interaction Coefficients

	T/ K	NB_2^*/ cm^3 mol^{-1}	$N^2B_3^*$/ cm^3 mol^{-1}	$-A_{2min}$/ cm^3 mol^{-1}	R_{2min}/ cm^3 mol^{-1}	$-A_{3min}$/ cm^3 mol^{-1}	R_{3min}/ cm^3 mol^{-1}
α-CD	293.15	1169	1047557	1247	2416	2601207	3648764
	298.15	830	639820	1600	2430	3050621	3690441
	303.15	484	218731	1949	2433	3480463	3699194
	308.15	543	288804	1898	2441	3435857	3724661
	313.15	663	436362	1786	2448	3310058	3746419
sucrose[a]	298.15	286	87000	498	783	360000	447000
glucose[a]	298.15	117	−	403	520	−	−
cellobiose[b]	298.15	267	−	355	622	−	−
β-CD[c]	298.15	6296	8330941	3420	2876	3162568	5168373
18C6[d]	298.15	278	226998	615	893	498048	271051

[a] Data from ref 35. [b] Data from ref 36. [c] Data from ref 13. [d] Data from ref 19.

$$G_{ij} = \int_0^\infty (g_{ij} - 1)4\pi r^2 \mathrm{d}r \tag{30}$$

where g_{ij} is the radial distribution function between species i and j, r is the distance between the centers of molecules i and j. These integrals can be evaluated following inversion procedure of the Kirkwood−Buff theory as described by Ben-Naim[38] from experimental data of chemical potential (and hence activity), partial molar volumes, and isothermal compressibility. Since these integrals are directly related to radial distribution function, they are very sensitive to molecular interactions. The precise and accurate activity coefficient data along with partial molar volume data of α-CD in aqueous solutions have been used to evaluate the KB integrals at different temperatures using the equations[38,39]

$$G_{AB}(A \neq B) = G_{BA} = RT\kappa_T - (\bar{V}_1\bar{V}_2/DV) \tag{31}$$

$$G_{ii} = G_{AB} + (1/x_i)\{(\bar{V}_j/D) - V\}, \quad i \neq j \tag{32}$$

where

$$D = 1 + x_i(\partial \ln \gamma_i/\partial x_i)_{P,T} \tag{33}$$

In above equations A stands for water and B stands for α-CD.

In these equations κ_T is the isothermal compressibility, $\bar{V}_i$ is the partial molar volume of component i, x_i is the mole fraction of component i, V is the molar volume of the mixture, T is the absolute temperature, R is the gas constant, and γ_i is the activity coefficient of component i in the mole fraction scale. As the isothermal compressibility of solutions contributes negligibly to the G_{ij} values, the κ_T values of solvents are being used in above equations. The values of KB integrals are plotted in Figure 8 as a function of concentration of α-CD at different temperatures, and the values obtained at infinite dilution are given in Table 5, which are found to be in close agreement with the osmotic second virial coefficients (given in Table 4) at different temperatures obtained using McMillan−Mayer theory of solutions.

The data are further processed to evaluate the limiting values of the G_{ij} functions for $x_2 \to 0$ at all studied temperatures by using the equations

$$G_{AA}^0 = \lim_{x_2 \to 0} G_{AA} = RT\kappa_{T,A} - {V_1}^0 \tag{34}$$

$$G_{AB}^0 = \lim_{x_2 \to 0} G_{AB} = RT\kappa_{T,A} - {\bar{V}_2}^0 \tag{35}$$

$$G_{BB}^0 = \lim_{x_2 \to 0} G_{BB} = RT\kappa_{T,A} + {V_1}^0 - 2{\bar{V}_2}^0 - {V_1}^0\left(\frac{\partial \ln \gamma_2}{\partial x_2}\right)_{T,P,x_2 \to 0} \tag{36}$$

G_{BB}^0 is related to the osmotic second virial coefficients B_2^* of α-CD through the equation

$$G_{BB}^0 = -2NB_2^* \tag{37}$$

where N is Avogadro's number.[38,40] The limiting values thus calculated agree well with the extrapolated values of Figure 8. On examination of the KB integrals for solute−solute (G_{BB}), solute−solvent (G_{AB}), and solvent−solvent (G_{AA}) interactions, it is noted that G_{AA}^0 remains almost constant as a function of temperature, while G_{AB}^0 varies little but G_{BB}^0 changes highly (becoming less negative), meaning an increase in α-CD−α-CD interactions. This is a clear indication of the existence of a hydrophobic effect in these solutions. At low temperature the deviation parameter Δ ($= G_{AA}^0 + G_{BB}^0 - 2G_{AB}^0$) is negative and goes through a maximum at 303.15 K. This indicates that at low-temperature some hydrophobic hydration (solute−solvent interaction) is present, the contribution of which is overcome by stronger solute−solute association as the temperature is increased.

The concentration variation of these integrals is small but definitely indicates the presence of solute−solvent interaction and solute association. It also indicates that interactions among bulk water molecules are of similar type and remain unaffected.

The mean square concentration fluctuations $N\langle(\Delta x)^2\rangle$ can be calculated from the three KB integrals using the equations

$$N\langle(\Delta x)^2\rangle = x_1x_2[1 + \rho x_1x_2(G_{AA} + G_{BB} - 2G_{AB})] \tag{38}$$

where x_1 is the mole fraction of solvent, ρ is the average number density, and N is the total number of molecules within which the concentration fluctuations are considered. The variation of mean square concentration fluctuation parameter, $N\langle(\Delta x)^2\rangle$ as a function of α-CD concentration is shown in Figure 9.

For an ideal solution ($G_{AA} = G_{BB} = G_{AB}$), $N\langle(\Delta x)^2\rangle$ is equal to x_1x_2 ($F = N\langle(\Delta x)^2\rangle/x_1x_2 = 1$). If the affinity between like species is stronger than unlike species, then the $N\langle(\Delta x)^2\rangle$ takes larger values than $x_1\ x_2$ ($F > 1$), and if the affinity between unlike species is stronger than like species, then the $N\langle(\Delta x)^2\rangle$ takes smaller values than x_1x_2 ($F < 1$). The quantity F can also be expressed in terms of thermodynamic properties as

$$\frac{1}{F} = \left(\frac{\partial \ln a_i}{\partial x_i}\right)_{T,P} = 1 + \left(\frac{\partial \ln \gamma_i}{\partial x_i}\right)_{T,P} = 1 + \frac{x_1x_2}{RT}\left(\frac{\partial^2 G^E}{\partial {x_i}^2}\right)_{T,P} \tag{39}$$

where a_i and γ_i are respectively the activity and activity coefficients of species i, G^E is the excess free energy of solution.[41,42] The concentration dependence of function F is shown in Figure 10.

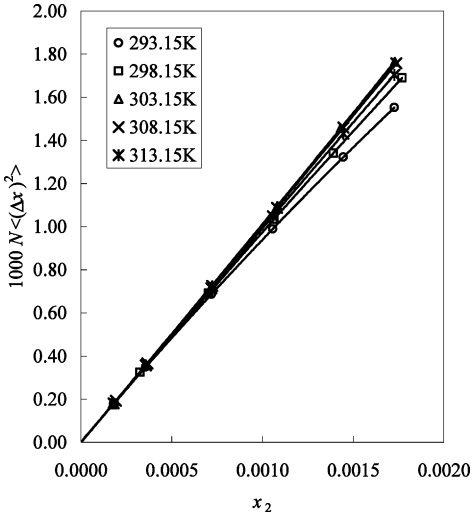

Figure 9. Plot of mean square concentration fluctuation parameter $N\langle(\Delta x)^2\rangle$ as a function of mole fraction of α-CD in aqueous α-CD solutions at different temperatures.

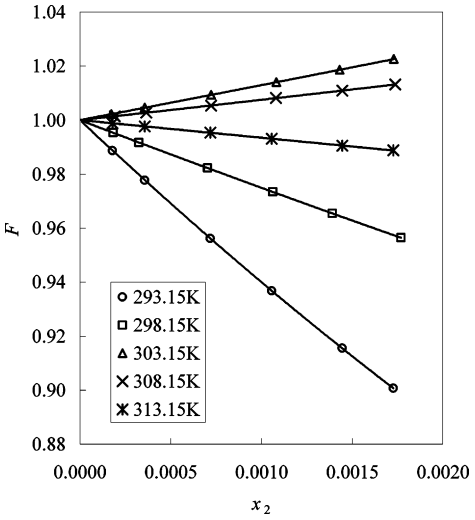

Figure 10. Plot of function F as a function of mole fraction of α-CD in aqueous α-CD solutions at different temperatures.

TABLE 5: Limiting Values of Kirkwood−Buff Integrals and Values of Osmotic Second Virial Coefficients for Aqueous α-CD Solutions at Different Temperatures

T/ K	G_{AB}^0/ cm^3 mol^{-1}	G_{AA}^0/ cm^3 mol^{-1}	G_{BB}^0/ cm^3 mol^{-1}	NB_2^*/ cm^3 mol^{-1}
293.15	−602.8	−16.87	−2338	1169
298.15	−606.3	−16.91	−1661	831
303.15	−607.1	−16.94	−967	483
308.15	−609.1	−16.98	−1068	534
313.15	−610.9	−16.98	−1325	662

These results reveal that at low temperatures, the hydrophobic hydration is present which decreases at higher temperatures, while the hydrophobic interaction effect is present at all temperatures and is maximum at the highest temperature studied as observed from partial molar excess entropy data (Figure 7).

It is interesting to examine the temperature dependence of (ln f_2) (activity coefficient of α-CD on the mole fraction scale) at various concentrations of α-CD in water. The data are shown in Figure 11. We note that (ln f_2) goes through a minimum at about 304 K for all the studied concentrations. We attribute this to a structural effect that may be associated with a change of one glucose unit (because of strain) inside the cavity and replacing the water molecules inside the cavity. This may be

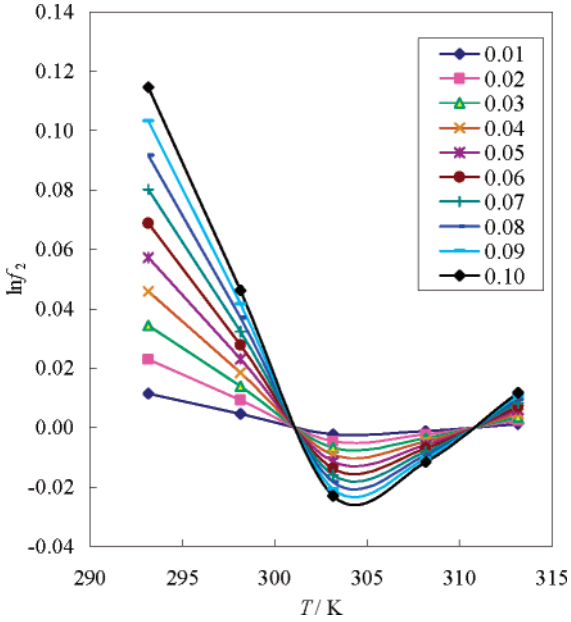

Figure 11. Plot of activity coefficient (ln f_2) of α-CD as a function of temperature in aqueous α-CD solutions at different concentrations (mol kg^{-1}).

true as it has not been possible to obtain hydration number values at 303.15 and 308.15 K. The other important observation is that (ln f_2) values are zero at 301 and 311 K for all the studied concentrations. The curves show similarity to optical density behavior exhibited by dyes in aqueous solutions showing more than one species in equilibrium. The ideal behavior seen at these temperatures can be viewed in terms of balancing of enthalpy and entropy changes yielding nearly zero values for excess free energies. Lumry and Rajender[43,44] have discussed the enthalpy−entropy compensation phenomenon in aqueous solutions and elaborated it as the ubiquitous property of water. They proposed a geometrical relaxation model to account large H−S fluctuation for aqueous solutions showing hydrophobic hydration; it is felt that our results of Figure 11 are the manifestation of the rearrangement of water molecules in the cavities accompanied by the conformational change of α-CD or the balance of hydrophobic hydration and interaction phenomena as against the thermal perturbation. More studies on variety of compounds are needed to find out the exact mechanism of enthalpy and entropy compensation phenomena.

4. Conclusion

Our experimental measurements of solvent activity indicate hydration of α-CD in aqueous solutions the extent of which is greatest at low temperatures. The activity coefficient of α-CD shows a peculiar temperature dependence showing a minimum at 304 K, while ideal mixing is indicated at 301 and 311 K. These are being attributed to the presence of structural changes occurring as a result of the rotational motion of glucose units causing rearrangement of water molecules residing in the cavity of α-CD. The calculations of excess free energy, excess heat, and excess entropy of solution indicate the dominance of enthalpy changes occurring in solution phase. The partial molar entropy values of α-CD increase with increase in temperature, indicating the presence of α-CD−α-CD (hydrophobic interaction) in solution phase. The concentration dependence of ΔH^E and $T\Delta S^E$ reveals the presence of compensation phenomenon. It is suggested that α-CD molecules may be present in a helix-type configuration and their hydration is being determined by

thermal and structural changes occurring with respect to solute as well as due to −H-bonding interactions with solvent water molecules. The applications of McMillan−Mayer and Kirkwood−Buff theories have been made to obtain a second virial coefficient for α-CD molecules. The affinity between two α-CD molecules initially increases with an increase in temperature and reveals the presence of hydrophobic interactions in harmony with partial molar entropy data. The variation in the concentration fluctuation parameter $N\langle(\Delta x)^2\rangle$ indicates again the presence of microheterogeneity in the solution phase. Lumry[45] has remarked on the uses of enthalpy−entropy compensation in protein research that entropy is equally as important as enthalpy and for which the scalar quantities of small-molecule chemistry can be replaced by the vector quantities that appear necessary to make biology possible. It is felt that these remarks apply equally well to the thermodynamic properties exhibited by cyclic glucose oligomers such as α-CD, especially in aqueous solutions. There is a need for accurate and meaningful measurements of these properties for many similar molecules which can be used as enzymatical model compounds in aqueous solution.

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Supporting Information Available: Calculations of free energy change (ΔG) of solution and corresponding heat change (ΔH) and the entropy change (ΔS) for aqueous α-CD solutions at 298.15 K; comparison of these values with those obtained from solubility and heat data reported in the literature. This material is available free of charge via the Internet at http://pubs.acs.org.

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