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Ammonium based ionic liquids act as compatible solvents for glycine peptides

T. Vasantha [a], Pankaj Attri [b], Pannuru Venkatesu [b,*], R.S. Rama Devi [a]

[a] Department of Chemistry, Sri Padmavathi Womens Degree and Post Graduate College, Tirupati 517 502, India
[b] Department of Chemistry, University of Delhi, Delhi 110 007, India

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ABSTRACT

In this article, we have reported the solubilities, apparent transfer free energies ($\Delta G'_{tr}$) and UV-visible absorption measurements of glycine peptides (GPs), such as glycine (Gly), diglycine (Gly_2), and cyclic glycylglycine (c(GG)) in aqueous ionic liquids (ILs), bearing sulfate and phosphate anions with ammonium cation, at $T = 298.15$ K. Values of solubility were obtained from density (ρ) measurements of GPs in water and in aqueous ILs. The ammonium ILs such as diethylammonium hydrogen sulfate (DEAS) $[(CH_3CH_2)_2NH][HSO_4]$, triethylammonium hydrogen sulfate (TEAS) $[(CH_3CH_2)_3NH][HSO_4]$, and triethylammonium dihydrogen phosphate (TEAP) $[(CH_3CH_2)_3NH][H_2PO_4]$ have been used in the present study. We observed the positive values of $\Delta G'_{tr}$ for Gly, Gly_2, and c(GG) from water to ILs. These results reveal that the unfavourable interactions are dominated between ILs and the GPs. This indicates that the ammonium based ILs stabilize the GP structure. Further, we have used the $\Delta G'_{tr}$ results to evaluate the transfer free energies ($\Delta g'_{tr}$) contribution of the peptide backbone unit, also known as glycyl residue, ($-CH_2C{=}ONH-$) as function of ILs concentration. Our results suggest that all the investigated ammonium ILs are compatible with GPs and act as stabilizers for GPs structure through exclusion of ILs from GPs' surface. Furthermore, UV-vis spectrophotometer measurements are used as evidence for the stability of GPs in aqueous ILs at $T = 298.15$ K.

1. Introduction

In recent years, ionic liquids (ILs) have been emerged as a novel class of biocompatible solvents in the scientific field. They are fluid salts at room temperature, and entirely composed of ionic species [1–5]. They have many fascinating properties which make them of fundamental interest to all chemists and bioengineers, since both the thermodynamics and kinetics of reactions carried out in ILs are different to those in conventional molecular solvents. The physicochemical properties of ILs are quite sensitive towards structure and nature of cations and anions of ILs. These ILs find wide range applications in various processes like organic synthesis, catalysis, separations and polymerization among a plethora of other uses [6–10]. Due to the ionic nature of the materials, ILs have essentially negligible vapour pressure and so can be envisioned as being useful in a variety of applications [11,12]. The potential utilization and applications of ILs are rapidly increasing in all modern scientific fields by several researchers such as separations [13] reactions [14–17], homogeneous two-phase catalysis [18] and extractions [19]. The activity, structure and stability of protein in aqueous IL solutions have been reported by various researchers [20–25].

Proteins are linear, large complex molecules; heterogeneous polymers are genetically mandated with 20 different naturally occurring amino acids in all living organisms, where residues are linked by covalent peptide bonds (–CO–NH–) [26–28]. In this context, ILs are found to be translating the protein functioning in therapeutic practice [1,2,23,24]. Therefore, the thermodynamic contributions of amino acid from water to IL solutions provide information about solute-solvent interactions, which are important in understanding the stability of proteins' structure and function [21,26,27]. To have a better understanding of the effect of ILs on GPs and to reveal the molecular interactions between ILs and protein functional groups, more detailed thermodynamic studies are still needed.

The main concept of this work is to explore the thermodynamic contribution of ILs on glycine peptides (GPs) and glycyl residue ($-CH_2C{=}ONH-$) from water to ILs by using the apparent transfer free energies ($\Delta G'_{tr}$) measurements. In this study, we have reported the effect of three novel class of ammonium based ILs such as diethylammonium hydrogen sulfate (DEAS) $[(CH_3CH_2)_2NH][HSO_4]$, triethylammonium hydrogen sulfate (TEAS) $[(CH_3CH_2)_3NH][HSO_4]$, and triethylammonium dihydrogen phosphate (TEAP) $[(CH_3CH_2)_3NH][H_2PO_4]$, on the GP compounds of glycine (Gly), diglycine (Gly_2), and cyclic glycylglycine c(GG),

* Corresponding author. Tel.: +91 11 27666646 142; fax: +91 11 2766 6605
E-mail addresses: pvenkatesu@chemistry.du.ac.in, venkatesup@hotmail.com (P. Venkatesu).

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by using the $\Delta G'_{tr}$ data at $T = 298.15$ K, which are determined through the solubility measurements. Further, we have estimated the transfer free energy ($\Delta g'_{tr}$) contribution of the glycyl residue from water to IL solutions by using the $\Delta G'_{tr}$ values of respective GPs. To address the mechanism events between GPs and ILs, we have also studied the UV-vis absorption measurements as a function of GPs concentration in each IL.

2. Materials and methods

2.1. Materials

The highest purity of all GPs were purchased from different commercial sources and used without further purification. The Gly (mass fraction purity > 0.99) and Gly_2 (mass fraction purity > 0.99) were obtained from Across Organics (USA) and c(GG) (mass fraction purity > 0.99) was purchased from Aldrich Chemical Co. (USA). High purity water was obtained from Nano pure-ultra pure water equipment, which was distilled and deionised with a resistivity of 18.3 Ω · cm for making the aqueous IL solutions. All the samples were carefully prepared by mass using a Mettler Toledo analytical balance, which measured with a precision of ±0.0001 g. The ILs were synthesized by using the methods described in the literature [29–31]. The entire ammonium family of ILs, namely DEAS (mass fraction purity 0.99), TEAS (mass fraction purity 0.99) and TEAP (mass fraction purity 0.99) of general type [amine] [anion] used in the present study were synthesized in our laboratory and the detailed procedure have been delineated previously [21].

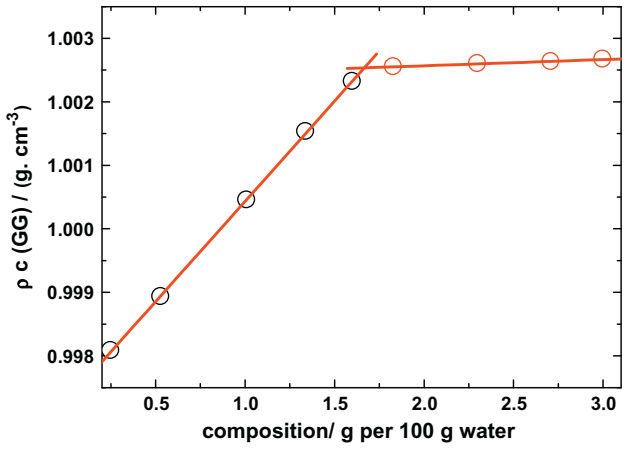


FIGURE 1. The schematic depiction to obtain the solubility limit of c(GG). Densities of c(GG) in water vs. composition of c(GG) in water at $T = 298.15$ K under atmospheric pressure. The solubility limit of the model compound was determined at the point of the intersection of the two fitted lines in each system. For the sake of simplicity and clarity of presentation, all the solubility curves for other systems are not shown.

2.2. Methods

2.2.1. Solubility measurements of GPs in water and aqueous ammonium ILs

Solubility measurements of GPs were performed in a similar manner to that of Nozaki and Tanford [32-34]. The detailed procedure used in the present study has been depicted elsewhere [27,28,35–37]. The concentrated ammonium IL samples are used as solvents for GPs. To each of the sample vials containing a fixed amount of solvent (water or aqueous IL solution, 2 cm^3) was added a weighed amount of a model compound of GPs to provide a series of mixtures with increasing composition of GPs mass. Each vial was closed with a Teflon-coated screw cap, then the cap was sealed with parafilm to ensure an air tight and water tight seal as well as to prevent evaporation. Accordingly, the samples were prepared such that approximately five vials would ultimately result in unsaturated solutions and the remaining vials in saturated solution. The vials containing the solutions were placed in a low temperature shaker equipped with a water bath (Metrex, New Delhi, India). The water bath temperature was retained at (298.15 ± 0.01) K with a constant shaking rate. After 36–48 h, the shaker was stopped, and the supernatant of each vial was removed through a syringe and filtered by 0.47 μm disposal filter (Millipore, Millex-GS), before measurements. The ρ values of the samples were measured at $T = 298.15$ K with a precision of ±0.00005 g · cm^{-3} using a vibrating tube densimeter (DMA-4500 M, Anton-Parr, Austria). The instrument was equipped with a built-in solid-state thermostat and a resident program with an accuracy of temperature of ±0.03 K. The densimeter was initially calibrated by measuring the ρ of atmospheric air and double distilled water, according to manufacture recommendations at $T = 298.15$ K. The observed value and the manufacture recommended values of ρ agreed well. The concentration of solute expressed g/100 g solvent and the uncertainty of the concentration of solute (GP) is lower than ±0.03. The IL concentration was expressed by mass/mass (IL in water, table 1S). The precision of the solubility limit is lower than ±0.8%. The solubility limit of the model protein compound c(GG) was determined at the point of the intersection of the two fitted lines in each system, as illustrated in figure 1.

TABLE 1
Glycine peptide solubilities (S_{GP}) in water and in ammonium aqueous ILs (expressed in mass/mass) and densities (ρ_{*GP}) at solubility limits at $T = 298.15$ K.

Solvent	GP	S_{GP} (g/100 g of solvent)				ρ_{*GP}/(g · cm^{-3})			
TEAP		0%	12.3%	19.0%	25.9%	0%	12.3%	19.0%	25.9%
	Gly	25.09[a]	12.9	7.6	4.3	1.08299	1.07843	1.10901	1.12501
	Gly_2	22.75[b]	7.1	3.7	1.8	1.07731	1.10202	1.10592	1.11017
	c(GG)	1.68[c]	1.31	1.040	0.822	1.00250	1.00423	1.10103	1.11046
DEAS			11.3%	17.8%	23.9%		11.3%	17.8%	23.9%
	Gly		7.2	2.8	1.1		1.12482	1.20535	1.26885
	Gly_2		9.7	5.5	3.3		1.11313	1.14870	1.15901
	c(GG)		1.09	0.739	0.521		1.00187	1.06566	1.11523
TEAS			12.1%	18.6%	24.6%		12.1%	18.6%	24.6%
	Gly		9.8	4.8	2.1		1.09202	1.10002	1.14143
	Gly_2		12.3	8.7	5.7		1.16835	1.19919	1.27950
	c(GG)		0.980	0.659	0.402		1.00069	1.02139	1.12344

[a] $S_{Gly} = 25.10$ ref. [32,41]; 25.09 ref. [33–35].
[b] $S_{Gly2} = 22.75$ ref. [35]; 22.66 ref. [34]; 22.67 ref.[45].
[c] $S_{c(GG)} = 1.68$ ref. [35,41]. Mass fraction purity > 0.99 for Gly, Gly_2, c(GTG); mass fraction purity = 0.99 for DEAS, TEAS, TEAP.

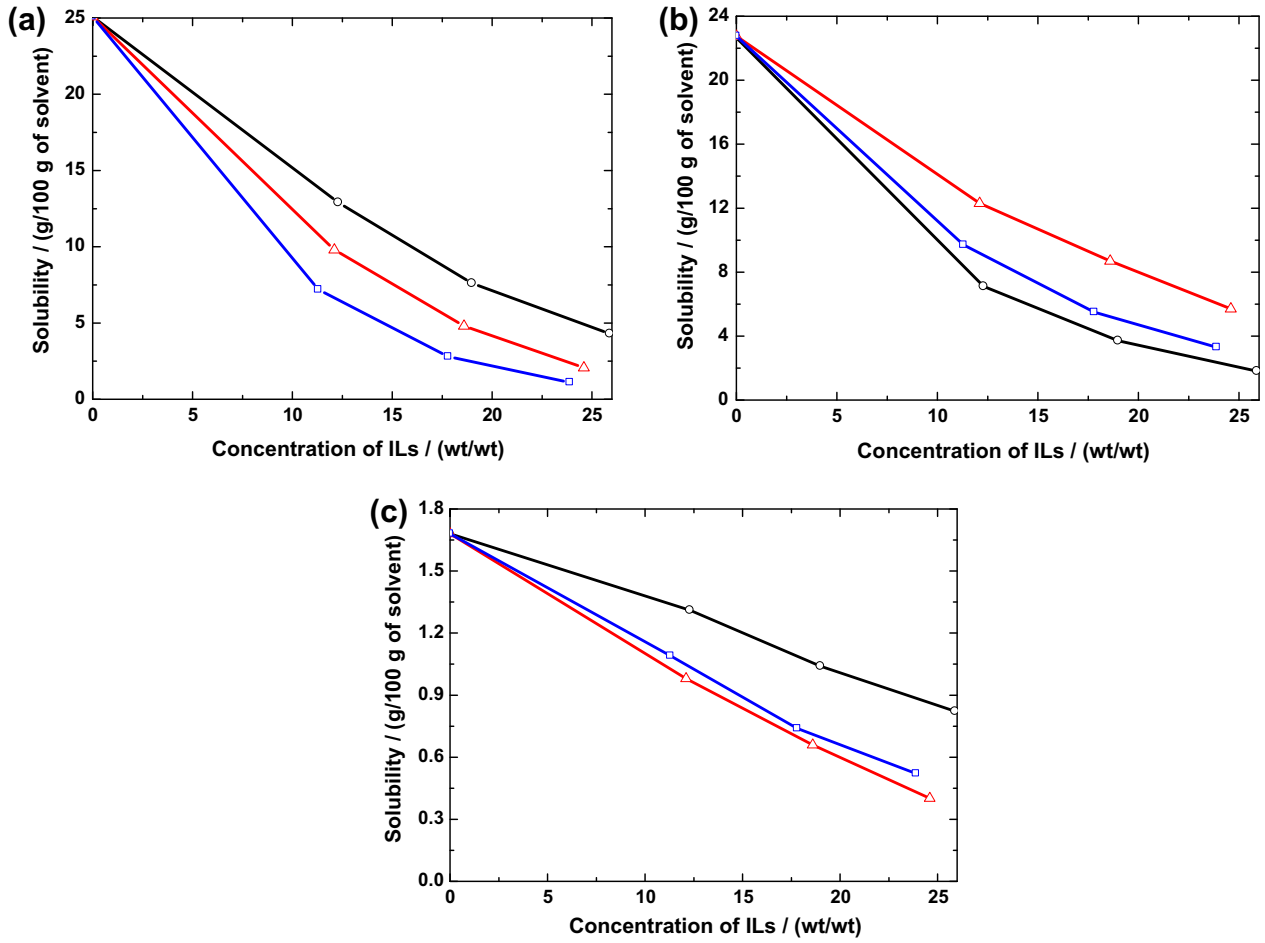


FIGURE 2. Solubility limits for (a) Gly, (b) Gly_2 and (c) c(GG) in ammonium aqueous solution of ILs: TEAP (○), DEAS (□) and TEAS (Δ) at $T = 298.15$ K. Solid lines show the smoothness of the solubility points.

2.2.2. UV-vis absorption measurements

The UV-vis spectrophotometer (UV-1800, SHIMADZU Co, Japan) was employed for absorbance measurements of the samples using a quartz cuvette cell of 1 cm path length. The UV-vis spectra were performed on a computer-controlled spectrometer. Appropriate amounts of samples were uniformly added to the quartz cell. The entire absorbance wavelength readings were made within the range of 190–500 nm. Spectrophotometer has matched quartz cells, with spectral bandwidth of 1 nm, wavelength accuracy of ±0.3 nm with automatic wavelength corrections.

3. Results and discussion

3.1. Solubility of glycine peptides (GPs) from water to ammonium ILs

Table 1S lists the concentration as well as experimental densities (ρ) of the samples of the GP in water and in aqueous ammonium IL solution. The density for each value was plotted as a function of concentration and the solubility limit of the GP was obtained at the point of junction of the two fitted lines for each system [33] as described in figure 1. Similarly, we have measured the solubility limits of each GP in water and in aqueous solutions at $T = 298.15$ K. The density ($\rho*$) of samples at the solubility limits and the solubility limits are presented in Table 1. The solubility limits of GPs in solvents are graphically illustrated in figure 2. The experimental results in figure 2 show that the solubility of Gly, Gly_2 and c(GG) decreases linearly with increasing the concentrations of IL solutions which indicates the dominance of salting-out effect. The salting-out of the solute reflects the increase in the stability of the native structure of GPs in the presence of ILs. The results in table 1 explicitly elucidate that the solubility of GPs in water decrease from Gly to Gly_2. The variations in the solubility from Gly to Gly_2 are due to the long chain in glycine peptides. Due to this, the peptide is only partially surrounded by water molecules since the vicinal space in the peptide molecule is already filled by the –NH–CH–CO– group to which the side chains are attached. As a result, the structure of the long chain glycine peptides leads to lower the values of solubility [38].

3.2. Apparent transfer free energy ($\Delta G'_{tr}$) of GPs from water to ammonium ILs

Transfer free energy measurements (ΔG_{tr}) have played a key role in understanding the effect of stabilization or destabilization of biomolecules in co-solvents [32–37,39–43]. Values of the solubility were used to obtain the apparent transfer free energy ($\Delta G'_{tr}$) of GPs from water to ammonium ILs at $T = 298.15$ K. Nozaki and Tanford [32-34,42] developed a transfer free energy model that has utilized to assess the transfer free energies of proteins from water to different co-solvents. A detailed description of the evaluating $\Delta G'_{tr}$ has been described elsewhere [35–37,44–48]. The uncertainty in $\Delta G'_{tr}$ is to be ±1.5%. The results of $\Delta G'_{tr}$ values obtained for GPs from water to ammonium ILs at $T = 298.15$ K are plotted in figure 3 and tabulated in table 2. Figure 3 depicts that

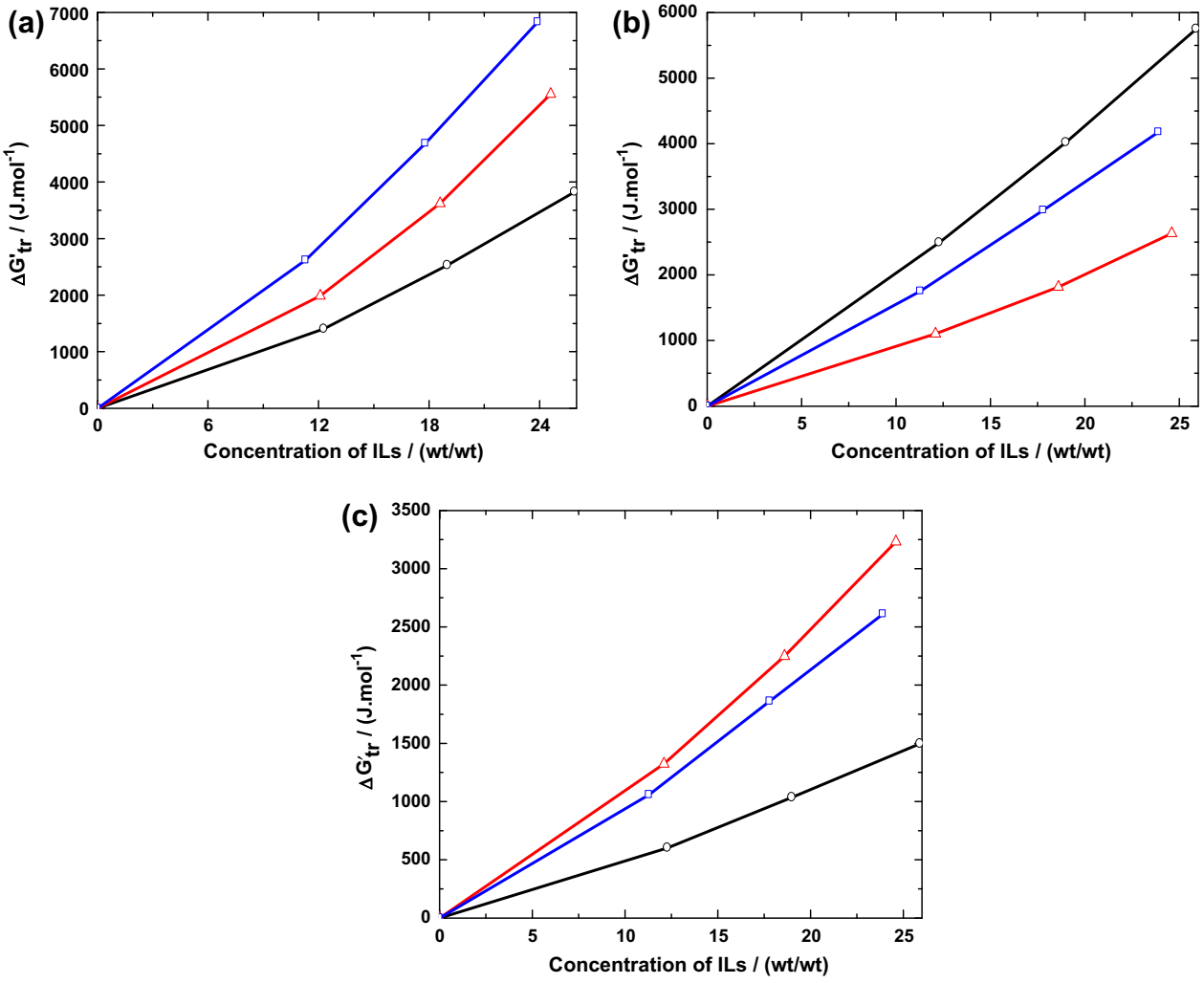


FIGURE 3. Apparent transfer free energies ($\Delta G'_{tr}$) for (a) Gly, (b) Gly_2 and (c) c(GG) in ammonium aqueous solution of ILs: TEAP (○), DEAS (□) and TEAS (Δ) at T = 298.15 K. Solid lines show the smoothness of the solubility points.

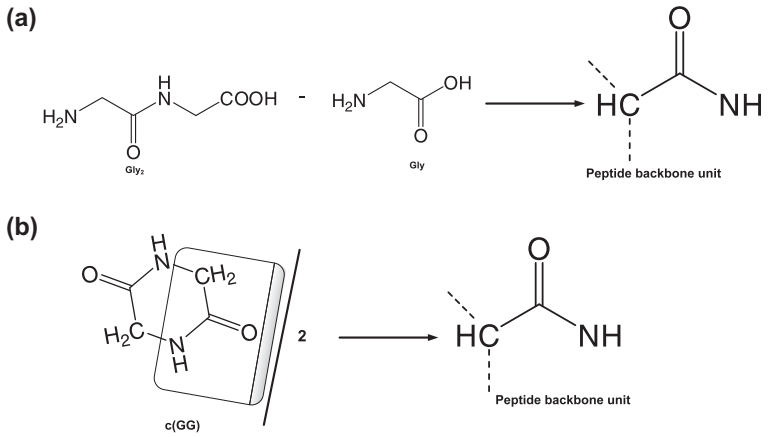
TABLE 2
Apparent transfer free energies $\Delta G'_{tr}$ of GPs from water to ammonium IL solutions (expressed in mass/mass) at T = 298.15 K.

Solvent	GP	$\Delta G'_{tr}$ (J · mol^{-1})		
TEAP		12.3%	19.0%	25.9%
	Gly	1405.46	2528.19	3827.63
	Gly_2	2492.33	4019.30	5750.15
	c(GG)	603.36	1037.03	1497.43
DEAS		11.3%	17.8%	23.9%
	Gly	2618.22	4684.19	6829.41
	Gly_2	1753.43	2985.19	4177.11
	c(GG)	1059.56	1861.34	2609.77
TEAS		12.1%	18.6%	24.6%
	Gly	1986.72	3622.48	5554.69
	Gly_2	1102.79	1815.84	2634.01
	c(GG)	1323.50	2248.56	3231.43

the $\Delta G'_{tr}$ values are positive for GPs from water to ammonium IL solutions at T = 298.15 K. We have observed that the $\Delta G'_{tr}$ values of GPs linearly increases with increasing concentration of ILs. The results show that there is unfavourable interaction between ILs and GPs that leads to stabilize the native structure of GPs.

The $\Delta G'_{tr}$ of the ILs for the simple Gly amino acid shows that DEAS is the powerful stabilizer, TEAS is moderate stabilizer, while TEAP is a week stabilizer. According to the Hofmister series we have $SO_4^{2-} > PO_4^-$ hence the sulfate ion has more stabilization tendency as compared to the phosphate ion group. We have observed the stability of Gly order as DEAS > TEAS > TEAP. The reason for the DEAS > TEAS is that, smaller cations have larger ion densities in the solvent, which in turn increase the number of anions on the surface of the GPs that results in stronger hydrogen bonding with the water molecules on the protein model surface, consequences in increasing the stability of Gly.

For Gly_2, the stability order is TEAP > DEAS > TEAS. As Gly_2 has more steric hindrance as compared to glycine, hence the ion radius is very important in this case for the stabilization of protein model compounds. According to Zhao [49], the ion radius of the SO_4^{2-} is ≈238 pm and that of $H_2PO_4^-$ is ≈240 pm, hence the SO_4^{2-} has more penetrating power as compared to $H_2PO_4^-$. This might be the reason why $H_2PO_4^-$ has a greater tendency to stabilize than SO_4^{2-}. The explanation for DEAS > TEAS is also same as illustrated above; therefore the order of stabilization of the Gly_2 are TEAP > DEAS > TEAS. In addition to this, $\Delta G'_{tr}$ value for c(GG) is TEAS > DEAS > TEAP, which is entirely different from the Gly_2, while there is some similarity in case of Gly. As in the case of c(GG), the Hofmister series plays a dominant role as $SO_4^{2-} > PO_4^-$ hence the sulfate ion has more stabilization tendency as compared to the phosphate ion group, whereas, the TEAS > DEAS mainly depends upon the nature of interaction between the both alkyl cation



SCHEME 1. Schematic illustration of determining the contribution of glycyl residue of (a) Glycine peptides and (b) c(GG).

TABLE 3
Transfer free energy (g'_{tr}) contribution of glycine residue of GPs from water to ammonium ILs (expressed in mass/mass) at T = 298.15 K.

Scheme	Solvent	$\Delta g'_{tr}$ /(J · mol^{-1})		
	TEAP	12.3%	19.0%	25.9%
1a		1086.87	1491.11	1922.52
1b		301.68	518.51	748.71
	DEAS	11.3%	17.8%	23.9%
1a		−864.78	−1699.00	−2652.30
1b		529.78	930.67	1304.88
	TEAS	12.1%	18.6%	24.6%
1a		−883.92	−1806.64	−2920.68
1b		661.75	1124.28	1615.71

and c(GG). These results emphasize that the stability order of the protein with ILs mainly depends upon the nature of ILs and proteins [23,50–53].

3.3. Transfer free energy ($\Delta g'_{tr}$) contribution of the glycyl residue from water to ammonium ILs solution

The transfer free energy ($\Delta g'_{tr}$) contribution of the peptide backbone unit (glycyl residue, –CH_2C═ONH–) is obtained as the difference between the values of $\Delta G'_{tr}$ corresponding to Gly and Gly_2 as a function of IL concentration [32-34]. The $\Delta g'_{tr}$ contribution of the glycyl residue is computed as the difference between

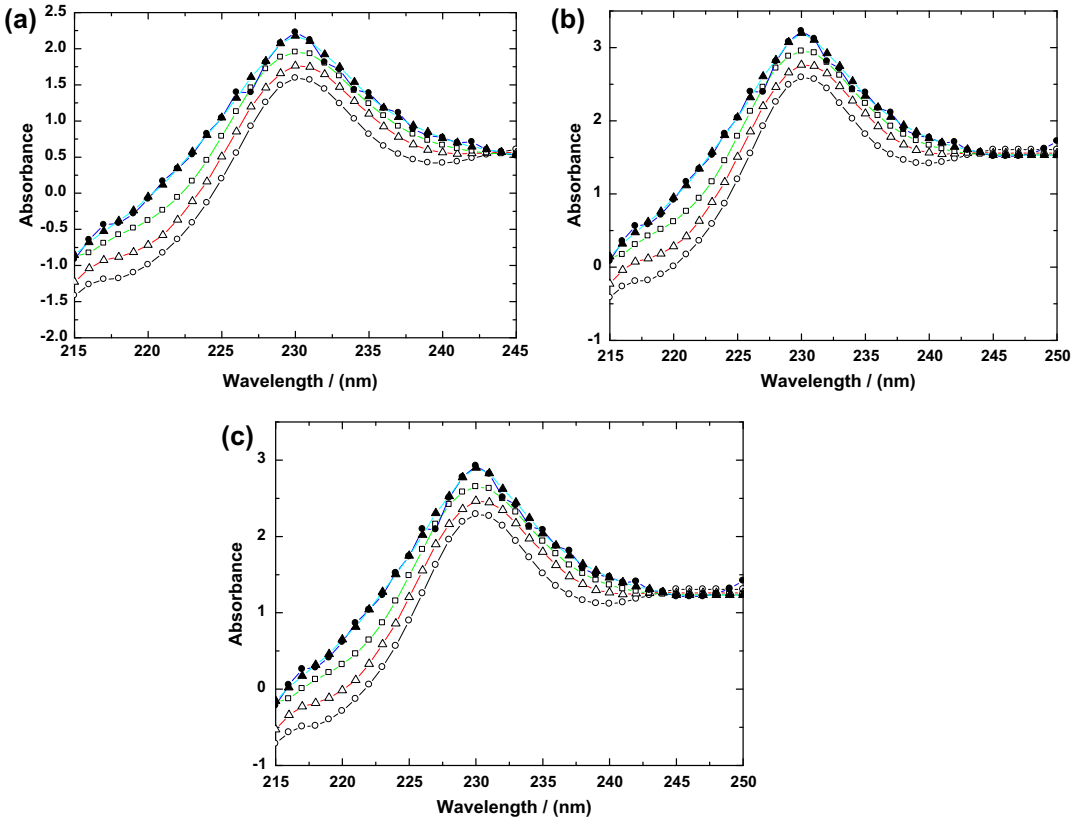


FIGURE 4. UV-vis spectra of Gly in (a) 12.3% of TEAP as function of Gly concentration: (○) = 12.0, (Δ) = 12.5, (□) = 12.8, (●) = 12.9, (▲) = 13.5; (b) 19.0% of TEAP as function of Gly concentration: (○) = 7.0, (Δ) = 7.2, (□) = 7.5, (●) = 7.6, (▲) = 7.8 and (c) 25.9% of TEAP as function of Gly concentration: (○) = 3.8, (Δ) = 4.0, (□) = 4.2, (●) = 4.3, (▲) = 4.6 at T = 298.15 K .

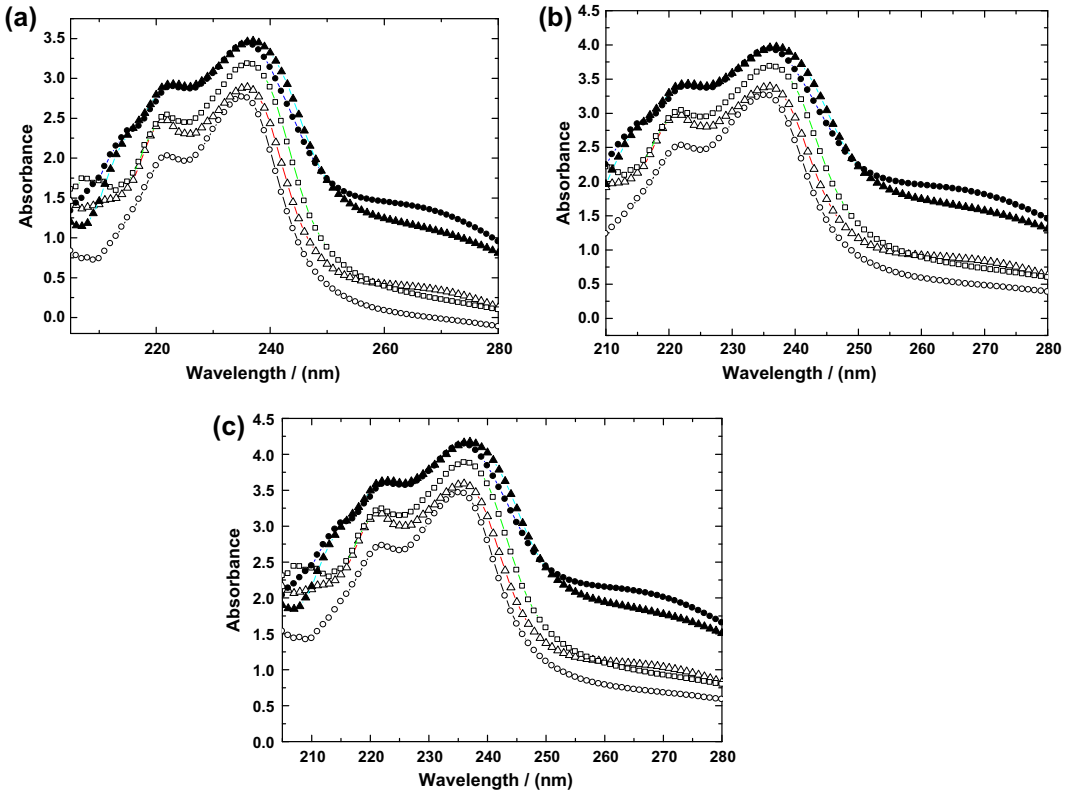


FIGURE 5. UV -vis spectra of Gly_2 in (a) 12.3% of TEAP as function of Gly_2 concentration: (○) = 6.5, (Δ) = 6.8, (□) = 7.0, (●) = 7.1, (▲) = 7.5; (b) 19.0% of TEAP as function of Gly_2 concentration: (○) = 3.0, (Δ) = 3.2, □ = 3.6, (●) = 3.7, (▲) = 4.1; (c) 25.9% of TEAP as function of Gly_2 concentration: (○) = 0.8, (Δ) = 1.5, □ = 1.7, (●) = 1.8, (▲) = 2.2 at T = 298.15 K.

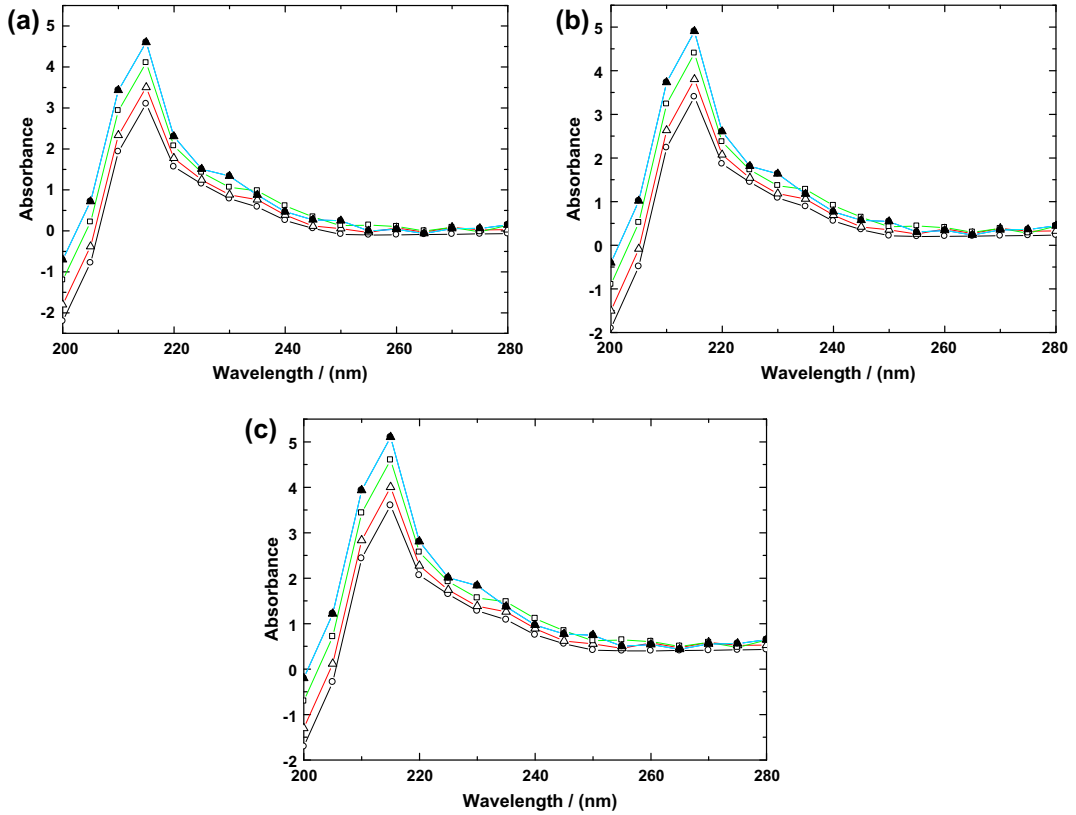


FIGURE 6. UV -vis spectra of c(GG) in (a) 12.3% of TEAP as function of c(GG) concentration: (○) = 1.0, (Δ) = 1.12, (□) = 1.20, (●) = 1.31, (▲) = 1.35; (b) 19.0% of TEAP as function of c(GG) concentration: (○) = 0.51, (Δ) = 0.72, (□) = 0.92, (●) = 1.04, (▲) = 1.12; (c) 25.9% of TEAP as function of c(GG) concentration: (○) = 0.41, (Δ) = 0.56, (□) = 0.76, (●) = 0.82, (▲) = 0.85 at T = 298.15 K.

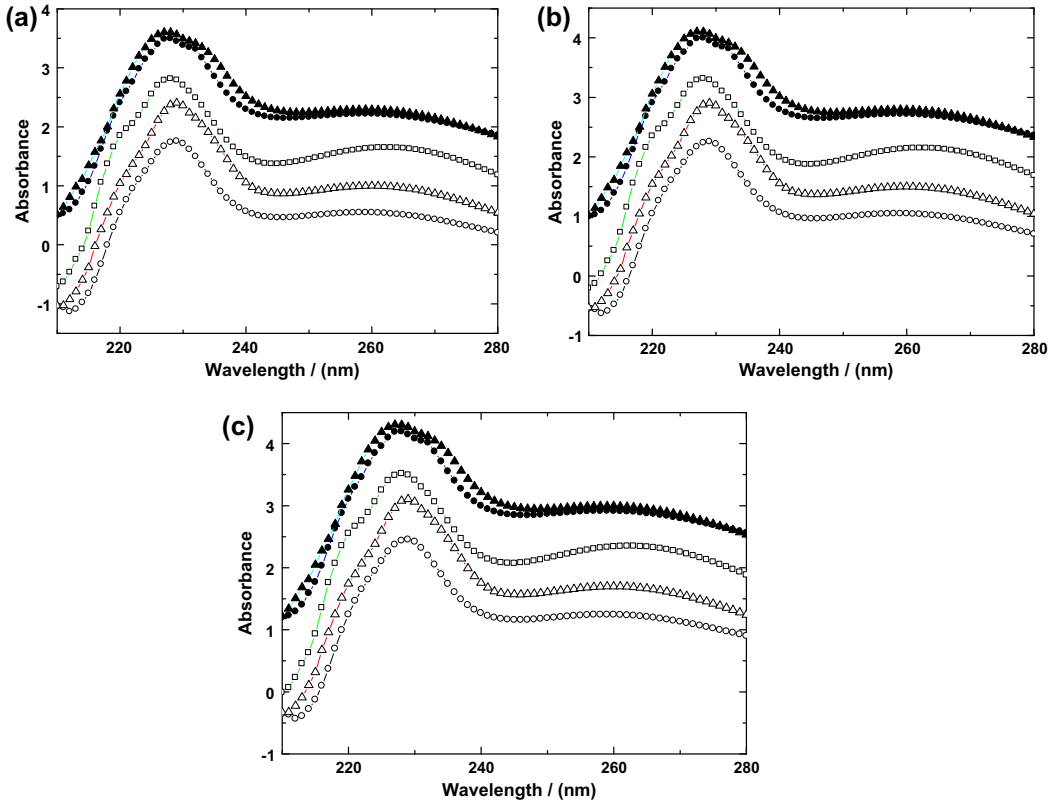


FIGURE 7. UV -vis spectra of Gly in (a) 11.3% of DEAS as function of Gly concentration: (○) = 6.5, (Δ) = 6.9, (□) = 7.1, (●) = 7.2, (▲) = 7.5; (b) 17.8% of DEAS as function of Gly concentration; (○) = 2.0, (Δ) = 2.2, (□) = 2.7, (●) = 2.8, (▲) = 3.2 (c) 23.9% of DEAS as function of Gly concentration: (○) = 0.5, (Δ) = 0.8, (□) = 1.0, (●) = 1.1, (▲) = 1.6 at T = 298.15 K.

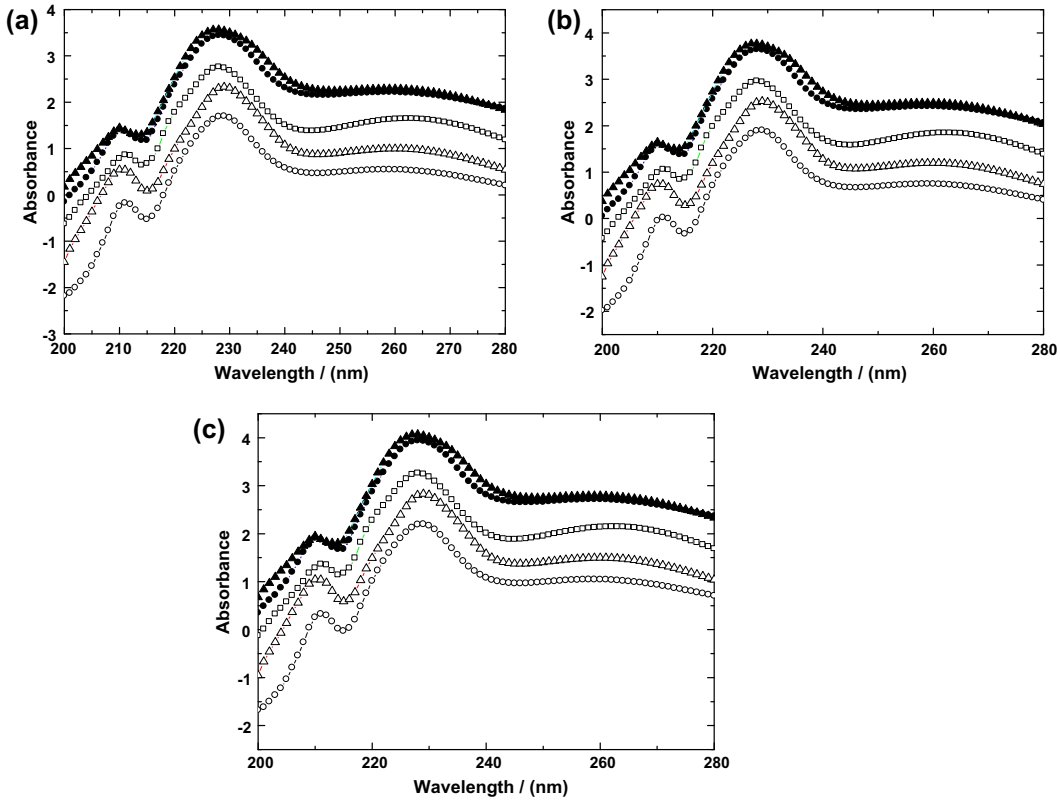


FIGURE 8. UV -vis spectra of Gly_2 in (a) 11.3% of DEAS as function of Gly_2 concentration:(○) = 9.0, (Δ) = 9.3, (□) = 9.6, (●) = 9.7, (▲) = 10.2; (b) 17.8% of DEAS as function of Gly_2 concentration: (○) = 4.8, (Δ) = 5.2, (□) = 5.4, (●) = 5.5, (▲) = 5.7; (c) 23.9% of DEAS as function of Gly_2 concentration: (○) = 2.8, (Δ)= 3.0, (□)= 3.2, (●) = 3.3, (▲) = 3.4 at T = 298.15 K.

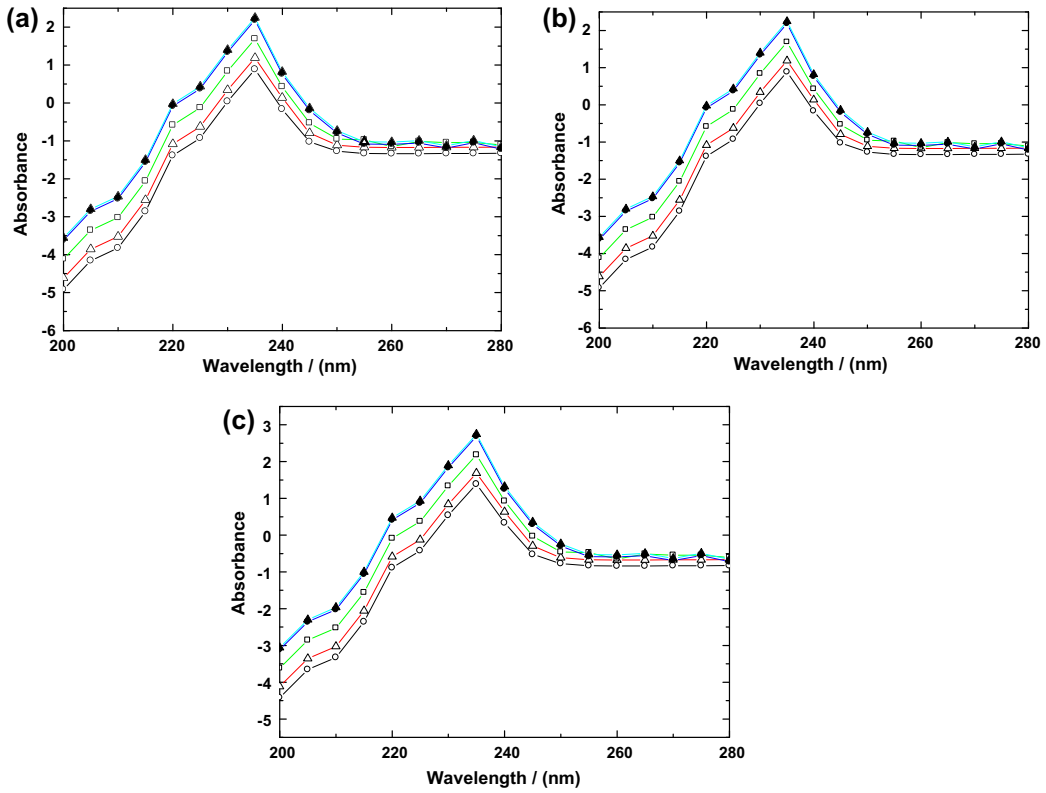


FIGURE 9. UV-vis spectra of c(GG) in (a) 11.3% of DEAS as function of c(GG) concentration: (○) = 0.52, (Δ) = 0.71, (□) = 0.96, (●) = 1.09, (▲) = 1.12; (b) 17.8% of DEAS as function of c(GG) concentration: (○) = 0.31, (Δ) = 0.42, (□) = 0.64, (●) = 0.73, (▲) = 0.84; (c) 23.9% of DEAS as function of c(GG) concentration: (○) = 0.25, (Δ) = 0.37, (□) = 0.43, (●) = 0.52, (▲) = 0.61 at T = 298.15 K.

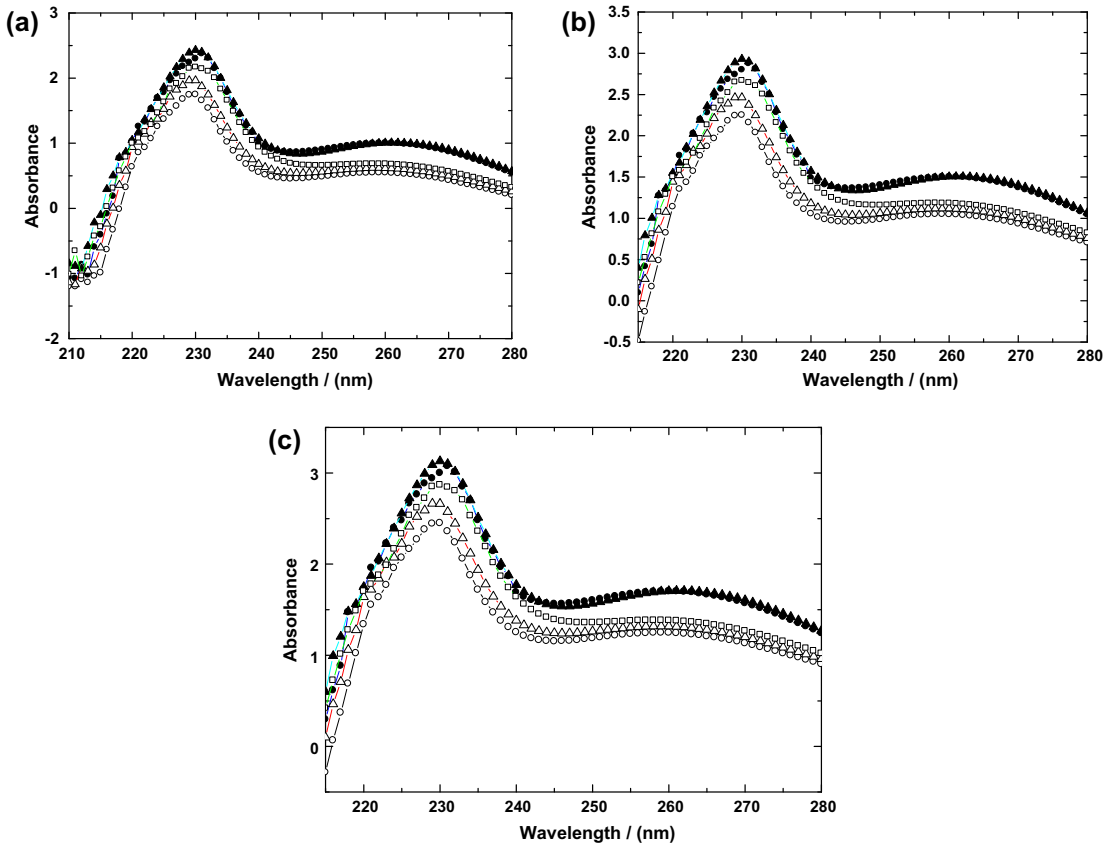


FIGURE 10. UV -vis spectra of Gly in (a) 12.1% of TEAS as function of Gly concentration: (○) = 9.0, (Δ) = 9.3, (□) = 9.7, (●) = 9.8, (▲) = 10.2; (b) 18.6% of TEAS as function of Gly concentration: (○) = 4.0, (Δ) = 4.2, (□) = 4.7, (●) = 4.8, (▲) = 5.0; (c) 24.6% of TEAS as function of Gly concentration: (○) = 1.2, (Δ) = 1.5, (□) = 1.9, (●) = 2.0, (▲) = 2.5 at T = 298.15 K.

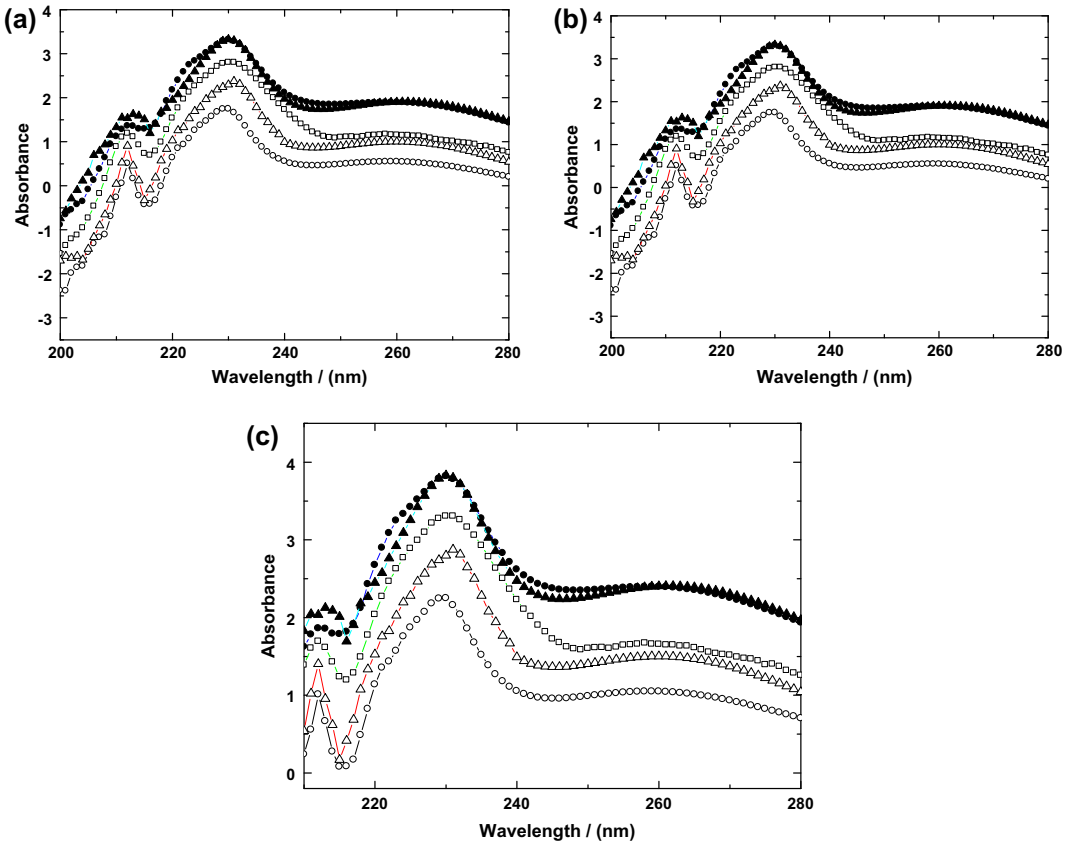


FIGURE 11. UV -vis spectra of Gly_2 in (a) 12.1% of TEAS as function of Gly_2 concentration: (○) = 11.5, (Δ) = 11.8, (□) = 12.2, (●) = 12.3, (▲) = 12.5; (b) 18.6% of TEAS as function of Gly_2 concentration: (○) = 8.0, (Δ) = 8.2, (□) = 8.6, (●) = 8.7, (▲) = 9.0; (c) 25.6% of TEAS as function of Gly_2 concentration: (○) = 4.8, (Δ) = 5.3, (□) = 5.6, (●) = 5.7, (▲) = 6.1 at T = 298.15 K.

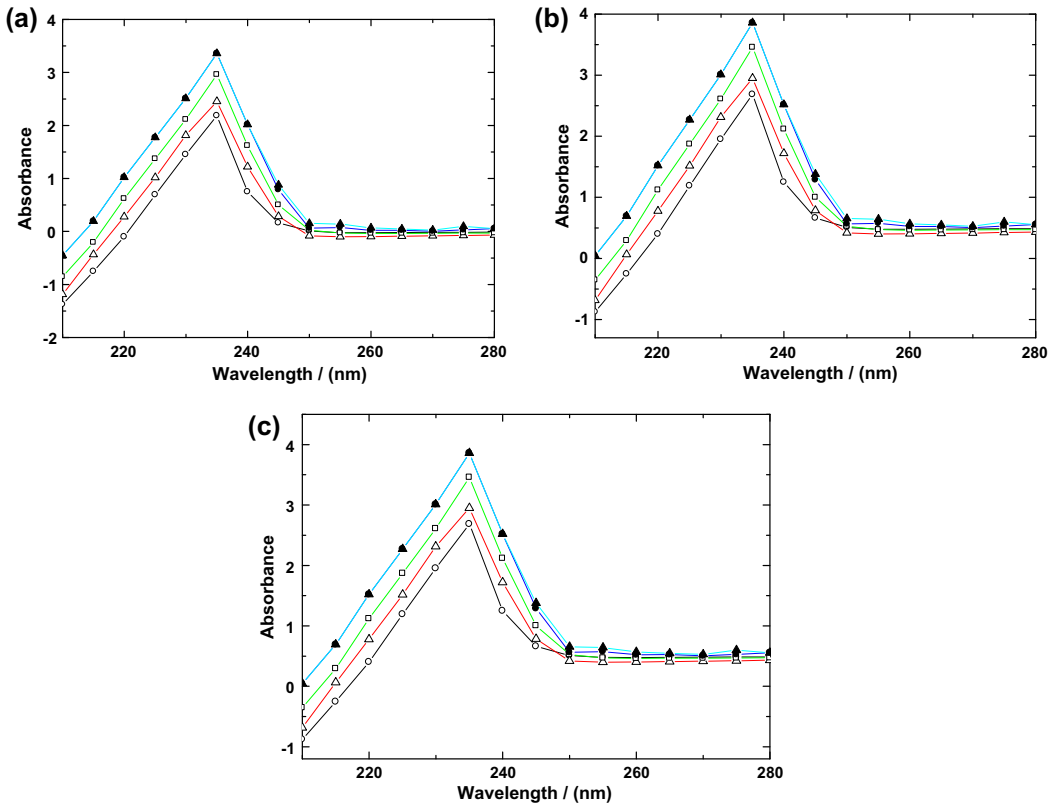


FIGURE 12. UV-vis spectra of c(GG) in (a) 12.1% of TEAS as function of c(GG) concentration: (○) = 0.42, (Δ) = 0.57, (□) = 0.73, (●) = 0.98, (▲) = 1.12; (b) 18.6% of TEAS as function of c(GG) concentration: (○) = 0.30, (Δ) = 0.41, (□) = 0.57, (●) = 0.65, (▲) = 0.71; (c) 24.5% of TEAS as function of c(GG) concentration: (○) = 0.10, (Δ) = 0.21, (□) = 0.35, (●) = 0.40, (▲) = 0.45 at T = 298.15 K.

the values of $\Delta G'_{tr}$ for Gly_2 and Gly, as shown in Scheme 1a. The evaluated $\Delta g'_{tr}$ values for the glycyl residue are collected in Table 3 at various IL concentrations. The results obtained in table 3 reveal that the $\Delta g'_{tr}$ values for the glycyl residue from water to TEAP are positive at all concentrations and obviously increase with increasing TEAP concentrations. In other words, glycine residue has a negative contribution for TEAS and DEAS at all concentrations of these ILs investigations. The positive contribution indicates that TEAP is a stabilizer while negative values attribute that TEAS and DEAS are destabilizers for glycine residue of glycine peptides. The TEAP exhibits unfavourable interactions with glycine residue whereas the other two ILs favourably interacts with this residue.

Further, we have used scheme 1b to evaluate the IL dependences of $\Delta g'_{tr}$ contribution of glycyl residue from the $\Delta G'_{tr}$ values of c(GG) model compound [54]. The results of these predicted $\Delta g'_{tr}$ from scheme 1b are also included in table 3. The $\Delta g'_{tr}$ values are positive for peptide backbone unit of c(GG) from water to the studied IL solutions; this contribution increases with increasing IL concentrations. Therefore, ILs interact unfavourably with the glycyl residue of c(GG). We have observed larger positive $\Delta g'_{tr}$ values for this residue in the presence of TEAS at all concentrations (for example, 661.75 $J \cdot mol^{-1}$ for 12.1% (m/m) TEAS), which indicates that TEAS acts as a strong stabilizer. Our data clearly indicate that DEAS is a moderate stabilizer (for example, 529.78 $J \cdot mol^{-1}$ for 11.3% (m/m) DEAS) while TEAP is a poor stabilizer (for example, 301.68 $J \cdot mol^{-1}$ for 12.3% (m/m) TEAP) for peptide backbone unit, glycyl residue.

3.4. UV-vis spectrophotometer

To address the effect of ILs on Gly, Gly_2, and c(GG) in detail, we have further explored the absorbance of the GPs as a function of IL concentration at close to, below and above the solubility limits in ILs by the UV-vis spectrophotometer. The UV-vis spectra of GPs are reported in figures 4 to 12 as function of ILs concentration at $T = 298.15$ K. The results in figure 4 show that only one peak is observed at ≈230 nm in TEAP at 12.3%, 19.0% and 25.9% in Gly. In this case, there is an increase in the absorption intensity with increase in the concentration of TEAP. Furthermore, we have observed the flattening of the absorption spectra band and this band significantly depends upon the concentration, and on the type of the GP used in the solution. Moreover, the results in figure 5a show that two peaks are observed at ≈220 and ≈230 nm for 6.5 g per 100 g of Gly_2 in TEAP 12.3% concentration. In the case of c(GG), the similar trend is followed as in the case of Gly which is shown in figure 6. The absorption band at ≈210 nm is observed in TEAP at 12.3%, 19.0% and 25.9% and at higher concentration near solubility limit, we have observed the flattening of the band.

We have used the various concentrations of DEAS or TEAS on Gly and Gly_2 to observe the change in the absorption band. The results in Figures 7, 8, 10 and 11 show that UV-vis spectrophotometer data for the Gly and Gly_2 is consistent with the solubility limits. In the case of Gly_2 in DEAS, one peak is observed slightly at ≈210 nm and another peak is observed at ≈230 nm (figure 8). Whereas, in the case of Gly in TEAS, we have observed a single peak at ≈230 (figure 9), while for Gly_2 for the same IL observed two peaks at ≈210 nm and ≈230 (figure 11). In the case of c(GG) in 11.3, 12.1 and 12.3% (m/m) respectively for DEAS, TEAS and TEAP, we have observed the flattening of the band at 1.09, 0.980, and 1.31 g, that is also well consistent with our $\Delta G'_{tr}$ data (Figures 6, 9 and 12). The results observed reveal that there is no change in the wavelength of the absorption spectra with addition of ILs to the sample; this reveals that the native structure of GPs are not disturbed by these studied ILs at all concentrations.

4. Conclusions

In this article, the interactions between glycine peptides: Gly, Gly_2, c(GG), and ILs: TEAP, DEAS, and TEAS are explored on the basis of solubility data. We have obtained the apparent transfer free energies ($\Delta G'_{tr}$) of GPs from water to ILs solutions from the solubility limits. Moreover, we have obtained the transfer free energies ($\Delta g'_{tr}$) of the peptide backbone unit contributions from the corresponding $\Delta G'_{tr}$ values of GPs. Our results clearly indicate that all ILs are biocompatible co-solvent for GPs and can stabilize the GP structures through unfavourable interactions between GP and IL. Our experimental data illustrate that there is no symmetry in ILs for the stability of GPs such as Gly, Gly_2 and c(GG). Hence the stability of GPs depends upon the nature of both GPs as well as ILs.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jct.2012.07.009.

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