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Ion-dipole complex effect on activity coefficient of L-methionine in aqueous NaCl and $NaNO_3$ solutions

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Abstract−The mean ionic activity coefficient (MIAC) ratios of NaCl and $NaNO_3$ in aqueous L-methionine solutions were measured using the potentiometric method. The MIAC ratio of the electrolyte in the aqueous L-methionine solution was reduced at low electrolyte concentrations, while its value increased at higher electrolyte concentrations. In contrast, the activity coefficient ratio of amino acid L-methionine decreased as the electrolyte concentration increased. At higher L-methionine concentration, the MIAC values were higher. Such variations in the activity coefficient ratio at higher electrolyte concentration can be attributed to the formation of an ion-dipole complex ($A^-(^+AA^-)C^+$). The electrolyte-perturbed-chain-statistical-associating-fluid-theory (electrolyte-PC-SAFT) model was used to calculate the MIAC of the electrolyte and activity coefficient of L-methionine in aqueous L-methionine/electrolyte solutions to accurately describe the experimental tendency. The consideration of the effect of an ion-pair complex did not show a significant difference in comparison with results obtained without it, but depicted a better description.

Keywords: Electrolyte, L-methionine, Ion-pair Complex, PC-SAFT, Mean Spherical Approximation

INTRODUCTION

An amino acid is the basic unit and a building block of complex biochemicals, such as peptides and proteins. Its behavior in a mixture depends on many factors, such as pH, chemical structure, solvent characteristics, and electrolyte type. Sulfur-containing L-methionine is an important precursor for all other sulfur-containing amino acids and their derivatives. In humans, L-methionine is associated with a decreased risk of proximal colon cancer in men and ovarian cancer in women [1-3]. L-methionine plays an important role in protein synthesis during pregnancy and is related to normal fetal growth in humans and animals [4-6].

The solubility of biological molecules in aqueous solutions is altered by adding salts that dissociate into cations and anions: a salting-in effect that increases the solubility proportionally compared with the salt concentration, and the salting-out effect which decreases the solubility with an increase in salt concentration. These effects mainly vary according to the type of dissociated cation and anion. The variation in solubility is owing to ions that influence the activity coefficient of biological molecules, which interact with water and dissociated ions (i.e., cations and anions) [7,8]. Experimental studies on the activity coefficient of amino acids are necessary for its process design. For these reasons, many studies [9-17] on mixtures containing electrolytes and amino acids have been reported.

There are many methods for measuring the activity coefficient of amino acids in aqueous electrolyte solutions: (1) the potentiometric method [9-13], consisting of electrochemical cells with an ion-selective electrode (ISE); (2) the isopiestic method [14,15] based on the principle that all components in the experimental chamber have the same vapor pressure; and (3) the vapor pressure osmometry (VPO) method [16,17] based on accurately determining the temperature difference between a drop of solvent and a drop of solution hanging on thermistors. The isopiestic method is used to measure the reliable activity coefficient of a solute in a solution containing non-volatile solutes such as electrolytes, amino acids and polymers at medium and high concentrations [15], but in dilute solutions large uncertainties may arise despite a long equilibrium time (approximately 6 days) [18]. Whereas, the VPO method has been used widely in dilute solutions and low-concentration ranges [19], but is limited in high-concentration range [18]. On the other hand, the potentiometric method using an ISE has advantages over the other two methods, such as rapidity and relative simplicity in performing an experiment. Furthermore, this method has proven to be effective for investigating the interactions between electrolytes and amino acids, which provides important information for the suitable design of equilibrium-based processes for the separation and concentration of amino acids [20].

In this study, to confirm the possibility of the L-methionine separation from fermentation broth by the solubility change (i.e., salting-out and salting-in effects) with adding NaCl and $NaNO_3$ salts, the potentiometric method with an ISE was used to measure the activity coefficient of L-methionine and the mean ionic activity coefficient (MIAC) of electrolytes (NaCl and $NaNO_3$) in aqueous solution because the difference of the activity coefficient leads to solubility change. The separation method by adding salts is a relatively easy and cheap process in comparison to other methods [21] like chromatography. In aqueous L-methionine/electrolyte solutions, there are various association phenomena, such as self-association of water and amino acid molecules, cross-association, hydration,

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Table 1. The chemical components used in this work

Chemical	CAS No.	Suppliers	Mass fraction purity	Purification method	Analysis method*
L-methionine	15985-39-4	Sigma-Aldrich	0.98	none	HPLC
NaCl	7647-14-5	Sigma-Aldrich	0.99	none	-
$NaNO_3$	7631-99-4	Sigma-Aldrich	0.99	none	-

* The analysis method was provided by the suppliers.

and ion-pair complexes between amino acids and ions dissociated from electrolytes. These interactions have a strong effect on the activity coefficient of each species (electrolytes and amino acids). Understanding the interaction between amino acids and electrolytes is particularly important for analyzing their separation and enrichment. Furthermore, the study of the nature of these interactions is critical to the design of biocompatible separation processes [22,23]. To describe these interactions, the electrolyte-perturbed-chain-statistical-associating-fluid-theory (electrolyte-PC-SAFT) [9,10,24] equation of state (EoS) combined with PM-MSA [25,26] was applied to calculate the MIAC of the electrolyte and activity coefficient of amino acids in electrolyte/amino acid/water solutions.

EXPERIMENTAL METHODS

1. Theory of the Experiments

The potentiometric method for measuring the activity coefficient of L-methionine and MIAC of the electrolyte consists of electrochemical cells with an ISE. The schematic design of the electrochemical cell is as follows:

$$\text{Cation-ISE} \mid \text{solutions} \mid \text{Anion-ISE} \tag{1}$$

According to the Nernst equation, the MIAC of the electrolyte (±, s) in binary (electrolyte/water, bin) and ternary (electrolyte/amino acid/water, ter) solutions is related to the electrochemical potential difference between the cation-ISE and anion-ISE.

$$\Delta E^{ter} = E^0 + S\ln(m_s \gamma_\pm^{ter}) \tag{2}$$

$$\Delta E^{bin} = E^0 + S\ln(m_s \gamma_\pm^{bin}) \tag{3}$$

where ΔE^0 is the difference between the standard potentials of the electrochemical cell. The slope S theoretically equals $\nu RT/nF$, and n, ν, R, and T are the number of electrons, sum of valances for ions, gas constant, and temperature, respectively. Subtracting Eq. (3) from Eq. (2) and rearranging the resulting equation yields the following expression:

$$\gamma_\pm^{ter}/\gamma_\pm^{bin} = \exp[(\Delta E^{ter} - \Delta E^{bin})/S] \tag{4}$$

The MIAC of the electrolyte in an amino acid/water mixture was obtained from the measured electromotive force (EMF) at fixed concentrations. The MIAC ratio of the electrolyte (±) depends on the concentration of the electrolyte and amino acid (AA), and is accurately represented by the following empirical expression [27]:

$$\begin{aligned} \nu\ln(\gamma_\pm^{ter}/\gamma_\pm^{bin}) &= C_1 m_{AA} + C_2 m_S m_{AA} + C_3 m_{AA}^2 \\ &\quad + C_4 m_S^2 m_{AA} + C_5 m_{AA}^3 + C_6 m_S m_{AA}^2 \end{aligned} \tag{5}$$

where C_i is the numerical constant. The activity coefficient of an amino acid was obtained from the ratio of the MIAC of the electrolyte using a cross-differential relation.

$$\nu\left(\frac{\partial \ln \gamma_\pm}{\partial m_{AA}}\right)_{m_S,\, T,\, P} = \left(\frac{\partial \ln \gamma_{AA}}{m_S}\right)_{m_{AA},\, T,\, P} \tag{6}$$

Combining Eqs. (5) and (6), the ratio of the activity coefficients of amino acids can be calculated as follows:

$$\begin{aligned} \ln(\gamma_{AA}^{ter}/\gamma_{AA}^{bin}) &= C_1 m_S + \frac{1}{2} C_2 m_S^2 + 2C_3 m_S m_{AA} \\ &\quad + \frac{1}{3} C_4 m_S^3 + 3C_5 m_S m_{AA}^2 + C_6 m_S^2 m_{AA} \end{aligned} \tag{7}$$

2. Materials

L-methionine (CAS No. 63-68-3) with 98% purity was obtained from Sigma-Aldrich. Sodium chloride (CAS No. 7647-14-5) and sodium nitrate (CAS No. 7631-99-4) were purchased from Sigma-Aldrich, and the purity of all electrolytes was 99%. L-methionine and the electrolytes were used without further purification. All the chemicals used are listed in Table 1. An ISE/pH meter (Orion 920A) with ±0.1 mV resolution and three ion-selective electrodes, i.e., sodium-ISE (Ross Na^+-ISE, glass body, Thermo Orion 84-11 model), chloride-ISE (Cl^--ISE, polymer body, Thermo Orion 94-17 model), and nitrate ion-selective electrode (NO_3^--ISE, polymer body, Thermo Orion 93-07 model), were used to measure the electrochemical potential (i.e. EMF) in electrochemical cell. Deionized water was distilled and purified using a Milli-Q® water purification system.

3. Measurement Procedure

The electrochemical potential at fixed electrolyte and amino acid

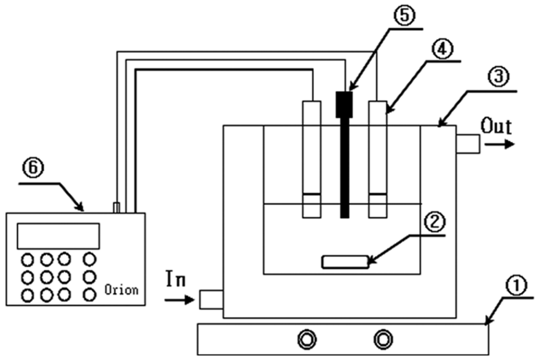

Fig. 1. Schematic view of the experimental setup.

① Magnetic stirrer	④ ISE
② Magnetic bar	⑤ Thermocouple
③ Jacketed glass beaker	⑥ Orion 920A

concentrations was measured by the addition of an amino acid within ±0.01 wt%. The solutions were continuously stirred using a magnetic bar to maintain a constant concentration and temperature in the solution (approximately 200 mL). The water-double jacket attached to the thermostat bath maintained a constant temperature at 298.15±0.1 K (see Fig. 1). The EMF between the cation-ISE and anion-ISE electrodes was determined only when the drift was less than 0.1 mV. For each set of experiments, the ISEs were calibrated using a linear regression of ΔE vs. $\ln(m_s \gamma_{\pm}^{bin})$ at each electrolyte molality m_s.

THERMODYNAMIC BACKGROUND

For aqueous L-methionine/electrolyte (NaCl and $NaNO_3$) systems, the electrolyte-PC-SAFT model defines the residual Helmholtz free energy as follows:

$$A^{res} = A^{PC\text{-}SAFT} + A^{Born} + A^{MSA} \tag{8}$$

where the superscripts PC-SAFT, Born, and MSA represent the contributions of PC-SAFT for describing the short-range interactions (repulsion, chain-connectivity, dispersion, and association), the Born equation for solvation contributions, and mean spherical approximation (MSA) for electrostatic interactions between ions, respectively. These terms are represented by PC-SAFT [28,29], Born equation [30], and PM-MSA [25,26].

As mentioned, various association phenomena exist in aqueous electrolyte/amino acid solutions, and these interactions are treated with electrolyte-PC-SAFT EoS [24]. The association scheme for water and amino acids is assumed to be a 4C association scheme (i.e., two lone electron pairs (e) of oxygen and two hydrogen atoms (H) for water, and two electron acceptors of the ammonium (N) group and two electron donors of the carboxylic (C) group for amino acids). Cations and anions were treated as one hard sphere with a S_i-association site. The ion-pair complex between an amino acid and ions is described as cross-association. All associations have been described in previous work [24].

The Helmholtz free energy A^{MSA} for long-range interactions between cations and anions was derived by Blum [25] and Blum and Hoeye [26]. They developed an MSA incorporated with a primitive model, in which the water molecule was assumed to be a continuous medium with a specified dielectric constant D. The Helmholtz free energy A^{MSA} is expressed by the primitive MSA [13]:

$$A^{MSA}/NkT = \frac{\alpha^2}{4\pi\rho}\left[\Gamma \Sigma_{ion} \frac{\rho_i z_i^2}{1+\Gamma d_{hi}} + \frac{\pi}{2\Delta}\Omega P_n^2 + \frac{\Gamma^3}{3\pi\rho}\right] \tag{9}$$

$$\alpha^2 = \frac{e^2}{DkT} \tag{10}$$

$$\Delta = 1 - \frac{\pi}{6}\Sigma_{ion}\rho_i d_{hi}^3 \tag{11}$$

$$4\Gamma^2 = \alpha^2 \Sigma_{ion}\rho_i \left[\frac{z_i - \frac{\pi}{2\Delta} d_{hi}^2 P_n}{1+\Gamma d_{hi}}\right]^2 \tag{12}$$

where d_{hi} is the diameter of the hydrated ion i in the aqueous solution. The shielding parameter Γ has a meaning similar to the inverse screening length of the Debye-Hückel theory and is calculated from the analytical solution of the nonlinear relations of P_n and Ω.

$$P_n = \frac{1}{\Omega}\Sigma_{ion}\frac{\rho_i d_{hi} z_i}{1+\Gamma d_{hi}} \tag{13}$$

$$\Omega = 1 + \frac{\pi}{2\Delta}\Sigma_{ion}\frac{\rho_i d_{hi}^3}{1+\Gamma d_{hi}} \tag{14}$$

In the mixture solutions, the pair-potential parameters σ_{ij} and ε_{ij} between segments can be defined by conventional combining rules:

$$\sigma_{ij} = 1/2(\sigma_i + \sigma_j) \tag{15}$$

$$\varepsilon_{ij} = (1 - k_{ij})\sqrt{\varepsilon_{ii}\varepsilon_{jj}} \tag{16}$$

where k_{ij} is a binary interaction parameter. The hydrogen bonding association parameters, $\varepsilon^{A_iB_j}$ and $\kappa^{A_iB_j}$ can also be defined as [31]

$$\varepsilon^{A_iB_j} = (\varepsilon^{A_iB_i} + \varepsilon^{A_jB_j})/2 \tag{17}$$

$$\kappa^{A_iB_j} = \sqrt{\kappa^{A_iB_i}\kappa^{A_jB_j}}\left[\frac{\sqrt{\sigma_i\sigma_j}}{(\sigma_i+\sigma_j)/2}\right]^3 \tag{18}$$

RESULTS AND DISCUSSION

1. Experiment

The ΔE^{bin} value was determined in an electrolyte/water binary mixture (i.e., aqueous electrolyte solution) without L-methionine, and ΔE^{ter} was determined in the electrolyte/amino acid/water ternary mixture by measuring the EMF between the cation-ISE and anion-ISE electrodes. The EMF for each concentration was measured over the electrolyte (±) molality range from 0.05 to 1.0 $m_{\pm}$ in

Table 2. The activity coefficient ratio of electrolyte in L-methionine aqueous solutions at 298.15 K[a,b]

L-methionine	NaCl					$NaNO_3$				
	0.1 m	0.3 m	0.5 m	0.7 m	1.0 m	0.1 m	0.3 m	0.5 m	0.7 m	1.0 m
0.025 m	0.9980	0.9990	1.0000	1.0010	1.0010	1.0000	0.9980	1.0000	1.0020	1.0000
0.05 m	0.9940	0.9970	0.9990	1.0010	1.0020	0.9980	1.0000	1.0020	1.0020	1.0020
0.1 m	0.9880	0.9940	0.9960	1.0000	1.0020	0.9921	0.9960	1.0000	1.0020	1.0040
0.15 m	0.9850	0.9900	0.9940	0.9980	1.0016	0.9842	0.9921	0.9960	1.0000	1.0020
0.2 m	0.9830	0.9870	0.9930	0.9970	1.0020	0.9803	0.9881	0.9940	0.9960	1.0000

[a] Standard uncertainties u for temperature and activity coefficient are u(T)=0.1 K and $u(\gamma)=0.005$.

[b] Relative standard uncertainty u_r for molality of NaCl and $NaNO_3$ is u(m)=0.01.

Table 3. The coefficient of the reduction equation for the mean ionic activity coefficient ratio

Electrolyte	RMSD (%)	C_1	C_2	C_3	C_4	C_5	C_6
NaCl	0.058	−0.230650	0.508247	−0.605363	−0.120161	3.458506	−0.797058
$NaNO_3$	0.091	−0.103156	0.539003	−1.364634	−0.244078	3.117254	−0.227884

Table 4. The activity coefficient ratio of L-methionine in electrolyte aqueous solutions at 298.15 K[a]

L-methionine	NaCl					$NaNO_3$				
	0.1 m	0.3 m	0.5 m	0.7 m	1.0 m	0.1 m	0.3 m	0.5 m	0.7 m	1.0 m
0.025 m	0.9760	0.9415	0.9219	0.9144	0.9206	0.9861	0.9723	0.9734	0.9856	1.0170
0.05 m	0.9760	0.9407	0.9192	0.9087	0.9080	0.9811	0.9571	0.9477	0.9486	0.9613
0.1 m	0.9784	0.9457	0.9245	0.9118	0.9039	0.9745	0.9373	0.9141	0.9005	0.8894
0.15 m	0.9837	0.9596	0.9442	0.9350	0.9279	0.9724	0.9308	0.9027	0.8833	0.8623
0.2 m	0.9922	0.9827	0.9792	0.9796	0.9824	0.9750	0.9375	0.9124	0.8953	0.8760

[a] Standard uncertainties u for activity coefficient is $u(\gamma)=0.005$.

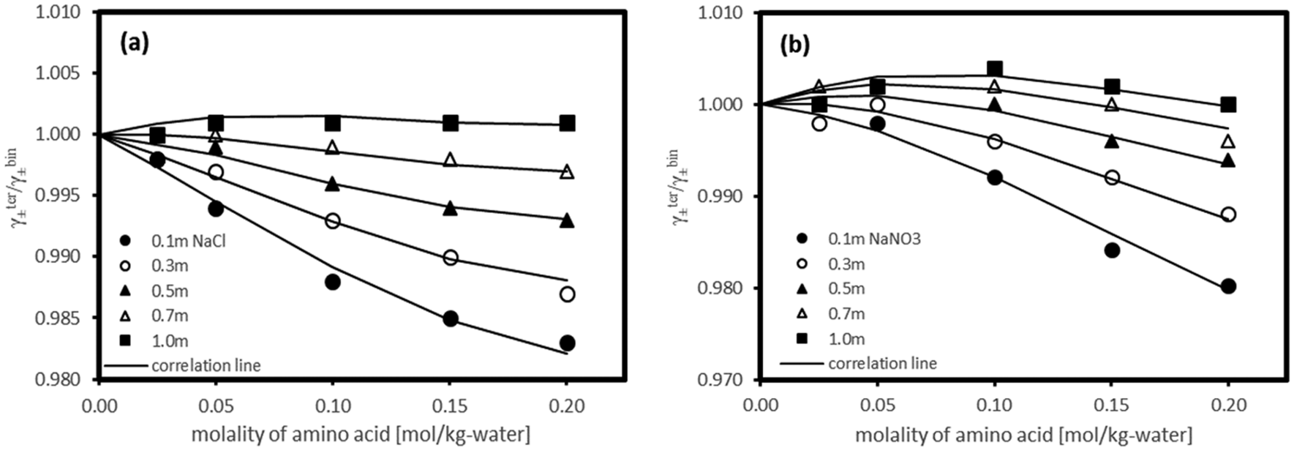

Fig. 2. The mean ionic activity coefficient ratio of (a) NaCl and (b) $NaNO_3$ in L-methionine aqueous solution.

approximately 0.2 $m_\pm$ increments and L-methionine (AA) molality range from 0.05 m_{AA} to 0.45 m_{AA} in 0.05 m_{AA} increments. The measured potential differences ΔE^{ter} and ΔE^{bin} for ternary and binary systems, respectively, were used to obtain the MIAC ratio $\gamma_\pm^{ter}/\gamma_\pm^{bin}$ of electrolytes (NaCl and $NaNO_3$) in an aqueous L-methionine solution. The experimental data for $\gamma_\pm^{ter}/\gamma_\pm^{bin}$ are presented in Table 2. By fitting the experimental $\gamma_\pm^{ter}/\gamma_\pm^{bin}$ data to Eq. (5), the C_i parameters were evaluated for each system and are presented in Table 3. The estimated parameters were used to generate the ratio of the activity coefficient of the L-methionine $\gamma_{AA}^{ter}/\gamma_{AA}^{bin}$ in aqueous electrolyte solutions (see in Table 4). As shown in Table 3, the values of the C_1 coefficient are negative for both electrolytes (NaCl and $NaNO_3$)/L-methionine/water mixtures. The C_1 coefficient represents the pair-wise interaction between L-methionine and electrolyte (NaCl and $NaNO_3$) molecules, and its negative value indicates the presence of an attractive force between these molecules [13,32].

Figs. 2 and 3 depict the effects of L-methionine and NaCl concentrations on the ratio of activity coefficients $\gamma_\pm^{ter}/\gamma_\pm^{bin}$ and $\gamma_{AA}^{ter}/\gamma_{AA}^{bin}$, respectively. Fig. 2 shows the fitted results for the MIAC ratio of the electrolyte (NaCl and $NaNO_3$) in the presence and absence of L-methionine, $\gamma_\pm^{ter}/\gamma_\pm^{bin}$, as a function of L-methionine molality for electrolyte/L-methionine/water systems. It was observed that $\gamma_\pm^{ter}/\gamma_\pm^{bin}$ was strongly affected by the presence of L-methionine. At electrolyte concentrations lower than 0.7 $m_\pm$, the $\gamma_\pm^{ter}/\gamma_\pm^{bin}$ of the electrolyte (NaCl and $NaNO_3$) was steadily reduced by the addition of L-methionine, while at high concentrations (1.0 $m_\pm$) it remained constant for NaCl, and slightly increased and then decreased for $NaNO_3$, as the concentration of L-methionine increased. This suggests that at higher electrolyte concentrations, the electrostatic ionic interactions are more shielded, and the effect of short-range interactions increases. Such changes in interaction result in a smaller effect of amino acids on the MIAC of NaCl and $NaNO_3$. At higher electrolyte concentrations, the formation of an ion-dipole complex owing to these interactions is favorable [33].

As shown in Fig. 3, the ratio of the activity coefficient $\gamma_{AA}^{ter}/\gamma_{AA}^{bin}$ of L-methionine is also affected by the presence of the electrolyte. At a particular concentration of L-methionine, its activity coefficient ratio reaches a minimum value at approximately 0.6 $m_\pm$ NaCl and 0.5 $m_\pm$ $NaNO_3$ when plotted against the electrolyte concentration. Similar behavior was observed for several electrolyte/amino acid/water systems [10,32,34]. These effects are caused by the results of the interaction between L-methionine, water, cations, and anions

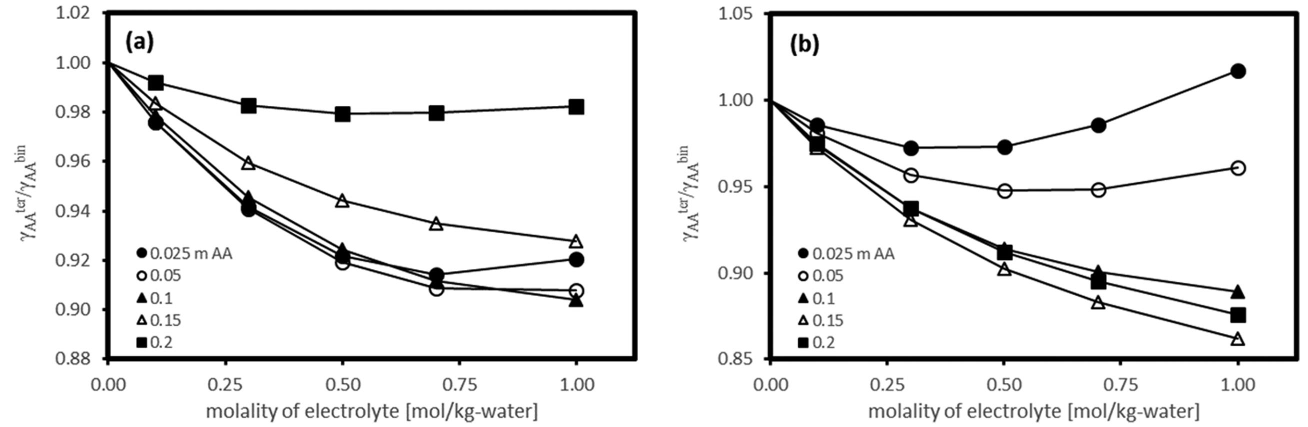

Fig. 3. The activity coefficient ratio of L-methionine in (a) NaCl and (b) $NaNO_3$ aqueous solution.

[24] The decrease in the activity coefficient ratio of L-methionine with an increase in NaCl electrolyte concentration is smaller at higher molarity of L-methionine and the electrolyte. This behavior may be caused by the fact that a higher concentration leads to the formation of ion-dipole pairs. The ion-pair complex (i.e., ion-dipole pair) weakens the forces between the charged ions and charged amine and carboxyl functional groups of amino acids that exists as zwitterions, which enhances the effect of the forces between the organic sections of the amino acid ions [35]. However, the opposite trend was observed for the $NaNO_3$ electrolyte concentration. This result, in turn, depends on the nature of the electrolyte ions (Cl^- and NO_3^-) and their interaction with L-methionine molecules.

The mutual effect of L-methionine and the electrolyte on the activity coefficient ratio is mainly governed by the interaction between these components and that with water, and most of those are due to ion-dipole interaction (i.e., ion-dipole pair interaction). The ion-pair complex is attributed to the formation of physically bonded ion pairs between ions and amino acids, via ion-dipole pair interactions. The variation in the activity coefficient owing to these interactions affects its solubility in aqueous electrolyte solutions. It is noteworthy that if $\gamma_{AA}^{ter}/\gamma_{AA}^{bin}$ is greater than unity, a salting-out effect is expected, and if it is less than unity, a salting-in effect is expected [20,24]. From the comparison presented in Fig. 3, smaller values of the activity coefficient ratio of L-methionine were observed in a NO_3-containing aqueous electrolyte solution than those observed in a Cl-containing aqueous electrolyte solution. Therefore, a higher solubility of L-methionine is expected in NO_3-containing aqueous electrolyte solutions [24].

2. Modeling

The electrolyte-PC-SAFT EoS [9,10,24,36] was employed to correlate the measured experimental data. Each expression for the MIAC of the electrolyte and activity coefficient of L-methionine was obtained from the chemical potential of each component, which was estimated from the partial derivative of the residual Helmholtz energy with respect to each component:

$$\mu_i^{res}(\mathrm{T, V})/\mathrm{kT}=\frac{1}{\mathrm{V}}\left(\frac{\partial \mathrm{A}^{res}/\mathrm{kT}}{\partial \mathrm{N}_i}\right)_{V,\,T,\,N_{i\neq j}} \tag{19}$$

Because the activity coefficients of ions and amino acids do not reach unity in the pure component state, they are obtained from the unsymmetrical condition as follows [37]:

$$\gamma_i'=\frac{\mathrm{V}^{l,\,\infty}_{m_\pm\to 0,\, m_{AA}\to 0}}{\mathrm{V}^l}\exp\left[\frac{\mu_i^{res}(\mathrm{T, V})-\mu_i^{res,\,\infty}(\mathrm{T, V})m_\pm\to 0,\ m_{AA}\to 0}{\mathrm{kT}}\right] \tag{20}$$

where the subscripts m_{AA} and $m_\pm$ indicate the molality of the amino acids and electrolytes in the aqueous solution. The MIAC of an electrolyte can be calculated as follows:

$$\gamma_\pm=(\gamma_+^{\nu_+}\cdot\gamma_-^{\nu_-})^{1/(\nu_++\nu_-)} \tag{21}$$

where v_+ and v_- are the stoichiometric numbers of cations and anions, respectively. The activity coefficients of amino acids and electrolytes are defined on a molality-based scale as follows [38]:

$$\gamma_i=\gamma_i'/[1+0.001\mathrm{M}_w(\mathrm{vm}_\pm+\mathrm{m}_{AA})],\ \text{for } i=\pm,\ \mathrm{AA} \tag{22}$$

where v is the sum of the stoichiometric number of ions (i.e., $v=v_++v_-$) and M_w is the molecular weight of water. Therefore, the MIAC of an electrolyte and activity coefficient of L-methionine are expressed as follows:

$$\ln\gamma_\pm^{ter}=\ln\gamma_\pm^{bin}+\ln\gamma_\pm^{ter\,\prime}-\ln\gamma_\pm^{bin\,\prime}+\ln\left(\frac{1+0.001\mathrm{M}_w\mathrm{vm}_\pm}{1+0.001\mathrm{M}_w(\mathrm{vm}_\pm+\mathrm{m}_{AA})}\right) \tag{23}$$

$$\ln\gamma_{AA}^{ter}=\ln\gamma_{AA}^{bin}+\ln\gamma_{AA}^{ter\,\prime}-\ln\gamma_{AA}^{bin\,\prime}+\ln\left(\frac{1+0.001\mathrm{M}_w\mathrm{vm}_{AA}}{1+0.001\mathrm{M}_w(\mathrm{vm}_\pm+\mathrm{m}_{AA})}\right) \tag{24}$$

where superscripts ter and bin denote the ternary and binary system, respectively.

The activity coefficient ratio of the electrolytes and L-methionine was modeled using the electrolyte-PC-SAFT EoS. The pure component parameters for each species were obtained from literature [36,39] and are listed in Table 5. In L-methionine/electrolyte/water solutions, the zwitterion ($^+AA^-$) of L-methionine, with both positively and negatively charged groups, forms ion-pair complexes ($^+AA^-+A^-C^+\leftrightarrow A^-(^+AA^-)C^+$) by bonding with cations (C^+) and anions (A^-). In this study, the ion-pair complex is considered to be a cross-association between ions and L-methionine. Therefore, the cross-association parameters ($\varepsilon_{ion,\,AA}^{assoc}$, $\kappa_{ion,\,AA}^{assoc}$) between amino acids and ions were introduced. The cross-association volume $\kappa_{ion,\,AA}^{assoc}$ was set to 0.001 based on literature [24,36,40,41] for the electro-

Table 5. The pure component parameters for electrolyte-PC-SAFT EoS

Chemicals	Pure parameters							Binary	ARD (%)*		
	S_i	m [-]	σ [Å]	ε/k [K]	ε^{AB}/k [K]	k^{AB} [-]	d_h [Å]	k_{AAw}	P^{sat}	ρ	γ_i
water	4	1.0175	3.0348	339.39	1,538.43	0.031733	-	-	0.25	0.21	-
L-methionine	4	9.3112	2.6300	336.52	3,212.46	0.035245	-	−0.1175	-	0.04	0.83
Na^+	8	1	1.6966	1,834.09	2,916.95	0.01	4.1905	-	-	-	-
Cl^-	7	1	3.3895	760.41	2,047.51	0.01	5.3896	-	-	-	-
NO_3^-	3	1	3.8142	1,666.89	1,811.04	0.01	4.0613	-	-	-	-

* ARD (%)=100%/n×$\Sigma_{i=1}^{n}|X_{exp}-X_{cal}|/X_{exp}$, X=$P^{sat}$ (saturated vapor pressure), ρ (density) and γ_i (activity coefficient)

Table 6. The calculated activity coefficient ratio of electrolyte and amino acid in aqueous solution using electrolyte-PC-SAFT EoS

Electrolytes	With ion-pair complex				Without ion-pair complex		
			ARD (%)			ARD (%)	
	l	$\varepsilon^{A_iB_j}$/k	$\gamma_\pm^{ter}/\gamma_\pm^{bin}$	$\gamma_{AA}^{ter}/\gamma_{AA}^{bin}$	l	$\gamma_\pm^{ter}/\gamma_\pm^{bin}$	$\gamma_{AA}^{ter}/\gamma_{AA}^{bin}$
NaCl	−0.0758	2,608.7255	0.0776	1.9101	−0.1774	0.2755	2.7210
$NaNO_3$	−0.0417	2,460.8707	0.1523	3.1986	−0.0939	0.2126	3.2547
Overall average			0.1150	2.5543		0.24405	2.9879

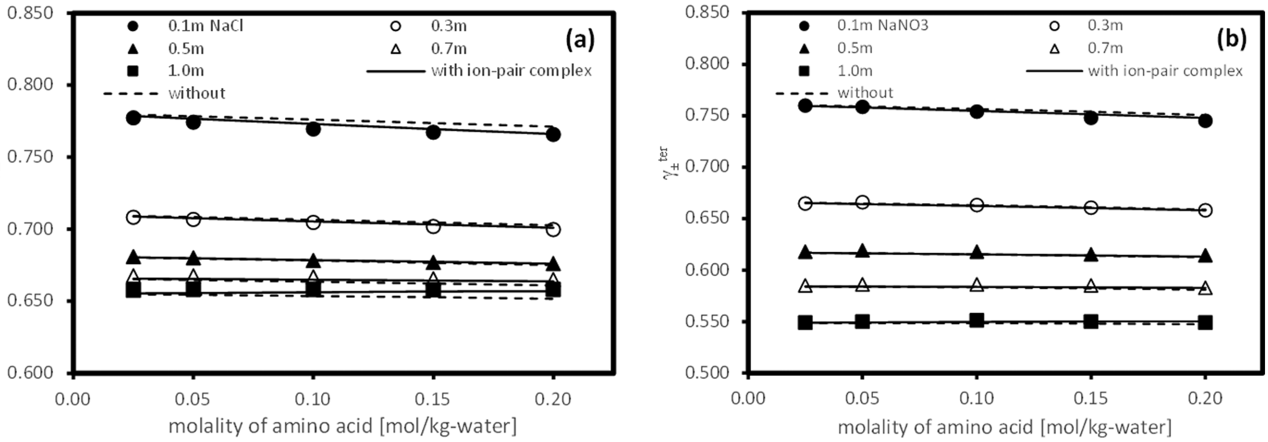

Fig. 4. The mean ionic activity coefficient of (a) NaCl and (b) $NaNO_3$ in L-methionine aqueous solution.

lyte solutions. The cross-association energy parameters between L-methionine and ions (cations and anions) are considered to be symmetric, $\varepsilon^{assoc}_{+,AA}=\varepsilon^{assoc}_{-,AA}$. Therefore, the unknown parameter $\varepsilon^{assoc}_{ion,AA}$ and binary interaction parameters were estimated by fitting the MIAC of the electrolyte. Additionally, the binary interaction parameters between the amino acids (AA) and ions (cations and anions) were assumed to be equal (i.e., $k_{cation,AA}=k_{anion,AA}$). Lastly, the unknown parameters are the cross-association energy parameter $\varepsilon^{assoc}_{ion,AA}$ and binary interaction parameter $k_{ion,AA}$, which were regarded as adjustable parameters.

The adjustable parameters and calculated absolute average relative deviation (ARD) errors are listed in Table 6. To confirm the effect of the ion-pair complex on the activity coefficient of L-methionine and the electrolytes, the calculated results were also reported without considering the ion-pair complex. The calculation results considering the ion-pair complex show ARD values of 0.12 and 2.55% for the MIAC of the electrolyte and for the activity coefficient of the amino acid, respectively, which were noticeably different from those without considering the ion-pair complex (0.24% ARD for the MIAC of the electrolyte, 2.99% ARD for the activity coefficient of the amino acid). These results may be owing to the description of ion-pair interactions. The cross-association strength between the ions (Na^+, Cl^-, and NO_3^-) and L-methionine, with an ammonium group ($-NH_3^+$) and carboxylic group ($-COO^-$), showed a value of approximately 5.2 kcal/mol for NaCl and 4.9 kcal/mol for $NaNO_3$. The cross-association between L-methionine and NaCl was much stronger than that between L-methionine and $NaNO_3$. This is attributed to the stronger surface charge density of the Cl^- anion owing to the small surface area of Cl^- (52.81 $Å^2$) compared with NO_3^- (76.68 $Å^2$). Surface areas were obtained using the estimation method described in literature [42].

Fig. 4 shows the results of the MIAC modeling of NaCl and $NaNO_3$ ($\gamma_\pm^{ter}$) in the presence of L-methionine. The electrolyte-PC-SAFT EoS accurately describes the variation in the MIAC of the electrolyte at different concentrations as a function of the L-methionine concentration. At a fixed electrolyte molality, the MIAC of

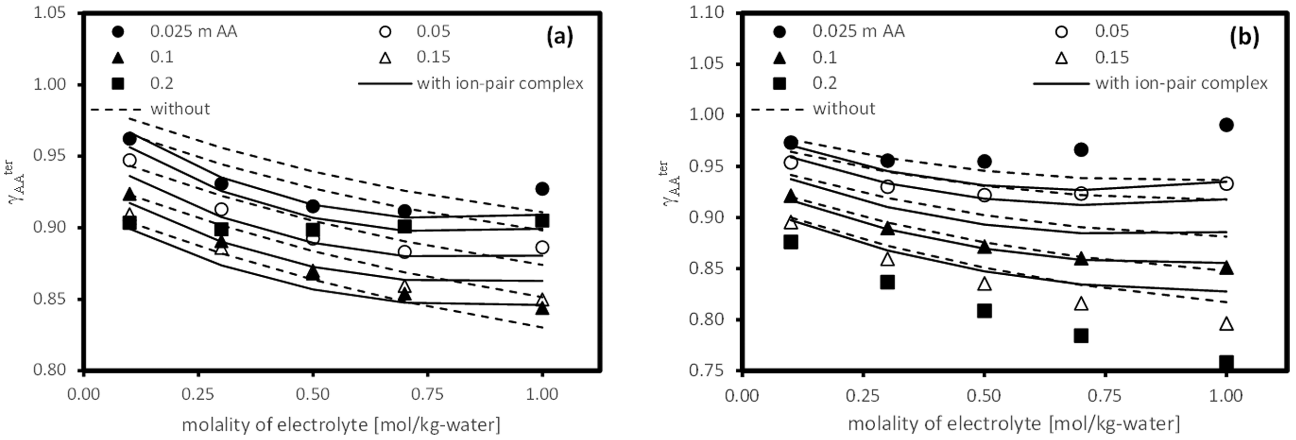

Fig. 5. The activity coefficient of L-methionine in (a) NaCl and (b) NaNO$_3$ aqueous solution.

the electrolyte was observed to decrease as the L-methionine concentration increased. This decrease is reduced at higher electrolyte concentration. The MIAC of the NaNO$_3$ electrolyte in the aqueous L-methionine solution was smaller than that of the NaCl electrolyte. This trend is accurately described by the electrolyte-PC-SAFT model. The consideration of the ion-pair complex shows a smaller value for ARD (%) compared with that without the ion-pair complex, but the difference is not very large or graphically visible.

As shown in Fig. 5, the activity coefficient of L-methionine γ_{AA}^{ter} decreases with increasing electrolyte concentration. This trend is more evident in the aqueous NaNO$_3$ solution. The electrolyte-PC-SAFT model, which considers the ion-pair complex, shows a better description in comparison to that without the ion-pair complex consideration, but the difference is minimal. The decrease in the activity coefficient of L-methionine with increasing electrolyte concentration suggests that the salting-in effect occurred. This behavior is similar to that of previously investigated electrolyte/amino acid/water systems reported in literature [34,37,43-47]. Based on these results, it was found that the NO$_3^-$ anion leads to a stronger salting-in effect than the Cl$^-$ anion.

CONCLUSIONS

The activity coefficients of the electrolytes NaCl and NaNO$_3$ and L-methionine in aqueous solutions were measured using the potentiometric method. The MIAC ratio of the electrolyte $\gamma_\pm^{ter}/\gamma_\pm^{bin}$ was steadily reduced by the addition of L-methionine at low electrolyte concentration, while its value increased at higher electrolyte concentration. In contrast, the activity coefficient of L-methionine showed a higher value as the electrolyte concentration increased. These variations in the MIAC of the electrolyte and activity coefficient of L-methionine at higher electrolyte concentrations were attributed to the formation of an ion-dipole complex. The electrolyte-PC-SAFT EoS was applied to calculate the MIAC of the electrolyte and activity coefficient of L-methionine in electrolyte/L-methionine/water systems, and accurately described the experimental trends. The consideration of the effect of an ion-pair complex, which has a considerable influence on the activity coefficient of amino acids and electrolytes in aqueous solutions, did not show a significant difference from the results obtained without its consideration; however, it provided a better description of the system.

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NOTES

The authors declare no competing financial interest.

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