A Simple Method to Reduce the Optimized Parameters of Aqueous Amino Acid Solutions Using Association EOSs

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ABSTRACT: *Bringing up dissociation/ association equilibria, four new correlated equations are suggested for fixing the parameters of less investigated amino acid systems in a given value for two association models including PC-SAFT and CPA EOSs. Correlated parameters including co-volume parameter, association volumes, and the number of segments are dependent on the molecular weight of amino acids and have derived optimizing and fitting the parameters of the much-used aqueous amino acid solution. Moreover, to indicate the applicability of offered new equations, these formulas are utilized to reduce the number of optimized parameters from six to four for less investigated amino acid solutions. In the case of PC-SAFT EOS, the number of segments and association volume are fixed in a specified value and used to adjust four other parameters of PC-SAFT EOS including the segment of diameter, association energy, dispersion energy, and binary interaction parameter for less investigated amino acid solutions. In the case of CPA model, the correlated parameters are co-volume parameter and association volume, and these two parameters are applied to optimize four other parameters of CPA model such as temperature-dependent energy parameter containing a_0 and c_1, association energy, and binary interaction parameter. Also, the solubility of studied systems is predicted at different temperatures for aqueous binary solutions. Furthermore, osmotic coefficients and water activity of these less investigated systems are evaluated. In the case of PC-SAFT model, the calculated AADs for liquid density, activity coefficient, water activity, osmotic coefficient, and solubility are 0.0032, 0.0864, 0.0058, 0.051, and $4.46*10^{-4}$, respectively. For CPA model, the AADs of these thermodynamic properties are 0.0117, 0.075, 0.0023, 0.16, and $2.79*10^{-4}$, respectively. Both models can reproduce the literature data as well, and though the CPA model is a semi-empirical EOS, it doesn't have irrelevant answers.*

KEYWORDS: *Amino acid; PC-SAFT; CPA; Optimized parameters; correlated equations*.

INTRODUCTION

Employment of aqueous amino acid solutions and their derivation is really considerable in many industrial and biological processes [1-3]. Hence, the researches in biotechnology have acquired lots of attention in order to advance a chemical process for purification and separation of aqueous amino acid solutions. The systems containing amino acids are the simplest structures among the bio-chemicals, and are so many similarities to complex bio-chemicals. Therefore, a precise description of thermodynamic properties of bio-chemicals like amino acids is so principal for designing and scaling up the bio-separation and chemical processes, and it is essential

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for obtaining knowledge of phase equilibria. Collecting all these thermodynamic properties is possible via thermodynamic modeling.

Throughout recent years, two basic types of thermodynamic models have been utilized for calculating different thermodynamic properties of aqueous amino acid solutions, i.e. equations of state (EOS) models, and excess Gibbs energy (g^E) models. One of the basically projects for presenting a specified view of both mentioned procedures was that of *Khoshkbarchi* and *Vera* [4]. The NRTL model [5], Pitzer model [6], Wilson model [7], and UNIFAC model [8] are also so useful among the g^E models applied in amino acids calculations. These models have effectively demonstrated their applicability in lots of systems including aqueous amino acids [9-17]. For instance, *Bowden et al.* [17] utilized solubility data of alpha-amino acids in binary water/ethanol solutions to compute the excess solubility via Gude and NRTL and Jouyban-Acree model. The NRTL and Gude models which are the empirical and regressed equations adjusted the data as well, and Jouyban-Acree model was less accurate. Besides, *Lenka* and *Sarkar* [15] determined the solubility data of L-asparagine monohydrate (LAM) in pure water and water/isopropanol mixtures in the temperature range from 298.15 K to 333.15 K via gravimetric procedure. They also applied the NRTL and UNIQUAC models to correlate the obtained experimental solubility data through adjusting binary parameters. They considered the fusion heat of LAM as an extra parameter for both models and estimated it along with binary interaction parameters. The calculated solubility data was reproduced truly in their study.

Although utilization of g^E models is so frequent due to their comprehensibility, these models are not able to examine the liquid density. So, other methods which are capable of calculating the liquid density and vapor pressure data should be investigated. Since the equations of state can compute the mentioned data applying the residual Helmholtz energy framework, and they do not have these difficulties, these models have obtained more attention in different thermodynamic properties calculations without any extra term.

In the case of equation of state utilization, lots of distinguished activities [18-29] are related to different models of Statistical Associating Fluid Theory (SAFT) [30-32] for calculating various thermodynamic properties in aqueous amino acid solutions. For illustration, *Ji* and *Feng* [19] utilized the SAFT EOS by extending the approach [33] which had been developed previously to describe the SAFT parameters for amino acids, and they examined the solubility of these solutions. In addition, *Held et al.* [25] used PC-SAFT EOS in order to simultaneously calculate various thermodynamic properties of 28 amino acid and oligopeptides solutions without considering dissociation /association equilibria. After a while, they [26] applied the parameters optimized in the literature [25], and they modeled pH and solubility in multi-solute amino acid solutions with different pIs [26].

Other equations of state related to thermodynamic modeling of amino acid solutions have been presented in the literature [34-41]. For example, *Valavi et al.* [41] applied Perturbed Hard Sphere Chain (PHSC) EOS to model the thermodynamic properties of aqueous amino acid solutions using the activity coefficient data, liquid density and solubility data. Moreover, osmotic coefficient, water activity, and vapor pressure of aqueous amino acid systems have been predicted in their work. In addition, *Park et al.* [34] and *Yeom et al.* [35] used hydrogen-bonding lattice fluid equation of state for modeling the aqueous amino acid solutions parameters. Additionally, *Pazuki et al.* [36] correlated the phase equilibria of peptides and amino acids in aqueous systems based on the perturbation theory of equation of state. Newly, we applied CPA EOS to compute aqueous amino acid solutions density, vapor pressure, activity coefficient, and solubility, without considering the dependency of solubility on pH value and propounding dissociation /association equilibria [42]. Following the presented study, a new perspective on CPA EOS was offered to calculate different thermodynamic properties of amino acid solutions taking into account the dissociation /association equilibria and dependency of solubility on pH value [43]. The model also was utilized to correlate the Δh and Δs through the optimization of 24 amino acids solubility data.

Now, following our previous study [43], the essence of ongoing project is evaluation the ability of four new equations correlated in this study in the case of the CPA EOS as well as the Perturbed-Chain Statistical Association theory to reduce the adjusted parameters of these models from six to four for amino acid solutions and illustrate the dependency of solubility on dissociation /association equilibria. To begin modeling, applying scheme 2B which has one donor site and one accepter site of electrons,

the molecules parameters are optimized for both EOSs (CPA equation of state and PC-SAFT EOS) utilizing the liquid density and saturated vapor pressure experimental data. The water molecules optimized parameters are available in the literature [43-45]. It should be mentioned that in water molecules with scheme 2B, the donor site is related to electrons of oxygen atom and the accepter site is relevant to two hydrogen atoms.

Secondly, exerting adjusted parameters of water molecules, PC-SAFT model and CPA EOS are used in typical and available water/amino acid system; five pure component parameters for amino acids along with one binary interaction parameter are optimized in the much-used water/amino acid mixture. Also, different schemes are propounded according to the structure of studied amino acids and their donor and accepter sites. It should be noted, the optimization procedure has been done formerly in reference [43] in the case of the CPA model, and the results of this study including two new correlated equations related to co volume parameter and association volume have been applied here. In the case of PC-SAFT EOS, the new optimized parameters and correlated equations for amino acid systems are presented here for the first time. Although optimizing the amino acids parameters has been exerted formerly by *Held et al.* [25] for PC-SAFT theory, these parameters could not establish a reasonable relation between optimized parameters and other factors, and they did not present a predictive result for calculating liquid density, solute activity coefficient, water activity, and osmotic coefficient at various temperatures and pressures. So, this manner is done again to present a predictive result in the case of PC-SAFT EOS.

After optimization process of some common and available aqueous amino acid solutions, two new equations related to molecular weight of amino acids are correlated for calculating the parameters of PC-SAFT EOS including the number of segments and association volume. In the case of CPA EOS, these correlated equations were presented in our previous work [43]. These equations which are related to co-volume and association volume are used here and the applicability of them are investigated.

Hence, in order to evaluate the applicability of correlated equations, these formulas are subsequently utilized to fix two parameters of less investigated amino acids in a given value and reduce the number of optimized parameters from six to four for both EOSs. In the case of PC-SAFT EOS, these fixed parameters containing the number of segments and association volume are used to adjust four other parameters of PC-SAFT EOS including the segment of diameter, association energy, dispersion energy, and binary interaction parameter for less investigated amino acid solutions. In the case of the CPA model, the correlated parameters are co-volume parameter and association volume. These two parameters are applied to optimize four other parameters of CPA model such as temperature-dependent energy parameter containing a_0 and c_1, association energy, and binary interaction parameter. Also, the solubility of studied systems is predicted at different temperatures for aqueous binary solutions, and the influence of pH value is studied for both models. Moreover, the osmotic coefficients of these less investigated systems are predicted. It can be observed, reducing the optimized parameters and calculating the thermodynamic properties is a successful process.

THERMODYNAMIC MODELLING

PC-SAFT and CPA EOSs

The common PC-SAFT EOS is a result of combining several various kinds of contributions containing the hard-core repulsion interactions, conventional attractive dispersion, and association interaction of water molecules as well as the association contribution of all other species which have hydrogen bonding. Therefore, all of these contributions should be considered through a successful theory. Hence, the residual Helmholtz energy a^{res} can be described as below [46, 47]:

$$a^{res} = a^{hc} + a^{disp} + a^{assoc} \quad (1)$$

The superscripts hc, disp, and assoc, pertain to the molecular interactions from the formation of the chain (hard-chain), the dispersion energy, and the association contributions, respectively. Moreover, the details of the equations concerning hard-chain, dispersion, and association terms of the PC-SAFT EOS have been described in references [46, 47].

Furthermore, the conventional combining rules of Berthelot-Lorenz are applied to calculate the dispersion energy (u) and diameter of segment (σ) in the mixture:

$$u_{ij} = \sqrt{u_{ii} u_{jj}} \left(1 - k_{ij}\right) \quad (2)$$

$$\sigma_{ij} = \frac{1}{2}\left(\sigma_{ii} - \sigma_{jj}\right) \quad (3)$$

here k_{ij} is temperature independent binary interaction parameter which is correlated using experimental data.

Likewise, applying simple combining and mixing rules of Wolbach and Sandler, the cross-association interactions containing association volume (k) and association energy (ε) between two associating substances can be described as follow:

$$\varepsilon^{A_iB_j} = \frac{1}{2}(\varepsilon^{A_iB_i} + \varepsilon^{A_jB_j}) \tag{4}$$

$$k^{A_iB_j} = \sqrt{k^{A_iB_i}k^{A_jB_j}}\left[\frac{\sqrt{\sigma_{ii}\sigma_{jj}}}{\frac{1}{2}(\sigma_{ii}+\sigma_{jj})}\right] \tag{5}$$

Also, the Cubic Plus Association equation of state established by *Kontogeorgis et al.* [48] in 1996 has been combined from a physical part proposed by Soave-Redlich-Kwong (SRK) [49] and an association term based on SAFT model [30, 31]. The equation which describes the thermodynamic properties of mixtures in terms of pressure (P) is as below:

$$P = \frac{RT}{V_m - b} - \frac{a(T)}{V_m(V_m + b)} - \tag{6}$$

$$P\frac{1}{2}\frac{RT}{V_m}\left(1+\rho\frac{\partial \ln g}{\partial \rho}\right)\times\sum_i x_i\sum_{A_i}\left(1-X_{A_i}\right)$$

Where V_m shows the molar volume, and ρ refers to molar density. Likewise, X_{Ai} and x_i are the mole fraction of molecule i not bonded at site *A* and the mole fraction of component i, respectively. Moreover, *g* is the radial distribution function, and it can be observed with exact explanations in the literature [48, 49]. In addition, *T* is temperature, and *R* indicates the gas constant. Additionally, *a(T)* demonstrates energy parameter which is temperature-dependent, and b is co-volume parameter. Furthermore, the combining rules of Berthelot-Lorenz are employed for computing the co-volume and energy parameters in the mixture.

$$b_{ij} = \frac{1}{2}(b_{ii} + b_{jj}) \tag{7}$$

$$a_{ij} = \sqrt{a_{ii}a_{jj}}(1 - k_{ij}) \tag{8}$$

Likewise, the cross association binary interactions including association volume (β) and association energy (ε) between two associating materials are determined as below:

$$\varepsilon^{A_iB_j} = \frac{1}{2}\left(\varepsilon^{A_iB_i} + \varepsilon^{A_jB_j}\right) \tag{9}$$

$$\beta^{A_iB_j} = \sqrt{\beta^{A_iB_i}\beta^{A_jB_j}}\left[\frac{\sqrt{b_{ii}b_{jj}}}{\frac{1}{2}(b_{ii}+b_{jj})}\right]^3 \tag{10}$$

It should be mentioned, the precise explanations about CPA EOS, thermodynamic properties calculations, and dissociation/association equilibria can be found in the literature [43, 48].

It should be mentioned, the reason of selecting these two models is nature of them. The PC-SAFT EOS is a theoretical model which considers the molecular interactions of components as well. Besides, this model takes into account the association interaction of species with a radial distribution function (g) which has theoretical base too, and hence it calculates the association interactions as well. So, it seems that this model can compute liquid density excellent. Moreover, the CPA EOS is a semi-empirical model and it is the strongest model among semi-empirical models. This model can also compute the association interactions with a radial distribution function which is not so powerful in comparison with PC-SAFT EOS. As yet, in the case of amino acids, it has not been presented a complete and principal thermodynamic comparison between these two selected models which are one of the strongest models in their categories. Likewise, following our previous study [43] which has investigated the applicability of CPA model for amino acids systems, the comparison of this model with PC-SAFT EOS is due to proficiency evaluation of a semi-empirical model like CPA EOS with a theoretical model in order to understand that a model like CPA has precise results.

RESULTS AND DISSCOTION

Pure water parameter optimization

Applying the original PC-SAFT EOS offered by Gross and Sadowski [46] for associating pure components such as water and alcohol, three non-associative parameters (m, σ, u/k_B) plus two additional associative parameters (k^{AB}, ε^{AB}/k_B) have to be adjusted for water molecules using saturated liquid density and vapor pressure experimental data. The optimized parameters of water molecules suggesting scheme 2B are similar to our previous works [44]. It should

be mentioned that water molecules with scheme 2B have one donor and one accepter sites, the donor site is related to electrons of oxygen atom and the accepter site is relevant to two hydrogen atoms.

Also, using CPA model [48], five pure component parameters such as association volume (β^{AB}), association energy (ε^{AB}), co-volume parameter (b), and temperature-dependent energy parameter containing a_0 and c_1 are optimized for water molecules applying scheme 2B [43].

Likewise, in more details, the optimization method which is followed in this study uses Nelder-Mead method [50] to optimize the relevant parameters. This technique is utilized for minimizing a function of *n* variables, which depends on the comparison of function quantities at the (n + 1) vertices of a universal simplex. It is followed *via* the substitution of the vertex with maximum value by another point. The simplex adjusts itself to the confined landscape, and contracts on to the ultimate minimum. The procedure is demonstrated to be useful and computationally compact. This method exerts "fmincon" code in Matlab program.

Amino acid parameter optimization

After water molecule parameters optimization, in the case of water/amino acid systems, we need five pure component parameters for each amino acid along with one binary interaction parameter between water and amino acid molecules (k_{ij}). The pure component parameters have been described in the above section for both models.

In this study, we propose four new correlated equations to reduce adjusted parameters of water/amino acid systems from six to four. In the case of the CPA model, the co-volume parameter (b) and association volume (β^{AB}) are two offered equations obtained in our previous work [43]. Also, for PC-SAFT EOS, the number of segments (m_{seg}) and association volume (k^{AB}) are two correlated equations presented in this study (see Appendix A). These parameters are dependent on the molecular weight of amino acids and have derived optimizing and fitting the parameters of the much-used aqueous amino acid solutions. Hence, for CPA EOS, the optimized parameters of water/amino acid solutions are association energy (ε^{AB}), temperature-dependent energy parameter containing a_0 and c_1, and k_{ij}. In addition, for PC-SAFT model, the adjusted parameters are association energy (ε^{AB}/k_B), diameter of segment (σ), dispersion energy (u/k_B), and k_{ij}. In addition, the objective function is using liquid density and solute activity coefficient data.

As it can be observed from Appendix A which is involved new parameters of the much-used amino acid solutions, number of the segment (m_{seg}), and association volume parameter (k^{AB}) increase with molecular weight increment. Also, a linear relation is seen between the molecular weight of amino acids and number of the segment. However, the relation of association volume and molecular weight of amino acids is in-linear. It is guessed, like CPA EOS, this observation is due to the degree of used mixing rules. The offered equations for PC-SAFT EOS are as follow:

$$m_{seg} = 0.00899M_A - 0.2180 \quad (11)$$

$$k^{AB} = 1.706??\times 10^{-7} M_A^3 - \quad (12)$$

$$3.838\times 10^{-5} M_A^3 + 0.0045M_A - 0.1449$$

Where, M_A is molecular weight of amino acid. Furthermore, the suggested equations for CPA EOS are as follow [43]:

$$b = 0.0357M_A - 2.0565 \quad (13)$$

$$\beta = -2.5667\times 10^{-5} M_A^2 - 0.0114M_A \quad (14)$$

These four equations can indicate the range of association volume and number of the segments in the case of PC-SAFT model as well as the co-volume parameter and association volume in the case of CPA model for linear and annular amino acids, and fix their value as a specified number. Subsequently, four other parameters of these amino acids are optimized considering association/dissociation equilibria via both EOSs. Hence, the number of the adjusted parameters are reduced from six to four and the results are in good agreement with experimental data. The calculated and optimized parameters of these less investigated amino acids are presented in Table 1 and 2 for PC-SAFT and CPA EOSs, respectively. These amino acids are L-Lysine, L-Aspartic Acid, Dl-Aspartic acid, L-Asparagine, Dl-β-Aminobutyric Acid, Dl-α-Aminobutyric Acid, α-Amino iso Butyric Acid, γ-Aminobutyric Acid, L-Proline, Dl-Proline, L-Hydroxyproline, L-Phenylalanine, Dl-Phenylalanine, L-Tyrosine, and L-Tryptophan. Investigating the association schemes of amino acids and according to their structure (the number

Table 1. Calculated and optimized parameters of PC-SAFT EOS for less investigated amino acids as well as the optimized parameters which are related to solubility (Δh/R, Δs/R)

	Calculated parameters from equations (11) and (12)				Correlated parameters of PC-SAFT EOS				
Amino acid	m_{seg}	K^{AB}	N	u/k_B	ε^{AB}/k_B	σ	$k_{ij,25\,°C}$	Δh/R	Δs/R
L-Lysine	1.0954	0.2253	3	339.06	4798.99	5.059	-0.1217	1484.32	1.2736
Dl-Aspartic acid	0.9795	0.1771	3	406.74	4840.44	7.7276	-0.2563	2903.22	2.6724
L-Aspartic acid	0.9795	0.1771	3	406.74	4840.44	7.7276	-0.2563	3022.59	2.7217
L-Asparagine	0.9707	0.1739	2	376.46	4841.4	5.0583	-0.0990	4189.49	8.5466
Dl-α-Aminobutyric Acid	0.7098	0.09869	2	421.53	2927.46	5.6682	-0.1683	-	-
α-Amino iso butyric Acid	0.7098	0.09869	2	421.00	2927.46	5.6980	-0.1823	-	-
γ-Aminobutyric Acid	0.7098	0.09869	2	421.00	2927.46	5.63119	-0.1738	-	-
Dl-β-Aminobutyric Acid	0.7098	0.09869	2	333.29	2925.41	5.6309	-0.2810	-	-
Dl-Proline	0.8178	0.1254	2	425.11	2643.18	5.5027	-0.1654	-	-
L-Proline	0.8178	0.1254	2	425.11	2643.18	5.5027	-0.1654	-	-
L-Hydroxiproline	0.9618	0.1706	3	435.19	3160.69	5.4943	-0.1057	682.61	-0.7170
Dl-Phenylalanine	1.2682	0.3211	2	395.99	4790.00	7.2286	-0.2244	1267.99	-2.6669
L-Phenylalanine	1.2682	0.3211	2	395.99	4790.00	7.2286	-0.2244	807.01	-3.9674
L-Tyrosine	1.4122	0.4263	3	399.99	4840.44	7.4072	0.05759	2924.018	-0.3258
L-Tryptophan	1.6195	0.6271	3	618.85	4840.39	4.9405	0.3137	1051.84	-3.7103

of donor and accepter sites), various schemes with 2, 3 or 4 associating sites are assumed for amino acid molecules

It should be noted, before offering these equations, "fmincon" code of Matlab could not go forward and stick in a while loop in the optimization process of some annular amino acids. This problem was solved after using these formulas and fixing two parameters.

After amino acid parameters optimization, the solubility of the amino acid an important factor in modeling of aqueous amino acids solutions is predicted at various temperatures for both EOSs.

Also, the Average Absolute Deviation (AAD) is described as below:

$$AAD = \left[\frac{1}{N_p} \sum_{i=1}^{N_p} | Y_{i.cal} - Y_{i.exp} | \right] \quad (15)$$

Where, *Y* is any type of thermodynamic property.

Also, using the parameters listed in Tables 1 and 2 related to less investigated amino acid solutions, the liquid densities, activity coefficient, water activity, osmotic coefficient, and solubility of mentioned aqueous amino acid solutions are examined for PC-SAFT and CPA EOSs taking into account the association/dissociation equilibria. The average absolute deviations (AADs) of these thermodynamic properties are summarized for PC-SAFT and CPA EOSs in Table 3.

To give in detail the correlated results, the predicted activity coefficient of Dl-α-Aminobutyric Acid, liquid density of L-Phenylalanine, water activity of L-Hydroxyproline, and solubility of L-Tyrosine and L-Asparagine are compared with experimental data in Figs. 1, 2, 3, 4, and 5, respectively for both models. As demonstrated in these figures, these thermodynamic properties can be correlated reasonably for both models.

CONCLUSIONS

The essence of this task is demonstrating the ability of PC-SAFT and CPA EOSs for calculation and prediction of liquid densities, water activity, solute activity coefficient, osmotic coefficient, and solubility of the less-used aqueous amino acid solutions. Likewise, four new equations are presented according to optimized parameters

Table 2: calculated and optimized parameters of CPA EOS for less investigated amino acids as well as the optimized parameters which are related to solubility (Δh/R, Δs/R). This table contains critical temperature estimated with the group contribution method by Marrero and Gani [51].

	Calculated parameters from equations (13) and (14)				Correlated parameters of CPA EOS					
Amino acid	b	β^{AB}	N	ε^{AB}	c_1	a_0	$k_{ij,25\,°C}$	Δh/R	Δs/R	T_C
L-Lysine	7.2666	0.08606	3	81.39	3.7896	0.2644	-0.4030	321.75	-2.6302	1049.44
Dl-Aspartic acid	6.8029	0.06935	3	10.04	1.8529	0.5851	-0.1479	3172.98	3.6925	1060.38
L-Aspartic acid	6.8029	0.06935	3	10.04	1.8529	0.5851	-0.1479	3161.14	3.26	1060.38
L-Asparagine	6.7678	0.06800	2	61.04	1.7713	0.4531	-0.5355	4175.89	8.5254	1045.16
Dl-α-Aminobutyric Acid	5.7337	0.03237	2	28.82	1.3352	0.6361	-0.3526	-	-	1025.8
α-Amino iso butyric Acid	5.7337	0.03237	2	28.83	1.2045	0.6520	-0.3915	-	-	1023.01
γ-Aminobutyric Acid	5.7337	0.03237	2	37.18	1.1452	0.7602	-0.3898	-	-	748.39
Dl-β-Aminobutyric Acid	5.7337	0.03237	2	36.45	1.3170	0.8031	-0.3493	-	-	714.47
Dl-Proline	6.1620	0.04521	2	52.73	1.2709	0.5941	-0.5615	-	-	746.87
L-Proline	6.1620	0.04521	2	52.73	1.2709	0.5941	-0.5615	-	-	746.87
L-Hydroxiproline	6.7326	0.06664	3	22.03	1.8099	0.7279	-0.3577	22.13	-2.9376	806.13
Dl-Phenylalanine	7.9472	0.1015	2	19.97	2.7397	0.3625	-0.0650	1248.32	-2.5503	737.58
L-Phenylalanine	7.9472	0.1015	2	19.97	2.7397	0.3625	-0.0650	737.58	-3.8367	737.58
L-Tyrosine	8.5177	0.09934	3	16.71	3.0911	0.9237	0.9192	3251.57	0.8190	1054.05
L-Tryptophan	9.3392	0.05837	3	50.26	3.4220	0.2052	0.1164	995.54	-3.9640	1077.02

of conventional amino acids. These equations are related to the molecular weight of amino acids, and they examine the relation of PC-SAFT EOS parameters including the number of segments, and association volume with the mentioned factor. Also, for the CPA model, the offered equations are based on co-volume parameter and association volume. These equations can reduce the number of optimized parameter from six to four in both models. In addition, osmotic coefficient, and water activity of these aqueous solutions are predicted with rational results for both models. Moreover, considering dissociation /association equilibria, the solubility of aqueous solutions including untypical amino acids is correlated at various temperatures. Clearly, it is shown that the both models are able to reproduce the experimental data accurately over a wide range of amino acid concentration and temperatures. As expected, the PC-SAFT can calculate the density better than CPA model. Also, the CPA model which is a semi-empirical one can compute other properties excellent in competition with a theoretical model like PC-SAFT.

APPENDIX A

This Appendix describes the process of obtaining equations 11 and 12 related to number of segment and association volume of PC-SAFT EOS.

After water molecules optimization procedure, the specific parameters of 24 linear and typical amino acids have been adjusted at atmospheric pressure and 298.15 K via PC-SAFT EOS applying the liquid densities, water activity, and amino acid activity coefficient of binary water/amino acid solutions. The parameters of pure compounds for PC-SAFT EOS are shown in Table 4.

Investigating the association schemes of amino acids and according to their structure (the number of donor and accepter sites), various schemes with 2, 3 or 4 associating sites are assumed for amino acid molecules.

It has to be implied that in the case of DL and L isomers, equivalent parameters have been presented [25, 41]. At first, the related parameters of one isomer are optimized, and then the fitted parameters are exerted for other isomer. For illustration, the optimized parameters of L-Serine, Dl-Valine, DL-Alanine, L-Leucine, L-Arginine,

Table 3: AADs for density, activity coefficient, water activity, osmotic coefficient, and solubility of less investigated aqueous amino acid solutions for PC-SAFT and CPA EOSs.

property	Amino acid	N_P	T(K)	PC-SAFT	CPA	ref
	Dl-Aspartic acid	1	298.15	0.0071	0.0078	[52]
	L-Aspartic acid	1	298.15	0.0037	0.008	[52]
	L-Asparagine	2	298.15	0.0039	0.0024	[53]
	Dl-α-Aminobutyric Acid	8	298.15	0.0025	0.0098	[54]
	α-Amino iso butyric Acid	4	298.15	0.0017	0.016	[55]
	γ-Aminobutyric Acid	4	298.15	0.0017	0.01	[55]
Density	L-Proline	8	298.15	0.0017	0.037	[56]
	L-Phenylalanine	4	298.15	0.0031	0.0091	[57]
	L-Tyrosine	5	298.15	0.0029	0.0082	[57]
	L-Tryptophan	4	298.15	0.0035	0.0087	[57]
	Total AAD			0.0032	0.0117	
	L-Lysine	17	298.15	0.1441	0.15	[58]
	Dl-α-Aminobutyric Acid	12	298.15	0.0062	0.0068	[59]
Activity coefficient	α-Amino iso butyric Acid	9	298.15	0.0055	0.0015	[60]
	γ-Aminobutyric Acid	14	298.15	0.1497	0.127	[61]
	Dl-β-Aminobutyric Acid	14	298.15	0.1215	0.098	[61]
	Dl-Proline	15	298.15	0.1516	0.1265	[62]
	L-Proline	20	298.15	0.10	0.0805	[63]
	L-Hydroxiproline	9	298.15	0.013	0.0099	[62]
	Total AAD			0.0864	0.075	
	L-Proline	5	298.15	0.0056	0.0019	[64]
Water activity	L-Hydroxiproline	5	298.15	0.006	0.0027	[64]
	Total AAD			0.0058	0.0023	
Osmotic coefficient	Dl-α-Aminobutyric Acid	12	298.15	0.051	0.16	[65]
	L-Lysine	3	298-373	0.0011	0.0008	[66]
	Dl-Aspartic acid	17	273-373	$5.04*10^{-5}$	0.0002	[52]
	L-Aspartic acid	17	273-373	0.0001	$3.49*10^{-5}$	[52]
Solubility	L-Asparagine	17	273-373	$7.16*10^{-5}$	0.0009	[53]
	L-Hydroxiproline	11	273-373	0.0025	0.0004	[67]
	Dl-Phenylalanine	17	273-373	$6.41*10^{-5}$	$4.06*10^{-5}$	[52]
	L-Phenylalanine	17	273-373	$4.52*10^{-5}$	0.0001	[53]
	L-Tyrosine	17	273-373	$4.65*10^{-5}$	$3.63*10^{-6}$	[52]
	L-Tryptophan	17	273-373	$2.36*10^{-5}$	$3.63*10^{-5}$	[53]
	Total AAD			$4.46*10^{-4}$	$2.79*10^{-4}$	

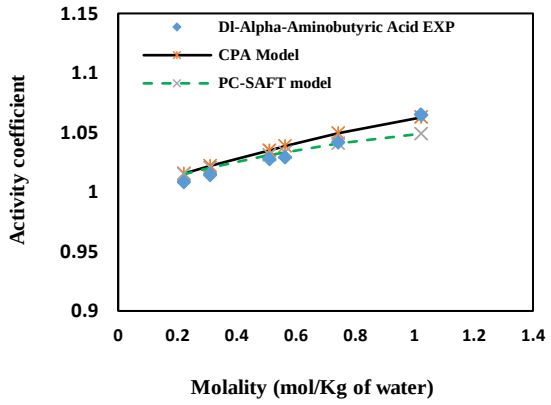

Fig. 1: Activity coefficient of Dl-α-Aminobutyric Acid at 298.15 K and 1 bar, at several molalities. Symbols are experimental data and solid lines are calculated applying PC-SAFT (-ˣ-) EOS and CPA model (-). (♦) Dl-α-Aminobutyric Acid [59].*

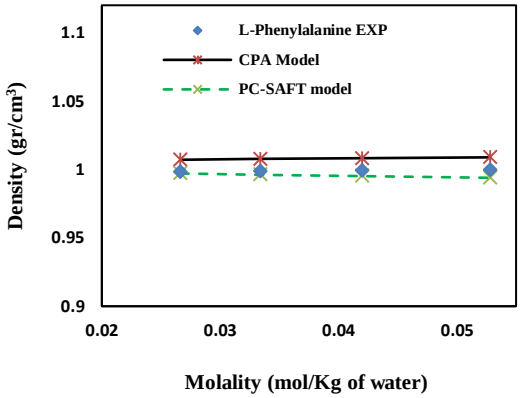

Fig. 2: Liquid density of L-Phenylalanine at 298.15 K and 1 bar, at several molalities. Symbols are experimental data and solid lines are calculated applying PC-SAFT (-ˣ-) EOS and CPA model (-). (♦) L-Phenylalanine [57].*

Dl-Methionine, L-Glutamic acid, and Dl-Threonine are applied for prediction of liquid density, activity coefficient, and water activity of their isomer.

It should be noted that introduced systems have been studied in the literature [25] formerly using PC-SAFT EOS, without propounding dissociation/association equilibria. In the subsequent work [26], the optimized parameters of the literature [25] have been applied to model solubility and pH in aqueous multi-solute amino acid solutions with different pIs. In details, at first, the binary aqueous mixtures have been considered at amino acids pI, and the effect of dissociation /association equilibria have been neglected. Then, related equations have been applied for ternary systems.

Since, these parameters could not establish a reasonable relation between optimized parameters and other factors, the parameters of these much-used amino acid solutions are adjusted again in this study.

Using the parameters listed in Table 4 related to common amino acid solutions which are similar to our previous work, the liquid densities, amino acid activity coefficient, water activity, and osmotic coefficient have been evaluated at 298.15 K and atmospheric pressure for PC-SAFT EOS. The Average Relative Deviations (ARDs) of liquid densities, solute activity coefficients, water activity, and osmotic coefficient are 0.29 %, 1.82 %, 0.083 %, and 6.84 % for PC-SAFT EOS. In addition, the results of this study can be compared with our previous work [43]. ARDs of density, solute activity coefficients, and water activity are 0.86 %, 1.76 % and 0.18 % for CPA EOS, respectively. As claimed by these data, our new investigation can satisfactorily produce favorable results in calculation of all reported thermodynamic properties along with covering numerous data in comparison with other works. Furthermore, liquid density, activity coefficient, and osmotic coefficient of these common amino acid solutions are predicted at other temperatures up to 333.15 K. The Average Relative Deviations (ARDs) of liquid densities, solute activity coefficients, and osmotic coefficient are 0.46 %, 7.31 %, and 25.2 % for temperatures changes up to 333.15 K. Besides, the simultaneous effects of temperature and pressure (0.35 MPa) on liquid density of L-glutamic acid are investigated. ARD is about 0.35 % in this case.

Also, the average relative deviation (ARD) is described as below:

$$ARD = 100 \times \left[\frac{1}{N_p} \sum_{i=1}^{N_p} \left| \frac{Y_{i.cal} - Y_{i.exp}}{Y_{i.exp}} \right| \right] \quad (16)$$

In this study, the enthalpy (Δh/R) and entropy (Δs/R) changes in dissolving process of mentioned systems have been correlated exerting solubility data according to Eq. (17), and the dissociation/association equilibria has been also considered.

$$x_i^{\pm} \gamma_i^{\pm} = \exp\left(\frac{\Delta s_{HA^{\pm}}}{R} - \frac{\Delta h_{HA^{\pm}}}{RT} \right) \quad (17)$$

Here, γ_i and x_i represent activity coefficient of zwitterions and mole fraction of zwitterions, respectively.

Table 4: PC-SAFT parameters of the much-used amino acids as well as the optimized parameters which are related to solubility (Δh/R, Δs/R).

Amino acid	m_{seg}	σ	u/k_B	N	ε^{AB}/k_B	K^{AB}	$k_{ij,25\,°C}$	Δh/R	Δs/R
Glycine	0.4238	5.6172	383.28	2	2927.47	0.0501	- 0.2123	1645.78	2.6812
Dl-alanine	0.5648	5.6774	393.15	2	2927.46	0.0755	- 0.1953	1141.71	0.4442
L-alanine	0.5648	5.6774	393.15	2	2927.46	0.0755	- 0.1953	1043.18	0.0884
β-alanine	0.4433	5.6503	393.16	2	2927.46	0.0755	- 0.2213	757.39	0.6798
Dl-serine	0.61532	5.5471	426.74	3	5648.01	0.0925	- 0.0985	2686.21	4.2579
L-serine	0.61532	5.5471	426.74	3	5648.01	0.0925	- 0.0985	1399.69	2.0604
Dl-valine	0.8779	5.7062	377.10	2	2241.08	0.1181	- 0.2209	1086.07	- 0.8256
L-valine	0.8779	5.7062	377.10	2	2241.08	0.1181	- 0.2209	774.38	- 3.2732
Dl-norvaline	0.8779	5.7062	377.10	2	2241.08	0.1181	- 0.2209	427.31	- 2.8337
Dl-leucine	1.0251	5.6849	440.68	2	2862.19	0.1830	- 0.1654	1178.24	- 2.6055
L-leucine	1.0251	5.6849	440.68	2	2862.19	0.1830	- 0.1654	540.60	- 3.8078
Dl-norleucine	1.0251	5.6849	440.68	2	2862.19	0.1830	- 0.1654	1442.48	- 1.5680
Dl-isoleucine	1.0251	5.6849	440.68	2	2862.19	0.1830	- 0.1654	1067.19	- 2.1274
L-isoleucine	1.0251	5.6849	440.68	2	2862.19	0.1830	- 0.1654	448.64	- 3.7548
L-cysteine	0.9090	5.6634	420.92	3	4860.70	0.1650	- 0.0667	3240.32	- 0.2926
Dl-glutamic acid	1.1533	5.6522	440.84	3	2862.20	0.2224	- 0.1421	4429.70	8.5005
L-glutamic acid	1.1533	5.6522	440.84	3	2862.20	0.2224	- 0.1421	3886.42	6.1623
L-histidine	1.1864	5.6629	440.50	3	2862.18	0.2567	- 0.1013	1921.22	0.9729
Dl-methionine	1.1743	5.6640	439.57	3	2862.74	0.2410	- 0.0438	1547.35	- 0.6401
L-methionine	1.1743	5.6640	439.57	3	2862.74	0.2410	- 0.0438	-	-
Dl-threonine	0.8980	5.6632	420.97	3	4860.70	0.1295	- 0.1269	-	-
L-threonine	0.8980	5.6632	420.97	3	4860.70	0.1295	- 0.1269	-	-
Dl-Arginine	1.2101	5.6479	331.64	4	6427.72	0.3805	- 0.1710	2132.84	2.9315
L-Arginine	1.2101	5.6479	331.64	4	6427.72	0.3805	- 0.1710	3296.73	6.8308

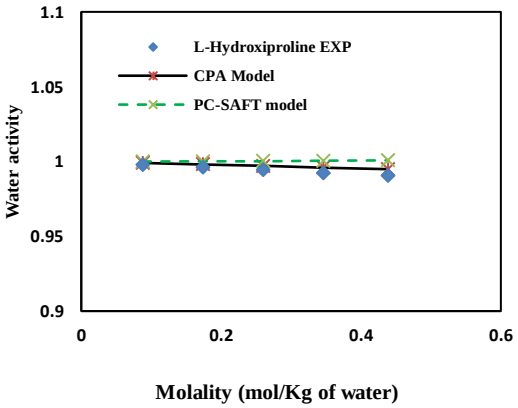

Fig. 3: Water activity of L-Hydroxyproline at 298.15 K and 1 bar, at several molalities. Symbols are experimental data and solid lines are calculated applying PC-SAFT (-ˣ-) EOS and CPA model (-*). (♦) L-Hydroxyproline [64].

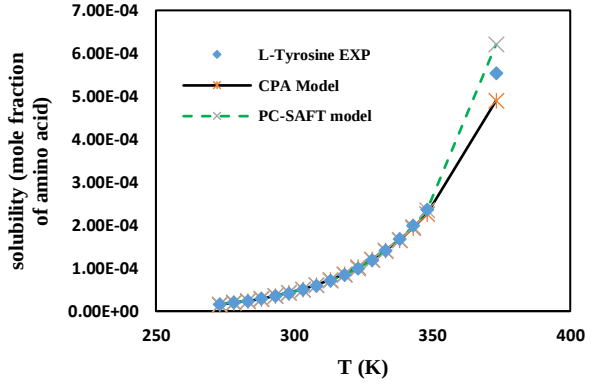

Fig. 4: Correlated and experimental solubility of L-Tyrosine in the aqueous solutions, at several temperatures. Symbols (♦) are experimental data [52] and solid line is calculated applying PC-SAFT (-ˣ-) EOS and CPA model (-*).

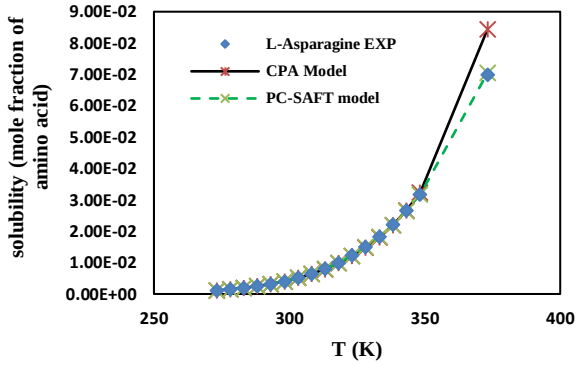

Fig.5: Correlated and experimental solubility of L-Asparagine in the aqueous solutions, at several temperatures. Symbols (♦) are experimental data [53] and the solid line is calculated applying PC-SAFT (-ˣ-) EOS and CPA model (-*-).

Furthermore, accounting dissociation/association equilibria at different pH values, $\Delta s_{HA^{\pm}}$ and $\Delta h_{HA^{\pm}}$ are entropy and enthalpy changes of amino acid zwitterions, respectively.

The ARDs of aqueous amino acid solubility is 2.65 %. It should be noted, similar to our previous work [43], the dissociation constant (K_a) is assumed invariant at different temperatures, and it is not added extra parameters for optimization.

Nomenclature

a_w	Water activity
m	Molality
M_A	Molecular weight of amino acid
N	Number of association sites, total number of particles
P	Pressure
T	Temperature, K
x_i	Mole fraction of chemical component i

ABBREVIATIONS

ARD	Average relative deviation
CPA	Cubic plus association
EOS	Equation of state
PC-SAFT	Perturbed chain statistical associating fluid theory
SAFT	Statistical associating fluid theory

GREEK LETTERS

γ	Activity coefficient
ϕ	Osmotic coefficient
$\varepsilon^{A_iB_j}$	Association energy parameter, K
ρ	Density, mol/m^3
φ	Fugacity coefficient

Superscripts

assoc	Association
m	Molality-based

Subscripts

cal	Calculation
exp	Experimental
i, j	Component indexes

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