wjert, 2024, Vol. 10 Issue 10, 29-60. Original Article ISSN 2454-695X

World Journal of Engineering Research and Technology
WJERT
www.wjert.org
SJIF Impact Factor: 7.029

PHYSICOCHEMICAL INVESTIGATION OF SOME AMINO ACIDS IN AQUEOUS SOLUTIONS OF AN ANTIVIRAL DRUG AT VARIOUS TEMPERATURES WITH THE MANIFESTATION OF DIVERSE MOLECULAR-INTERACTIONS

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Article Received on 28/07/2024 **Article Revised on 18/08/2024** **Article Accepted on 08/09/2024**

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ABSTRACT

The interaction between the amino acids L-serine and L-threonine and drug molecule amantadine hydrochloride was studied in aqueous medium. A comparative study was performed. It is quite difficult to understand the different degree of interactions of two molecules with structural similarities. To understand the interactions, we studied Density, Viscosity, Conductance as well as surface tension at various concentrations of amino acid molecules and at infinite dilution of the drug molecule. The deep investigation through the calculation of thermodynamic parameters such as apparent molar volume, viscosity beta coefficient, conductance and surface tension helped to determine the structure making and structure breaking interactions in the ternary solution system. A higher interaction in case of L- threonine and the drug molecule was observed.

1. INTRODUCTION

Understanding the underlying mechanism and drug interaction in a living system the study of drug-protein interaction is a leading factor.[1] The interaction between biomolecules and drugs

significantly influences drug toxicity, excretion rates, and pharmaceutical efficacy within living organisms. This interplay is a critical aspect of the emerging field of multi-targeted drug discovery. These interactions are based on various physiological processes and the specific nature of receptors for the drug molecules. The building blocks of the protein molecules must show effect on the solvation of protein and interactions taking place with the proteins and other molecules such as drug molecules. The mechanisms underlying these processes are not yet fully understood. Chemists are actively investigating these interactions by studying different physiological processes.[2-6]

Amantadine hydrochloride (ADM) exhibits a distinctive, rigid ring system composed of three fused cyclohexane rings. These rings adopt the chair conformation. Interestingly, amantadine is considered the smallest repeating unit within the diamond lattice. Amantadine or 1-aminoadamantine is a drug molecule of symmetrical C-10 primary amine with an unusual cyclic structure which is used as an antiviral agent used against the infection with influenza type A virus and to improve symptoms at the early diagnosis of infection, as well as in the management of herpes zoster. It has mild anti-parkinsonism activity.[7, 8] Amantadine inhibits two critical steps of viral infection. Early inhibition is associated with blocking virus uncoating. The molecular basis for this effect involves drug accumulation within endosomes, resulting in an increase in endosomal pH. Essentially, amantadine behaves as a lysosomotropic substance.[9] The drug is absorbed from the gut easily but its metabolism takes a long time and few side effects were recorded such as insomnia, dizziness, depression, confusion, and, in a few cases, and hallucinations.[8]

Cellular processes, such as metabolism, immune response, synaptic plasticity, cell growth, proliferation, and apoptosis, are regulated by complex signal transduction networks. These networks consist of molecules and large protein complexes that respond to biological or chemical stimuli within the cell's immediate environment.[10] Proteins are the biopolymers and which are made up of amino acids. Thus, understanding the interaction of the drug with the amino acids can open way of the further study of protein drug interactions. Here in this study our primary objective is to investigate the interactional behaviour of amino acids with the ADM molecule of biological and industrial significance. We have taken two naturally occurring amino acids Serine and threonine to study the interactions with the ADM molecule in the aqueous medium to understand the drug protein interactions.

2. Experimental details

2.1. Materials

The compounds under investigation included Amantadine hydrochloride ($C_{10}H_{18}ClN$, M.W. 187.71 g/mol), L-Serine ($C_3H_7NO_3$, M.W. 105.09 g/mol), and L-Threonine ($C_4H_9NO_3$, M.W. 119.12 g/mol), all sourced from Sigma-Aldrich, India, Germany. The purity of these compounds was reported to be between 0.98 and 0.99 in mass fraction. Solution preparations were conducted using doubly distilled deionized water with a conductivity of approximately 0.7 μS/cm. Further purification of these experimental chemicals, including the drug and amino acids, was deemed unnecessary. Prior to use, all chemicals were dried under vacuum over blue silica gel for a minimum of 72 hours at room temperature. Comprehensive details regarding the chemicals utilized in the experimental samples are presented in Table 1.

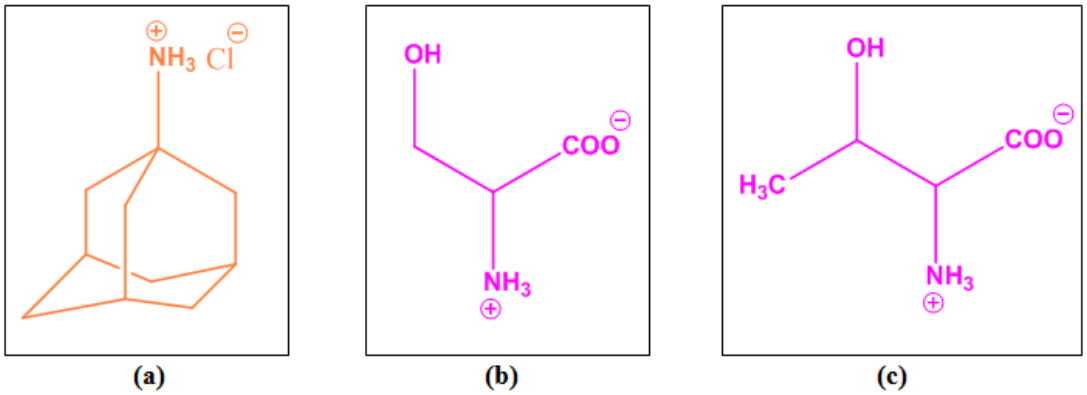


Figure 1: Chemical structure of (a) Amantadine Hydrochloride, (b) L-Serine and (c) L-Threonine.

Table 1: Details of Name, Attribution, CAS Number and Mass Fraction of Materials Studied.

SL. No.	Name of Chemicals	CAS NO.	Supplier	Purity Percentage	Molar mass(g/mole)
1	Amantadine hydrochloride ($C_{10}H_{18}ClN$)	665-66-7	Sigma Aldrich (India)	≥ 99%	187.71
2	L-Serine ($C_3H_7NO_3$)	56-45-1	Sigma Aldrich (Germany)	≥98%	105.09
3	L-Threonine ($C_4H_9NO_3$)	72-19-5	Sigma Aldrich (Germany)	≥ 98%	119.12

2.2. Apparatus and procedure

Preparation of experimental solution mixtures involved the precise combination of known volumes of solutions within airtight stoppered bottles, with measures taken to prevent

evaporation during the course of measurements. Mass measurements for stock solutions were conducted with a Mettler AG-285 electronic balance, offering a precision of ±0.01 mg. Dilution of stock solutions of ionic liquid and amino acids facilitated the creation of various concentration sets. The determination of density values allowed for the conversion of molarity to molality, with an associated standard uncertainty in molality of ±0.0001 mol·kg^{-1}, accounting for mass purity considerations.

The investigation involved the determination of densities (ρ) for experimental aqueous systems and solutions of varying concentrations across different temperatures, utilizing a vibrating-tube Anton Paar Density-Meter (DMA 4500 M).[11] This instrument exhibited an overall uncertainty in density of ±0.00093 g·cm^{-3}, calibrated using doubly distilled deionized degassed water and hot dry air. Temperature control, with a precision of ±0.01 K, was facilitated through an integrated Peltier device.

For viscosity (η) measurements, a Brookfield DV-III Ultra Programmable Rheometer, equipped with a spindle size 42 and offering an accuracy of ±1%, was employed. Prior calibration against known viscosities of water and aqueous $CaCl_2$ solutions was conducted to ensure accuracy.[12] Temperature regulation during viscosity assessments was achieved using a Brookfield Digital TC-500 temperature thermostat bath.

The specific conductivity of solutions was determined using a Systronics-308 conductivity meter, operating at a frequency of 1 kHz and possessing an accuracy of ±1%. Calibration and determination of the cell constant followed the methodology suggested by Lind et al.[13], with values maintained within the range of 0.09 to 1.00 cm^{-1} using a freshly prepared 0.01 M KCl aqueous solution. Solutions were contained within a dip-type immersion conductivity cell (CD-10) with a cell constant of (0.1 ± 0.001) cm^{-1}, with temperature control ensured via a temperature-regulated water bath.

Surface tension measurements of both mixed and pure experimental solutions, across different concentrations, were conducted using a K9 digital Tensiometer (Kruss GmbH, Hamburg, Germany), boasting an accuracy of ±0.3 mN/m. The platinum ring detachment technique was employed for surface tension determination. Calibration of the tensiometer with doubly distilled water yielded a surface tension value of 71.2 mN/m[14], consistent with literature values. The precise setup of the tensiometer, positioned in a controlled environment akin to that required for sensitive laboratory balances, ensured accuracy, alongside the

maintenance of a clean, dust-free atmosphere conducive to precise surface tension measurements.

3. RESULTS AND DISCUSSIONS

Table S1 provides the physical parameters of binary mixtures at various mass fractions (w = 0.001, 0.003, 0.005) of aqueous Amantadine Hydrochloride (AMD) solutions at three distinct temperatures (293.15, 298.15 K, 303.15 K, and 308.15 K).

Tables S2-S4 lists the experimentally determined values of density (ρ), and viscosity (η) for L-Serine and L-Threonine, as a function of concentration (molality), across different mass fractions of aqueous AMD mixtures at the specified temperatures.

3.1. Apparent molar volume

The volumetric properties, specifically the apparent molar volume (Φ_v) and the limiting apparent molar volume (Φ_v^0), are fundamental parameters in elucidating interactions within solution systems. The apparent molar volume is a composite of the geometric volume of the solute molecule and the volumetric alterations in the solvent resulting from interactions with the solute at the solute-solvent interface. Consequently, Φ_v values are derived from solution densities using the equation[15]:

$$\Phi_V = \frac{M}{\rho} - \frac{1000(\rho - \rho_0)}{m\rho\rho_0}$$

In this expression, M represents the molar mass of the solute, m is the molality of the solution, ρ denotes the density of the solution comprising amino acids, AMD, and H_2O, and ρ_0 is the density of the aqueous drug mixture (AMD and H_2O).

The systems investigated exhibit positive and substantial Φ_v values (Table S5-S7), indicative of significant solute-solvent interactions. At a constant temperature and consistent mass fraction of aqueous AMD, Φ_v values exhibit a decreasing trend with increasing molality (m) of the amino acids. Moreover, Φ_v increases concomitantly with rising temperatures and higher mass fractions of aqueous AMD. This relationship between Φ_v and $\sqrt{\mathbf{m}}$ is linear and can be fitted to the Masson equation[16]:

$$\Phi_V = \Phi_V^{\,0} + S_V * \sqrt{m}$$

Here, S_V^* denotes the experimental slope, and Φ_v^0 represents the limiting apparent molar volume at infinite dilution, which is a measure of solute-solvent interactions in the absence of solute-solute interactions.

The data presented in Table 2 and Figure 2 indicate that Φ_v^0 values are both large and positive for the amino acids studied, with the highest values observed for L-Threonine in the aqueous AMD system at all temperatures. This suggests stronger solute-solvent interactions for L-Threonine compared to L-Serine within the same solvent system. Additionally, the Φ_v^0 values are significantly larger than the S_V^* values, which are small and positive at all temperatures. As temperature increases, the S_V^* values decrease, implying a weakening in solute-solute interaction strength.

Table 2: Limiting molar volume (ϕ_V^0), viscosity-*B* and viscosity-*A* co-efficient and of (L-Serine + AMD + H_2O) and (L-Threonine + AMD + H_2O) systems in aqueous AMD solutions of mass fractions, W = 0.001, 0.003, 0.005 at temperatures 293.15 *K*, 298.15 *K*, 303.15 *K* and 308.15 *K* and atmospheric pressure 0.1 MP_a.

Temperature T (K^b)	$\phi_V^0 \times 10^6$ ($m^3\ mol^{-1}$)	$S_V^* \times 10^6$ ($m^3\ mol^{-3/2}\ kg^{1/2}$)	*B* ($dm^3\ mol^{-1}$)	*A* ($dm^{3/2}\ mol^{-1/2}$)
W_1=0.001 **(L-Serine+ AMD + H_2O) System**				
293.15	61.31	18.28	0.567	0.039
298.15	62.54	16.11	0.6900	0.035
303.15	63.48	16.03	0.787	0.034
308.15	64.61	15.80	0.86	0.032
W_1=0.003 **(L-Serine + AMD + H_2O)**				
293.15	62.34000	17.37	0.7290	0.037
298.15	63.45	15.98	0.834	0.033
303.15	64.63	14.21	0.955	0.030
308.15	65.25	13.78	1.035	0.029
W_1=0.005 **(L-Serine + AMD + H_2O)**				
293.15	63.42	15.95	0.894	0.035
298.15	65.03	10.91	0.999	0.031
303.15	66.22	10.45	1.112	0.028
308.15	67.20	10.09	1.227	0.028
W_1=0.001 **(L-Threonine + AMD + H2O)**				
293.15	74.47	16.74	0.605	0.042
298.15	75.71	15.78	0.7070	0.041
303.15	76.72	14.29	0.828	0.040
308.15	77.93	13.85	0.938	0.039
W_1=0.003 **(L-Threonine + AMD + H_2O)**				
293.15	75.77	13.69	0.7530	0.040
298.15	77.01	12.33	0.856	0.039
303.15	78.21	10.94	0.973	0.038
308.15	79.36	9.54	**1.101**	0.036

W_1=0.005 **(L-Threonine + AMD + H_2O)**				
293.15	77.09	10.14	0.901	0.037
298.15	78.26	8.55	1.02	0.037
303.15	79.47	8.20	**1.129**	0.036
308.15	80.51	7.71	**1.275**	0.035

Standard errors for limiting molar volume (ϕ_V^0), experimental slopes, S_V^*, Falkenhagen coefficient(***A)***and viscosity ***B***-coefficients(***B)*** are given in parenthesis. Mass fractions of AMD in aqueous solution; Combined standard uncertainty in molality according to stated purity u(m) =±0.0129 mol kg^{-1}. Standard uncertainty in temperature u(T) = ± 0.01 ***K***. Standard uncertainty in pressure(p)= ±0.01 ***MPa***.

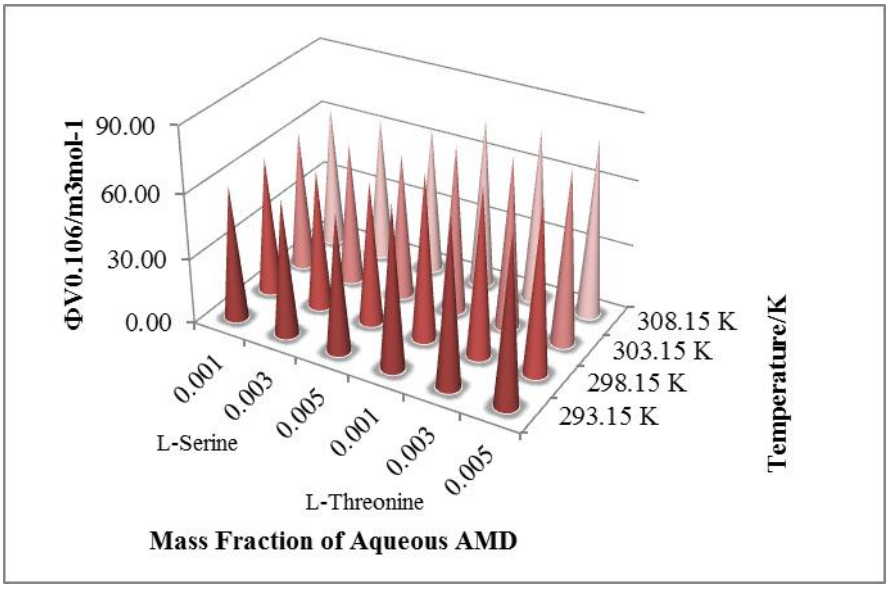


Fig 2: Plot of ϕ_V^0 vs of different mass fraction (*W*) of aqueous AMD vs of temperature (*T/K*).

Interactions between amino acids and AMD can be categorized into three distinct types according to the Co-sphere[17,18] overlap model: ion-hydrophilic interactions between the -NH_3^+ or -COO^- groups of amino acids and the hydrophilic portion of AMD; ion-hydrophobic interactions between the -NH_3^+ or -COO^- groups of amino acids and the hydrophobic groups of AMD; and hydrophobic-hydrophobic interactions between the hydrophobic groups of AMD and those of amino acids. The third type of interaction is more pronounced for L-Threonine than for L-Serine due to the larger hydrophobic portion present in L-Threonine.

The variation of Φ_v^0 with temperature can be modeled using the polynomial equation:

$$\Phi_V^{\ 0} = a_0 + a_1 T + a_2 T^2$$

Where, T denotes the temperature in Kelvin, and a_0, a_1, and a_2 are empirical coefficients dependent on the solute and the mass fraction of cosolute AMD. These coefficients are tabulated in Table 3 for both amino acids in aqueous AMD.

The limiting apparent molar expansibilities Φ_E^0 are evaluated as:

$$\Phi_E^0 = \left(\frac{\delta \Phi_V^0}{\delta T}\right)_P = a_1 + 2a_2 T$$

Table 3: Values of various coefficients of equation-3 for L-Serine and L-Threonine in different mass fraction (W) of aqueous AMD mixtures.

Aq. IL Mixture (W)	$a_0 \times 10^6/m^3\ mol^{-1}$	$a_1 \times 10^6/m^3\ mol^{-1}K^{-1}$	$a_2 \times 10^6/m^3\ mol^{-1}K^{-2}$	$a_0 \times 10^6/m^3$ mol-1	$a_1 \times 10^6/m^3\ mol^{-1}K^{-1}$	$a_2 \times 10^6/m^3\ mol^{-1}K^{-2}$
	(L-Serine + AMD + H_2O)			(L-Threonine + AMD + H_2O)		
0.001	-92.5551	0.8181	-0.0010	-19.3883	0.4082	-0.0003
0.003	-438.431	3.1446	-0.0049	-75.7114	0.7806	-0.0009
0.005	-579.138	4.0388	-0.0063	-107.604	1.0111	-0.0013

Mass fractions of AMD in aqueous solution; Standard uncertainties in molality according to stated purity u(m) = ±0.0129 mol kg^{-1}. Standard uncertainty in temperature u(T) = ± 0.01 *K*. Standard uncertainty in pressure(p)= ±0.01 *MPa*. Standard uncertainty values of *u* are: *u* (*T*) =±0.01 *K*.

Hepler's criterion is employed to assess the long-range structure-making and structure-breaking potentials of a solute in a mixed system through the sign of $\left(\frac{\delta \Phi E0}{\delta T}\right)_P$ [19]:

$$\left(\frac{\delta \Phi E0}{\delta T}\right)_P = 2a_2$$

A negative sign is indicative of a structure-breaker, while a positive sign suggests a structure-maker.[20] Table 4 reveals that the values of $\left(\frac{\delta \Phi E0}{\delta T}\right)_P$ for both amino acids under study are negative, classifying them as structure-breakers. This indicates that these amino acids disrupt the solvent structure, thereby enhancing solute-solvent interactions.

Table 4: Values of ($\delta\phi E^0/\delta T$) *P* for L-Serine and L-Threonine in different mass fraction (W1) of aqueous AMD mixtures at 293.15K, 298.15 *K* 303.15 *K* and 308.15 *K* and atmospheric pressure 0.1 MP_a.

Aq.Drug Mixture (W1)	$(\delta\phi E_0/\delta T)P \times 10^6/m^3\ mol^{-1}\ K^{-2}$	
	L-Serine + Aq.AMD	L-Threonine + Aq. AMD
0.001	-0.0020	-0.0006
0.003	-0.0098	-0.0018
0.005	-0.0126	-0.0026

Mass fractions of AMD in aqueous solution; Combined standard uncertainty in molality according to stated purity u(m) = ±0.0129 mol kg^{-1}. Standard uncertainty in temperature u(T) = ± 0.01 *K*. Standard uncertainty in pressure (p)= ±0.01 *MPa*.

3.2. Viscosity

The study of viscosity coefficients across varying molalities and temperatures provides valuable insights into ionic hydration and structural interactions in aqueous electrolytic solutions, particularly within ionic hydration cospheres.[21-24] Tables S2-S4 present viscosity (η) values for AMD in aqueous solutions of amino acids (L-Serine and L-Threonine) at temperatures of 293.15 K, 298.15 K, 303.15 K, and 308.15 K. Experimental results indicate that viscosity increases with the molality of amino acids. This trend is attributed to the increased frequency of molecular collisions at higher amino acid molalities, leading to kinetic energy dissipation and greater molecular aggregation, which, in turn, raises the solution viscosity.

To analyze the observed viscosity data, the Jones-Dole equation is employed[25]:

$$\frac{\eta}{\eta_0} = 1 + A\sqrt{m} + Bm$$

where η and η_0 denote the viscosities of the solution and solvent, respectively, and m represents solution molality. The experimental values of $\frac{\frac{\eta}{\eta_0}-1}{\sqrt{m}}$ for solution mixtures at 0.001, 0.003, and 0.005 molalities of aqueous amino acids at the specified temperatures are presented in Tables S5-S7. These values are positive and increase with both the concentration of AMD and temperature, suggesting stronger hydrophobic interactions between the alkyl chains of L-Serine and L-Threonine.

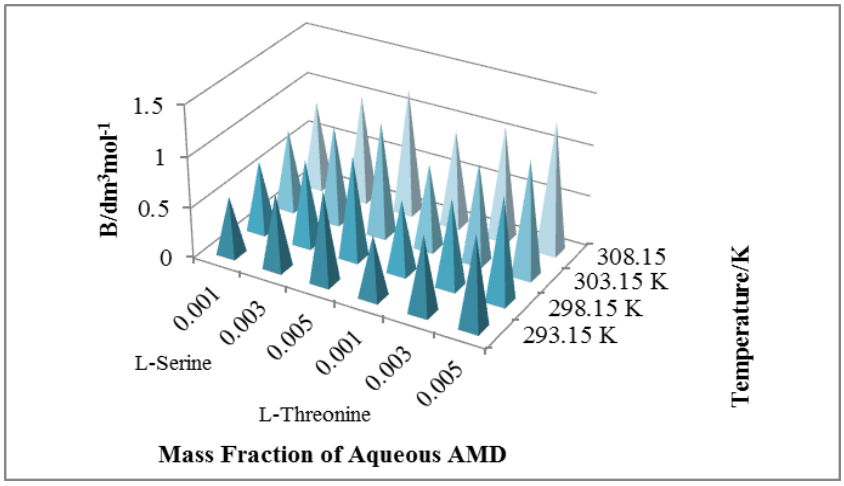


Fig. 3: Plot of Viscosity coefficient-*B* vs different mass fraction (*W*) of aqueous AMD vs temperature (*T/K*).

Rearranging the Jones-Dole equation yields:

$$\frac{\left(\frac{\eta}{\eta_0}-1\right)}{\sqrt{m}} = A + B\sqrt{m}$$

Here, the viscosity A-coefficient (Falkenhagen coefficient) indicates long-range Coulombic forces and signifies solute-solute interactions, while the B-coefficient, an adjustable parameter, reflects effective hydrodynamic volume and solute-solvent interactions, influenced by solute molecule size, shape, and structure.[26] The study's positive B-coefficient values under all conditions, which exceed the A-coefficient values, highlight the dominance of solute-solvent interactions over solute-solute interactions.[27] This trend is reinforced as both the B-coefficient and solution viscosity increase with rising temperatures and amino acid molalities, indicating enhanced solute-solvent interactions.

Table 5: Values of B/ϕ_V^0 for L-Serine and L- Threonine in different mass fraction (W1) of aqueous AMD mixtures at different temperatures and atmospheric pressure 0.1 MPa.

Temperature T (K)	Values of B/ϕ_V^0					
	(W_1) 0.001	**(W_2) 0.003**	**(W_3) 0.005**	**(W_1) 0.001**	**(W_2) 0.003**	**(W_3) 0.005**
	L-Serine + Aq.AMD			**L-Threonine + Aq. AMD**		
293.15K	9.2481	11.6939	14.0965	8.1241	9.9380	11.6876
298.15K	11.0329	13.1442	15.3621	9.3383	11.1154	13.0335
303.15K	12.3976	14.7764	16.7925	10.7925	12.4409	14.2066
308.15K	13.3106	15.8621	18.2589	12.0364	13.8735	15.8365

Mass fractions of AMD in aqueous solution; Combined standard uncertainty in molality according to stated purity u(m) = ±0.0129 mol kg^{-1}. Standard uncertainty in temperature u(T) = ± 0.01 *K*. Standard uncertainty in pressure (p)= ±0.01 *MPa*.

Table 6: Values of (*dB/dT*) for L-Serine and L-Threonine in different mass fraction (W) of aqueous AMD mixtures at 293.15K, 298.15 *K*, 303.15 *K* and 308.15*K* and atmospheric pressure 0.1 MP_a.

Aq.Drug Mixture (W)	*(dB/dT)*	
	L-Serine + Aq.AMD	L-Threonine + Aq. AMD
0.001	0.019	0.022
0.003	0.020	0.023
0.005	0.022	0.024

Mass fractions of AMD in aqueous solution; Combined standard uncertainty in molality according to stated purity u(m) = ±0.0129 mol kg^{-1}. Standard uncertainty in temperature u(T) = ± 0.01 *K*. Standard uncertainty in pressure (p)= ±0.01 *MPa*.

Table 7: Values of ($\bar{V}_1^0$–$\bar{V}_2^0$), $\Delta\mu_1^{0\neq}$, $\Delta\mu_2^{0\neq}$, $T\Delta S_2^{0\neq}$ and $\Delta H_2^{0\neq}$ for L-Serine and L-Threonine in different mass fraction (W) of aqueous AMD mixtures at four different temperatures and atmospheric pressure 0.1 *MPa.*

Parameters	W1=0.001				W2=0.003				W3=0.005			
	293.15K	298.15K	303.15K	308.15K	293.15K	298.15K	303.15K	308.15K	293.15K	298.15K	303.15K	308.15K
L-Serine												
$(\bar{V}_1^0$–$\bar{V}_2^0)$ $10^6/m^3.mol^{-1}$	-42.96	-44.17	-45.09	-46.19	-43.61	-44.70	-45.85	-46.44	-44.24	-45.82	-46.99	-47.94
$\Delta\mu_1^{0\neq}$/kJ.mol^{-1}	7.83	7.86	7.88	8.02	7.96	7.97	8.06	8.15	8.10	8.11	8.19	8.30
$\Delta\mu_2^{0\neq}$/kJ.mol^{-1}	88.85	106.92	121.89	136.07	108.50	124.13	142.39	157.85	127.29	142.95	160.07	180.60
$T\Delta S_2^{0\neq}$/kJ.mol^{-1}	-918.23	-933.90	-949.56	-965.22	-975.16	-991.80	-1008.43	-1025.06	-1037.99	-1055.69	-1073.39	-1091.10
$\Delta H_2^{0\neq}$/kJ.mol^{-1}	-1007.09	-1040.82	-1071.45	-1101.29	-1083.66	-1115.93	-1150.82	-1182.91	-1165.28	-1198.64	-1233.46	-1271.70
L-Threonine												
$(\bar{V}_1^0$–$\bar{V}_2^0)$ $10^6/m^3.mol^{-1}$	-56.24	-57.45	-58.44	-59.62	-57.16	-58.38	-59.55	-58.11	-59.25	-60.44	-61.45	-58.11
$\Delta\mu_1^{0\neq}$/kJ.mol^{-1}	7.81	7.84	7.86	8.00	7.94	7.96	8.04	8.07	8.09	8.16	8.27	8.07
$\Delta\mu_2^{0\neq}$/kJ.mol^{-1}	96.19	111.63	130.07	149.85	114.05	129.62	147.53	131.20	148.84	165.68	190.79	131.20
$T\Delta S_2^{0\neq}$/kJ.mol^{-1}	-1051.82	-1069.76	-1087.70	-1105.64	-1088.82	-1107.39	-1125.96	-1144.53	-1146.83	-1166.39	-1185.95	-1205.51
$\Delta H_2^{0\neq}$/kJ.mol^{-1}	-1148.02	-1181.39	-1217.77	-1255.49	-1202.87	-1237.01	-1273.49	-1314.51	-1278.04	-1315.24	-1351.63	-1396.31

Mass fractions of AMD in aqueous solution; Combined standard uncertainty in molality according to stated purity u(m) = ±0.0129 mol kg^{-1}. Standard uncertainty in temperature u(T) = ± 0.01 *K*. Standard uncertainty in pressure(p)= ±0.01 *MPa*

Viscosity A- and B-coefficients, derived from linear least-squares analysis of $\frac{\frac{\eta}{\eta_0}-1}{\sqrt{m}}$ versus $\sqrt{m}$, are listed in Table 1 for AMD solutions at the studied temperatures. Figures 3 illustrate the variation of B values as a function of amino acid molalities at the specified temperatures. The positive B-coefficient values across all solutions denote strong solute-solvent interactions between amino acids and AMD, consistent with the results derived from Φ_v^0 values. The smaller negative A-coefficient values further underscore the predominance of solute-solvent interactions over solute-solute interactions. Higher B-coefficient values at increased viscosities suggest that solute molecules are more effectively solvated by solvent molecules, enhancing solute-solvent interactions with increasing temperatures and amino acid concentrations.[28] The B-values for AMD in aqueous L-Threonine solutions are significantly higher than those in aqueous L-Serine solutions, indicating stronger solute-solvent interactions in the former.

The viscosity B-coefficient, particularly its first derivative with respect to temperature dB/dT (Table 6), provides insights into the nature of solute-solvent interactions, distinguishing between structure-making and structure-breaking behaviors.[29-31] Negative dB/dT values indicate structure-making (kosmotropic) properties, whereas positive values denote structure-breaking (chaotropic) properties. The positive dB/dT values observed for AMD in aqueous amino acid solutions imply that AMD acts as a structure-breaker in these mixtures. Additionally, a high B/ Φ_v^0 ratio (Table 5) indicates the formation of a primary solvation shell as a structure disruptor.[32]

The free energy of activation per mole of solvent for viscous flow ($\Delta\mu_1^{0\neq}$) is calculated using[33]:

$$\eta_0 = \left(\frac{hN_A}{\bar{V}_1^0}\right)\exp\left(\frac{\Delta\mu_1^{0\neq}}{RT}\right)$$

Rearranging this yields:

$$\Delta\mu_1^{0\neq} = RT\ln\left(\frac{\eta_0\bar{V}_1^0}{hN_A}\right)$$

Feakins et al. provide an expression based on the transition state theory for the relative viscosity of electrolyte solutions[34,35]:

$$B = \left(\bar{V}_1^0 - \bar{V}_2^0\right) + \bar{V}_1^0 \left[\frac{\Delta\mu_1^{0\neq} - \Delta\mu_2^{0\neq}}{RT}\right]$$

From this, we derive:

$$\Delta\mu_2^{0\neq} = \Delta\mu_1^{0\neq} + \left(\frac{RT}{\bar{V}_1^0}\right)\left[B - \left(\bar{V}_1^0 - \bar{V}_2^0\right)\right]$$

The values of $\Delta\mu_2^{0\neq}$ in Table 7 are positive and significantly higher than those of $\Delta\mu_1^{0\neq}$, indicating stronger interactions between AMD and the amino acids (L-Threonine and L-Serine) in the ground state compared to the transition state. In the ground state, solute and solvent molecules are more tightly bound. The increasing $\Delta\mu_1^{0\neq}$ with amino acid molality suggests a more structured ground state with higher amino acid concentrations. The entropy of activation ($\Delta S_2^{0\neq}$) and enthalpy of activation ($\Delta H_2^{0\neq}$) are calculated using[36]:

$$\Delta S_2^{0\neq} = -\frac{d\left(\Delta\mu_2^{0\neq}\right)}{dT}$$

$$\Delta H_2^{0\neq} = \Delta\mu_2^{0\neq} + T\Delta S_2^{0\neq}$$

The positive values of ($\Delta S_2^{0\neq}$) and ($\Delta H_2^{0\neq}$) suggest that the formation of the transition state is associated with bond-breaking and increasing disorder. According to Feakins' model, the fact that $\Delta\mu_2^{0\neq}$ exceeds $\Delta\mu_1^{0\neq}$ indicates that AMD acts as a structure breaker[37,38] consistent with the dB/dT characteristics observed in aqueous L-Threonine and L-Serine mixtures.

3.3. Electrical conductance

The nature of interactions between solute and solvent, and whether the components act as structure-makers or structure-breakers in a specific solvent, can be deduced through a study of electrical conductance. This investigation examines the interactions between the antiviral drug (AMD) and aqueous solutions of the amino acids L-serine (L-Ser) and L-threonine (L-Thr) across four different temperatures. Conductance measurements offer valuable insights into the interaction and transport phenomena within the (L-Ser + AMD + H_2O) and (L-Thr + AMD + H_2O) ternary systems.[39]

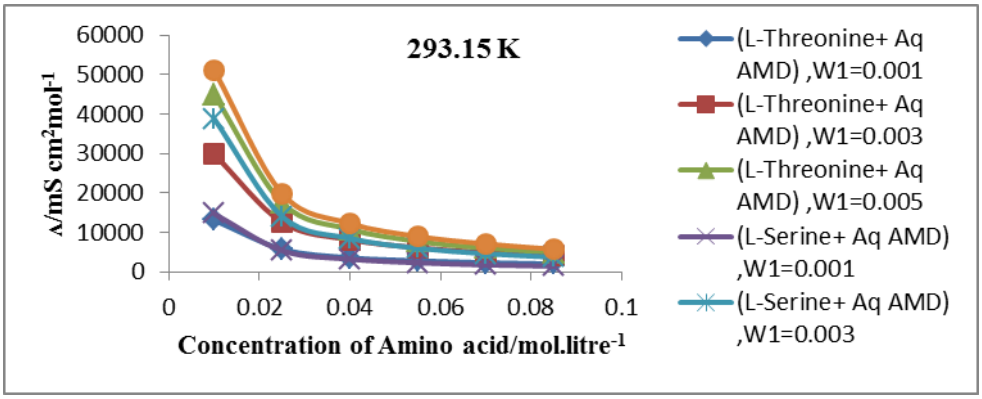


Fig. 4: Plot of molar conductance vs concentration of Amino acids in different mass fraction (*W*) in aqueous AMD at 293.15 K.

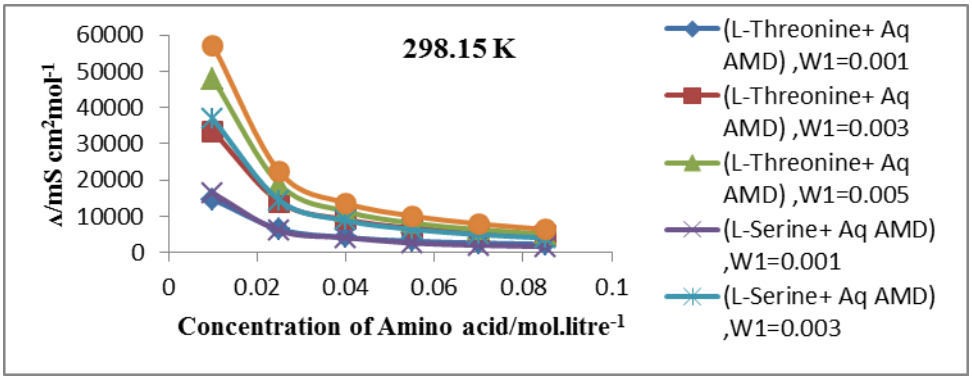


Fig. 5: Plot of molar conductance vs concentration of Amino acids in different mass fraction (*W*) in aqueous AMD at 298.15 K.

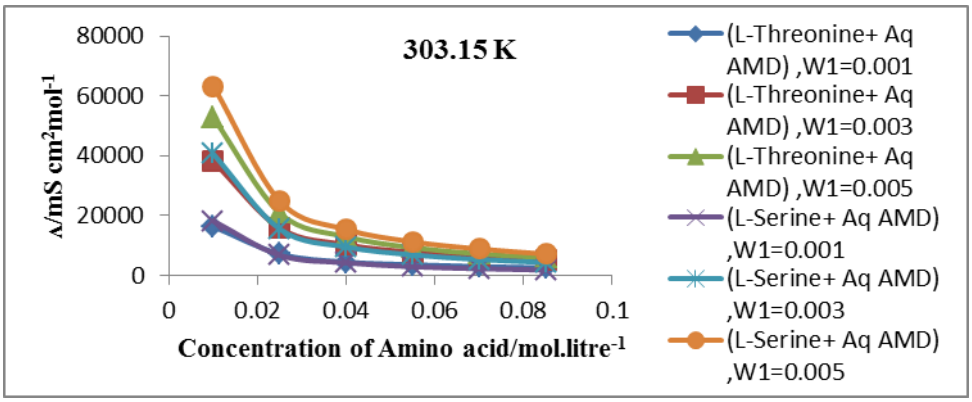


Fig. 6: Plot of molar conductance vs concentration of Amino acids in different mass fraction (*W*) in aqueous AMD at 303.15 K.

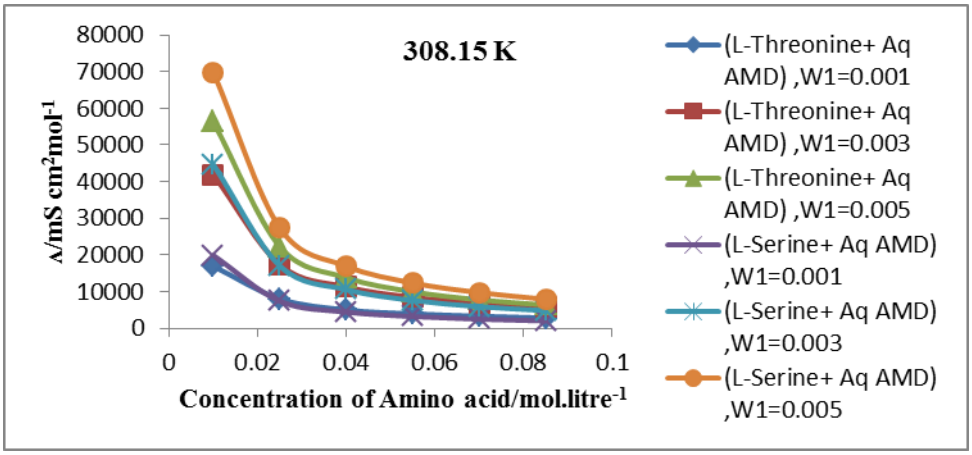


Fig. 7: Plot of molar conductance vs concentration of Amino acids in different mass fraction (*W*) in aqueous AMD at 308.15 K.

Table S8 presents the molar conductance (Λ) values of AMD in various molalities of aqueous L-Ser and L-Thr solutions [40]. The data reveal that molar conductance decreases as the concentration of L-Ser and L-Thr increases. Interestingly, L-Ser solutions show higher molar conductance values compared to L-Thr solutions under all experimental conditions.

Figures 4-7 depict the variation of molar conductance (Λ) with different molalities of L-Ser and L-Thr in aqueous AMD solutions (0.001, 0.003, 0.005 molality) at 293.15 K, 298.15 K, 303.15 K, and 308.15 K. The results indicate that Λ values increase with rising temperatures for all experimental systems and with increasing concentrations of amino acids and AMD solutions. However, the incremental addition of either L-Ser or L-Thr to the AMD solution results in a consistent decrease in molar conductance values.[41] This trend is primarily influenced by the mobility of ions in solution, notwithstanding the formation of ionic substances upon the addition of aqueous L-Ser or L-Thr solutions.

The observed decline in molar conductance values can be attributed to solute–solvent interactions governed by ion-hydrophilic, ion-hydrophobic, and hydrophobic-hydrophobic interactions within the solution mixtures. The formation of molecular associations reduces the mobility of ionic substances, thus explaining the observed conductance behavior. Consequently, the conductometric study substantiates findings derived from investigations of density, viscosity, and surface tension.

3.4. Surface tension

The data for surface tension in aqueous solutions of both amino acids at T = 298.15 K is shown in Table S9. Figure 7 illustrates the variation of surface tension for the amino acids in aqueous AMD solutions as a function of molality at 298.15 K. It is observed that as the concentration of L-serine increases, so does its surface tension, whereas L-threonine displays an opposite trend.

The nature of the limiting slopes ($\partial\sigma/\partial m$) of surface tension concerning concentration indicates the solute's hydrophobic or hydrophilic properties, revealing the predominant surface interactions.[42, 43] Table 8 provides the limiting slopes calculated from data in highly dilute regions.

L-serine shows positive ($\partial\sigma/\partial m$) values, typical of electrolytes and highly polar hydrophilic substances.[44] This is explained by favorable interactions between zwitterionic groups and the polar solvent. On the other hand, L-threonine, with its higher hydrocarbon content, shows hydrophobic characteristics, leading to its migration and adsorption at the liquid–air interface. Consequently, L-threonine shows negative ($\partial\sigma/\partial m$) values.

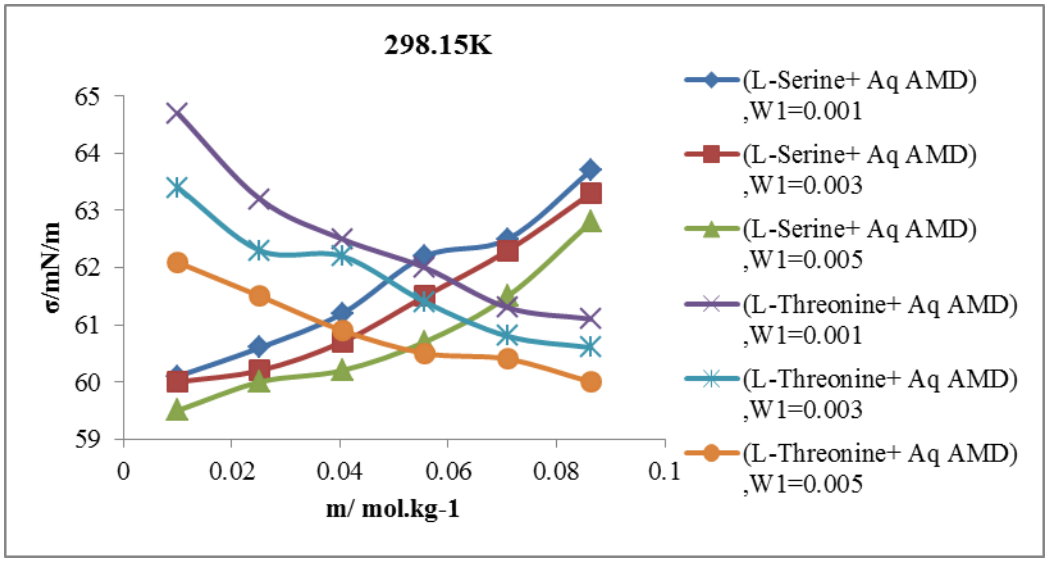


Fig. 8: Plot of Surface Tension (σ) of L-Serine and L-Threonine as a function of different mass fraction (W) of aqueous AMD.

Table 8: Limiting Slopes (∂σ/∂m) of the Surface Tension of the Aqueous Solutions of α-Amino Acids.

(∂σ/∂m)	L-Serine	L-Threonine
0.001	-0.691	0.705
0.003	-0.551	0.674
0.005	-0.404	0.614

Mass fractions of AMD in aqueous solution; Combined standard uncertainty in molality according to stated purity u(m) = ±0.0129 mol kg^{-1}. Standard uncertainties in temperature u(T) = ± 0.01 *K*. Standard uncertainty in pressure (p)= ±0.01 *MPa.*

4. CONCLUSION

The investigation of the interactions between amino acids and drug molecule performed in aqueous ternary system. The interactions at the infinite dilution were determined by conducting the experiment at very low concentration of the drug in water. The apparent molar volume calculated was in favour of the strong solute-solvent interaction and which was confirmed again by the determination of the positive values of the limiting apparent molar expansibilities (Φ_E^0) as well as viscosity B values. The interactions of the drug with both the amino acids were found as structure breaker due to the disruption of the primary solvation sphere. The further calculation of the thermodynamic parameters such as entropy and enthalpy of activation supported the fact of structure breaking phenomena. However, the conductometric study also supported the fact of strong solute-solvent interaction. The opposite trends of surface tension values for the two amino acids are due to the structural differences. The L-threonine, due to its higher hydrophobic content, shows hydrophobic characteristics. The overall study signified the higher interaction of the L-threonine with the amantadine hydrochloride compared to the L-serine.

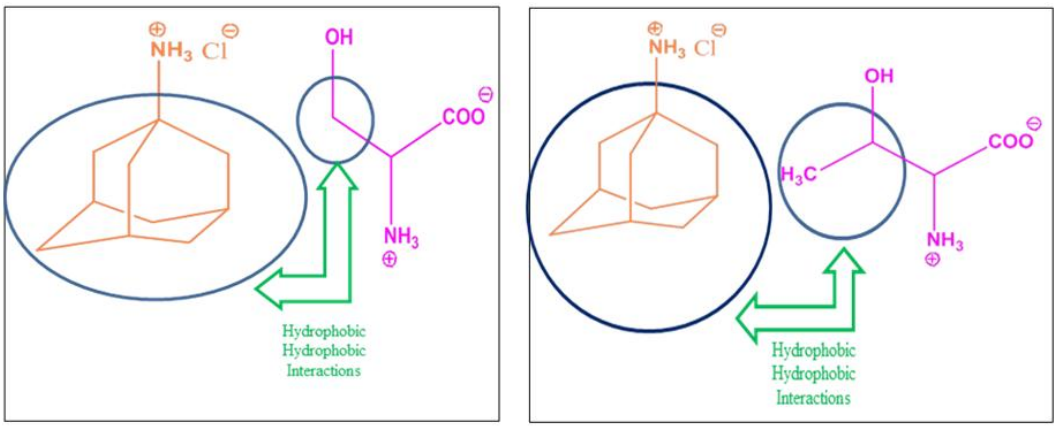


Figure 8: Plausible interaction between AMD with L-Serine and L-Threonine.

Table S1: Density (ρ), Viscosity (η) of aqueous pure AMD solutions of mass fractions W = 0.001, 0.003, 0.005 at temperatures 293.15, 298.15K, 303.15K and 308.15K.

Mass fraction(W)	Temperature (K)	Density (ρ) $\times 10^{-3}$ Kg.m^{-3}	Viscosity (η) mPa.S
0.001	293.15	0.99823	0.54023
	298.15	0.99702	0.51839
	303.15	0.99569	0.4962
	308.15	0.9941	0.47369
0.003	293.15	0.99831	0.55910
	298.15	0.99718	0.53268
	303.15	0.99575	0.52185
	308.15	0.99418	0.48832
0.005	293.15	0.99838	0.57766
	298.15	0.99723	0.54969
	303.15	0.99586	0.53728
	308.15	0.99426	0.50430

Standard uncertainty in molality according to stated purity u(m) = ±0.0129 mol kg^{-1}. Standard uncertainty in temperature u(T) = ± 0.01 *K*.

Table S2: Density (ρ), and Viscosity (η) of (AMD+Ser+H_2O) and (AMD +Thr+H_2O), systems in aqueous AMD solutions of mass fractions W_1=0.001, W_2=0.003, W_3=0.005, at 293.15K, 298.15K, 303.15K and 308.15K.

	(AMD+Ser+H_2O) system, W_1=0.001		(AMD +Thr+H_2O) system, W_1=0.001	
Molality (Mol/Kg)	Density (ρ)$\times 10^{-3}$ Kg.m^{-3}	Viscosity (η) mPa.S	Density (ρ) $\times 10^{-3}$ Kg.m^{-3}	Viscosity (η) mPa.S
	Temperature – 293.15 K		**Temperature – 293.15 K**	
0.0101	0.99865	0.54625	0.99866	0.54575
0.0252	0.99925	0.55153	0.99928	0.55228
0.0404	0.99983	0.55681	0.99988	0.55766
0.0556	1.00040	0.56231	1.00046	0.56372
0.0709	1.00095	0.56713	1.00103	0.56977
0.0863	1.00148	0.57171	1.00160	0.57468
	Temperature – 298.15 K		**Temperature – 298.15 K**	
0.0101	0.99743	0.52347	0.99744	0.52393
0.0252	0.99802	0.52992	0.99804	0.53061
0.0404	0.99859	0.5359	0.99863	0.53659
0.0556	0.99915	0.54188	0.99920	0.54257
0.0709	0.99969	0.54671	0.99976	0.54832
0.0863	1.00023	0.55245	1.00031	0.55429
	Temperature – 303.15 K		**Temperature – 303.15 K**	
0.0101	0.99609	0.50176	0.99610	0.50199
0.0252	0.99667	0.50800	0.99670	0.50939
0.0404	0.99723	0.51447	0.99727	0.51608
0.0556	0.99777	0.52116	0.99784	0.52301
0.0709	0.99830	0.52692	0.99839	0.52900

0.0863	0.99882	0.53314	0.99893	0.53521
	Temperature – 308.15 K		**Temperature – 308.15 K**	
0.0101	0.99449	0.47927	0.99450	0.47973
0.0252	0.99505	0.48554	0.99508	0.48739
0.0404	0.99560	0.49226	0.99564	0.49458
0.0556	0.99613	0.49898	0.99619	0.50199
0.0709	0.99664	0.50546	0.99673	0.50846
0.0863	0.99714	0.51147	0.99726	0.51539

Standard uncertainty in molality according to stated purity u(m) = ±0.0129 mol kg^{-1}. Standard uncertainty in temperature u(T) = ± 0.01 *K*.

Table S3: Density (ρ), and Viscosity (η) of (AMD+Ser+H_2O) and (AMD +Thr+H_2O), systems in aqueous AMD solutions of mass fractions W_1=0.001, W_2=0.003, W_3=0.005, at 293.15K, 298.15K, 303.15K and 308.15K.

	(AMD+Ser+H_2O) system, W_1=0.003		**(AMD +Thr+H_2O) system, W_1=0.003**	
	Temperature – 293.15 K		**Temperature – 293.15 K**	
Molality (Mol/Kg)	**Density (ρ) ×10^{-3} Kg.m^{-3}**	**Viscosity (η) mPa.S**	**Density (ρ) ×10^{-3} Kg.m^{-3}**	**Viscosity (η) mPa.S**
0.0101	0.99872	0.56506	0.99873	0.56529
0.0252	0.99931	0.57216	0.99934	0.57285
0.0404	0.99988	0.57857	0.99993	0.57949
0.0556	1.00043	0.58543	1.00051	0.5868
0.0709	1.00097	0.59206	1.00108	0.59297
0.0863	1.00150	0.59822	1.00164	0.59982
	Temperature – 298.15 K		**Temperature – 298.15 K**	
0.0101	0.99758	0.53866	0.99759	0.53912
0.0252	0.99816	0.54602	0.99818	0.54694
0.0404	0.99872	0.55337	0.99876	0.55451
0.0556	0.99926	0.56071	0.99933	0.56163
0.0709	0.99979	0.56735	0.99989	0.56896
0.0863	1.00031	0.57377	1.00044	0.57606
	Temperature – 303.15 K		**Temperature – 303.15 K**	
0.0101	0.99614	0.52831	0.99615	0.52877
0.0252	0.99671	0.53613	0.99673	0.53705
0.0404	0.99726	0.54418	0.99730	0.54579
0.0556	0.99779	0.55245	0.99786	0.55406
0.0709	0.99831	0.55979	0.99841	0.56117
0.0863	0.99883	0.56735	0.99895	0.56942
	Temperature – 308.15 K		**Temperature – 308.15 K**	
0.0101	0.99456	0.49481	0.99457	0.49528
0.0252	0.99511	0.50245	0.99514	0.50407
0.0404	0.99565	0.51077	0.99570	0.51285
0.0556	0.99618	0.51885	0.99625	0.52116
0.0709	0.99669	0.52495	0.99679	0.52969
0.0863	0.99719	0.53279	0.99732	0.53774

Standard uncertainty in molality according to stated purity u(m) = ±0.0129 mol kg^{-1}. Standard uncertainty in temperature u(T) = ± 0.01 *K*.

Table S4: Density (ρ), and Viscosity (η) of (AMD+Ser+H_2O) and (AMD +Thr+H_2O), systems in aqueous AMD solutions of mass fractions W_1=0.001, W_2=0.003, W_3=0.005, at 293.15K, 298.15K, 303.15K and 308.15K.

	(AMD+Ser+H_2O) system, W_3=0.005		(AMD +Thr+H_2O) system, W_3=0.005	
	Temperature – 293.15 K		Temperature – 293.15 K	
Molality (Mol/Kg)	Density (ρ) ×10^{-3} Kg.m^{-3}	Viscosity (η) mPa.S	Density (ρ) ×10^{-3} Kg.m^{-3}	Viscosity (η) mPa.S
0.0101	0.99878	0.58452	0.99879	0.58475
0.0252	0.99936	0.59320	0.99939	0.59343
0.0404	0.99992	0.60187	0.99998	0.60233
0.0556	1.00046	0.61031	1.00056	0.61077
0.0709	1.00099	0.61806	1.00112	0.61851
0.0863	1.00151	0.62512	1.00168	0.62603
	Temperature – 298.15 K		Temperature – 298.15 K	
0.0101	0.99762	0.55681	0.99763	0.55727
0.0252	0.99819	0.56552	0.99822	0.56621
0.0404	0.99874	0.57445	0.99879	0.5756
0.0556	0.99929	0.58315	0.99936	0.58406
0.0709	0.99983	0.5916	0.99992	0.5932
0.0863	1.00035	0.60005	1.00047	0.6021
	Temperature – 303.15 K		Temperature – 303.15 K	
0.0101	0.99624	0.54464	0.99625	0.54533
0.0252	0.99679	0.55406	0.99682	0.55474
0.0404	0.99733	0.56346	0.99738	0.56438
0.0556	0.99786	0.57308	0.99794	0.57445
0.0709	0.99839	0.58200	0.99848	0.58383
0.0863	0.99890	0.59114	0.99902	0.59343
	Temperature – 308.15 K		Temperature – 308.15 K	
0.0101	0.99463	0.51193	0.99464	0.51262
0.0252	0.99517	0.52116	0.99520	0.52254
0.0404	0.99570	0.53107	0.99575	0.53268
0.0556	0.99623	0.54119	0.99629	0.54280
0.0709	0.99672	0.54904	0.99682	0.55314
0.0863	0.99723	0.55801	0.99735	0.56369

Standard uncertainty in molality according to stated purity u(m) = ±0.0129 mol kg^{-1}. Standard uncertainty in temperature u(T) = ± 0.01 *K*.

Table S5: Apparent molar volume (φ_V) and (η_r-1)/$\sqrt{c}$ of (AMD+Ser+H_2O) system and (AMD +Thr+H_2O) systems in aqueous AMD solutions of mass fractions W_1=0.001, W_2=0.003, W_3=0.005, at 293.15K, 298.15K, 303.15K and 308.15K.

	(AMD+Ser+H_2O) system, W_1=0.001		(AMD +Thr+H_2O) system, W1=0.001	
	Temperature – 293.15 K		Temperature – 293.15 K	
Molality (Mol/Kg)	$\varphi_V \times 10^6$ ($m^3 mol^{-1}$)	(η_r-1)/$\sqrt{c}$ $dm^{3/2} mol^{-1/2}$	$\varphi_V \times 10^6$ ($m^3 mol^{-1}$)	(η_r-1)/$\sqrt{c}$ $dm^{3/2} mol^{-1/2}$
0.0101	63.1007	0.09753	76.1458	0.10187
0.0252	64.2659	0.12710	77.1010	0.14069
0.0404	65.0301	0.15206	77.8062	0.16078
0.0556	65.5393	0.17540	78.4666	0.18469
0.0709	66.1012	0.19117	78.9677	0.20587
0.0863	66.6882	0.20424	79.2758	0.21772
	Temperature – 298.15 K		Temperature – 298.15 K	
0.0101	64.1323	0.10188	77.1921	0.11086
0.0252	65.0993	0.14675	78.3516	0.15530
0.0404	65.8155	0.17649	78.8577	0.18334
0.0556	66.3033	0.20201	79.4287	0.20790
0.0709	66.8539	0.21629	79.8793	0.22828
0.0863	67.1970	0.23602	80.2735	0.24844
	Temperature – 303.15 K		Temperature – 303.15 K	
0.0101	65.1717	0.11585	78.2477	0.12061
0.0252	65.9399	0.15640	78.8052	0.17424
0.0404	66.6079	0.19150	79.6665	0.20796
0.0556	67.2581	0.22303	80.0328	0.23917
0.0709	67.7581	0.24359	80.5112	0.25972
0.0863	68.1875	0.26570	80.9239	0.28040
	Temperature – 308.15 K		Temperature – 308.15 K	
0.0101	66.2234	0.12158	79.3189	0.13148
0.0252	67.1971	0.16401	80.0813	0.18896
0.0404	67.6652	0.20328	80.7435	0.22791
0.0556	68.2259	0.23599	81.2039	0.26330
0.0709	68.8202	0.26278	81.5924	0.28710
0.0863	69.3113	0.28357	81.9474	0.31240

Standard uncertainty in molality according to stated purity u(m) = ±0.0129 mol kg^{-1}. Standard uncertainty in temperature u(T) = ± 0.01 *K*.

Table S6: Apparent molar volume (φ_V) and (η_r-1)/$\sqrt{c}$ of (AMD+Ser+H_2O) system and (AMD +Thr+H_2O) systems in aqueous AMD solutions of mass fractions W_1=0.001, W_2=0.003, W_3=0.005, at 293.15K, 298.15K, 303.15K and 308.15K.

	(AMD+Ser+H_2O) system, W_1=0.003		(AMD +Thr+H_2O) system, W_1=0.003	
	Temperature – 293.15 K		Temperature – 293.15 K	
Molality (Mol/Kg)	$\varphi_V\times10^6$ (m^3mol^{-1})	(η_r-1)/$\sqrt{c}$ $dm^{3/2}\,mol^{-1/2}$	$\varphi_V\times10^6$ (m^3mol^{-1})	(η_r-1)/$\sqrt{c}$ $dm^{3/2}\,mol^{-1/2}$
0.0101	64.1026	0.11059	77.1469	0.11479
0.0252	65.0672	0.15387	77.9017	0.16182
0.0404	65.7814	0.18169	78.5569	0.19012
0.0556	66.4507	0.20953	79.0120	0.22033
0.0709	66.9607	0.23255	79.3958	0.23916
0.0863	67.3960	0.25056	79.7464	0.26086
	Temperature – 298.15 K		Temperature – 298.15 K	
0.0101	65.1345	0.11620	78.1925	0.12492
0.0252	65.9004	0.16435	79.1509	0.17538
0.0404	66.5663	0.20158	79.6070	0.21254
0.0556	67.2146	0.23288	79.9721	0.24052
0.0709	67.7131	0.25558	80.3051	0.26735
0.0863	68.1412	0.27488	80.6231	0.29008
	Temperature – 303.15 K		Temperature – 303.15 K	
0.0101	66.1790	0.12744	79.2544	0.13636
0.0252	66.7457	0.17892	80.0143	0.19018
0.0404	67.3635	0.22116	80.4217	0.23676
0.0556	67.9910	0.25832	80.7655	0.27175
0.0709	68.4782	0.28411	81.0867	0.29447
0.0863	68.7805	0.30918	81.3977	0.32316
	Temperature – 308.15 K		Temperature – 308.15 K	
0.0101	66.6585	0.13658	80.3279	0.14616
0.0252	67.4884	0.18865	80.8883	0.20978
0.0404	67.9634	0.23690	81.2469	0.25841
0.0556	68.3732	0.27473	81.5692	0.29516
0.0709	68.9032	0.30610	81.8788	0.32966
0.0863	69.3706	0.33272	82.1828	0.35742

Standard uncertainty in molality according to stated purity u(m) = ±0.0129 mol kg^{-1}. Standard uncertainty in temperature u(T) = ± 0.01 *K*.

Table S7: Apparent molar volume (φ_V) and (η_r-1)/$\sqrt{c}$ of (AMD+Ser+H_2O) system and (AMD +Thr+H_2O) systems in aqueous AMD solutions of mass fractions W_1=0.001, W_2=0.003, W_3=0.005, at 293.15K, 298.15K, 303.15K and 308.15K.

	(AMD+Ser+H_2O) system, W_1=0.005		(AMD +Thr+H_2O) system, W_1=0.005	
	Temperature – 293.15 K		Temperature – 293.15 K	
Molality (Mol/Kg)	$\varphi_V\times10^6$ (m^3mol^{-1})	(η_r-1)/$\sqrt{c}$ $dm^{3/2}$ $mol^{-1/2}$	$\varphi_V\times10^6$ ($m^3.mol^{-1}$)	(η_r-1)/$\sqrt{c}$ $dm^{3/2}$ $mol^{-1/2}$
0.0101	65.1045	0.12264	78.1480	0.12670
0.0252	65.8685	0.17614	78.7025	0.17883
0.0404	66.5329	0.21699	79.0567	0.22124
0.0556	67.1796	0.24953	79.3749	0.25334
0.0709	67.6768	0.27386	79.8242	0.27737
0.0863	68.1039	0.29209	80.0989	0.29812
	Temperature – 298.15 K		Temperature – 298.15 K	
0.0101	66.1391	0.13320	79.1966	0.14164
0.0252	66.7041	0.18793	79.5516	0.19602
0.0404	67.3200	0.23241	80.1086	0.24306
0.0556	67.5794	0.26787	80.3366	0.27527
0.0709	67.8555	0.29761	80.5911	0.30895
0.0863	68.2583	0.32442	80.8585	0.33766
	Temperature – 303.15 K		Temperature – 303.15 K	
0.0101	67.1846	0.14060	80.2588	0.15352
0.0252	67.9535	0.20305	80.8174	0.21134
0.0404	68.3698	0.25057	81.1747	0.25935
0.0556	68.7223	0.29217	81.3121	0.30342
0.0709	68.9078	0.32374	81.6600	0.33696
0.0863	69.2528	0.35374	81.8692	0.36875
	Temperature – 308.15 K		Temperature – 308.15 K	
0.0101	68.2429	0.15478	81.3366	0.16861
0.0252	68.8122	0.21689	81.6951	0.23442
0.0404	69.1796	0.27218	82.0035	0.28839
0.0556	69.32640	0.31983	82.3032	0.33369
0.0709	69.97377	0.35764	82.6001	0.37524
0.0863	70.14139	0.38543	82.7765	0.41392

Standard uncertainty in molality according to stated purity u(m) = ±0.0129 mol kg^{-1}. Standard uncertainty in temperature u(T) = ± 0.01 *K*.

Table S8: Molar conductivities of (AMD+Ser+H_2O) system and (AMD +Thr+H_2O) systems in aqueous AMD solutions of mass fractions W_1=0.001, W_2=0.003, W_3=0.005, at 293.15K, 298.15K, 303.15K and 308.15K.

Molar conductivities(mS cm^2mol^{-1})								
	(AMD+Ser+H_2O) system, W_1=0.001				**(AMD+Thr+H_2O) system, W_1=0.001**			
Molarity (moles/L)	**293.15K**	**298.15K**	**303.15K**	**308.15K**	**293.15K**	**298.15K**	**303.15K**	**308.15K**
0.0101	14760.00	16390.00	18190.00	19910.00	13160.00	14660.00	16350.00	16930.00
0.0252	5444.00	6040.00	6732.00	7396.00	5776.00	6452.00	7164.00	8000.00
0.0404	3252.50	4117.50	4222.50	4422.50	3622.50	4182.50	4485.00	5017.50
0.0556	2347.27	2614.55	2920.00	3214.55	2841.82	3163.64	3560.00	3947.27
0.0709	1801.43	2014.29	2244.29	2482.86	2372.86	2658.57	2964.29	3292.86
0.0863	1458.82	1625.88	1814.12	2004.71	2061.18	2316.47	2554.12	2820.00
	(AMD+Ser+H_2O) system, W_2=0.003				**(AMD+Thr+H_2O) system, W_2=0.003**			
Molarity (moles/L)	**293.15K**	**298.15K**	**303.15K**	**308.15K**	**293.15K**	**298.15K**	**303.15K**	**308.15K**
0.0101	38790.00	36770.00	40610.00	44660.00	29810.00	33380.00	38120.00	41930.00
0.0252	14080.00	14400.00	15488.00	17036.00	12612.00	13972.00	15804.00	17328.00
0.0404	8505.00	8850.00	9512.50	10545.00	8187.50	9125.00	10267.50	11277.50
0.0556	6029.09	6385.45	6878.18	7598.18	6158.18	6727.27	7727.27	8449.09
0.0709	4645.71	4970.00	5340.00	5912.86	4967.14	5557.14	6085.71	6992.86
0.0863	3762.35	4051.76	4350.59	4811.76	4240.00	4720.00	5323.53	5831.76
	(AMD+Ser+H_2O) system, W_3=0.005				**(AMD+Thr+H_2O) system, W_3=0.005**			
Molarity (moles/L)	**293.15K**	**298.15K**	**303.15K**	**308.15K**	**293.15K**	**298.15K**	**303.15K**	**308.15K**
0.0101	51060.00	57080.00	63310.00	69830.00	44900.00	47810.00	52740.00	56320.00
0.0252	19904.00	22240.00	24836.00	27356.00	17552.00	18784.00	20828.00	22288.00
0.0404	12302.50	13665.00	15360.00	16947.50	10840.00	11345.00	12920.00	13790.00
0.0556	9009.09	10072.73	11236.36	12363.64	7770.91	8141.82	9289.09	9947.27
0.0709	7118.57	7931.43	8855.71	9724.29	6054.29	6351.43	7214.29	7751.43
0.0863	5764.71	6405.88	7171.76	7921.18	4940.00	5177.65	5896.47	6340.00

Standard uncertainty in molality according to stated purity u(m) = ±0.0129 mol kg^{-1}. Standard uncertainty in temperature u(T) = ± 0.01 *K*.

Table S9: Surface tension of (AMD+Ser+H_2O) and (AMD+Thr+H_2O) systems in aqueous AMD solutions of mass fractions W_1=0.001, W_2=0.003, W_3=0.005, at 298.15K.

	(AMD+Ser+H_2O) system			**(AMD+Thr+H_2O) system**		
Molarity (moles/litre)	**W_1=0.001**	**W_2=0.003**	**W_3=0.005**	**W_1=0.001**	**W_2=0.003**	**W_3=0.005**
0	64.7	63.4	62.1	60.1	60.0	59.5
0.0101	63.2	62.3	61.5	60.6	60.2	60.0
0.0252	62.5	62.2	60.9	61.2	60.7	60.2
0.0404	62.0	61.4	60.5	62.2	61.5	60.7
0.0556	61.3	60.8	60.4	62.5	62.3	61.5
0.0709	61.1	60.6	60.0	63.7	63.3	62.8
0.0863	64.7	63.4	62.1	60.1	60.0	59.5

Standard uncertainty in molality according to stated purity u(m) = ±0.0129 mol kg^{-1}. Standard uncertainty in temperature u(T) = ± 0.01 *K*.

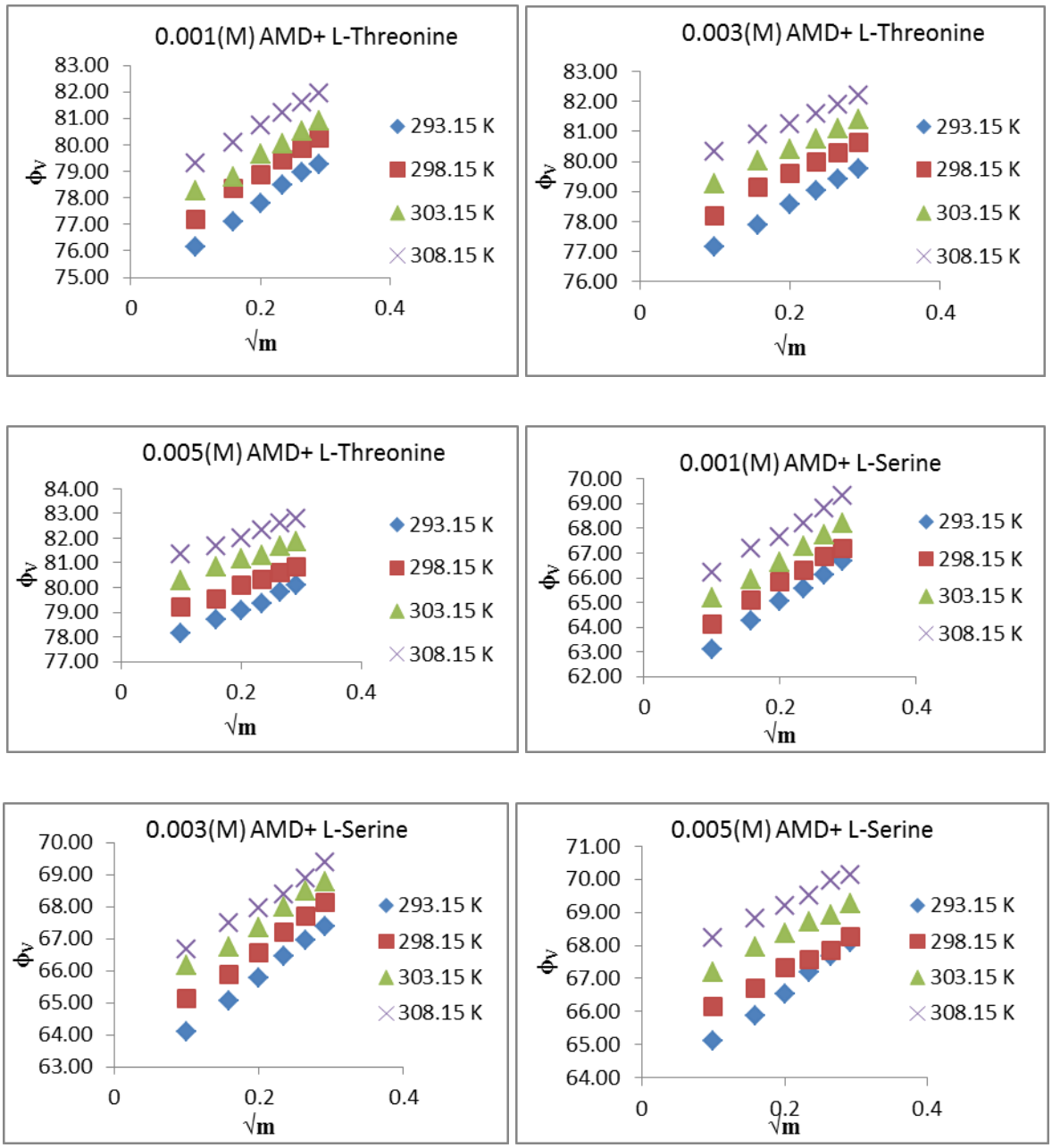
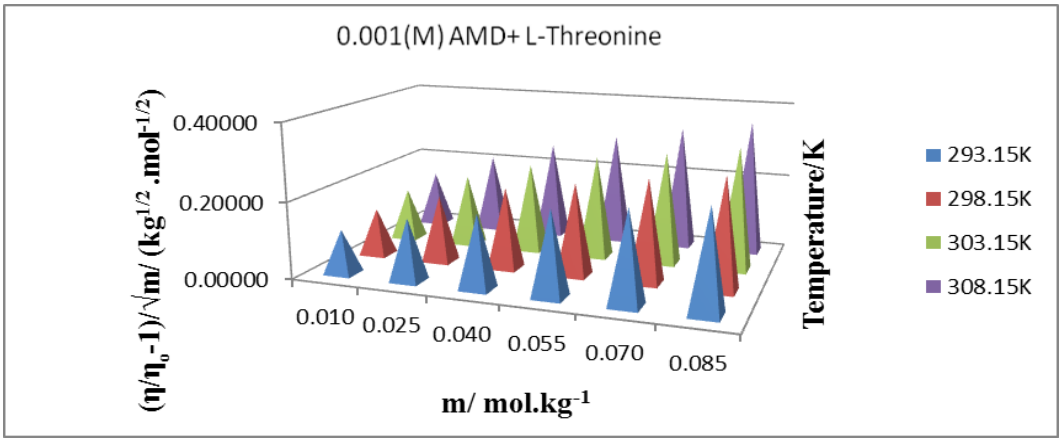
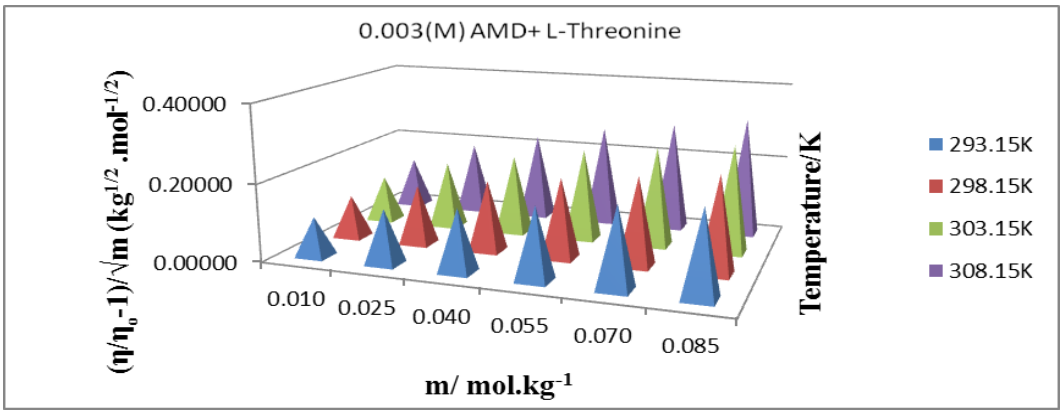
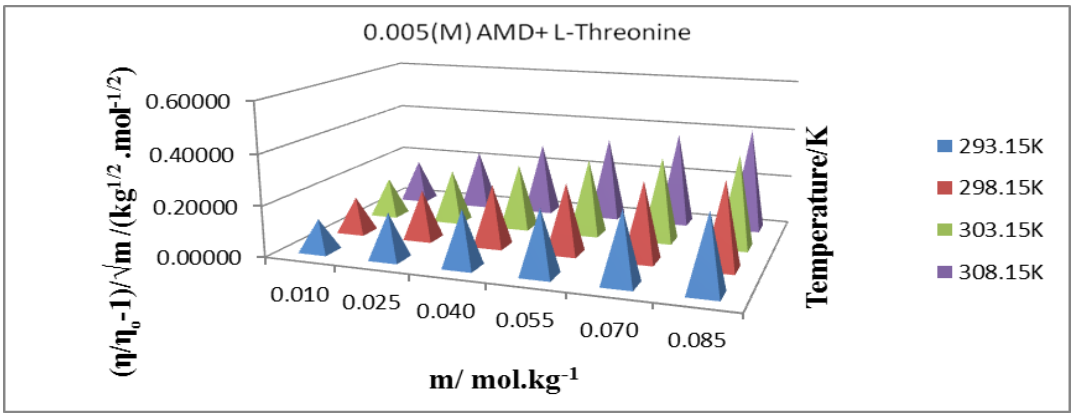
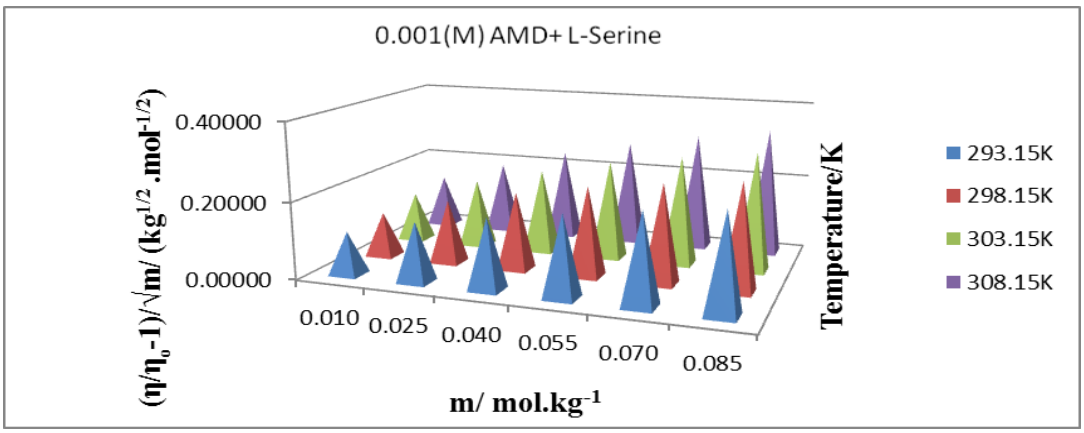


Figure S1: Plot of (φ_V) Vs √m of (AMD+L-Thr+H_2O), (AMD+L-Ser+H_2O) systems in aqueous AMD solutions of mass fractions W_1=0.001, W_2=0.003, W_3=0.005, at 293.15K 298.15K, 303.15K and 308.15K.


0.001(M) AMD+ L-Threonine
(η/η0 -1)/√m/ (kg1/2 .mol-1/2)
0.40000
0.20000
0.00000
0.010
0.025
0.040
0.055
0.070
0.085
m/ mol.kg-1
Temperature/K
293.15K
298.15K
303.15K
308.15K


0.003(M) AMD+ L-Threonine
(η/η0 -1)/√m (kg1/2 .mol-1/2)
0.40000
0.20000
0.00000
0.010
0.025
0.040
0.055
0.070
0.085
m/ mol.kg-1
Temperature/K
293.15K
298.15K
303.15K
308.15K


0.005(M) AMD+ L-Threonine
(η/η0 -1)/√m /(kg1/2 .mol-1/2)
0.60000
0.40000
0.20000
0.00000
0.010
0.025
0.040
0.055
0.070
0.085
m/ mol.kg-1
Temperature/K
293.15K
298.15K
303.15K
308.15K


0.001(M) AMD+ L-Serine
(η/η0 -1)/√m/ (kg1/2 .mol-1/2)
0.40000
0.20000
0.00000
0.010
0.025
0.040
0.055
0.070
0.085
m/ mol.kg-1
Temperature/K
293.15K
298.15K
303.15K
308.15K

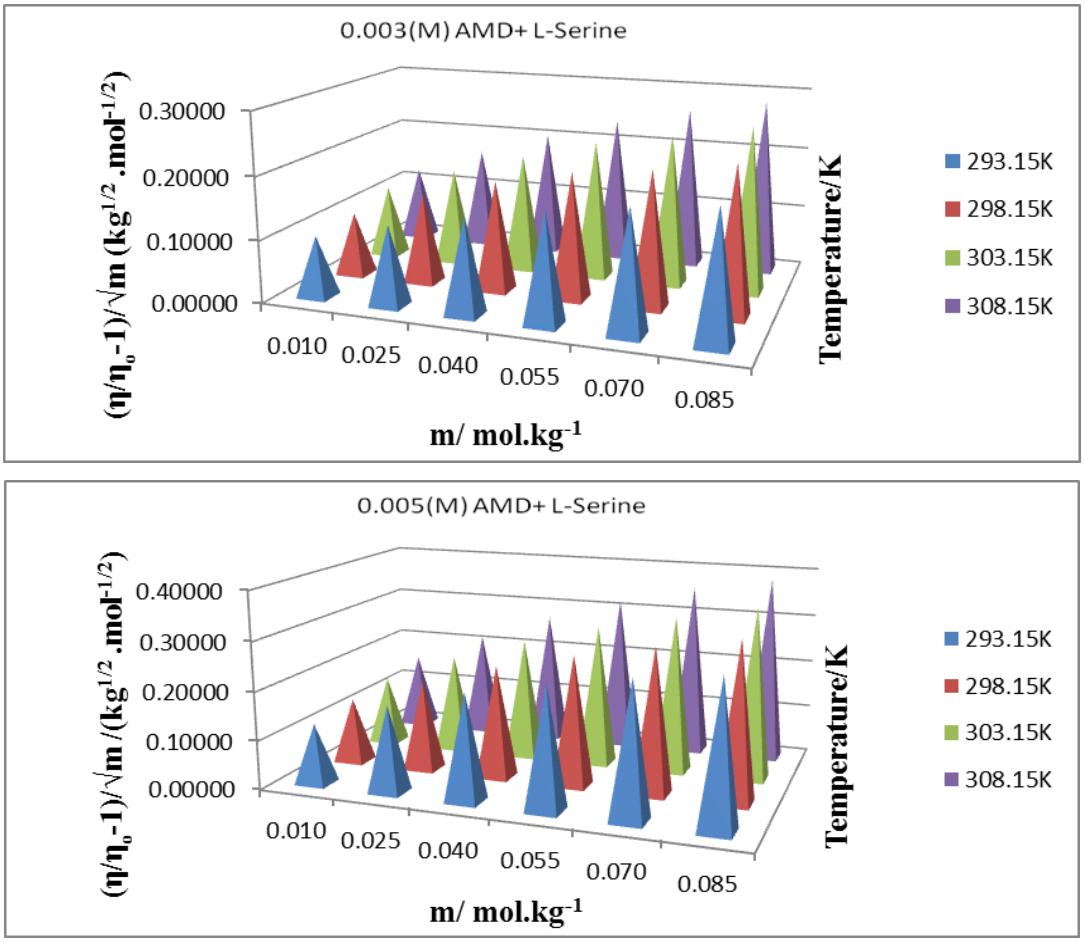


Figure S2: Plot of $[(\eta/\eta_0)-1]/\sqrt{c}$ Vs $\sqrt{m}$ of (AMD+L-Thr+H_2O) and (AMD+L-Ser+H_2O) systems in aqueous AMD solutions of mass fractions W_1=0.001, W_2=0.003, W_3=0.005, at 293.15K 298.15K, 303.15K and 308.15K.

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