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CHEMICAL THERMODYNAMICS AND THERMOCHEMISTRY

# Partial and Apparent Molar Volume of Azithromycin in Its Solutions in Ethanol, 1-Propanol, and 1-Butanol at 300.15, 305.15, 310.15 K and Ambient Pressure

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**Abstract**—The densities and ultrasound velocities in azithromycin solutions in ethanol, 1-propanol and 1-butanol at various concentrations and at three different temperatures ($T$ = 300.15, 305.15, and 310.15 K) have been measured. Based on the data obtained, various derived acoustical parameters viz, acoustic impedance ($Z$), adiabatic compressibility (β), intermolecular free length ($L_f$), free volume ($V_f$), Rao's constant ($R$), Wada's constant ($W$), partial molar volume ($V_\Phi$), and hence apparent molar volume ($V_\Phi^0$) of the solute have been calculated. The results are discussed on the basis of the nature of solute-solvent interactions.

**Keywords:** acoustical, molecular interaction, acoustic impedance, azithromycin, partial molar volume, apparent molar volume

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## INTRODUCTION

Studies of intermolecular interactions play an important role in understanding the interactions that take place in solutions. Changes in density, viscosity, ultrasound velocity and other parameters from temperature and concentration have been considered by many scientists and shed light on the structural changes occurring in solutions [1–5].

The choice of a suitable solvent is of primary scientific interest in order to obtain the required efficiency, selectivity and kinetics of a chemical process. The presence of hydrogen bonds in polar solvents has a significant effect on the dielectric, physicochemical and acoustic properties of mixtures. Alcohols are widely used as solvents in chemical and pharmaceutical industries, during extraction [6–8], as dispersing agents for nanomaterials [9–12] and for the synthesis of other organic compounds [13–16]. A large number of studies devoted to alcohols and their mixtures at various temperatures and pressures have been carried out using densimetry, viscometry, spectroscopy, and computer chemistry [17–29]. In clinical medicine, undesirable drug–alcohol interactions are of common concern [30]. Heavy drinking and its combined effect with the antibiotics resulted into deadly incidental and intentional poisoning. When a new drug is synthesized, drug-alcohol interactions should be thoroughly studied [30, 31].

Azithromycin (Fig. 1) is a macrolide antibiotic similar in structure to erythromycin. Azithromycin has increased activity against Gram-negative bacteria compared with erythromycin, while maintaining activity against Gram-positive organisms. Azithromycin is characterized by good oral bioavailability, excellent tissue penetration and persistence, and long elimination half-lives [32]. Azithromycin demonstrates good results in vitro against Zika and Ebola viruses [33] and severe respiratory diseases. Recently, the evaluation of azithromycin as a drug for the COVID-19 therapy has started [34–37].

Therefore, in the present article we report the experimental densities, ultrasonic velocities and the derived parameters of azithromycin solutions of various concentrations and at different temperatures: 300.15, 305.15, and 310.15 K in ethanol, 1-propanol, and 1-butanol.

## EXPERIMENTAL

In the present study, the chemicals used are ethanol, 1-propanol, and 1-butanol, are of AR grade. These chemicals were used without any further purification. The details of these chemicals are given in Table 1. All the solutions were prepared gravimetrically and are kept hermetically sealed to prevent contact with moisture from the air and evaporation. Solutions were prepared using CONTECH CA 224 analytical balance (e ± 0.0001 g). The solutions of different

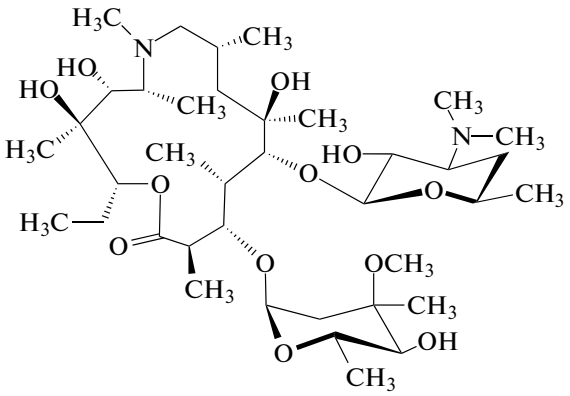

**Fig. 1.** Structure of azithromycin.

molality viz, 0.0144, 0.0275, 0.0394, 0.0503, 0.0602, 0.0694, 0.0779, 0.0858, 0.0931, and 0.1 of azithromycin were prepared in ethanol, 1-propanol, and 1-butanol. The solutions were gently stirred on a magnetic stirrer before measurements. Care was taken to avoid contamination during mixing. The estimated uncertainty of molality value is $u(m) = \pm 1 \times 10^{-3}$.

Densities were measured using calibrated pycnometer with nominal volume of 10 $cm^3$. The ultrasonic velocity ($u$) was measured on digital ultrasonic pulse echo velocity meter (Vi Microsystems Pvt. Ltd. model VCT-70) at 2 MHz with an accuracy of 0.1% (2 ± 0.0001 MHz). The estimated uncertainity of ultrasonic velocity is within $u(m) = \pm 1.09$ m $s^{-1}$. The instrument has a built-in thermostat to maintain the temperature (±0.1 K). Ultrasonic velocity meter was calibrated with triple distilled water and pure methanol at 300.15, 305.15, and 310.15 K.

## RESULTS AND DISCUSSION

The comparison of experimentally obtained values of densities (ρ) and ultrasonic velocity ($U$) of pure liquids with literature values is presented in Table 2.

The experimentally determined values of density (ρ), ultrasonic velocity ($u$) for all solutions of the drug at different concentrations and at $T$ = 300.15, 305.15, and 310.15 K are listed in Table 3. The data on density and ultrasonic velocity were used to calculate acoustical parameters [45] viz., acoustic impedance ($Z$), adiabatic

**Table 1.** Specification and mass fraction purity[a] of chemical samples

| S.N. | Chemical name | Source | CAS no. | $M$, g/mol | Fraction purity |
|---|---|---|---|---|---|
| 1 | Ethanol | Merck | 64-17-5 | 46.07 | ≥99.9% |
| 2 | 1-Propanol | Merck | 71-23-8 | 60.10 | ≥99.5% |
| 3 | 1-Butanol | Merck | 71-36-3 | 74.12 | ≥99.5% |
| 4 | Azithromycin | — | 83905-01-5 | 749 | |

[a] Purity as provided by supplier.

**Table 2.** Comparison of experimental densities (ρ) and ultrasonic velocity ($u$) of pure liquids with interpolated literature values at 300.15, 305.15, and 310.15 K and atmospheric pressure

| Liquids | $\rho \times 10^{-3}$, kg $m^{-3}$ | | $u$, m $s^{-1}$ | |
|---|---|---|---|---|
| | exp. | literature | exp. | literature |
| | 300.15 K | | | |
| Ethanol | 0.7810 | 0.7893 [38] | 1128.2 | 1127.4 [39] |
| 1-Propanol | 0.7962 | 0.798 [39] | 1188.1 | 1189.2 [38] |
| 1-Butanol | 0.8042 | 0.8069 [38] | 1227.9 | 1225.8 [13] |
| | 305.15 K | | | |
| Ethanol | 0.7875 | 0.7873 [38] | 1108.9 | 1109.4 [38] |
| 1-Propanol | 0.7959 | 0.7955 [40] | 1170.1 | 1169.7 [38] |
| 1-Butanol | 0.7942 | 0.7946 [42] | 1203.2 | 1203 [44] |
| | 310.15 K | | | |
| Ethanol | 0.7853 | 0.7855 [38] | 1093.1 | 1092.9 [43] |
| 1-Propanol | 0.7879 | 0.7873 [41] | 1098.3 | 1093 [41] |
| 1-Butanol | 0.7955 | 0.7945 [41] | 1188.9 | 1189.5 [43] |

**Table 3.** Molality ($m$), density (ρ), ultrasonic velocity ($u$), adiabatic compressibility (β), acoustic impedance ($Z$), intermolecular free length ($L_f$), free volume ($V_f$), Rao's constant ($R$), Wada's constant ($W$), and partial molar volume ($V_Φ$) for the solution of drug in ethanol, 1-propanol, and 1-butanol at 300.15, 305.15, 310.15 K and atmospheric pressure

| $m$, mol kg$^{-1}$ | ρ, kg/m$^3$ | $u$, m s$^{-1}$ | $Z \times 10^{-5}$, kg m$^{-2}$ s$^{-1}$ | $\beta \times 10^{10}$, m$^2$ N$^{-1}$ | $L_f \times 10^{11}$, m | $V_f \times 10^6$, m$^3$ mol$^{-1}$ | $R$ | $W$ | $V_Φ \times 10^{-6}$, m$^3$ mol$^{-1}$ |
|---|---|---|---|---|---|---|---|---|---|
| Ethanol, $T = 300.15$ K | | | | | | | | | |
| 0.014 | 772.63 | 1149.19 | 8.879 | 9.592 | 9.901 | 2.718 | 0.0393 | 1.407 | 55.123 |
| 0.028 | 780.02 | 1159.15 | 9.042 | 9.499 | 9.804 | 2.830 | 0.0390 | 1.411 | 54.191 |
| 0.039 | 791.74 | 1172.63 | 9.284 | 9.352 | 9.653 | 3.008 | 0.0384 | 1.412 | 53.958 |
| 0.050 | 800.31 | 1182.52 | 9.464 | 9.247 | 9.545 | 3.116 | 0.0380 | 1.412 | 53.755 |
| 0.060 | 805.45 | 1188.75 | 9.575 | 9.181 | 9.476 | 3.181 | 0.0378 | 1.413 | 53.58 |
| 0.069 | 817.74 | 1202.89 | 9.837 | 9.041 | 9.332 | 3.264 | 0.0372 | 1.414 | 53.392 |
| 0.078 | 824.88 | 1211.52 | 9.994 | 8.943 | 9.230 | 3.453 | 0.0369 | 1.416 | 53.25 |
| 0.086 | 830.31 | 1218.25 | 10.115 | 8.875 | 9.160 | 3.538 | 0.0367 | 1.417 | 53.128 |
| 0.093 | 836.14 | 1225.81 | 10.249 | 8.810 | 9.093 | 3.633 | 0.0365 | 1.419 | 52.994 |
| 0.102 | 842.88 | 1234.06 | 10.402 | 8.723 | 9.004 | 3.852 | 0.0362 | 1.421 | 52.842 |
| Ethanol, $T = 305.15$ K | | | | | | | | | |
| 0.014 | 720.34 | 1077.28 | 7.760 | 10.289 | 10.619 | 2.534 | 0.0422 | 1.438 | 55.669 |
| 0.028 | 733.45 | 1092.57 | 8.013 | 10.102 | 10.426 | 2.661 | 0.0414 | 1.440 | 55.383 |
| 0.039 | 742.31 | 1103.04 | 8.188 | 9.975 | 10.296 | 2.820 | 0.0410 | 1.444 | 55.125 |
| 0.050 | 754.02 | 1116.44 | 8.418 | 9.815 | 10.131 | 2.935 | 0.0403 | 1.446 | 54.918 |
| 0.060 | 770.31 | 1135.21 | 8.745 | 9.600 | 9.909 | 3.042 | 0.0395 | 1.448 | 54.683 |
| 0.069 | 778.67 | 1145.35 | 8.918 | 9.495 | 9.800 | 3.108 | 0.0391 | 1.449 | 54.515 |
| 0.078 | 788.88 | 1157.86 | 9.134 | 9.351 | 9.651 | 3.302 | 0.0386 | 1.451 | 54.271 |
| 0.086 | 801.79 | 1172.74 | 9.403 | 9.190 | 9.486 | 3.416 | 0.0380 | 1.451 | 54.129 |
| 0.093 | 805.74 | 1178.53 | 9.496 | 9.142 | 9.436 | 3.501 | 0.0378 | 1.456 | 53.97 |
| 0.102 | 822.32 | 1197.20 | 9.845 | 8.941 | 9.229 | 3.758 | 0.0371 | 1.457 | 53.81 |
| Ethanol, $T = 310.15$ K | | | | | | | | | |
| 0.014 | 715.46 | 1063.38 | 7.608 | 10.359 | 10.692 | 2.517 | 0.0425 | 1.351 | 56.163 |
| 0.028 | 728.62 | 1078.68 | 7.859 | 10.169 | 10.496 | 2.644 | 0.0417 | 1.353 | 55.856 |
| 0.039 | 740.31 | 1092.39 | 8.087 | 10.002 | 10.324 | 2.812 | 0.0411 | 1.355 | 55.559 |
| 0.050 | 748.89 | 1102.72 | 8.258 | 9.882 | 10.200 | 2.915 | 0.0406 | 1.357 | 55.335 |
| 0.060 | 756.89 | 1112.31 | 8.419 | 9.770 | 10.084 | 2.989 | 0.0402 | 1.359 | 55.056 |
| 0.069 | 768.76 | 1126.05 | 8.657 | 9.617 | 9.926 | 3.068 | 0.0396 | 1.361 | 54.843 |
| 0.078 | 777.74 | 1136.86 | 8.842 | 9.485 | 9.790 | 3.256 | 0.0392 | 1.363 | 54.604 |
| 0.086 | 784.61 | 1145.27 | 8.986 | 9.392 | 9.693 | 3.343 | 0.0389 | 1.365 | 54.43 |
| 0.093 | 794.89 | 1157.58 | 9.201 | 9.267 | 9.565 | 3.453 | 0.0384 | 1.367 | 54.253 |
| 0.102 | 802.94 | 1167.07 | 9.371 | 9.157 | 9.452 | 3.670 | 0.0380 | 1.369 | 54.043 |
| 1-Propanol, $T = 300.15$ K | | | | | | | | | |
| 0.014 | 796.27 | 1100.54 | 8.763 | 9.308 | 9.607 | 2.801 | 0.0382 | 1.472 | 71.532 |
| 0.028 | 806.27 | 1112.39 | 8.969 | 9.189 | 9.485 | 2.926 | 0.0377 | 1.473 | 71.271 |
| 0.039 | 815.13 | 1123.23 | 9.156 | 9.084 | 9.376 | 3.097 | 0.0373 | 1.475 | 71.053 |
| 0.050 | 825.99 | 1136.60 | 9.388 | 8.960 | 9.248 | 3.216 | 0.0368 | 1.477 | 70.794 |
| 0.060 | 830.84 | 1142.59 | 9.493 | 8.901 | 9.187 | 3.282 | 0.0366 | 1.478 | 70.606 |
| 0.069 | 836.27 | 1150.62 | 9.622 | 8.841 | 9.125 | 3.338 | 0.0364 | 1.483 | 70.433 |
| 0.078 | 843.99 | 1160.88 | 9.798 | 8.740 | 9.021 | 3.533 | 0.0361 | 1.487 | 70.212 |
| 0.086 | 855.99 | 1176.65 | 10.072 | 8.608 | 8.885 | 3.647 | 0.0356 | 1.492 | 69.986 |
| 0.093 | 862.56 | 1185.10 | 10.222 | 8.540 | 8.815 | 3.748 | 0.0353 | 1.494 | 69.851 |
| 0.102 | 868.27 | 1192.51 | 10.354 | 8.468 | 8.741 | 3.968 | 0.0351 | 1.496 | 69.636 |

**Table 3.** (Contd.)

| $m$, mol kg$^{-1}$ | ρ, kg/m$^3$ | $u$, m s$^{-1}$ | $Z \times 10^{-5}$, kg m$^{-2}$ s$^{-1}$ | $\beta \times 10^{10}$, m$^2$ N$^{-1}$ | $L_f \times 10^{11}$, m | $V_f \times 10^6$, m$^3$ mol$^{-1}$ | $R$ | $W$ | $V_\Phi \times 10^{-6}$, m$^3$ mol$^{-1}$ |
|---|---|---|---|---|---|---|---|---|---|
| 1-Propanol, $T = 305.15$ K | | | | | | | | | |
| 0.014 | 750.27 | 1035.71 | 7.771 | 9.878 | 10.196 | 2.639 | 0.0405 | 1.438 | 73.292 |
| 0.028 | 762.27 | 1049.98 | 8.004 | 9.720 | 10.032 | 2.766 | 0.0399 | 1.441 | 72.859 |
| 0.039 | 774.84 | 1065.72 | 8.258 | 9.556 | 9.864 | 2.943 | 0.0392 | 1.444 | 72.546 |
| 0.050 | 781.99 | 1074.59 | 8.403 | 9.464 | 9.768 | 3.044 | 0.0389 | 1.446 | 72.123 |
| 0.060 | 791.99 | 1086.49 | 8.605 | 9.337 | 9.637 | 3.128 | 0.0384 | 1.448 | 71.814 |
| 0.069 | 805.99 | 1103.06 | 8.891 | 9.173 | 9.468 | 3.217 | 0.0378 | 1.449 | 71.528 |
| 0.078 | 813.99 | 1112.72 | 9.057 | 9.062 | 9.354 | 3.407 | 0.0374 | 1.451 | 71.189 |
| 0.086 | 830.56 | 1131.67 | 9.399 | 8.872 | 9.157 | 3.539 | 0.0367 | 1.451 | 70.869 |
| 0.093 | 837.41 | 1141.19 | 9.556 | 8.797 | 9.080 | 3.638 | 0.0364 | 1.456 | 70.615 |
| 0.102 | 843.72 | 1148.94 | 9.694 | 8.715 | 8.995 | 3.856 | 0.0362 | 1.457 | 70.389 |
| 1-Propanol, $T = 310.15$ K | | | | | | | | | |
| 0.014 | 731.74 | 1005.29 | 7.356 | 7.356 | 10.454 | 2.574 | 0.0415 | 1.412 | 74.266 |
| 0.028 | 739.99 | 1015.03 | 7.511 | 7.511 | 10.334 | 2.685 | 0.0411 | 1.413 | 73.877 |
| 0.039 | 748.56 | 1025.61 | 7.677 | 7.677 | 10.210 | 2.844 | 0.0406 | 1.416 | 73.571 |
| 0.050 | 756.27 | 1034.85 | 7.826 | 7.826 | 10.100 | 2.944 | 0.0402 | 1.417 | 73.246 |
| 0.060 | 763.74 | 1043.73 | 7.971 | 7.971 | 9.994 | 3.016 | 0.0398 | 1.419 | 73.012 |
| 0.069 | 773.19 | 1054.69 | 8.155 | 8.155 | 9.869 | 3.086 | 0.0394 | 1.419 | 72.693 |
| 0.078 | 780.84 | 1063.78 | 8.306 | 8.306 | 9.751 | 3.269 | 0.0390 | 1.421 | 72.442 |
| 0.086 | 787.99 | 1072.19 | 8.449 | 8.449 | 9.652 | 3.358 | 0.0387 | 1.422 | 72.209 |
| 0.093 | 795.99 | 1082.02 | 8.613 | 8.613 | 9.552 | 3.458 | 0.0383 | 1.424 | 72.046 |
| 0.102 | 805.13 | 1092.87 | 8.799 | 8.799 | 9.426 | 3.680 | 0.0379 | 1.425 | 71.747 |
| 1-Butanol, $T = 300.15$ K | | | | | | | | | |
| 0.014 | 804.21 | 1198.42 | 9.638 | 9.216 | 9.512 | 2.829 | 0.0378 | 1.513 | 89.285 |
| 0.028 | 819.36 | 1216.20 | 9.965 | 9.042 | 9.333 | 2.973 | 0.0371 | 1.514 | 88.999 |
| 0.039 | 826.5 | 1224.86 | 10.123 | 8.959 | 9.247 | 3.140 | 0.0368 | 1.515 | 88.769 |
| 0.050 | 831.93 | 1231.50 | 10.245 | 8.896 | 9.182 | 3.239 | 0.0366 | 1.515 | 88.567 |
| 0.060 | 839.07 | 1240.28 | 10.407 | 8.813 | 9.097 | 3.314 | 0.0363 | 1.517 | 88.416 |
| 0.069 | 849.36 | 1252.39 | 10.637 | 8.704 | 8.984 | 3.390 | 0.0358 | 1.517 | 88.212 |
| 0.078 | 856.21 | 1261.75 | 10.803 | 8.615 | 8.892 | 3.584 | 0.0356 | 1.52 | 88.021 |
| 0.086 | 862.55 | 1269.79 | 10.953 | 8.543 | 8.818 | 3.675 | 0.0353 | 1.522 | 87.857 |
| 0.093 | 877.64 | 1287.62 | 11.301 | 8.393 | 8.663 | 3.813 | 0.0347 | 1.522 | 87.685 |
| 0.102 | 883.07 | 1295.15 | 11.437 | 8.326 | 8.594 | 4.036 | 0.0346 | 1.525 | 87.568 |
| 1-Butanol, $T = 305.15$ K | | | | | | | | | |
| 0.014 | 747.93 | 1113.51 | 8.328 | 9.909 | 10.228 | 2.631 | 0.0406 | 1.461 | 90.982 |
| 0.028 | 756.21 | 1125.16 | 8.509 | 9.798 | 10.113 | 2.744 | 0.0402 | 1.467 | 90.715 |
| 0.039 | 771.07 | 1143.34 | 8.816 | 9.603 | 9.912 | 2.929 | 0.0394 | 1.47 | 90.393 |
| 0.050 | 774.50 | 1148.27 | 8.893 | 9.555 | 9.863 | 3.015 | 0.0393 | 1.473 | 90.215 |
| 0.060 | 782.21 | 1158.57 | 9.062 | 9.454 | 9.758 | 3.089 | 0.0389 | 1.477 | 89.914 |
| 0.069 | 794.35 | 1173.72 | 9.323 | 9.307 | 9.607 | 3.171 | 0.0383 | 1.479 | 89.643 |
| 0.078 | 804.79 | 1188.08 | 9.562 | 9.166 | 9.461 | 3.369 | 0.0379 | 1.486 | 89.472 |
| 0.086 | 818.79 | 1204.94 | 9.866 | 8.999 | 9.289 | 3.489 | 0.0372 | 1.487 | 89.286 |
| 0.093 | 829.07 | 1217.33 | 10.093 | 8.885 | 9.171 | 3.602 | 0.0368 | 1.489 | 89.074 |
| 0.102 | 831.03 | 1222.19 | 10.157 | 8.848 | 9.132 | 3.798 | 0.0367 | 1.495 | 88.878 |

**Table 3.** (Contd.)

| $m$, mol kg$^{-1}$ | ρ, kg/m$^3$ | $u$, m s$^{-1}$ | $Z \times 10^{-5}$, kg m$^{-2}$ s$^{-1}$ | $\beta \times 10^{10}$, m$^2$ N$^{-1}$ | $L_f \times 10^{11}$, m | $V_f \times 10^6$, m$^3$ mol$^{-1}$ | $R$ | $W$ | $V_\Phi \times 10^{-6}$, m$^3$ mol$^{-1}$ |
|---|---|---|---|---|---|---|---|---|---|
| 1-Butanol $T = 310.15$ K | | | | | | | | | |
| 0.014 | 725.64 | 1012.28 | 7.346 | 10.213 | 10.542 | 2.553 | 0.0419 | 1.408 | 93.989 |
| 0.028 | 733.93 | 1025.17 | 7.524 | 10.095 | 10.420 | 2.663 | 0.0414 | 1.415 | 93.595 |
| 0.039 | 742.5 | 1036.39 | 7.695 | 9.973 | 10.293 | 2.820 | 0.0410 | 1.419 | 93.184 |
| 0.050 | 750.21 | 1048.69 | 7.867 | 9.865 | 10.182 | 2.920 | 0.0405 | 1.422 | 92.838 |
| 0.060 | 757.64 | 1063.40 | 8.057 | 9.760 | 10.074 | 2.992 | 0.0402 | 1.425 | 92.446 |
| 0.069 | 767.64 | 1075.82 | 8.258 | 9.631 | 9.941 | 3.064 | 0.0396 | 1.429 | 92.129 |
| 0.078 | 746.21 | 1088.35 | 8.121 | 9.885 | 10.203 | 3.124 | 0.0408 | 1.433 | 91.815 |
| 0.086 | 753.36 | 1099.19 | 8.281 | 9.781 | 10.096 | 3.210 | 0.0405 | 1.436 | 91.551 |
| 0.093 | 761.27 | 1112.05 | 8.466 | 9.676 | 9.988 | 3.307 | 0.0400 | 1.441 | 91.279 |
| 0.102 | 770.5 | 1124.77 | 8.666 | 9.543 | 9.850 | 3.521 | 0.0396 | 1.445 | 91.032 |

**Table 4.** The apparent molal volume of azithromycin drug in alcoholic solution at different temperature ($T$ = 300.15, 305.15, and 310.15 K)

| Sr. no. | Solvent | 300.15 K | | | 305.15 K | | | 310.15 K | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | $V_\Phi^0 \times 10^{-6}$, m$^3$/mol | $-S_m$ | $R^2$ | $V_\Phi^0 \times 10^{-6}$, m$^3$/mol | $-S_m$ | $R^2$ | $V_\Phi^0 \times 10^{-6}$, m$^3$/mol | $-S_m$ | $R^2$ |
| 1 | Ethanol | 296.2 | 183.6 | 0.999 | 309.8 | 216.7 | 0.999 | 315.3 | 246.4 | 0.999 |
| 2 | 1-Propanol | 297.8 | 199.4 | 0.998 | 313.8 | 246.7 | 0.997 | 345.4 | 349.0 | 0.999 |
| 3 | 1-Butanol | 318.9 | 219.1 | 0.996 | 338.3 | 342.4 | 0.997 | 346.9 | 289.1 | 0.998 |

compressibility (β), intermolecular free length ($L_f$), free volume ($V_f$), Rao's constant ($R$), Wada's constant ($W$), and partial molar volume ($V_m$) by the following equations:

$$\beta = 1/u^2\rho, \quad (1)$$

$$Z = u\rho, \quad (2)$$

$$L_f = K_T\sqrt{\beta}, \quad (3)$$

where $K_T$ is temperature dependent constant known as Jacobson's constant

$$K_T = (93.875 + 0.375T) \times 10^{-8},$$

where $T$ is absolute temperature, free volume

$$V_f = [M_{eff}u/K\eta]^{1/2}, \quad (4)$$

where $M_{eff}$ is effective molecular weight, Rao's constant:

$$R = \left(\frac{M}{\rho}\right)(u)^{1/3}, \quad (5)$$

Wada's constant:

$$W = \frac{M(B)^{-1/7}}{\rho}, \quad (6)$$

where $M$ is molecular weight of solute, partial molar volume of azithromycin:

$$V_\Phi = \frac{M_2}{\rho} + \frac{(\rho_0 - \rho)}{m\rho_0\rho}. \quad (7)$$

It is observed from Table 3 that the densities and ultrasonic velocities increase with concentration. Same types of the trends are observed at $T$ = 300.15, 305.15, and 310.15 K. The product of density and ultrasonic velocity is the acoustic impedance ($Z$). $Z$ increases gradually with increase in concentration and decreases with increase in temperature. This reflects the structure making action through strong hydrogen bonding [46]. Adiabatic compressibility (β) varies inversely to ultrasonic velocity and density (Eq. (2)). With the increase in the molality of the solution, β decreases linearly at the studied temperature. Naik et al. also reported the same trend in the values of β [1]. This indicates the closer packing of the molecules [47]. Intermolecular free length ($L_f$) is the indicator of the interactions between the solute and solvent due to association between the molecules through H-bonding. With the increase in the concentration, the decrease in the $L_f$ values reflects the strong solute- solvent interactions. From the Table 3, it is observed that the value of $V_f$ increases with increase in the concen-

tration for all studied alcoholic solutions. This may be due to the dispersive forces of the component molecules. The decrease in the Rao's constant and the increase in the Wada's constant values confirms that these alcohols are associated in solution due to dipole–dipole interaction and hydrogen bonding.

The partial molar volume ($V_\varphi$) of the drug in ethanol, 1-propanol, and 1-butanol were calculated from the density measurements at the different temperatures by using Eq. (7). These $V_\varphi$ values are listed in Table 3. By using the values of the partial molar volumes, the apparent molar volumes ($V^0\varphi$) of the drug were evaluated by using Masson's equation [48] given below:

$$V_\varphi = V^0\varphi + S_m. \quad (8)$$

When $V_\varphi$ are plotted against molality, the intercept on $Y$ axis and slope gives the values of the apparent molar volume, $V^0\varphi$ and $S_m$, respectively. The negative values of the $S_m$ listed in Table 4 confirm the drug–solvent interactions [2].

## CONCLUSION

In the present work, densities and ultrasonic velocity in the solutions of azitromycin in ethanol, 1-propanol, and 1-butanol were experimentally determined at various concentrations and temperatures ($T$ = 300.15, 303.15, and 310.15 K). By using these values, acoustical parameters of the drug are calculated over the entire concentration range. The obtained data are interpreted in terms of molecular interactions between the drug and the alcohols. The negative values of the apparent molar volume of the solute confirmed the presence of strong H-bonding between the drug and alcohol [49]. The strength of H bonding increases with increase in the concentration and temperature. The extent intermolecular interactions is higher in 1-butanol than in other solvents. The temperature also play the major effect on these interactions.

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