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Study of some Thermodynamic Properties of Vitamin B3 in Aqueous Deep Eutectic Solvent Solutions at T = (288.15 to 318.15) K

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Deep eutectic solvents (DESs), known for their eco-friendliness and innovative qualities, have shown promise for use in drug systems. This study aims to investigate experimentally some thermodynamic properties of solutions formed by vitamin B3 in aqueous deep eutectic solvent by the measurements of the speed of sound and density (accuracy in speed of sound and density measurements with values of 1 m s^{-1} and 0.05 kg m^{-3}). DESs included (choline chloride/malonic acid (ChCl/MA (1:1)), choline chloride/oxalic acid (ChCl/OA (1:1)), choline chloride/ethylene glycol (ChCl/EG (1:2)), and choline chloride/glycerol (ChCl/G (1:2)) in aqueous solutions across a temperature range of (288.15 to 318.15) K. By utilizing the Redlich-Meyer equation and correlating apparent molar volume ($V\phi$) and apparent molar isentropic compressibility (κ_φ) values, several key parameters including standard partial molar volume (V_φ^0), and partial molar isentropic compressibility (κ_φ^0) were determined. Furthermore, apparent molar isobaric expansion (E_φ^0), and Hepler's constant were computed from these derived parameters. Additionally, Hansen solubility parameters were calculated to predict the solubility of the drug within the solvent medium. Overall, the results suggest a substantial interaction between vitamin B3 and the ChCl/MA system.

Keywords: Nicotinic acid (vitamin B3), Deep eutectic solvents, Standard partial molar volume, Partial molar isentropic compressibility, Hansen solubility parameter

INTRODUCTION

Nicotinic acid (vitamin B3), commonly known also as niacin, is an imperative compound with multiple physiological impacts involving various systems, biosynthesis, metabolic reactions, therapeutic fields, and several drug preparations [1]. In addition, it finds widespread applications as an important factor in the repairing of Vit B3, healthy skin, proper functioning of the nervous system, and an additive in food, cosmetics, and forage [2,3]. Plasma triglyceride levels and density lipoprotein cholesterol (LDL-c) were also lower in the presence of Vit B3, which causes the increase in the levels of high-density lipoprotein cholesterol (HDL-c) [4,5].

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Given that a majority of biological processes occur in aqueous environments, and hydration is a critical factor in biological systems, comprehending the precise roles and mechanisms of action of vitamins can be a complex endeavor. One approach to shedding light on these complexities is to investigate the thermophysical properties of vitamins in fluids, particularly in aqueous media, with a focus on variations in solvation or hydration layers. These variations are crucial factors influencing numerous biological structures and processes, especially in the presence of co-solvents. Conducting thermodynamic analyses of such systems yields valuable insights into drug-cosolvent interactions across various domains. Exploring volumetric, ultrasonic, and related parameters allows us to elucidate the interplay between drugs and solvents. This knowledge, in turn, can inform the design of innovative drug systems with

applications in the field of pharmacy.

Deep eutectic solvents (DESs), ionic liquids (ILs), and organic solvents are the three main types into which co-solvents can be divided. Organic solvents, commonly used in numerous systems, often possess characteristics such as volatility, toxicity, and flammability. On the other hand, ILs represent a class of salts that hold promise as innovative solvents and for various other applications. Nevertheless, this category of solvents tends to be expensive and challenging to prepare [6,7]. Over the past decade, deep eutectic solvents (DESs) have garnered significant attention across various scientific disciplines due to their distinctive properties, which encompass biodegradability, biocompatibility, cost-effectiveness, and a straightforward preparation process [7,8]. These solvents are often described as clear, homogenous liquids that are produced via the combination of two or more chemicals that develop strong intermolecular contacts, one of which functions as a hydrogen bond donor (HBD) and the other as an acceptor of hydrogen bonds (HBA) [9].

In this context, the influence of deep eutectic solvents (DESs) as innovative co-solvents on the behavior of biological compounds stands as a crucial matter within the realm of physical chemistry. The study of volumetric and acoustic properties has been firmly established as a valuable method for investigating the intermolecular interactions between solute and solvent molecules in fluid systems [10-13]. Physicochemical and thermodynamic studies help clarify the complex nature of molecular interactions and the different kinds of interactions that take place in mixtures [14,15]. However, the existing literature contains limited information regarding the physical properties of aqueous solutions of Vitamin B3 in the presence of deep eutectic solvents (DESs).

This work focuses on study the Vit B3 in water and (DESs + water) systems. Four choline chloride-based (ChCl) DESs including ChCl/ethylene glycol (EG), ChCl/glycerol (G), ChCl/malonic acid (MA) and ChCl/oxalic acid (OA) were selected to investigate the Vit B3 behavior in DESs aqueous solutions using density and speed of sound measurements. The experimentally obtained data has been employed to calculate various derived thermodynamic parameters. These thermophysical parameters encompass the apparent molar volume (V_φ), standard partial molar volume (V_φ^0), apparent molar isentropic compressibility (κ_φ), and standard partial isentropic compressibility κ_φ^0 values. Furthermore, Hansen solubility parameters (HSP) were employed to assess the interactions of Vitamin B3 in the solvent medium. These parameters are valuable for predicting solvent performance in manufacturing processes and can offer insights into solvent behavior in various other domains of endeavor. The derived parameters were utilized to investigate the influence of deep eutectic solvents (DESs) on the interactions between Vitamin B3 and the solvent systems.

EXPERIMENTAL

2. Chemicals

The materials used in this study included glycerol, ethylene glycol, oxalic acid, malonic acid, nicotinic acid, choline chloride, and absolute ethanol. For detailed information about these materials, please refer to Table 1.

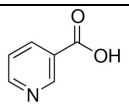
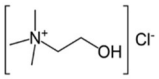
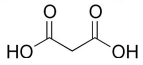
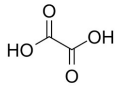
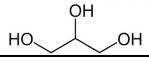
Preparation of the DESs

The two components (HBA and HBD) were combined in a glass vessel that was jacketed and had a mechanical stirrer. The stirrer was operated at 350 rpm and 353.15 K to create a homogenous liquid phase that was free of solid particles. This process was used to manufacture the deep eutectic solvents (DESs) for this study. The DESs investigated in this research were formulated using the following molar ratios: ChCl/MA (1:1), ChCl/OA (1:1), ChCl/G (1:2), and ChCl/EG (1:2) [16]. The HNMR spectra depicted in Figs. S-1, S-2, S-3, and S-4 (provided in the supporting information) demonstrate the successful synthesis of these DESs.

Apparatus and Procedure

Using an uncertainty of ± 0.1 mg, the solutions with different molalities were created using the AW 220 Shimadzu balance (GR220, Japan). The binary solution of Vitamin B3 in water covered a molality range from m = 0.0000 to 0.1791 mol kg^{-1} and was prepared using freshly distilled water. Ternary aqueous solutions with different molalities of Vitamin B3 were created by incorporating the specified DESs (ChCl/MA, ChCl/OA, ChCl/G, and ChCl/EG) listed in Table 2.

Table 1. A summary of the Used Chemicals

Chemical name	Abbreviation	Supplier	CAS No.	Mass fraction (purity)	Structure
Nicotinic acid	Vit B3	Merck	59-67-6	>0.99	
Choline chloride	ChCl	Merck	67-48-1	>0.99	
Malonic acid	MA	Merck	141-82-2	>0.99	
Oxalic acid	OA	Merck	144-62-7	>0.99	
Ethylene glycol	EG	Merck	107-21-1	>0.99	
Glycerol	G	Merck	56-81-5	>0.99	

The suppliers were provided with the purities of the used components.

The produced solutions were kept in sealed containers to avoid moisture contamination. The solutions were mixed for ten minutes at room temperature before measurements were taken. The quantity of the medication per kilogram of solvent (water or combinations of DES and water) is known as the molality of vitamin B3. Next, using a high-precision vibrating tube digital densimeter, the DSA 5000 (Anton Paar, Austria), running at a frequency of around 3 MHz, the density and sound speed in the produced solutions were measured experimentally. The sensitivity of the DSA 5000 allowed for accuracy in density and speed of sound measurements, with values of 0.05 kg m^{-3} and 1 m s^{-1}, respectively.

RESULTS AND DISCUSSION

Density and Speed of Sound Results

To determine the apparent molar volumes of Vit B3 across various molalities (0.50, 1.00, and 1.50 mol kg^{-1}) within ternary solutions consisting of (ChCl/MA, ChCl/OA, ChCl/EG, ChCl/G), we conducted experiments to measure the density, denoted as d, at various temperatures (T = 288.15 to 318.15 K) as detailed in Table S-I. In these systems, Vit B3 serves as the solute, while DESs act as co-solvents. Table S-I presents the experimental data, which reveals a decrease in system densities at elevated temperatures. The calculation of apparent molar volumes, V_φ, involves utilizing the experimentally determined density data in the following equation:

$$V_\varphi = \frac{M}{d} - \left[\frac{(d - d_0)}{m d d_0}\right] \quad (1)$$

in this equation, the symbol denoting apparent molar volume is V_φ, where M stands for the solute's molality, d_0 and d for the solute's density and the solvent's density (kg m^{-3}) of the ternary solution under study, respectively. Table S-I provides a list of calculated apparent molar volume values, clearly demonstrating an increase in magnitude with rising temperature and molality of DESs. These positive values of V_φ indicate stronger solute-solvent interactions.

In addition, the standard partial molar volume V_φ^0 was adequately correlated by using the Redlich-Meyer polynomial equation as follows [29]:

$$V_\varphi = V_\varphi^0 + B_v m \quad (2)$$

The symbol B_v represents a parameter within the equation. We employed a least-squares analysis to determine the values of this parameter, and the results are provided in Table 3. The

Table 2. Common Properties of DESs Used in this Work at Different Temperatures and 871 hPa[a]

DES designation	Molar ratio of liquid solutions	Melting Point (K)	Water mass fraction percent	Molar mass (g mol^{-1})[a]	T (K)	10^{-3} d (kg·m^{-3}) (exp)	10^{-3} d (kg m^{-3}) (Lit)	u (m s^{-1}) (exp)	u (m s^{-1}) (Lit)
ChCl/EG	1.00:2.00	207.15	0.05%	87.921	293.15	1.119560	1.1171 [17]	1920.22	
					298.15	1.115745	1.1174 [18]	1909.74	1911.04 [20]
							1.1184 [19]		
					303.15	1.112824	1.1145 [18]	1897.56	
							1.1114 [17]		
					308.15	1.109846	1.1109 [21]	1886.14	
							1.1116 [18]		
ChCl/MA	1.00:1.00	243.68	0.02%	121.842	293.15	1.228541	1.1851 [17]	1942.81	
							1.234 [22]		
					298.15	1.225823	1.231 [22]	1929.56	1962.69 [23]
									1912.14 [24]
					303.15	1.222756	1.1786 [17]	1915.78	
							1.228 [22]		
					308.15	1.219645	1.224 [22]	1902.82	
ChCl/OA	1.00:1.00	229.65	0.26%	114.828	293.15	1.210321	1.205 [22]	1932.42	
					298.15	1.206612	1.202 [22]	1918.95	1925.00 [23]
					303.15	1.203489	1.199 [22]	1905.75	
					308.15	1.200123	1.195 [22]	1895.23	
ChCl/G	1.00:2.00	233.15	0.13%	107.937	298.15	1.186564	1.1920 [25]	2012.48	2012.59 [23]
							1.19085 [26]		
							1.181 [27]		
							1.19575 [28]		2001.29 [28]
					303.15	1.183645	1.1895 [25]	2001.17	2080 [27]
							1.18807 [28]		
							1.19290 [28]		1990.23 [28]
					308.15	1.180879	1.1867 [25]	1989.99	
							1.18528 [26]		
							1.19015 [28]		1979.24 [28]
					313.15	1.178231	1.1838 [25]	1978.85	1976 [27]
							1.18249 [28]		
							1.18740 [28]		1968.30 [28]
					318.15	1.175512	1.1814 [25]	1967.74	
							1.17970 [26]		
							1.18465 [28]		1957.38 [28]

Standard uncertainties (u) for each variable are u (T) = 0.001 K; u (p) = 10 hPa. The combined standard uncertainty for the average of n density measurements u (ρ) = 0.05 g cm^{-3} and speed of sound u (u) = 1 m s^{-1}. Standard uncertainty (u) for DESs composition was estimated to be less than $5 \cdot 10^{-2}$ mole ratio. Standard uncertainty (u) for water content was estimated to be less than %0.02.

[a]Molar mass of DESs = x_1 M_1 + x_2 M_2. x_1 and M_1; mole fraction and molar mass of ChCl. x_2 and M_2; mole fraction and molar mass of HBD.

The melting point is expressed for the solidus (formation of the first liquid) or liquids (disappearance of last crystals).

The density and speed of sound were measured for the liquid state of the prepared DESs.

values of V_φ^0 and B_v represent interactions within the systems, respectively. It is widely recognized that hydrophilic-hydrophilic interactions contribute positively to V_φ^0 and B_v, while hydrophobic-hydrophobic and hydrophobic–hydrophilic interactions have a negative impact [30]. The positive values of V_φ^0 for Vit B3, as shown in Table 3, indicate the presence of ion–dipole interactions between solute and solvent molecules, contributing positively to V_φ^0.

Figure 1 presents 2-D plots depicting the variation of V_φ^0 with temperature for the studied systems at a DES molality of 1 mol kg^{-1}. It is evident that the V_φ^0 values increase at elevated temperatures and molality levels of DESs. Specifically, for Vit B3, the V_φ^0 value is notably higher in the presence of ChCl/MA compared to the other investigated DESs.

The introduction of DES increases the V_φ^0 values, signifying robust interactions within these systems. The functional groups within the HBD section of the employed DESs each contribute to drug interactions. In the case of ChCl/MA, its two COOH functional groups (which exhibit less intramolecular interaction compared to oxalic acid) may be a significant factor in establishing stronger interactions with the COOH group of Vit B3, as opposed to the other DESs. To gain a deeper understanding of these interactions, further investigation through spectroscopic studies, molecular dynamic simulations, and computational studies is essential in identifying the dominant functional groups involved in the interaction between Vit B3 and DESs.

In addition, a comparison of V_φ^0 data for aqueous Vit B3 solutions with available literature data was given in Fig. 2. There is good agreement between the experimental and reported data in the literature [31,32].

Another essential property is the partial molar transfer $\Delta_{tr}V_\varphi^0$, which provides insights into the interactions between the solute and co-solvent. The $\Delta_{tr}V_\varphi^0$ values for Vit B3 in both binary and ternary solutions have been calculated as follows:

$$\Delta_{tr}V_\varphi^0 = V_{\varphi\,(\text{In ternary DES solution})}^0 - V_{\varphi\,(\text{in water})}^0 \qquad (3)$$

The transfer volume ($\Delta_{tr}V_\varphi^0$) values have been documented in Table 3.

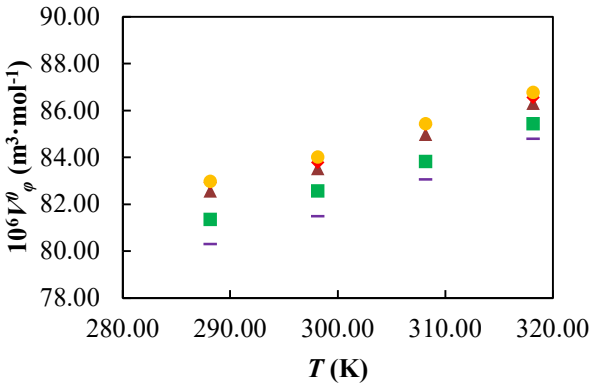


Fig. 1. The comparison of the standard partial molar volumes, V_ϕ^0, of Vit B3 in binary and ternary aqueous DESs solutions (1.00 mol kg^{-1}) at different temperatures; (-), binary solution; (■), ChCl/G; (▲), ChCl/EG; (♦), ChCl/OA; (●), ChCl/MA.

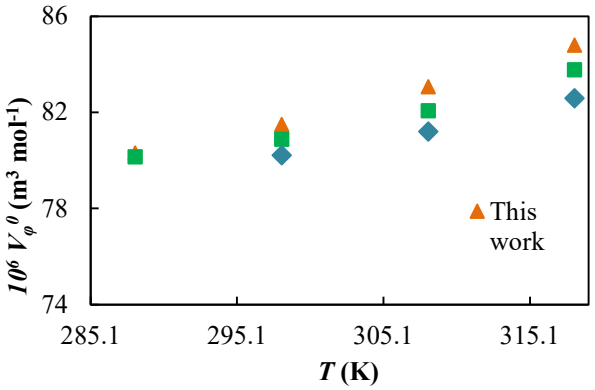


Fig. 2. The comparison of the standard partial molar volumes, V_ϕ^0, of Vit B3 in water (experimental and reported data) at different temperatures.

The cosphere overlap model proposes several kinds of interactions between the solute and the co-solvent, as follows, in line with the model created by Friedman and Krishnan [33,34].

(i) The ion-ion interactions might take place between Vit B3's carboxylate groups and the ions inside the DESs.

(ii) The ion-hydrophobic interactions are the interactions that are seen between the hydrophobic part of vitamin B3 and the ions that are included inside the DESs.

Table 3. Standard Partial Molar Volumes, V_{φ}^{0}, $\Delta_{tr} V^{0}_{\varphi}$, the Experimental Parameter $B_{v,}$ and the Corresponding Standard Deviations $\sigma(V_{\varphi})$ for Vit B3 in Solvents Contain (Water and Water + DESs) at T = (288.15 to 318.15) K and at Ambient Pressure (P = 871 hPa)

T (K)	$10^6 V^0_{\varphi}$ (m^3 mol^{-1})	$10^6 B_v$ (m^3 g mol^{-2})	$10^6 \Delta_{tr} V^0_{\varphi}$ (m^3 mol^{-1})	$\sigma(V_{\varphi})$
		Vit B3 in water		
288.15	80.30	17.16	-	0.24
298.15	81.49	22.28	-	0.27
308.15	83.06	16.64	-	0.17
318.15	84.79	13.57	-	0.15
		Vit B3 in 0.50 mol kg^{-1} aqueous ChCl/G solution		
288.15	80.44	24.44	0.14	0.06
298.15	81.78	28.20	0.29	0.06
308.15	83.23	32.66	0.17	0.14
318.15	85.01	30.61	0.22	0.10
		Vit B3 in 1.00 mol kg^{-1} aqueous ChCl/G solution		
288.15	81.35	35.18	1.05	0.06
298.15	82.57	33.46	1.08	0.03
308.15	83.83	33.52	0.77	0.07
318.15	85.44	26.62	0.65	0.06
		Vit B3 in 1.50 mol g^{-1} aqueous ChCl/G solution		
288.15	82.82	21.41	2.52	0.13
298.15	83.72	25.08	2.23	0.07
308.15	84.93	23.57	1.87	0.07
318.15	86.17	22.96	1.38	0.11
		Vit B3 in 0.50 mol kg^{-1} aqueous ChCl/EG solution		
288.15	80.97	18.39	0.67	0.07
298.15	82.45	21.78	0.96	0.13
308.15	84.09	24.87	1.03	0.06
318.15	85.98	22.26	1.19	0.07
		Vit B3 in 1.00 mol kg^{-1} aqueous ChCl/EG solution		
288.15	82.57	20.45	2.27	0.04
298.15	83.53	25.55	2.04	0.09
308.15	84.99	20.83	1.93	0.05
318.15	86.31	18.01	1.52	0.07
		Vit B3 in 1.50 mol kg^{-1} aqueous ChCl/EG solution		
288.15	83.87	10.01	3.57	0.08
298.15	84.47	20.10	2.98	0.05
308.15	86.38	7.78	3.32	0.08
318.15	87.31	11.08	2.52	0.09
		Vit B3 in 0.50 mol kg^{-1} aqueous ChCl/OA solution		
288.15	81.53	18.48	1.23	0.11
298.15	83.31	13.95	1.82	0.07
308.15	84.34	24.17	1.28	0.12
318.15	86.46	21.83	1.67	0.05
		Vit B3 in 1.00 mol kg^{-1} aqueous ChCl/OA solution		
288.15	82.93	17.30	2.63	0.07
298.15	83.78	24.88	2.29	0.16
308.15	85.39	18.78	2.33	0.08
318.15	86.56	23.63	1.77	0.09
		Vit B3 in 1.50 mol kg^{-1} aqueous ChCl/OA solution		
288.15	84.09	14.67	3.79	0.10
298.15	84.88	21.55	3.39	0.17
308.15	86.43	20.47	3.37	0.05
318.15	87.51	17.85	2.72	0.04

Table 3. Continued

	Vit B3 in 0.50 mol kg^{-1} aqueous ChCl/MA solution			
288.15	81.95	17.01	1.65	0.06
298.15	83.41	19.60	1.71	0.03
308.15	84.74	17.84	1.68	0.03
318.15	86.52	23.38	1.73	0.05
	Vit B3 in 1.00 mol kg^{-1} aqueous ChCl/MA solution			
288.15	82.98	18.61	2.68	0.05
298.15	84.02	22.34	2.53	0.02
308.15	85.44	20.06	2.38	0.05
318.15	86.77	22.13	1.98	0.05
	Vit B3 in 1.50 mol kg^{-1} aqueous ChCl/MA solution			
288.15	84.41	12.60	4.11	0.15
298.15	85.40	15.59	3.91	0.05
308.15	86.62	20.05	3.56	0.07
318.15	87.87	14.35	3.08	0.10

Standard uncertainties (u) for each variable are u (T) = 0.001 K; u (p) = 1.5 kPa. Standard uncertainty (u) for DESs composition was estimated to be less than $5 \cdot 10^{-2}$ mole ratio. The Vit B3 molality was defined as; mole of drug per kg of solvent ((water) and (DES + water mixtures)).

(iii) Hydrophobic-hydrophobic interactions occur between the drug's organic portion and the DESs.

(iv) Interactions between the drug's hydrophobic group and the hydrophilic end of the DESs are known as hydrophobic-hydrophilic interactions.

The cosphere overlap model shows that ion-ion and ion-hydrophilic interactions are more important than hydrophobic-hydrophobic and ion-hydrophobic interactions, as all of the obtained values for our systems at all temperatures are positive.

The below-mentioned polynomial equation shows the variation of V_φ^0 with temperature [35]:

$$V_\varphi^0 = A + BT + CT^2 \quad (4)$$

In Eq. (4), A, B, and C represent the parameters for the V_φ^0 values, determined through least-squares analysis. The resulting parameter values are presented in Table 4.

Taking the derivative with respect to temperature in Eq. (4) allows for the calculation of the apparent molar isobaric expansion E_φ^0:

$$E_\varphi^0 = \left(\frac{\partial V_\varphi^0}{\partial T}\right)_p = B + 2CT \quad (5)$$

Table 5 reports the apparent molar isobaric expansion data that were so computed from the aforementioned equation, and Fig. 3 shows the data visually. The analysis of Fig. 3 illustrates the variation of E_φ^0 *versus* the temperature for investigated systems at molality 1 (mol kg^{-1}) of DESs. In the present case, E_φ^0 values are positive which suggests that active interactions exist between the Vit B3 and aqueous DES solutions.

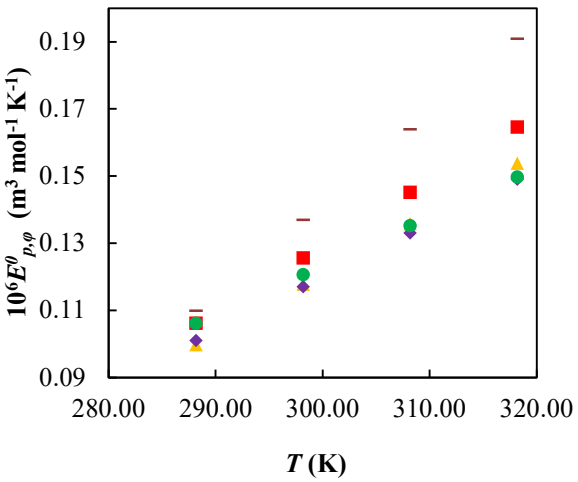


Fig. 3. The comparison of the apparent molar isobaric expansions, E^0_φ of Vit B3 in binary and ternary aqueous DESs solutions (1.00 mol·kg^{-1}) at diferent temperatures; (-), binary solution; (■), ChCl/G; (▲), ChCl/EG; (♦), ChCl/OA; (●), ChCl/MA.

Table 4. The Parameters A, B, and C for the Temperature Dependence Fitting of the V_{φ}^{0} Values Using Least-squares Analysis

	Parameters		
Systems	A	B	$10^2\,C$
Vit B3 in water	160.71	-0.67	0.14
Vit B3 in 0.50 mol kg^{-1} aqueous ChCl/G solution	137.61	-0.52	0.11
Vit B3 in 1.00 mol kg^{-1} aqueous ChCl/G solution	131.76	-0.46	0.10
Vit B3 in 1.50 mol kg^{-1} aqueous ChCl/G solution	128.28	-0.40	0.09
Vit B3 in 0.50 mol kg^{-1} aqueous ChCl/EG solution	126.91	-0.45	0.10
Vit B3 in 1.00 mol kg^{-1} aqueous ChCl/EG solution	128.51	-0.42	0.09
Vit B3 in 1.50 mol kg^{-1} aqueous ChCl/EG solution	124.15	-0.38	0.08
Vit B3 in 0.50 mol kg^{-1} aqueous ChCl/OA solution	113.96	-0.36	0.09
Vit B3 in 1.00 mol kg^{-1} aqueous ChCl/OA solution	120.19	-0.36	0.08
Vit B3 in 1.50 mol kg^{-1} aqueous ChCl/OA solution	116.46	-0.32	0.07
Vit B3 in 0.50 mol kg^{-1} aqueous ChCl/MA solution	111.98	-0.33	0.08
Vit B3 in 1.00 mol kg^{-1} aqueous ChCl/MA solution	112.57	-0.31	0.07
Vit B3 in 1.50 mol kg^{-1} aqueous ChCl/MA solution	110.57	-0.28	0.07

Standard uncertainties (u) for each variable are u (T) = 0.001 K; u (p) = 1.5 kPa.

Table 5. The Apparent Molar Isobaric Expansions ($E_{p,\varphi}^{0}$) and Hepler's Constants $\left(\partial^2 V_{\varphi}^{0} / \partial T^2\right)_p$ for Vit B3 in Binary and Ternary Aqueous DESs Solutions at T = (288.15 to 318.15) K and at Ambient Pressure (P = 871 hPa)

	$10^6\,E_{p,\varphi}^{0}$ (m^3 mol^{-1} K^{-1})				$10^2\left(\partial^2 V_{\varphi}^{0} / \partial T^2\right)_p$
Systems	288.15 K	298.15 K	308.15 K	318.15 K	(m^6 mol^{-2} K^{-2})
Vit B3 in water	0.1099	0.1369	0.1639	0.1909	0.270
Vit B3 in 0.50 mol kg^{-1} aqueous ChCl/G solution	0.1186	0.1406	0.1626	0.1846	0.220
Vit B3 in 1.00 mol kg^{-1} aqueous ChCl/G solution	0.1061	0.1256	0.1451	0.1646	0.195
Vit B3 in 1.50 mol kg^{-1} aqueous ChCl/G solution	0.0871	0.1041	0.1211	0.1381	0.170
Vit B3 in 0.50 mol kg^{-1} aqueous ChCl/EG solution	0.1360	0.1565	0.1770	0.1975	0.205
Vit B3 in 1.00 mol kg^{-1} aqueous ChCl/EG solution	0.0998	0.1178	0.1358	0.1538	0.180
Vit B3 in 1.50 mol kg^{-1} aqueous ChCl/EG solution	0.0976	0.1141	0.1306	0.1471	0.165
Vit B3 in 0.50 mol kg^{-1} aqueous ChCl/OA solution	0.1327	0.1497	0.1667	0.1837	0.170
Vit B3 in 1.00 mol kg^{-1} aqueous ChCl/OA solution	0.1010	0.1170	0.1330	0.1490	0.160
Vit B3 in 1.50 mol kg^{-1} aqueous ChCl/OA solution	0.0964	0.1109	0.1254	0.1399	0.145
Vit B3 in 0.50 mol kg^{-1} aqueous ChCl/MA solution	0.1264	0.1424	0.1584	0.1744	0.160
Vit B3 in 1.00 mol kg^{-1} aqueous ChCl/MA solution	0.1061	0.1206	0.1352	0.1497	0.145
Vit B3 in 1.50 mol kg^{-1} aqueous ChCl/MA solution	0.0965	0.1095	0.1225	0.1355	0.130

Standard uncertainties (u) for each variable are u (T) = 0.001 K; u (p) = 1.5 kPa. Standard uncertainty (u) for DESs composition was estimated to be less than $5{\cdot}10^{-2}$ mole ratio.

The higher the value of apparent molar isobaric expansivity, the more regular the solute molecules are in the solution, which causes the solution to expand. By adding solute to the solution, a structure like a regular lattice is formed in which all species are in place and at a certain distance, which is the reason for the expansion of the solution. The results for this quantity show that as the temperature increases the quantity increases "the solute molecules in the solution become more spaced apart and the expandability increases". This quantity decreases with increasing amount of DES, which may be due to the interactions that occur between the solvent and the DES. The structure breaking or making properties of the various solutes with the E_{φ}^{0} values can be interpreted. The following thermodynamic expression, given by Hepler, is a crucial descriptor for characterizing the solute's role in either promoting or disrupting the structure of the solvent in the bulk. It is represented as follows [36]:

$$\left(\frac{\partial E_{\varphi}^{0}}{\partial T}\right)_{p}=\left(\frac{\partial^{2}V_{\varphi}^{0}}{\partial T^{2}}\right)_{p}=2C \tag{6}$$

The values of this constant for all systems have been obtained and are presented in Table 5. Positive values of $\left(\partial^{2}V_{\varphi}^{0}/\partial T^{2}\right)_{p}$ indicate structure-making behavior, while negative values imply structure-breaking behavior when the solute is introduced into the aqueous solution of DESs. The positive values of $\left(\partial^{2}V_{\varphi}^{0}/\partial T^{2}\right)_{p}$ for Vit B3 in solutions infer the structure-making affinity. By adding solute to the solution, the structure of the solute forms a neat arrangement inside the solution, which is called structure making, like a regular lattice in which all species are in place at regular intervals. In this regard, the higher the quantity of Hepler, the greater the structure making of solute in solution, and implies the regular been strengthened as follows: ChCl/G > ChCl/EG > ChCl/OA > ChCl/MA.

Vit B3 experimental density and sound speed data in aqueous DES solutions were recorded at different temperatures between 288.15 K and 318.15 K. The following formula was used to get the partial molar isentropic compressibilities using these data. This parameter expresses how resistant the solution is overall to variations in pressure and, in turn, to variations in density and volume [37].

$$\kappa_{\varphi}=\frac{(\kappa_{s}\rho_{0}-\kappa_{s0}\rho)}{m\rho\rho_{0}}+\frac{\kappa_{s}M}{\rho} \tag{7}$$

where, κ_{s0} and κ_{s} represents adiabatic or isentropic compressibility of the solvent and solution, respectively. The following equation, given by Newton- Laplace has been used to evaluate the isentropic compressibility, κ_s (Pa^{-1}) values [38]:

$$\kappa_{s}=\frac{1}{\rho u^{2}} \tag{8}$$

In this case, u stands for sound speed. The forces and chemical bonds that bind atoms to molecules are the basic drivers of sound speed in a liquid medium. Computed parameters like isentropic compressibility, denoted as κ_s (Pa^{-1}), offer valuable insights into the molecular interactions within a liquid. The calculated values of the partial molar isentropic compressibility, κ_{φ}, are provided in Table S-II. As observed in Table S-II, the values of κ_{φ} are negative and exhibit an increase with both the molalities of Vit B3 and temperature. The ultrasonic behavior of a solution primarily arises from the effect of pressure on bulk water molecules. The negative κ_{φ} values indicate that water molecules around Vit B3, as the solute, are less compressible than water molecules in the bulk. This is explained by the theory that DES and ions do not depend on pressure and that, as a result of the charge on the ions and the existence of DESs, electrostricted water molecules have already undergone their maximum compression. To correlate the κ_{φ} values, the Redlich-Meyer equation was applied as follows [39].

$$\kappa_{\varphi}=\kappa_{\varphi}^{0}+B_{\kappa}m \tag{9}$$

in this equation, κ^{0}_{φ} is the standard partial isentropic compressibility, B_{κ} is the empirical parameters. The values of these parameters along with the standard deviation's values for κ_{φ} are listed in Table S-II. Figure 4 indicates the variation of κ^{0}_{φ} versus the temperature for investigated systems at molality 1 (mol kg^{-1}) of DESs. The amount of the solute-solvent interactions is expressed using κ_{φ}^{0} values whatever

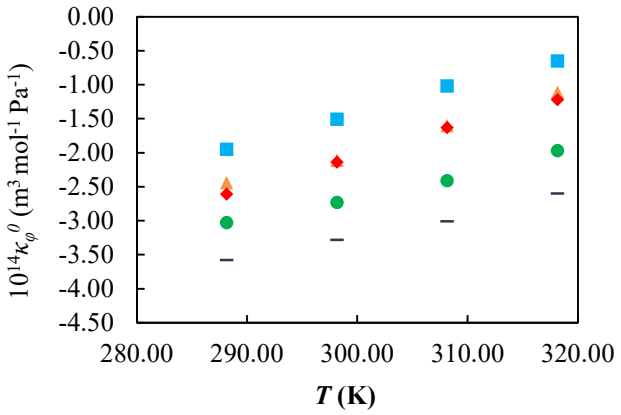


Fig. 4. The comparison of the partial molar isentropic compressibility, κ_ϕ^0 of Vit B3 in aqueous DESs solutions (1.00 mol kg^{-1}) at different temperatures; (-), binary solution; (■), ChCl/G; (▲), ChCl/EG; (♦), ChCl/OA; (●), ChCl/MA.

these values are lower; the interactions that occur will also be stronger. In the systems studied in this work, the κ_φ^0 values are decreased with increasing temperature.

The partial molar transfer isentropic compressibility $\Delta_{tr}\kappa_\varphi^0$ of Vit B3 in ternary to binary solutions was computed by the relation:

$$\Delta_{tr}\kappa_\varphi^0 = \kappa_\varphi^0(\text{In ternary DES solution}) - \kappa_\varphi^0(\text{in water}) \quad (10)$$

Table 6 shows the results of these computations. Positive transfer values are observed when the concentration of DESs increases.

The standard deviation (σ) is used in this study to evaluate the applicability and precision of the computations. The following formula can be used to determine the precise value:

$$\sigma(X) = \sqrt{\frac{\sum_{i=0}^{last(m)} (X_i^{\exp} - X_i^{cal})^2}{N-n}} \quad (11)$$

Here, n and N represent the number of parameters and experimental data points, respectively. The terms X_i^{cal} and $X_i^{\exp}$ refer to the calculated and experimental values of the parameters V_φ and κ_φ. The standard deviations for all the investigated systems are detailed in Tables 3 and 6. The above equation is employed to assess the deviations between the experimental data and the values obtained from the Redlich-Meyer model.

Hansen Solubility Parameters Results

Various methods exist for assessing solute-solvent interactions, with the Hansen solubility parameter (HSP) being widely favored for solvent selection. These solubility parameters were initially introduced by Hildebrand, emphasizing the principle that 'like dissolves like [40]. This parameter, originally introduced by Hildebrand and further refined by Hansen [41], is known as the Hildebrand-Hansen solubility parameter. Solubility parameters are commonly computed using the following relationship and can be found using mathematical or experimental methods:

$$\delta^2 = \frac{E_{coh}}{V_m} = \frac{\Delta H_{vap} - RT}{V_m} \quad (12)$$

In this equation, E_{coh} represents the intermolecular forces, specifically adhesion energy, while V_{m} stands for molar volume, and ΔH_{vap} represents the enthalpy of evaporation. Furthermore, R and T denote the universal gas constant and temperature (in Kelvin), respectively.

The solute-solvent interactions in the systems under study are clarified by the solubility parameter that Hansen and Hildebrand established. It encompasses adhesion energy density, which is the sum of energies needed to overcome dispersion forces (δ_{d}), breaking of hydrogen bonds between molecules (δ_{h}), and the dipolar interactions (δ_{p}) [42]:

$$\delta_t^2 = \delta_d^2 + \delta_p^2 + \delta_h^2 \quad (13)$$

This equation may be used to determine the mutual solubility of solute *i* and solvent *j*:

$$\Delta\delta_{ij} = \sqrt{4(\delta_d^i - \delta_d^j)^2 + (\delta_p^i - \delta_p^j)^2 + (\delta_h^i - \delta_h^j)^2} \quad (14)$$

The methods based on the contribution of different functional groups are applied to calculate δ_{h}, δ_{p}, and δ_{d}. Thus, δ_{d} is obtained from the following equation:

Table 6. The Partial Molar Isentropic Compressibility κ^0_φ, $\Delta_{tr}\,\kappa^0_{\varphi,}$ Experimental Parameter $B_{k,}$ and the Corresponding Standard Deviations σ (κ_φ) for Vit B3 in Binary and Ternary Aqueous DESs Solutions at T = (288.15 to 318.15) K and at Ambient Pressure (P = 871 hPa)

T (K)	$10^6\,\kappa^0_\varphi$ ($m^3\,mol^{-1}$)	$10^6\,B_k$ ($m^3\,kg\,mol^{-2}$)	$10^6\,\Delta_{tr}\,\kappa^0_\varphi$ ($m^3\,mol^{-1)}$	σ (κ_φ)
		Vit B3 in water		
288.15	-3.58	16.02	-	0.06
298.15	-3.28	17.41	-	0.03
308.15	-3.01	19.84	-	0.04
318.15	-2.60	19.23	-	0.05
		Vit B3 in 0.50 mol kg^{-1} aqueous ChCl/G solution		
288.15	-2.53	10.37	1.05	0.02
298.15	-2.12	11.92	1.16	0.03
308.15	-1.59	11.17	1.42	0.03
318.15	-1.18	11.36	1.42	0.02
		Vit B3 in 1.00 mol kg^{-1} aqueous ChCl/G solution		
288.15	-1.95	4.25	1.63	0.05
298.15	-1.51	4.57	1.77	0.04
308.15	-1.02	4.05	1.99	0.05
318.15	-0.65	4.98	1.95	0.03
		Vit B3 in 1.50 mol kg^{-1} aqueous ChCl/G solution		
288.15	-1.66	5.58	1.92	0.03
298.15	-1.19	5.44	2.09	0.02
308.15	-0.71	5.33	2.30	0.03
318.15	-0.23	6.61	2.37	0.03
		Vit B3 in 0.50 mol kg^{-1} aqueous ChCl/EG solution		
288.15	-2.58	9.12	1.00	0.03
298.15	-2.06	8.16	1.22	0.05
308.15	-1.59	9.21	1.42	0.04
318.15	-1.15	9.96	1.45	0.05
		Vit B3 in 1.00 mol kg^{-1} aqueous ChCl/EG solution		
288.15	-2.44	11.67	1.14	0.04
298.15	-2.11	12.73	1.17	0.04
308.15	-1.60	10.70	1.41	0.03
318.15	-1.11	10.58	1.49	0.03
		Vit B3 in 1.50 mol kg^{-1} aqueous ChCl/EG solution		
288.15	-2.28	10.17	1.30	0.07
298.15	-2.00	13.61	1.28	0.03
308.15	-1.35	10.93	1.66	0.04
318.15	-0.81	10.90	1.79	0.02
		Vit B3 in 0.50 mol kg^{-1} aqueous ChCl/OA solution		
288.15	-2.75	10.20	0.83	0.04
298.15	-2.39	9.78	0.89	0.04
308.15	-1.98	7.99	1.03	0.05
318.15	-1.64	7.54	0.96	0.04

Table 6. Continued

	Vit B3 in 1.00 mol kg^{-1} aqueous ChCl/OA solution			
288.15	-2.61	9.44	0.97	0.03
298.15	-2.14	7.43	1.14	0.05
308.15	-1.60	5.90	1.41	0.06
318.15	-1.22	6.21	1.38	0.05
	Vit B3 in 1.50 mol kg^{-1} aqueous ChCl/OA solution			
288.15	-2.26	7.80	1.32	0.05
298.15	-1.94	10.61	1.34	0.06
308.15	-1.51	10.78	1.50	0.04
318.15	-1.08	9.72	1.52	0.05
	Vit B3 in 0.50 mol kg^{-1} aqueous ChCl/MA solution			
288.15	-3.01	10.76	0.57	0.04
298.15	-2.62	10.71	0.66	0.04
308.15	-2.24	10.79	0.77	0.04
318.15	-1.83	9.52	0.77	0.05
	Vit B3 in 1.00 mol kg^{-1} aqueous ChCl/MA solution			
288.15	-3.03	14.38	0.55	0.02
298.15	-2.73	14.55	0.55	0.01
308.15	-2.41	15.67	0.60	0.04
318.15	-1.97	14.83	0.63	0.06
	Vit B3 in 1.50 mol kg^{-1} aqueous ChCl/MA solution			
288.15	-2.54	9.90	1.04	0.02
298.15	-2.10	11.88	1.18	0.06
308.15	-1.65	11.67	1.36	0.03
318.15	-1.30	11.60	1.30	0.03

Standard uncertainties (u) for each variable are u (T) = 0.001 K; u (p) = 1.5 kPa. Standard uncertainty (u) for DESs composition was estimated to be less than $5 \cdot 10^{-2}$ mole ratio.

$$\delta_d = \frac{\sum F_d}{V_m} \quad (15)$$

Here, F_d represents the constant dispersion component of molar adsorption and V_m is molar volume. The interactions involving polar groups are further characterized using the following relationship:

$$\delta_p = \frac{\sqrt{\sum F_p^{\,2}}}{V_m} \quad (16)$$

here, F_p is the constant polar component of molar adsorption. δ_h can also be obtained from the following equation:

$$\delta_h = \sqrt{\frac{\sum E_h}{V_m}} \quad (17)$$

where E_h is the hydrogen bond adhesion energy per structural group. Using the literature [43], we can calculate the solubility parameters for different materials.

In this study, the parameters δ_d, δ_p, and δ_h were obtained from various sources, and some were determined using the method Hoftyzer-Van Krevelen for Vit B3 drug and the DESs, as summarized in Table 7. Differences between the solubility parameter of the drug and the solvents (water and water + DESs) were calculated using Eq. (14) and are presented in Table 8.

The Hansen solubility parameter is a valuable tool for predicting solubility based on the compatibility of the dispersion, polar, and hydrogen bonding characteristics between a solute and a solvent. The HSP is often represented

Table 7. The Calculated HSP for the Materials Used

Systems	δ_d	δ_p	δ_h	δt
Vit B3	18.895	7.556	10.824	23.049
Water	15.500	16.000	42.300	47.810
Water + ChCl/MA	16.435	5.128	17.673	24.673
Water + ChCl/OA	16.411	5.483	18.274	25.166
Water + ChCl/EG	16.704	5.385	22.172	28.278
Water + ChCl/G	17.641	5.588	24.415	30.635

Table 8. The calculated Δδ for Vit B3 Drug and Solvents (Water and Water + DESs)

Systems solute	Water	Water + ChCl/MA	Water + ChCl/OA	Water + ChCl/EG	Water + ChCl/G
Nicotinic acid	33.289	8.776	9.191	12.357	13.960

as a point in a three-dimensional space, with axes corresponding to the dispersion, polar, and hydrogen bonding components. Solvents can also be represented in this space based on their HSP values. The closer the HSP values of a solute and a solvent are, the more likely they are to be miscible or soluble. The results in Table 8 clearly indicate that $\Delta\delta$ values suggest a robust interaction between Vit B3 and the solvent (water + DES (ChCl/MA)) compared to the other systems. In other words, the strength of the interaction between Vit B3 and the solvents can be ranked as follows: Vit B3 + water + ChCl/MA > Vit B3 + water + ChCl/OA > Vit B3 + water + ChCl/EG > Vit B3 + water + ChCl/G. These findings are consistent with experimental results.

CONCLUSIONS

This article presents an exploration of the ultrasonic and volumetric properties of nicotinic acid in both water and aqueous deep eutectic solvent (DES) solutions. An essential aspect of pharmaceutical production involves investigating drug-cosolvent interactions, and this study employs straightforward volumetric and ultrasonic methods to gain deeper insights into these interactions. The V_φ values, calculated for the drug in aqueous DES solutions, exhibit an increase with rising temperature and molalities of nicotinic acid. The cosphere overlap model, which is based on transfer parameters, was used to analyze these interactions and showed that ion-ion and ion-hydrophilic interactions predominated over hydrophobic and ion-hydrophobic interactions. The Helpers constant's positive values imply that the medication functions as a structural builder. Moreover, the outcomes of the ultrasonic investigations closely correspond with the findings of the partial molar volume investigations. Additionally, the Hansen solubility parameters were calculated for the systems under investigation. Both experimental and Hansen solubility parameters point to strong interactions between nicotinic acid and the solvent (water + DES (ChCl/MA)), relative to other systems. These findings have significant implications for the pharmaceutical industry, as the thermodynamic analysis of the studied system plays a crucial role in drug development.

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