



Enthalpic interactions of N,N-dimethylformamide in aqueous glucose and sucrose solutions at 298.15 K

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ABSTRACT

Enthalpies of dilution of N,N-dimethylformamide (DMF) in aqueous sucrose and glucose solutions have been determined using an isothermal calorimeter (4400 IMC) at 298.15 K. The values of dilution enthalpy were used to determine homogeneous enthalpic interaction coefficients which characterize the interactions of examined DMF in aqueous sugar solutions. The results show that enthalpic pair interaction coefficients h_2 of DMF are all positive in aqueous sugar solutions and pass through a maximum, respectively, at $m \approx 0.5 \text{ mol kg}^{-1}$ of sucrose and at $m \approx 0.55 \text{ mol kg}^{-1}$ of glucose in mixed solvents. In the meantime the h_2 coefficients of DMF in aqueous sucrose solutions are more positive than that in aqueous glucose solutions. The variations of the enthalpic pairwise interaction coefficients with the mass fraction of sugar in mixtures are interpreted in terms of solute–solute and solute–solvent interactions.

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1. Introduction

The folding, structural stability, and dynamics of globular proteins are thought to be extensively controlled by the interactions of the macromolecule with water. Various added substances affect these interactions and consequently alter the structural stability of proteins. It is well known that sugar and polyhydric alcohols can increase the thermal stability of proteins or reduce the extent of their denaturation by other reagents [1–4]. Some trends correlating the stabilizing potency of sugars and polyols with the number or configuration of the hydroxy groups have also been noted [5]. However, there are numerous exceptions [6,7] and not all proteins respond equally to a given compound. Thus our understanding of the stabilization mechanism of proteins is still incomplete.

Among various physical parameters, these thermodynamic parameters have been recognized as being sensitive to structural changes occurring in solutions. The thermodynamic properties associated with the stabilization process in the presence of a large amount of sugars are difficult to interpret, because of the large number of interactions that can occur and which contribute to the overall thermodynamic properties of the protein in each state. Studies on simple compounds that model some specific aspect of a protein can provide estimates of the contributions from particular functional groups on the protein. N,N-Dimethylformamide (DMF)

can serve as a model compound of peptides to obtain information on protein systems. As a continuation of that work [8–11], the present study is aimed at examining the homogenous enthalpic interaction coefficients of DMF in aqueous glucose and sucrose solutions of different compositions.

2. Experimental

2.1. Materials and sample preparation

DMF (analytical grade, >99.5 mass%) were stored over activated 4Å° molecular sieves in order to keep them dry. Glucose and sucrose (analytical reagents, >99 mass%) were dried over P₂O₅ in a vacuum desiccator for 72 h at room temperature before use. Both of them were used without further purification. The water used for the preparation of solutions was deionized and distilled using a quartz sub-boiling purifier.

Both the aqueous solutions, which were used as mixed solvents (water + sugar), and the DMF solutions (DMF + sugar + water) were prepared by mass using a Mettler AE 200 balance precise to ±0.1 mg. All the solutions were degassed and used within 12 h after preparation.

2.2. Calorimetric procedure

The enthalpies of dilution of DMF in aqueous sugar solutions were measured with an isothermal calorimeter (model 4400 IMC, Calorimeter Science Corporation, USA) at 298.15 K. This apparatus

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Table 1
Enthalpic interaction coefficients of DMF in aqueous glucose solutions at 298.15 K.

m (glucose) (mol kg ⁻¹)	h_2 (J kg mol ⁻²)	h_3 (J kg ² mol ⁻³)	h_4 (J kg ³ mol ⁻⁴)	r
0.0000	679.60	-7.72	-16.81	0.9998
0.2653	792.83	-141.71	29.94	0.9998
0.5545	849.05	-226.46	59.96	0.9996
0.8642	763.29	-125.43	19.06	0.9999
1.1362	705.51	-90.52	-12.08	0.9999
1.3830	669.32	-78.36	10.17	0.9998
1.6399	600.33	-121.54	14.95	0.9998

consists of a calorimeter unit immersed in a water bath controlled within $\pm 1 \times 10^{-3}$ K. The flow-mixing system is comprised of two CSC 4442 flow mixing cells [12,13] and two syringe pumps (model: 260D, ISCO Inc., USA). The IMC data acquisition software was provided by Calorimetry Sciences Corporation. The scheduler/monitor program of pumps was developed by our group. The variation in flow rates of the syringe pumps is less than 0.2%. The flow rates were determined by weighing the masses of liquids through the pump with 5 min. The relative mean deviation of thermal powers determined was 0.3%. Detail of testing of the calorimeter was reported elsewhere [14].

The enthalpies of dilution $\Delta_{\text{dil}}H_m$ can be obtained by the following equation [15]:

$$\Delta_{\text{dil}}H_m = \frac{P}{C_i f_2} \quad (1)$$

where P is the dilution thermal power (μW), C_i is the concentration of the solution before dilution (mol kg⁻¹), f_2 is the flow rate of DMF solution (mg s⁻¹). The concentration of the solution before dilution C_i was calculated from the equation:

$$C_i = \frac{m_i}{1 + m_i M} \quad (2)$$

So the enthalpies of dilution $\Delta_{\text{dil}}H_m$ can be given by

$$\Delta_{\text{dil}}H_m = \frac{P(1 + m_i M)}{m_i f_2} \quad (3)$$

where m_i is the initial molality of the DMF solution (mol kg⁻¹), M is the molar mass of DMF (kg mol⁻¹). The uncertainties of all $\Delta_{\text{dil}}H_m$ values owing to duplicate runs at each initial molality and the slight variations of flow rates are within 1%. The final molality m_f was calculated from the equation:

$$m_f = \frac{m_i f_2}{f_1(m_i M_2 + 1) + f_2} \quad (4)$$

where f_1 is the flow rate of diluent (aqueous sugar solution).

3. Results and discussion

An excess thermodynamic property can be expressed as a virial expansion of pairwise, triplet and quadruplet, etc. interaction coefficients, which account for all the variations of the solute–solute and solute–solvent interactions according to the McMillan–Mayer theory [16,17]. If aqueous sugar solution is regarded as solvent, the

excess enthalpy per kg of solvent (H^E) of a solution containing DMF at molality m is given by

$$H^E = h_2 m^2 + h_3 m^3 + h_4 m^4 + \dots \quad (5)$$

where h_2 , h_3 , h_4 , etc. are enthalpic pairwise, triplet and quadruplet interaction coefficients, respectively.

Eq. (5) can be rearranged to give

$$H_m^E(m) = \frac{H^E}{m} = h_2 m + h_3 m^2 + h_4 m^3 + \dots \quad (6)$$

The molar enthalpy of dilution ($\Delta_{\text{dil}}H_m$) of the solution from an initial molality (m_i) to a final molality (m_f), is therefore given by

$$\begin{aligned} \Delta_{\text{dil}}H_m &= H_m^E(m_f) - H_m^E(m_i) \\ &= h_2(m_f - m_i) + h_3(m_f^2 - m_i^2) + h_4(m_f^3 - m_i^3) + \dots \end{aligned} \quad (7)$$

The experimental values of $\Delta_{\text{dil}}H_m$ of DMF in aqueous glucose and sucrose solutions together with the initial and final molalities are listed in [supplementary data](#). The enthalpic interaction coefficients calculated from Eq. (7) using the least-squares procedure are given in [Tables 1 and 2](#). As there are some difficulties in the interpretation of higher coefficients [18], only the pairwise coefficient h_2 is considered.

The h_2 values of DMF in pure water is 679.60 J kg mol⁻² and the difference comparing to that of the literature [19] result from using a different experimental approach and concentration range. The h_2 coefficients are considered as enthalpic contributions to the coefficients of the excess Gibbs free energy and a measure of the global effect constituting a sum of the following processes: the partial dehydration of the solutes and the further direct interaction caused by the short-range molecular forces [20]. For DMF, which has two alkyl groups, the hydrophobic–hydrophobic interactions dominate the pair-wise interaction of DMF in pure water and these interactions are expected to result in a positive contribution to h_2 . The partial dehydrations of the hydration shell of the DMF are endothermic processes due to the prevailing release of structured water from the hydration cospheres to the bulk, which lead to a positive contribution to h_2 . Hence, the h_2 value of DMF in pure water is positive.

From [Fig. 1](#), it can be clearly seen that the trend of the h_2 coefficients of DMF in aqueous sucrose solutions is similar to that of the h_2 coefficients of DMF in aqueous glucose solutions. The enthalpic

Table 2
Enthalpic interaction coefficients of DMF in aqueous sucrose solutions at 298.15 K.

m (sucrose) (mol kg ⁻¹)	h_2 (J kg mol ⁻²)	h_3 (J kg ² mol ⁻³)	h_4 (J kg ³ mol ⁻⁴)	r
0.0000	679.60	-7.72	-16.81	0.9998
0.1561	791.55	-124.20	23.07	0.9999
0.3233	840.51	-145.18	24.06	0.9998
0.4805	924.45	-246.11	59.17	0.9998
0.7306	913.58	-225.97	47.54	0.9999
0.9714	822.77	-149.74	24.14	0.9999
1.2318	747.47	-121.54	14.95	0.9999

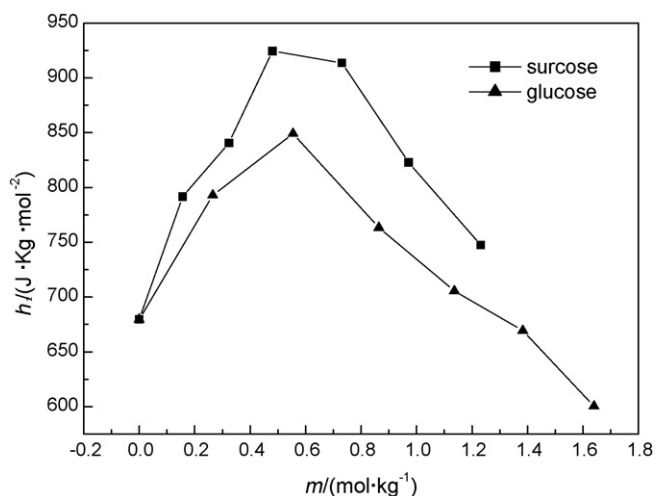


Fig. 1. Variations in enthalpic pair interaction coefficients (h_2) of DMF with the molality (m) of solute in aqueous solutions at 298.15 K.

pair interaction coefficients h_2 of DMF are all positive in aqueous sugar solutions and pass through a maximum, respectively, at $m \approx 0.5 \text{ mol kg}^{-1}$ of sucrose and at $m \approx 0.55 \text{ mol kg}^{-1}$ of glucose in mixed solvents. In the meantime the h_2 coefficients of DMF in aqueous sucrose solutions are more positive than that in aqueous glucose solutions.

Comparison between the interactive properties of solutes, such as DMF, in water and in aqueous sugar solutions is useful for obtaining a better understanding for the factors promoting the stabilization of biopolymers in such solutions. In the ternary solutions under investigation (DMF + sugar + water), besides the interaction between two DMF molecules, a DMF molecule can also interact with a sugar molecule because h_2 is a measure of the solvent mediated solute–solute interaction. The overall effect on h_2 reflects the equilibrium among the following superimposed processes:

- (i) hydrophobic–hydrophobic interaction between two DMF molecules (an endothermic process leading to a positive contribution to h_2);
- (ii) the direct interaction between DMF molecules and sugar molecules. This direct interaction is comprised of three types of interaction: (a) hydrophilic–hydrophilic interaction between the polar group of the DMF and the hydroxyl group of the sugar molecule (an exothermic process leading to a negative contribution to h_2); (b) hydrophobic–hydrophilic interaction between the apolar group of DMF and the hydroxyl group of the sugar molecule (an endothermic process leading to a positive contribution to h_2); (c) hydrophobic–hydrophobic interaction between the apolar group of DMF and the alkyl group of the sugar molecule (an endothermic process leading to a positive contribution to h_2);
- (iii) the partial dehydrations of the hydration shell of the DMF and the sugar molecule (an endothermic process also leading to a positive contribution to h_2).

Some authors concluded that polyhydroxy compounds have a structure-breaking effect in water. Taylor and Rowlinson [21] found that a strong hydrogen bonding exists between sugar and surrounding water molecules, which is stronger than the hydrogen bonding within the water molecule itself. Using the foregoing descriptions, the partial dehydrations of the hydra-

tion shell of the DMF is more difficult in sugar solution than in water, which gives more positive contribution to h_2 . Investigation [22] found hydrophobic–hydrophobic interaction is stronger in aqueous sugar solutions than in water. So the h_2 coefficients of DMF in aqueous sugar solutions are more positive than that in water. With the increase of sugar concentrations, the hydrophilic–hydrophilic interactions increase significantly and cancel part of the hydrophobic–hydrophobic interactions, which leads to the maximum value of h_2 , respectively, at $m \approx 0.5 \text{ mol kg}^{-1}$ of sucrose and at $m \approx 0.55 \text{ mol kg}^{-1}$ of glucose in mixed solvents.

From Fig. 1, it can be clearly seen that the rule of the h_2 coefficients for DMF in aqueous sucrose solutions is similar to that of the h_2 coefficients for DMF in aqueous glucose solutions, but there exist some distinctions in their interaction behaviors. These can be attributed primarily to the similarities and discrepancies in the structures of sucrose and glucose. The h_2 values for them seem to depend on the number and position of equatorial (e) and axial (a) –OH groups in the anomeric form, which is predominant in solution. The extent of hydration of saccharide molecules depends on their conformations and configurations of their hydroxyl groups, and e -OH groups are more readily hydrated than a -OH groups. According to Hisashi's study [23], the number of e -OH groups of sucrose is bigger than that of glucose. Obviously the extent of hydration of sucrose is stronger than that of glucose. Dehydrations of the hydration shell of the sucrose are more endothermic than that of glucose. So the h_2 coefficients of DMF in aqueous sucrose solutions are more positive than that in aqueous glucose solutions.

The h_2 coefficients for DMF in aqueous sucrose solutions reach a maximum in advance than that in aqueous glucose solutions. This may be due to the fact that for solutions of the same concentration, aqueous sucrose solutions contain about twice the number of OH groups compared to aqueous glucose solutions. Hydrophilic–hydrophilic interactions in sucrose solutions give a more negative contribution to h_2 than that in aqueous glucose solutions, so values of h_2 for DMF in aqueous sucrose solutions reach a minimum in advance.

4. Conclusion

Enthalpies of dilution of DMF in aqueous sucrose and glucose solutions have been determined using an isothermal calorimeter (4400 IMC) at 298.15 K. Experiential enthalpies of dilution varying with the concentration of sugar were correlated with the virial expansion equation. Enthalpic interaction coefficients h_2 , h_3 , and h_4 in the equations are obtained, and the values of the pairwise enthalpic interaction coefficient h_2 have been discussed. Hydrophobic–hydrophobic interaction is stronger in aqueous sugar solutions than in water, so the h_2 coefficients of DMF in aqueous sugar solutions are more positive than that in water. The different structures of sucrose and glucose make a contribution to their different values of h_2 . The number of e -OH groups of sucrose is bigger than that of glucose, so the h_2 coefficients of DMF in aqueous sucrose solutions are more positive than that in aqueous glucose solutions. For solutions of the same concentration, aqueous sucrose solutions contain about twice the number of OH groups compared to aqueous glucose solutions, so values of h_2 for DMF in aqueous sucrose solutions reach a minimum in advance.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tca.2008.10.021.

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