

PREDICTION OF LIQUID-LIQUID EQUILIBRIA FOR POLYETHYLENE GLYCOL BASED AQUEOUS TWO-PHASE SYSTEM BY ASOG AND UNIFAC METHOD

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Abstract - Liquid-Liquid equilibrium data were obtained for the polyethylene glycol₂₀₀₀(PEG2000)-sodium citrate-water system at 298.15, 308.15 and 318.15 K. The effect of temperature on binodal and tie line data was studied and published in a previous article (Murugesan and Perumalsamy, 2005). The interaction parameters of ASOG and UNIFAC models were estimated using the LLE data of PEG₂₀₀₀-sodium citrate-water system and are used to predict the LLE data for PEG₆₀₀₀-sodium citrate-water system at 298.15, 308.15 and 318.15 K (literature data). The predicted LLE data by both ASOG and UNIFAC models showed good agreement with the experimental and literature data.

Keywords: Liquid-Liquid equilibria; Polyethylene glycol; Sodium citrate; ASOG; UNIFAC

INTRODUCTION

Liquid-liquid extraction has been gaining importance in biochemical engineering as a result of the development of aqueous two-phase systems for the purification and isolation of macromolecules, such as protein, recombinant DNA, nucleic acid and antibiotics etc., Aqueous two-phase systems are formed when two hydrophilic components are mixed with water at above the threshold concentration (Albertsson, 1971). Due to their high water content, aqueous two-phase systems provide a gentle and protective environment for the separation/purification of biological materials. Aqueous two-phase systems were first applied by Albertsson (1971) to recover biomolecules. Generally the salt based aqueous two phase systems (ATPS) were made using polyethylene glycol with salt consisting

of selective cations namely, ammonium, potassium or sodium and anions such as phosphate, sulphate or carbonates etc. These salts, however, led to high concentration of sulphate and phosphate salts in the effluent streams, causing environmental problems. Recently, Porto et al (2008) and Tubio et al (2007) Murugesan and Perumalsamy (2005) Zafarani-Moattar et al (2004, 2008) have used citrate, as a substitute for phosphate and sulphate salts to form aqueous two phase system with polyethylene glycol (PEG). Since citrates are biodegradable and nontoxic, PEG + citrate salts form environmentally safe aqueous two-phase systems, more suitable for the extraction of biological materials. However, only a very limited amount of research work has been reported using citrate salts. The PEG-Citrate salt based aqueous two phase system was used for the purification of Bovine Serum albumin (BSA) and

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reported in a previous article (Perumalsamy and Murugesan, 2007). Porto et al (2008) used PEG/Citrate systems to remove proteases from a *Clostridium perfringens* fermentation broth. Tubio et al (2007) studied the effect of different factors such as polyethyleneglycol molecular weight, pH, tie line length, temperature and the presence of an inorganic salt on the protein partition coefficient. Recently Zafarani-Moattar et al. (2008) measured the equilibrium data of aqueous polypropylene glycol(PPG)-sodium citrate system at different temperatures, and used Merchuk expression for reproducing the experimental binodal data. In the present work, the group contribution methods, namely, Analytical Solution Of Groups (ASOG) and UNiversal Functional Activity Coefficient (UNIFAC) method were used for the prediction of the behavior of aqueous PEG₆₀₀₀-sodium citrate-water system, where the interaction parameters of the system were estimated using the LLE data of PEG₂₀₀₀-sodium citrate-water system. The liquid-liquid equilibrium data and the phase behaviour for PEG₂₀₀₀-sodium citrate-water system at 298.15, 308.15 and 318.15K temperatures were reported in a previous article (Murugesan and Perumalsamy, 2005). The literature data were taken from Zafarani-Moattar et al.(2004). They measured the equilibrium data of aqueous PEG₆₀₀₀-sodium citrate system at different temperatures, however, they made use of osmotic virial and UNIQUAC equations with or without Debye-Huckel term

Several models for the activity coefficient have been proposed for the polymer-polymer systems, but only few attempts only have been made for the thermodynamic modeling of aqueous polymer-inorganic salt systems. Aqueous polymer-salt systems have several advantages over the polymer-polymer systems due to the larger differences in density, greater selectivity, lower viscosity, lower cost and the larger relative size of the drops (Franco et al, 1996). Due to the size differences between the smaller molecules of salt and the polymer, the thermodynamic behavior of polymer-salt systems is more complicated. Several models for the estimation of activity coefficients have been proposed, involving the combinatorial and free volume effects in one term. There are mainly two kinds of models based on osmotic virial expansions and lattice theories proposed in literature. Osmotic virial expansions, using the osmotic pressure of a solvent in the solution, have been used in describing the phase behavior of two-phase systems. Edmond and Ogston (1968) proposed a virial expansion to predict phase diagrams of aqueous mixtures of Polyethylene

glycol and Dextran . King et al. extended this model and used for the prediction of biomolecule partitioning whereas Haynes et al. (1989) included a higher order virial coefficient in the above model to obtain a phase diagram [King et al., (1988), Haynes et al., (1989), Wu et al., (1996)].

The prediction of phase diagrams of polymer – polymer systems is mainly based on the Flory – Huggins theory, the UNIQUAC and the UNIFAC model [Haghtalab., (2001), Fredenslund., (1977)]. They are the widely used Lattice models. The extended UNIQUAC, UNIFAC and NRTL models have also been used for the prediction of phase behavior of the aqueous two-phase polymer-salt systems. In the present work, Liquid-Liquid equilibrium data were obtained for the polyethylene glycol₂₀₀₀(PEG2000)-sodium citrate-water system at 298.15, 308.15 and 318.15 K. The effect of temperature on binodal and tie line data was studied and published in a previous article (Murugesan and Perumalsamy, 2005). The UNIFAC and ASOG (Analytical Solution of Groups) method suggested by and Kojima and Tochigi, [Novak et al., (1987), Kojima et al., (1979)], was applied for the prediction of phase behavior of the aqueous PEG₆₀₀₀-sodium citrate-water system at equilibrium.

THERMODYNAMIC FRAMEWORK

Several models are available for the calculation of activity coefficients. Some are empirical such as those proposed by Margules and Van Laar (Noval et al., 1987); others, use the local composition concept, such as Wilson (1964) and NRTL (Renon and Prausnitz, 1968); still others, such as UNIQUAC (Haynes et al, 1989), have a more theoretical basis; and finally, some, such as ASOG (Derr and Deal, 1969; Kojima and Tochigi, 1979) and UNIFAC (Fredenslund et al, 1977), use the group contribution method, in which the activity coefficients are calculated from the contributions of the various groups making up the molecules of the solution. The concept of local composition states that due to intermolecular forces and differences in molecular sizes the composition of the system in the neighbourhood of a given molecule is not the same as that of bulk composition.

The group contribution method is more effective in the prediction of activity coefficients of the components compared to other methods. The effectiveness of this method depends on the division of solution into number of interacting groups. As the mutual behavior of interacting groups cannot be

determined experimentally, only certain thermodynamic models can be used, where the interaction parameters are determined from the behavior of a real system. The ASOG method (Kojima, 1979) as well as the UNIFAC method (Fredenslund, 1977) has found a wide application in practice.

ASOG and UNIFAC methods have a wide range of applications with temperatures between 2°C and 155°C, pressures upto 10 atm. This approach was mainly used for vapour-liquid equilibria at normal operating conditions. In the present case the UNIFAC interaction parameters used are those estimated using vapour-liquid equilibrium data obtained under normal operating conditions. The same parameters can be used for the prediction of solid-liquid equilibria also, but liquid-liquid equilibria cannot be predicted using the same interaction parameters. Hence, it was necessary to develop a unique (Magnussen et al, 1981) parameter table based on liquid-liquid equilibrium data, which is the major limitation of the model (Renon et al, 1968).

A given activity coefficient model should be able to predict any type of equilibrium using the same available parameters. Fredenslund et al (1977) compiled the UNIFAC group interaction parameters based on VLE data, which cannot be extended for the prediction of liquid-liquid equilibria. Hence it was necessary to estimate the interaction parameters for every liquid-liquid system involved. Moreover, the group contribution approach for mixtures with polymers is different from core UNIFAC, and hence it requires completely new interaction parameters to be estimated. Oishi and Prausnitz (1978) successfully applied the UNIFAC model for the polymer solutions.

The ASOG and UNIFAC methods are based on the assumption that the contribution to the activity coefficient of component *i* can be separated into two parts, namely, combinatorial part and residual part.

$$\ln \gamma_i = \ln \gamma_i^C + \ln \gamma_i^R \quad (1)$$

The size or shape of the molecule is accounted in the combinatorial part and the actual interaction between the groups is accounted in the residual part. Since the contribution of the combinatorial part to the overall activity coefficient is small, it is mostly considered for mixture of molecules of various sizes.

ASOG Method

The group fraction is defined as

$$X_k = \frac{\sum_{i=1}^N x_i v_{ki}}{\left(\sum_{i=1}^N x_i \sum_{m=1}^g v_{mi} \right)} \quad (2)$$

where v_{ki} is the content of the group *k* in molecules of component *i*, *N* is the number of components and *g* is the number of various groups in the mixture.

$$\ln \gamma_i^R = \sum_{m=1}^g v_{mi} \left(\ln \Gamma_m - \ln \Gamma_m^{(i)} \right) \quad (3)$$

where Γ_m is the activity coefficient of group *m* in the mixture and $\Gamma_m^{(i)}$ is the activity coefficient of group *m* in pure compound *i*.

The Flory – Huggins equation is used for the estimation of combinatorial part of the activity coefficient,

$$\ln \gamma_i^C = \ln v_i^{FH} - \ln \sum_{j=1}^N x_j v_j^{FH} + \frac{1 - v_i^{FH}}{\sum_{j=1}^N x_j v_j^{FH}} \quad (4)$$

where v_i^{FH} is the measure of the size of molecule *i*, defined as the number of atoms in the molecule (except for hydrogen atoms). The value of v_{ki} represents the number of atoms (other than hydrogen atoms), in group *k* of substance *i*.

$$\ln \Gamma_m = 1 - \ln \sum_{n=1}^g (X_n a_{mn}) - \sum_{n=1}^g \left(\frac{X_k a_{km}}{\sum_{n=1}^g X_n a_{kn}} \right) \quad (5)$$

These parameters were evaluated as temperature dependent using the expression

$$\ln a_{mn} = \alpha_{mn} + \frac{\beta_{mn}}{T} \quad (6)$$

which holds for $m=n$ that $\alpha_{mn} = \beta_{mn} = 0$.

UNIFAC Method

This method is also based on the above mentioned relationship (eqns 1, 2, 3). The

UNIQUAC equation is used for the estimation of the combinatorial part,

$$\ln \gamma_i^C = \left(\frac{\ln \Phi_i}{x_i} + 1 - \frac{\Phi_i}{x_i} \right) - \frac{1}{2} z q_i \left(\frac{\ln \Phi_i}{\theta_i} + 1 - \frac{\Phi_i}{\theta_i} \right) \quad (7)$$

where

$$\Phi_i = \frac{x_i r_i}{\sum_{i=1}^N x_i r_i} \quad \theta_i = \frac{x_i q_i}{\sum_{i=1}^N x_i q_i} \quad (8)$$

Quantities q_i and r_i are proportional to the surface area and volume of molecule i , found on the basis of values R_k and Q_k of the corresponding individual groups in the i -th molecule using the relationship

$$r_i = \sum_{k=1}^g v_{ki} R_k \quad q_i = \sum_{k=1}^g v_{ki} Q_k \quad (9)$$

where v_{ki} is the number of k groups in the molecule of component i

$$\ln \Gamma_m = Q_m \left\{ 1 - \ln \left(\sum_{k=1}^g \Theta_k^g \Psi_{mk} \right) - \sum_{k=1}^g \frac{\Theta_k^g \Psi_{mk}}{\sum_{j=1}^g \Theta_k^g \Psi_{jk}} \right\} \quad (10)$$

$$\text{where } \Theta_k^g = \frac{X_k Q_k}{\sum_{j=1}^g Q_j X_j} \quad (11)$$

and the interaction parameter Ψ_{jk} is considered to be temperature dependent having the following form

$$\Psi_{jk} = \exp \left(\frac{-a_{jk}}{T} \right) \quad (12)$$

The Surface and Volume Parameters

For PEG, the values for the volume and surface parameters, which are required in the UNIFAC equation, are estimated using group contribution method as adopted by Van Krevelen and Hofsteyn (1976) and are given in Table 1. The values of

volume and surface parameters for Na^+ were reported by H. Zerres et al. (1994); whereas the same for citrate ion were estimated by M.T. Zafarani Moattar (2004), using group contribution method. The estimated values of volume and surface for Na^+ and citrate ions are also given in Table 1.

Estimation of Model Parameters

The equilibrium data for PEG₂₀₀₀-sodium citrate-water system at different temperatures were used to estimate the interaction parameters of the ASOG and the UNIFAC equations by minimizing the following objective function:

$$\text{O.F.} = \sum_i \left[\frac{\left[(x_1 \gamma_1)_i^I - (x_1 \gamma_1)_i^{II} \right]^2}{(x_1 \gamma_1)_i^{II}} \right] + \sum_i \left[\frac{\left[(x_2 \gamma_2)_i^I - (x_2 \gamma_2)_i^{II} \right]^2}{(x_2 \gamma_2)_i^{II}} \right] + \sum_i \left[\frac{\left[(x_3 \gamma_3)_i^I - (x_3 \gamma_3)_i^{II} \right]^2}{(x_3 \gamma_3)_i^{II}} \right] \quad (13)$$

where I and II represent the two aqueous phases, and j is the number of tie lines and the equilibrium condition used is

$$(x_i \gamma_i)^I = (x_i \gamma_i)^{II} \quad (14)$$

The values of the interaction parameters obtained using the ASOG method is given in Table 2 and 3 and that of UNIFAC method is given in Table 4. Using the estimated interaction parameters, the phase diagrams for PEG₆₀₀₀-sodium citrate-water system at different temperatures were predicted. The average deviation of the predicted results by UNIFAC method and ASOG method are given in Table 5 and 6 respectively. The deviation is defined by the following equation:

$$\text{Dev} = \frac{1}{N} \sum_{i=1}^N \left| x_i^{\text{cal}} - x_i^{\text{exp}} \right| * 100 \quad (15)$$

where N is the number of experimental points and the superscripts 'exp' and 'cal' denote the experimental and calculated values respectively.

Table 1: Group parameter for PEG, salt and water

Group	H ₂ O	CH ₂ OH	CH ₂ OCH ₂	Na ⁺	Sodium citrate
R _k	0.920	1.674	1.593	0.095	5.764
Q _k	1.400	1.740	1.320	0.143	5.116

Table 2: Interaction parameter α_{mn} of ASOG method for the system PEG₂₀₀₀(1)–sodium citrate(2)-water(3)

m/n	CH ₂ OH	CH ₂ OCH ₂	Na ⁺	(C ₆ H ₅ O ₇) ³⁻	H ₂ O
CH ₂ OH	0.0000	1.1707	0.8649	0.9645	1.0158
CH ₂ OCH ₂	0.9006	0.0000	-0.3420	0.9608	-0.3554
Na ⁺	1.0499	-0.4516	0.0000	2.2241	-0.8907
(C ₆ H ₅ O ₇) ³⁻	1.0107	0.7380	2.8446	0.0000	-0.0481
H ₂ O	0.7997	-2.2099	-0.1230	0.1473	0.0000

Table 3: Interaction parameter β_{mn} of ASOG method for the system PEG₂₀₀₀(1)–sodium citrate(2)-water(3)

m/n	CH ₂ OH	CH ₂ OCH ₂	Na ⁺	(C ₆ H ₅ O ₇) ³⁻	H ₂ O
CH ₂ OH	0.0000	1.0004	0.9995	0.9999	1.00099
CH ₂ OCH ₂	0.9996	0.0000	0.9944	0.9997	1.01773
Na ⁺	1.0003	0.9976	0.0000	1.0033	0.98619
(C ₆ H ₅ O ₇) ³⁻	1.0001	1.0003	1.0081	0.0000	0.99186
H ₂ O	0.9993	0.9875	0.9936	0.9963	0.00000

Table 4: Interaction parameters a_{jk} of the UNIFAC equation for the PEG₂₀₀₀(1)-sodium citrate(2)-water(3) system

j/k	CH ₂ OH	CH ₂ OCH ₂	Na ⁺	(C ₆ H ₅ O ₇) ³⁻	H ₂ O
CH ₂ OH	0.0000	3.7541	1.9622	17.2052	1.9845
CH ₂ OCH ₂	6.4244	0.0000	68.1963	725.0347	15.0194
Na ⁺	0.0279	-23.2776	0.0000	-53.8425	27.4332
(C ₆ H ₅ O ₇) ³⁻	1.6738	-84.8722	-63.2657	0.0000	186.1067
H ₂ O	1.7457	7.8546	-8.1667	-224.8808	0.0000

Table 5: Comparison of experimental results with the calculated results using UNIFAC method for the PEG-sodium citrate-water based system.

S.No	ATPS System	PEG Average molecular weight	T(K)	Average Deviation (%)	Maximum Deviation (%)	Overall Deviation (%)	Reference
1	PEG ₂₀₀₀ -sodium citrate-water	2000	298.15	0.6538	0.7021	0.5958	Murugesan and Perumalsamy (2005)
			308.15	0.4467	0.4903		
			318.15	0.6869	0.7217		
2	PEG ₆₀₀₀ -sodium citrate-water	5886	298.15	0.6926	0.8546	0.8784	Zafarani-Moattar et al (2004)
			308.15	1.0064	1.2863		
			318.15	0.9363	1.2578		

Table 6: Comparison of the experimental results with the calculated results using ASOG method for the PEG-sodium citrate-water based system.

S.No	ATPS System	PEG Average molecular weight	T(K)	Average deviation (%)	Maximum Deviation (%)	Overall Deviation (%)	Reference
1	PEG ₂₀₀₀ -sodium citrate-water	2000	298.15	0.7783	0.8216	0.8492	Murugesan and Perumalsamy (2005)
			308.15	0.8482	0.8956		
			318.15	0.9210	0.9723		
2	PEG ₆₀₀₀ -sodium citrate-water	5886	298.15	0.8568	0.9279	1.3341	Zafarani-Moattar et al (2004)
			308.15	1.0908	1.2651		
			318.15	2.0547	2.3698		

RESULTS AND DISCUSSION

The binodal data, representing the minimum concentration required for the formation of two phases at temperatures 293.15, 303.15 and 313.15 K and the tie line compositions at temperatures 293.15, 303.15 and 313.15 K were determined. The LLE data for PEG₂₀₀₀-sodium citrate-water system at different temperatures and the effect of temperature on phase behaviour were described in an earlier article (Murugesan and Perumalsamy, 2005). The effect of temperature on the binodal curves of the investigated aqueous PEG₂₀₀₀-sodium citrate system is represented in Fig.1, which shows that an increase in temperature expands the two-phase area of binodal curve. The experimental tie line data at 298.15 K are shown in Fig. 2, as an example. Also the effects of temperature on tie line data are shown in Fig. 3. The Figure shows that the slope and the length of the tie line increases with temperature rises. In aqueous two-phase system, PEG and salt are predominantly present in the top and bottom phase respectively, due to the increase in hydrophobicity of PEG molecules with increase in temperature. Voros et al.(1993) and Mishima et al. (1995) reported similar results for other aqueous PEG-salt systems.

The obtained deviations showed that both ASOG and UNIFAC methods can be satisfactorily used to

predict the LLE data of the PEG (with different molecular weights)-sodium citrate-water systems at the studied temperature range. The model parameters were estimated from PEG₂₀₀₀-sodium citrate-water system based LLE data and they were used to predict the PEG₆₀₀₀-sodium citrate-water system based LLE data. Hence it is proved that both ASOG and UNIFAC models can predict the dependence of the phase diagram on the polymer molecular weights using only one set of parameters. A comparison between the experimental and calculated data by ASOG and UNIFAC method is shown in Fig. 4 and 5 respectively for the PEG-sodium citrate-water based systems. In Fig 4 and 5, the points are the experimental results and the curves represent the values calculated using the ASOG and UNIFAC methods respectively. Figures 4 and 5 show that the binodal moves towards the lower concentrations with an increase in the polymer molecular weight. Thus the group contribution approach for the prediction of phase equilibria can be satisfactorily applied to PEG₂₀₀₀-sodium citrate-water based aqueous two-phase systems containing various groups of components. In the present work both ASOG and UNIFAC models showed good agreement with the experimental data for the polymer-salt based aqueous two-phase system at different temperatures and estimating new interaction group parameters.

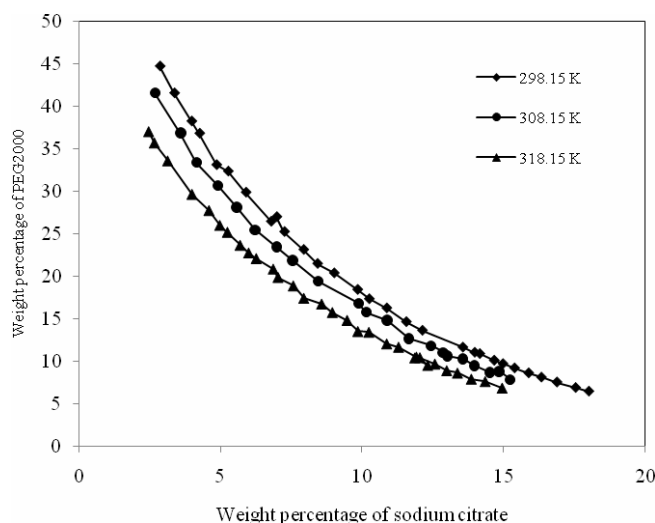


Figure 1: Binodal curves for the PEG₂₀₀₀-sodium citrate-water system at 298.15, 308.15 and 318.15 K.

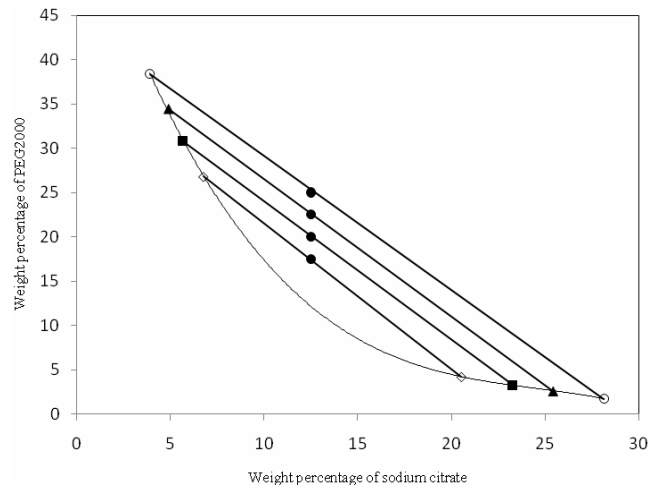


Figure 2: Phase diagram for the PEG₂₀₀₀-sodium citrate-water system at 298.15 K

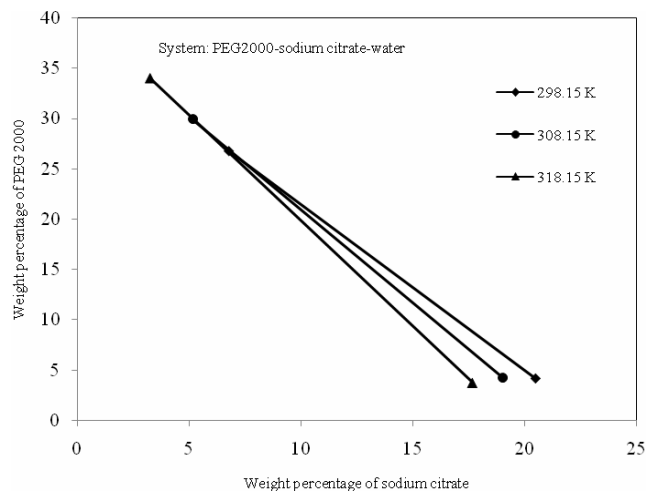


Figure 3: Effect of temperature on the tie lines for the PEG₂₀₀₀-sodium citrate-water system

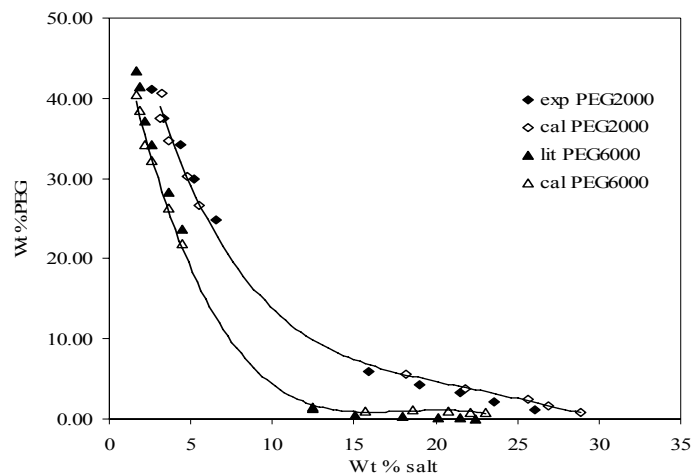


Figure 4: Comparison of experimental tie line data with the calculated values using UNIFAC method for the PEG-sodium citrate-water based system at 308.15 K

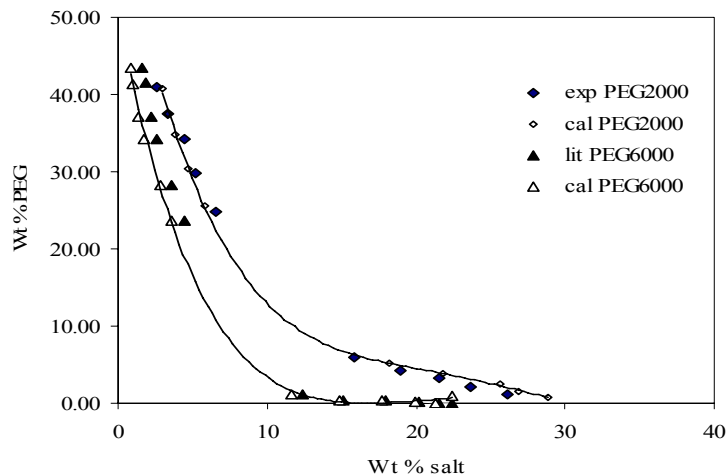


Figure 5: Comparison of the experimental tie line data with the calculated values using ASOG method for the PEG-sodium citrate-water based system at 308.15K

CONCLUSION

The binodal data and tie line data for the system PEG₂₀₀₀-sodium citrate-water at 298.15, 308.15 were obtained. The effect of temperature on LLE data has been studied. It was found that the expansion of two-phase area was observed with an increase in temperature. It was also observed that the slope and length of the tie lines increased with increasing temperature. Further, the group contribution methods, namely, Analytical Solution Of Groups (ASOG) and UNIFAC method were used to predict the behavior of aqueous PEG₆₀₀₀-sodium citrate system. The interaction parameters were estimated using the LLE data of PEG₂₀₀₀-sodium citrate system and associated with the existing VLE parameters. Hence these models seem to be more convenient to predict the dependence of the phase diagram on molecular weight. Even though, the correlated results of both models show satisfactory agreement with the experimental data, this agreement was slightly better, when UNIFAC method was employed.

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NOMENCLATURE

List of Symbols

a_0, a_1, a_2	coefficients
a_{mn}, a_{kn}	interaction parameters defined in eqn (7)
g	number of groups
n	refractive index
N	number of components
O.F	objective function
q_i	volume of molecule i
Q_k	relative surface area of group k
r_i	surface area of molecule i
R_k	relative volume of group k
W	weight fraction
x_i	mole fraction of component i
X	group fraction
z	coordination number

Greek Letters

γ	activity coefficient
Γ	group activity coefficient
α_{mn}, β_{mn}	interaction parameter between group m and n
v_{ki}	content of the group k in molecules of component i
Θ_i	fraction of surface area of component i

ϕ_i	volume fraction
Ψ_{mk}	parameter in the UNIFAC equation

Subscripts

m, n, i, j,	groups, polymer, salt and
k	water
p, s	polymer, salt

Superscripts

C, R	combinatorial, residual
cal	calculated
exp	experimental
g	group k
(i)	pure compound i
FH	Flory – Huggins

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