The Effect of Sodium Chloride on Ion Association of Lysine and Arginine Ionizable Side Chains Amino Acids with Dehydro-L-ascorbic Acid in Aqueous Solution at Different Temperatures

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Abstract
Molar conductance (Λ) of ionizable side chains amino acids, lysine (Lys) and arginine (Arg) with dehydroascorbic acid (DHA) in water and in NaCl solutions was measured at temperatures range 298 K to 313 K. The limited molar conductance (Λₒ) and the constant of the ions association (K_A) are calculated using the Shedlovsky techniques. The dynamic radius of the concerned ion (R) is calculated by used Stokes–Einstein relation. The heat of association, the Gibbs free energy, the change of entropy and activation energy (ΔHₒ/ₖ J mol⁻¹, ΔGₒ/ₖ J mol⁻¹, ΔSₒ/ₖ J K⁻¹ mol⁻¹, and ΔEₒ/ₖ J mol⁻¹) respectively), also calculated. The data show increases the molar conductance with increase in temperature and decreasing in values at addition of DHA to Lys and Arg solutions. The association ions in NaCl solutions appear to increase in radius and decrease in diffusion coefficient relative to water solutions. ΔEₒ shows in most samples a positive value for the association and the values in NaCl solutions has lower relative to the water solutions. ΔGₒ is a trend to decrease with an increase in DHA concentration in water and NaCl solutions. The ion association is exothermic reaction relative to the negative value of ΔHₒ. The ΔSₒ and ΔHₒ results, for Lys and Arg solutions, show decreasing in values at increase in DHA concentration in water and NaCl solutions. ΔGₒ (kJ mol⁻¹), ΔSₒ (J K⁻¹ mol⁻¹), ΔHₒ (kJ mol⁻¹), and ΔEₒ (kJ mol⁻¹)

Keywords: Amino acids, ascorbic acid, dehydroascorbic acid, conductance measurements.

تأثير اضافة كلوريد الصهديهم على الارتباط الابيوني للحامضين الأمينيين Lys و Arg ذو المجاميع الجانبية المتأينة مع حامض الديهدرواسكربوكليك في المحاليل المائية عند درجات حرارة مختلفة

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الخلاصة
تم قياس التوصيلية المولارية للحامضين الأمينيين Arg و Lys ذو المجاميع الجانبية المتأينة مع حامض الديهدرواسكربوكليك في محاليلها المائية والملحية عند درجات حرارة (298 K to 313 K) و تم حساب التوصيلية المولارية المحددة و ثابت الارتباط باستخدام طريقة (Shedlovsky method) اما صفر. القطر الديناميكي للارتباط تم حسابه باستخدام معادلة (Stokes–Einstein Eq.)، أيضا تم حساب الدوال الترموديناميكية (التغير في الطاقة الحرة ΔGₒ, التغير في حزوة الارتباط ΔHₒ, التغير في الحرارة الارتباط ΔSₒ). نتدرج في المحاليل المائية والملحية، نتدرج في درجات حرارة نتدرج في الارتباط ΔEₒ士兵

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1. Introduction

Amino acids (AAs) are the main components of food. AAs represent the principle building blocks required for biosynthesis of protein [1]. In another side, vitamin C is contributing to various cellular functions and essential as an antioxidant [2].

Ascorbic acid (AA) and dehydroascorbic acid (DHA) are the chemical material source forms of vitamin C. The human diet is abundant by AA and DHA [3]. DHA is made from AA in the gastrointestinal tract lumen (GIL). The GIL is the basic site for absorption of AA and DHA. In addition to that, DHA is formed when an oxidants reacts with AA in the GIL [4]. DHA (Figure-1) is different from AA in hydrophilic property, because it is present in a deprotonated form. So, it can easily transfer through the membranes of the cell, and interacted by alkali compounds (e.g. to oxalic acid and threonic acid) [5]. In the human body, both DHA and AA have iterative antivirals biological activity but DHA also has neuroprotective effects. Nowadays DHA is organized as an investigations drug with no recognized indications. Both AAs and vitamin C are water-soluble, and they are co-existence in some metabolic reactions, medication, and food. In addition to that vitamin C improves an effect on increasing AAs absorption from the oral given dose [6].

Life on earth stands on water, hydrophobic interactions and hydrogen bonds (HB). HB has a central role in numerous biological processes. HB effects on transport of the membrane, drugs distribution in the biological environment and other different contributions [7]. Applications of HB in drug design are currently taking an interest [8]. Therefore, information about ion association of the interactions between DHA and amino acids as HB is very important since searching the interaction between drugs can help us to have them in a normal use [9], and because the interaction of AAs with DHA play an important role in biochemical environment. Many searches study the ion association between amino acids and different biological molecules [10-12]. Since searching in ion association is key to knowledge the intermolecular interactions, structure-function relationships and structural biology. It is also assist in drugs design that binds with targets selectively.

This search reports the conductance measurements, the dynamic radiuses of the concerned ions, ion association constant and thermodynamic properties for DHA acid association with some ionizable side chains α-AAs (Lysine, Lys and Arginine, Arg) in water solution and sodium chloride solutions in the range 298–313 K of temperatures.

**Figure 1**-Dehydro-L-ascorbic acid (DHA).

2. Materials and methods

Lysine (Lys), arginine hydrochloride (Arg) (an ionizable-α-amino acid) and ascorbic acid (AA), were obtained from BDH company with a purity proximate to 99.9 %. Deionized water used in all
solutions has specific conductance, in the range of (3–4 µS/cm). The specific conductivity, κ (µS/cm), was measured by digital conductivity bridge (with a dip type immersion conductivity cell). All the solutions of lysine, arginine hydrochloride amino acids and dehydroascorbic acid were prepared at different concentrations (2–5x10⁻³ mol/L) by dissolving the required amount of the sample in distilled deionized water. A thermostat water bath (GFL/D30938) device was used through conductivity measurements in the range of temperature (298–313 K). The measurements of weights using in preparation of solutions were complete by using a digital electrical balance (Sartorius RC 210D). All measurements had done at least in triplicates. A method used for preparation of DHA, carry out as follows:

"Ten grams of ascorbic acid is dissolved in 300 ml of solvent, and 15 g of activated charcoal is added. Oxygen or air is bubbled through the solution at a flow rate of 20 ml / min for 30-60 min while the solution is gently stirred with a magnetic stirrer. At the completion of the reaction the solution is filtered [13]."

The oxidation reaction of AA to DHA in the presence of activated charcoal as a catalyst can be seen in equation represented by (Figure-2). The concentration of DHA in a solution determined by 2:6-dichlorophenolindophenol titrimetric analysis method [14].

![Figure 2](image_url)

**Figure 2**-Schematic illustration the oxidation reaction equation of AA to DHA.

### 3 Results and discussion

#### 3.1 Association constants.

Lysine (Lys) and arginine (Arg) amino acids have a polar ionizable side chains that can participate in hydrophobic interaction or hydrogen bonding to water, and to other AAs [15]. In other side DHA can accept a multiple HBs.

The predominate state of Lys and Arg in neutral solution can be shown in (Figure-3).

![Figure 3](image_url)

**Figure 3**-L-α-amino acid: A-lysine, B-arginine

The conductance and viscosity as transport properties of solutions are important because it provides values as useful information about ionic association. Understanding these properties provides a fundamental to the investigation of hydrogen bonding in the biological and chemical environment [16].
The physical properties of water used in the preparation of solutions are given in Table-1 as reported in searches [17, 18].

| T/K  | ρ0 / g m⁻³ | η / gm⁻¹s⁻¹ | D      |
|------|-------------|--------------|--------|
| 298  | 0.9971      | 0.8903       | 78.30  |
| 303  | 0.9957      | 0.7974       | 76.55  |
| 308  | 0.9941      | 0.7194       | 74.83  |
| 313  | 0.9923      | 0.6531       | 73.15  |

The conductance values of ionic substances in dilute solutions with a wide range of temperature allow the determination of thermodynamic and association constants [19]. HBs increase in solution as a result to increase in the molar concentration. So the conductivity values analyzed at (2-5×10⁻⁵M) for DHA to (2×10⁻³M) of lysine and arginine amino acids in water and in (2×10⁻³M) NaCl solutions. The solubility of AAs in water is very variable. So amino acids are affected at addition of inorganic salt by increase the solubility of AAs in a solution and this effect on transport properties of solutions [20]. Association constant Kₐ is valued by uses a numerous of equations. Shedlovsky Equation 1 [21], is used to calculate Kₐ:

\[
\frac{1}{\Lambda(S(Z))} = \frac{1}{\Lambda^0} + \frac{K_A C^{A/2}}{\Lambda^0}
\]

Where Λ (S cm⁻² mol⁻¹), is the molar conductivity, C (mol dm⁻³), the solution concentration, Λ⁰ (S cm⁻² mol⁻¹), the limited molar conductance, Kₐ (dm³ mol⁻¹), the constant of ion association, f±, and S(Z) are coefficient factors.

A, f±, and S(Z) are calculated using Equations 2-4:

\[
A = \frac{1000k}{c}
\]

\[
-\log f_\pm = \frac{A^{\sqrt{1}}}{1 + BR^{\sqrt{1}}}
\]

\[
A = \frac{1.8247 \times 10^6}{(DT)^{3/2}} ; \quad B = \frac{0.5209 \times 10^{10}}{\sqrt{DT}}
\]

\[
S(Z) = \left(\frac{Z}{2} + \sqrt{1 + \left(\frac{Z}{2}\right)^2}\right)^2
\]

\[
Z = \left[\frac{S}{\Lambda^0}\right] \sqrt{CA}; \quad S = aA_0 + \beta ; \quad \beta = \frac{62501}{\eta\sqrt{DT}} ; \quad a = \frac{0.8204 \times 10^6}{(DT)^{3/2}}
\]

Where: R (m), is the dynamic radius for ion association, K (μS cm⁻¹), is the specific conductivity, D, is the dielectric constant, C (mol dm⁻³), is molar concentration, η (g m⁻¹ s⁻¹), is the viscosity, and T (K), is the absolute temperature.

In the case of S (Z), the degree of dissociation γ, can be calculated using equation 5:
The value obtained from Equation 1, compared with Fuoss–Kraus equation, Equation 6 [22], and the result is very closer.

The dynamic radius of the concerned ion (Association distance) R, for diffusing species can result with using Stokes–Einstein equation, Equation 7 [23].

\[ R_\pm = \frac{kT}{6\pi\eta D} \]  

Where D (m² s⁻¹), is the diffusion coefficient, k (J K⁻¹), is the Boltzmann constant, T (K), is the absolute temperature, and \( \eta \) (kg m⁻¹ s⁻¹), is the dynamic viscosity.

In this search, it is used the \( \eta \), values based on the viscosity of water as listed in Table-1.

"Both diffusion and conductance involve the movement of ions, and as such, a connection between them exists. At infinite dilution, where interionic forces vanish, we may attribute to any given ion a characteristic drag, proportional to velocity, which resists motion through the solvent" [24]. So the diffusion coefficient values of diffusing species can be given by Einstein – Smoluchowski, Equation 8 [25].

\[ D = \mu K_B T \]  

Where, \( \mu \) (m² V⁻¹ s⁻¹), is the ionic mobility at infinitive dilution, \( k_B \) (eV K⁻¹), is the Boltzmann constant, and T (K), is the absolute temperature.

Since, \( \mu \), can be calculated according to Equation 9 [26].

\[ \mu = \frac{\lambda}{k_F} \]  

Where: \( \lambda \) (S cm² mol⁻¹), is the ionic molar conductivity, z, is the charge of ion and F (Coulomb mol⁻¹), is Faraday constant.

The diffusion coefficient results from Einstein–Smoluchowski relation and the dynamic radius of the diffusing species \( R_\pm \), products from Stokes–Einstein equation calculation is shown in Table-2.

**Table-2:** Values of diffusion coefficients, \( D/10^{-9} \) m²/s, and the dynamic radius of the diffusing species, \( R/10^{-10} \) m, of Lysine and Arginine amino acids in water and in 2×10⁻¹ M NaCl.

| T/K | Diffusing species | D | R | D | R | D | R | D | R |
|-----|------------------|---|---|---|---|---|---|---|---|
| 298 | Arg/water        | 0.187 | 13.20 | 0.194 | 14.51 | 0.195 | 16.31 | 0.199 | 17.97 |
|     | Arg/NaCl         | 0.115 | 21.39 | 0.118 | 23.86 | 0.121 | 26.28 | 0.125 | 28.62 |
|     | Arg-DHA/water    | 0.164 | 15.00 | 0.168 | 16.80 | 0.172 | 18.50 | 0.176 | 20.32 |
|     | Arg-DHA/NaCl     | 0.103 | 23.88 | 0.105 | 26.81 | 0.108 | 29.44 | 0.111 | 32.23 |
|     | Lys/water        | 0.249 | 09.88 | 0.254 | 11.10 | 0.260 | 12.23 | 0.265 | 13.50 |
|     | Lys/NaCl         | 0.146 | 16.85 | 0.150 | 18.77 | 0.153 | 20.78 | 0.157 | 22.78 |
|     | Lys-DHA/water    | 0.236 | 10.42 | 0.241 | 11.68 | 0.246 | 12.93 | 0.251 | 14.25 |
|     | Lys-DHA/NaCl     | 0.134 | 13.97 | 0.157 | 17.93 | 0.161 | 19.75 | 0.165 | 21.68 |

As shown in (Figure-1) DHA is a neutral molecule and the molar conductivity closer to zero while Lys and Arg amino acid at neutral pH (Figure-3) contains more than one of a positive α-ammonium group, so the molar conductivity is higher. And as a reason we take the conductivity of Lys and Arg solution to comparative with the conductivity of ion association between Lys-DHA, and Arg-DHA in water and NaCl solutions.

The molar conductivity, \( \Lambda \), and the association constant \( K_A \) (Calculated by using Eq.1), of ion association in water and in NaCl solutions at different temperature are listed in Table-3.
Table 3-The molar conductivity, $\Lambda / S \text{ cm}^2 \text{ mol}^{-1}$, the association constant, $K_A / \text{dm}^3 \text{ mol}^{-1}$ and the limiting molar conductivity, $\Lambda^0 / S \text{ cm}^2 \text{ mol}^{-1}$, of different solutions at different temperature relative to DHA concentration.

| C/10^{-3} M | DHA | T/K | $\Lambda$ | $K_A$ | $\Lambda$ | $K_A$ | $\Lambda$ | $K_A$ |
|-------------|-----|-----|-----------|-------|-----------|-------|-----------|-------|
| 298         | 303 | 308 | 313       |       |           |       |           |       |
| 0           | 133 | -   | 137       | -     | 141       | -     | 147       | -     |
| 2           | 107 | 1236| 110       | 1170  | 114       | 1094  | 120       | 988   |
| 3           | 073 | 2259| 077       | 2022  | 080       | 1897  | 085       | 1698  |
| 4           | 081 | 2612| 085       | 2293  | 069       | 2048  | 075       | 1742  |
| 5           | 043 | 4652| 046       | 4079  | 050       | 3478  | 055       | 2908  |
| $\Lambda^0$ | 230 | 232 | 235       | 242   | 247       | -     |           |       |
| Lys (2x10^{-3} M)/water | | | | | | | | |
| 0           | 095 | -   | 098       | -     | 102       | -     | 107       | -     |
| 2           | 068 | 1090| 071       | 1021  | 075       | 0980  | 081       | 0874  |
| 3           | 047 | 1955| 051       | 1686  | 055       | 1543  | 060       | 1363  |
| 4           | 034 | 3209| 037       | 2768  | 041       | 2393  | 047       | 1895  |
| 5           | 027 | 4340| 030       | 3591  | 034       | 2965  | 040       | 2228  |
| $\Lambda^0$ | 140 | 143 | 149       | 155   |           |       |           |       |
| Lys (2x10^{-3} M)/NaCl | | | | | | | | |
| 0           | 195 | -   | 198       | -     | 202       | -     | 208       | -     |
| 2           | 177 | 1089| 181       | 1016  | 185       | 0992  | 191       | 0946  |
| 3           | 118 | 2115| 121       | 2014  | 124       | 1960  | 130       | 1812  |
| 4           | 089 | 3119| 092       | 2524  | 096       | 2733  | 102       | 2460  |
| 5           | 069 | 4456| 072       | 4228  | 075       | 3857  | 080       | 3457  |
| $\Lambda^0$ | 362 | 364 | 369       | 375   |           |       |           |       |

The limiting molar conductivity, as an approximation, is related to the molar conductance and the molar concentration $(C)$ square root by [27]:

$$\Lambda = \Lambda^0 - A\sqrt{C}$$

Where, $A$ is a constant. The plot of this relation can be seen in the Figures-(4, 5) below.

![Figure 4](image1.png)

**Figure 4**-The dependence of $\Lambda$ (S cm$^2$ mol$^{-1}$), on $C^{1/2}$ (mol dm$^{-3}$)$^{1/2}$, of Lys: DHA, A- in water, B- in NaCl solutions at 298 K.
The molar conductivity of Lys and Arg appear decreasing in values at the addition of DHA, Table-3, and the values more decreasing at increase DHA concentration in dilute solutions. And this accustomed to those substances which have more probability for multiple hydrogen bonds display lower conductance relative to substances don’t have or less probability. The limited molar conductance showed increasing in values at increase temperature and decreasing in values for association constant $K_A$. The reason is due to the decrease of solution viscosity, and increase in the mobility of ions or condensed extent of ion solvation in solutions. The increase in thermal energy as a result lead to more bond breaking, so the ions have more mobility and frequency. Table-2 showed that the dynamic radiuses of the concerned ions increase as diffusion of the ions increase related to chang3e in temperature, and the $R$ of AAs in NaCl solutions have increased in size and decrease in diffusion coefficient and this accustomed to increase AAs solubility as compared with the same solutions in water.

3.2 Thermodynamic functions.

The chemical and physical properties of HB in solutions redirect the comprehensive intermolecular changes as a result of formation of HB.

HB not only effects on the dynamic properties but also the thermodynamic properties of solutions because of the frequent break and reformation of HBs [16]. HB is abundant in solutions. It is found in the main biological and chemical processes. HBs as strength take a site between the covalent bond and van der Waals interaction. So this strength of HB takes a range of energies that permits fast dissociation and association under ambient conditions. Like fast HB dynamics are essential in a wide-ranging of systems, so it can acknowledgment the properties of water and biological solutions [29]. The activation energy ($\Delta E_S$), which is mean as the accessible energy size for an interaction to come to pass in a chemical environment is calculated from S. A. Arrhenius equation [28]. So the $-\Delta E_S/2.303R$ value is related to the log $\Lambda$ and $1/T$ through Equation 11.

$$\log \Lambda = -\left(\frac{\Delta E_S}{2.303R}\right)\left(\frac{1}{T}\right) + \log A$$ \hspace{1cm} (11)

Where: A, Arrhenius factor, T (K), is the absolute temperature, R (J K$^{-1}$ mol$^{-1}$), is the universal gas constant, $\Delta E_S$ (kJ mol$^{-1}$), Arrhenius activation energy, and $\Lambda$ (S cm$^2$ mol$^{-1}$), is the molar conductance. The plot of this relation can be seen in the Figures-(6, 7) below.
The linear relationship between log Λ and 1/T (K⁻¹), for Lys: DHA, A- in water and B- in NaCl solutions.

Figure 6

The linear relationship between log Λ and 1/T (K⁻¹), for Arg: DHA, A- in water and B- in NaCl solutions.

Figure 7

The association enthalpy ΔH° (kJ mol⁻¹), represents the association heat change when one mole of a compound result from elements and calculated by used Van't Hoff’s expression [28]. So the −ΔH°/2.303R value is related to the log K_A and 1/T through relation 12.

\[
\log K_A = -\left(\frac{\Delta H^o}{2.303R}\right)\left(\frac{1}{T}\right) + \left(\frac{\Delta S^o}{2.303R}\right)
\]

12

The plot of this relation can be seen in Figures-(8,9) below.

Figure 8-The linear relationship between log K_A and 1/T (K⁻¹), for Lys: DHA, A- in water and B- in NaCl solutions.
The linear relationship between log $K_A$ and $1/T$ (K$^{-1}$), for Arg: DHA, A- in water and B- in NaCl solutions.

The change in Gibbs free energy $\Delta G^\circ$ (KJ mol$^{-1}$), refers to the usable energy of the association interaction in a solution is obtained from Eq. 13 [28].

$$\Delta G^\circ = -RT\ln K_A$$  

Equation-14 [29] is used to evaluation the entropy change, $\Delta S^\circ$ (J K$^{-1}$mol$^{-1}$), as a measure of randomness.

$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$$

Thermodynamic results for $\Delta G^\circ$ and $\Delta S^\circ$, are calculated at 298 K, and the data obtained from equations (11-14) are listed in Table-4.

**Table 4**-Thermodynamic parameters: $\Delta G^\circ$ (kJ mol$^{-1}$), $\Delta S^\circ$ (J K$^{-1}$mol$^{-1}$), $\Delta H^\circ$ (kJ mol$^{-1}$), and $\Delta E_s$ (kJ mol$^{-1}$), of different solutions relative to AA concentration.

| DHA | Thermodynamic parameters | $\Delta E_s$ | $\Delta H^\circ$ | $\Delta G^\circ$ | $\Delta S^\circ$ |
|-----|--------------------------|-------------|--------------|----------------|----------------|
| C<10$^{-2}$ M | Lys (2×10$^{-3}$ M) / water | | | | |
| 2 | 05.72 | -12.15 | -17.64 | 18.43 |
| 3 | 07.51 | -14.30 | -19.13 | 16.21 |
| 4 | 10.01 | -21.44 | -19.49 | -06.54 |
| 5 | 13.22 | -25.02 | -20.92 | -13.76 |
| | Lys (2×10$^{-3}$ M) / NaCl | | | | |
| 2 | 03.22 | -05.36 | -17.26 | 67.75 |
| 3 | 04.65 | -07.51 | -19.10 | 38.89 |
| 4 | 06.61 | -10.72 | -19.84 | 30.60 |
| 5 | 07.86 | -15.37 | -20.68 | 17.82 |
| | Arg (2×10$^{-3}$ M) / water | | | | |
| 2 | 08.93 | -06.01 | -17.33 | 37.99 |
| 3 | 11.44 | -20.37 | -18.79 | -05.30 |
| 4 | 17.15 | -28.59 | -20.00 | -20.83 |
| 5 | 21.44 | -35.74 | -20.75 | -50.30 |
| | Arg (2×10$^{-3}$ M) / NaCl | | | | |
| 2 | 04.65 | -06.79 | -17.28 | 35.20 |
| 3 | 05.00 | -07.86 | -18.97 | 37.28 |
| 4 | 07.51 | -12.51 | -19.93 | 24.90 |
| 5 | 07.15 | -12.87 | -20.82 | 26.68 |

From Table-4 the results show that:
The ΔE_S, appears in most samples a positive value for the association and this refers to a higher mobility and conductivity values of ions in the solutions [28]. The activation energy of the association process in NaCl solutions has lower values relative to the same solutions in water and this refers to the increase in solubility of amino acids under study.

The values of ΔG°, have the tendency to decrease with increase in DHA concentration in water and NaCl solutions, this refers to a transfer of the free solvent molecules to the bulk solvent [28] and increases in HBs formation related to increase in association constant. ΔG°, has negative values, this point to that the association is preferred rather than the dissociation in water and NaCl solutions.

The ΔH° shows negative values in water and NaCl solutions, and this refers to exothermic association interaction. ΔH° of the association process in NaCl solutions increase in values relative to the same solutions in water and this can be connected to raise solubility of amino acids. HBs have a tendency to associate the molecules in the solution so they have fewer random interaction and this accustomed to increase AAs solubility as compared with the same solutions in water.

ΔH°, ΔG°, ΔS°, and ΔE_S, also calculated. ΔE_S, appears in most samples a positive value for the ion association, and the association process in NaCl solutions has lower values relative to the same solutions in water and this refers to the increase in solubility of amino acids under study. The values of ΔG°, have the tendency to decrease with increase in DHA concentration in water and NaCl solutions, related to a transfer of the free solvent molecules to the bulk solvent and increase in HBs formation as the increase in association constant. ΔG°, has negative values, this point to that the association process is preferred in water and NaCl solutions.

The ΔH° shows an exothermic association interaction in water and NaCl solutions. ΔH° of the association process in NaCl solutions increase in values relative to the same solutions in water and this can be connected to raise solubility of amino acids. HBs have a tendency to associate the molecules in the solution so they have fewer random (ΔS°) as comparative to solution with no hydrogen bonding or lower, and this is seen at increase in DHA concentration in water and NaCl solutions.

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