Density, Viscosity and Speed of Sound of Acetaminophen-Propylene Glycol Solutions at 293.15 K Temperature

T. R. Pandit[1, a)] and V. A. Rana[2, b)]

[1, 2] *Department of Physics, Electronics and Space Science, School of Sciences, Gujarat University, Ahmedabad-380009, Gujarat, India*

[a)]Corresponding author: tanmaypandit@gujaratuniversity.ac.in,
b)varana@gujaratuniv*ersity.ac.in*

Abstract. Physical and acoustical properties of drug – solvent mixtures are useful in the field of pharmaceutical sciences to examine their functions and performance. Measurements of physical properties: density, viscosity and ultrasonic velocities for the solutions of acetaminophen and propylene glycol at a constant temperature of 293.15 K were carried out. Precise density results are used to evaluate thermodynamic properties specific gravity (S_G), specific volume (S_v); for all solutions. Allied parameters of ultrasonic velocity for all solutions have also been evaluated. Results were analyzed to obtain some structural information of prepared drug - solvent mixtures and examined in view of their applicability in the field of pharmaceutical sciences.

INTRODUCTION

Physical and acoustical properties like density, viscosity and ultrasonic velocity of solutions of pharmaceutical molecules in polar / non-polar solvents provide valuable information about solute-solvent interaction. [1] This information is useful for drug formulations, drug dosages, synthesis [2] and predicting the absorption and transport of drugs in the biological tissues. [3] Apart from this; the study of ultrasonic velocity and allied parameters for drug – solvent interactions are important to understand the behaviour of biomolecules and physico-chemical nature of solutions. [4]

Acetaminophen (APAP) formerly known as "Paracetamol" is selected for the present study as it is the most common drug used globally in case of fever and pain. APAP has also secured its position in the WHO's essential medicines listing. [5] APAP is white crystalline odorless powder and bitter in taste. The chemical formula of APAP is $C_8H_9NO_2$ and its molecular weight is 151.17 gm / mol. [6] Structure of APAP in Ball-Stick model is shown in **Fig.-1**. APAP is a pain reliever and used to treat many conditions such as headache, colds, fever, etc. APAP is generally safe medicine compared to aspirin and according to its recommended dosage i.e. 2 gm per day (infant) and 4 gm per day (adults) [7] Actual mechanism of action of APAP in human body is not completely known. In order to maintain the stability of APAP drug; it is necessary to select solvent having glass transition temperature (T_g) lower than that of APAP (T_g = 295.63 K) [8] and hence; Propylene Glycol (PG) having T_g = 160 K [9] has been selected as a solvent for present study.

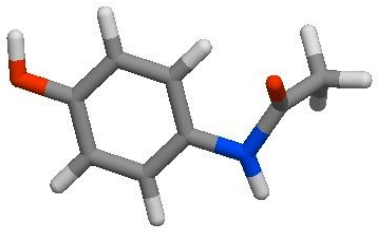

FIGURE 1. Structure of acetaminophen (APAP) in Ball-Stick model

MATERIALS AND METHODS

PG was procured from "High Purity Laboratory Chemicals (HPLC), Mumbai, Maharashtra, India" and APAP in powder was bought from "Farmson Pharmaceuticals Gujarat Pvt. Ltd., Vadodara, Gujarat, India". The solubility of APAP in PG is 1.15 gm / 10 ml. as reported in [10] and with reference to that; 11 different concentrations were prepared using different weights of APAP. The concentrations of APAP are then converted into molarity (M) using formulae described by E. M. Cheng et al. [11] and also reported in **Table - 1**. Measurements of density (ρ), viscosity (η) and speed of sound (u) were carried out using Pycnometer, Ostwald's Viscometer and Digital Ultrasonic Velocity meter (Vi Microsystems, India) respectively. Experimental setup and methodology as described by Rana and Chaube [12] has been followed to perform these measurements. Allied parameters have been evaluated using the formulae as stated in [13]

TABLE 1. Weight of APAP used for preparing the solutions and their conversion into molarity

Weights of APAP in PG	Molarity
0 mg	0 M
115 mg	0.076 M
230 mg	0.152 M
345 mg	0.228 M
460 mg	0.304 M
575 mg	0.380 M
690 mg	0.456 M
805 mg	0.532 M
920 mg	0.608 M
1035 mg	0.684 M
1150 mg	0.760 M

RESULTS AND DISCUSSION

Measured values of physical properties for PG at 293.15 K temperature i.e. ρ (1.0374 gm cm^{-3}), η (0.5476 cm^2 s^{-1}) and u (1748.96 m s^{-1}) are in good agreeent with the literature values of ρ = 1.0361 gm cm^{-3} [14], η = 0.581 cm^2 s^{-1} [14] and u = 1644.1 m s^{-1} (at 303.15 K) [15], which authenticates the experimental setup as well as the outcomes of this study.

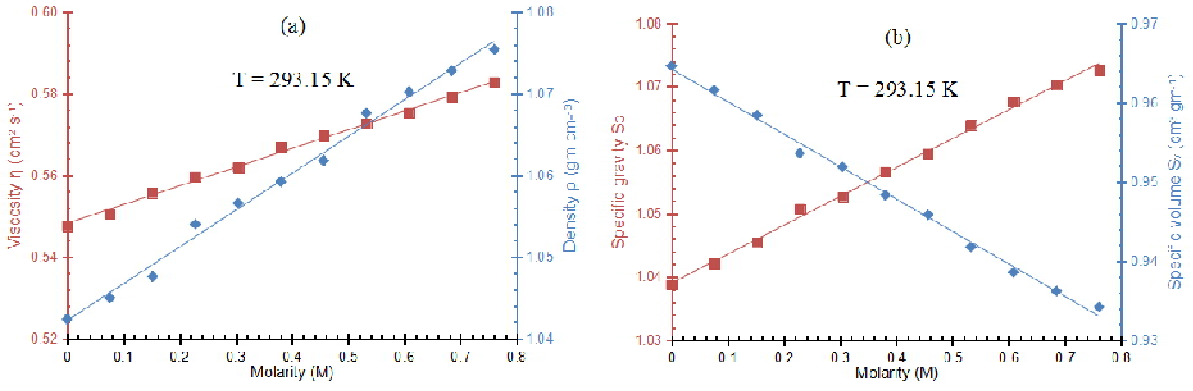

FIGURE 2. **(a)** Viscosity, Density and **(b)** specific gravity, specific volume for all molar solutions of APAP-PG at 293.15 K temperature

Figure - 2 (a) depicts the viscosity and density values of APAP-PG solutions at 293.15 K temperature. Density increases with rise in concentration which can be attributed to increasing weight of APAP in the solutions. Accurately determined density values are used to evaluate thermodynamical parameters such as specific gravity (S_G) and specific volume (S_V) and their values are represented in Fig.-2(b). Linear decrement in S_v and increment in S_G

with concentration can be observed from the results. Decrement in S_v with concentration suggest weak solute-solute interaction in APAP and similar behaviour has been observed in our previous study for paracetamol - water solutions. [16] Obtained results of density and thermodynamical parameters are helpful to identify purity of substances. [17] Viscosity data of drug-solvent mixtures (in the form of cough syrup, ointment, etc.) of varying concentrations is widely used by drug manufacturer, because it helps in forecasting the behaviour of formulation when user consumes it. As it can be seen from **Fig.-2(a)** that the values of viscosity increases as a function of concentration (with minor variation).

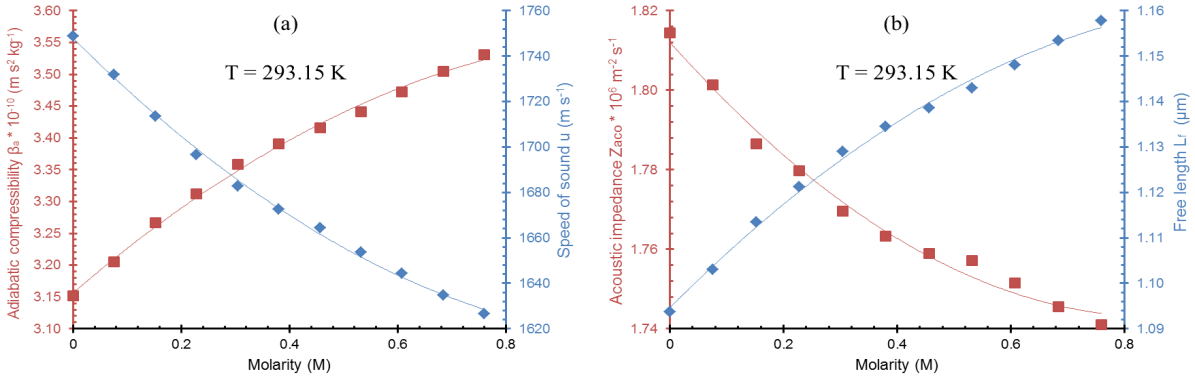

FIGURE 3. **(a)** Speed of sound, adiabatic compressibility and **(b)** free length, acoustic impedance for all solutions of APAP-PG at 293.15 K temperature

Measurement of speed of sound enables determination of some acoustical parameters; which are found to be very sensitive to molecular interactions.[18] Hence such results are of importance for the study of molecular interaction strength in the solution. Using the values of speed of sound; various acoustical parameters like adiabatic compressibility (β_a), free length (L_f), acoustical impedance (Z_{aco}), viscous relaxation time (τ_η), free volume (V_f), molar volume (V_M), Rao's constant (R), Wada's constant (W), apparent molar volume (Φ_V) and apparent molar compressibility (Φ_k) were also calcualted using the formulae prescribed in [13]. **Figure – 3 (a)** represents the speed of sound (u) and adiabatic compressibility (β_a) and **Fig.–3(b)** shows free length (L_f) and acoustic impedance (Z_{aco}) for different concentrations at 293.15 K temperature.

TABLE 2. Acoustic parameters for APAP-PG solutions at 293.15 K temperature

Molarity (M)	**τ_η (10^{-14} s)**	**V_f (10^{-5} ml mole^{-1})**	**V_M (10^{-4})**	**R (10^{-3})**	**W (10^{-6})**	**Φ_v**	**Φ_k (10^{-6})**
0	23.01	0.81	5.19	6.26	22.83	------	-------
0.076	23.53	0.85	5.43	6.52	23.92	-12992.42	-4.16
0.152	24.21	0.87	5.67	6.78	25.03	-6406.63	-2.09
0.228	24.71	0.91	5.88	7.01	26.01	-4211.38	-1.39
0.304	25.16	0.95	6.11	7.27	27.09	-3113.75	-1.04
0.380	25.63	0.98	6.34	7.53	28.15	-2455.16	-0.83
0.456	25.94	1.03	6.57	7.79	29.19	-2016.11	-0.68
0.532	26.27	1.07	6.78	8.02	30.15	-1702.51	-0.58
0.608	26.63	1.11	7.01	8.27	31.20	-1467.30	-0.51
0.684	27.06	1.15	7.23	8.52	32.24	-1284.36	-0.45
0.760	27.44	1.19	7.45	8.77	33.28	-1138.01	-0.40

Decrease in speed of sound, increase in adiabatic compressibility and free length with concentration designates weak solute-solvent interaction due to increase in internal pressure; suggests the increase of cohesive forces which hurdles structural rearrangement. [19] This is very important oucome as internal pressure is the fundamental property of solution which offers an exceptional source for inspecting the solution phenomena. Increase in viscous relaxation time (τ_n) also supports such kind of interactions. Other evaluated parameters are reported in **Table - 2.**

Increase in free volume and molar volume with concentration confirming their dependance on effective mass. Rao's constant (R) and Wada's constant (W) increases linearly with the concentration and confirms that solute-solvent interaction takes place in the system and also supports the above mentioned facts. [20] Values of apparent molar volume (Φ_v) and compressibility (Φ_K) increase with concentration indicates positive volume trasnfer to solvent (PG) with higher APAP concentration. Hydroxyl group (at the junction of APAP) is under the influence of the electrostatic field produced by the charged groups of PG which are less compressible in the bulk solution and it may be the reason for the negative values of Φ_v and Φ_K. [21]

CONCLUSION

Experimental data at 293.15 K temperature of density, viscosity and speed of sound for acetaminophen-propylene glycol solutions have been reported. Several acoustic parameters have been calculated from the measured data. Density and viscosity were found to increase with the concentration and weak solute-solute interaction has been revealed through thermodynamic parameters. Speed of sound found to decrease with concentration of APAP; which results increase in adiabatic compressibility, free length due to internal pressure suggests weak solute-solvent interaction. Results indicated that the properties of propylene glycol are influenced by its interactions with acetaminophen.

ACKNOWLEDGEMENT

Authors are thankful to the funding agencies DST, New Delhi and UGC, New Delhi for providing financial assistance through DST - FIST (LEVEL - 1) project (SR/FST/PSI-001/2006) and DRS - SAP program grant [No.F.530/10/DRS/2010(SAP-1)] respectively, to develop experimental facilities which was utilized to carry out this work. Authors are also thankful to Prof. P. N. Gajjar, Head, Department of Physics, University School of Sciences, Gujarat University, Ahmedabad for his constant encouragement.

REFERENCES

1. W. Curatolo, Pharm. Sci. Tech. Today, **1.9** (1998), pp. 387-393.
2. M. J. Iqbal and M.A. Chaudhry, J. Chem. Thermodyn., **41** (2009), pp. 221-226.
3. R. B. Tôrres, A.C.M. Marchiore, and P.L.O. Volpe, J. Chem. Thermodyn., **38** (2006), pp. 526-541.
4. C. M. Dudhe and K.C. Patil, Int. J. Pharm. Pharm. Sci. Res., **2** (2012), pp. 76-78.
5. World Health Organization, 2017.
6. C. M. McLoughlin, W.A.M. McMinn, and T.R.A. Magee, Powder Technol., **134** (2003), pp. 40-51.
7. F. M. Russell, F. Shann, N. Curtis, and K. Mulholland, Bull. World Health Organ., **81** (2003), pp. 367-372.
8. M. L. Williams, F.L. Robert, and J.D. Ferry, J. Am. Chem. Soc., **77** (1955), pp. 3701-3707.
9. P. D. Martino, G.F. Palmieri, and S. Martelli, Chem. Pharm. Bull., **48** (2000), pp. 1105-1108.
10. A. Jouyban, Handbook of Solubility Data for Pharmaceuticals (CRC Press, 2009).
11. E. M. Cheng, M. Fareq, F. S. Abdullah, F. H. Wee, S. F. Khor, Y. S. Lee, M. Afendi, M. Shukry, A. B. Shahriman, and W. Khairunizanm, IEEERFM, 2013, pp. 409–413.
12. V. A. Rana and H. A. Chaube, J. Mol. Liq., **173** (2012), pp. 71-76.
13. A. Ali, S. Hyder, and A. K. Nain, J. Mol. Liq., **79** (1999), pp. 89-99.
14. D. R. Lide, CRC Handbook of Chemistry and Physics (CRC Boca Raton, 2012).
15. D. S. Kumar and D. K. Rao, (2007).
16. Pandit, T. R., and V. A. Rana. "Acoustical properties of aqueous solutions of paracetamol at different temperatures.".
17. R. Francesconi, A. Bigi, K. Rubini, and F. Comelli, J. Chem. Eng. Data, **50** (2005), pp. 1932-1937.
18. G. Arul and L. Palaniappan, (2005).
19. P. S. Naidu and K. R. Prasad, (2004).
20. J. P. Singh and R. Sharma, Rn, **10** (2013), pp. 1026.
21. H. Rodríguez, A. Soto, A. Arce, and M.K. Khoshkbarchi, J. Solution Chem., **32** (2003), pp. 53-63.