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# Volumetric studies of antibiotics in aqueous media

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ABSTRACT

Acoustical and volumetric studies of antibiotics; dimetridazole (DMZ) and metronidazole (MNZ) were carried out to understand the various interactions present in antibiotic's aqueous solutions. Density and speed of sound of antibiotic solutions in water with the molality ranging (0.01–0.05 mol $kg^{-1}$) were measured over the temperature range from 293.15 K to 313.15 K. Volumetric and acoustical properties like apparent molar volume ($V^{\phi}$), adiabatic compressibility factor ($K_s$), isentropic compressibility ($K^{\phi}$), partial molar volume ($V^{o\phi}$) and partial molar compressibility ($K^{o\phi}$) of antibiotics were calculated from the experimental data of density and sound velocity. The derived data has been discussed in terms of solute-solute and solute-solvent interactions. The $V^{\phi}$ values are positive and $K^{\phi}$ values are negative for both antibiotics, indicative of strong solute-solvent interactions and closely packed structure of antibiotics in water.

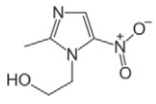


## 1. Introduction

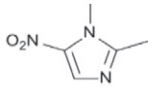
Solubility is a basic physico-chemical property that has significant applications to different industries like biological, chemical, pharmaceutical and environmental. It has been noted that by the addition of solute, changes occur in the structure of solvent. Presence of solute may either make or break the structure of solvent. The structural aspects of the liquid can be inferred from the density and sound velocity of the solutions at different solute concentrations and temperature as these properties give information about the intermolecular forces [1,2].

Thermodynamic properties like apparent molar volume and apparent molar isentropic compressibility of any solution can be evaluated by different volumetric properties of the system by which the co-solvent action and solute–solvent interactions can better be understood [3]. It gives a useful and reliable tool to study the properties of solutions of amino acids, drugs, polymers etc. The solubility data also serve to construct mathematical models that help to optimize solvent composition selection in pharmaceutical technology [4].

Globally, infections in gastrointestinal tract by different parasites and bacteria are responsible for major morbidity and deaths. 5-Nitroimidazoles, a set of medicines like tinidazole, dimetridazole, secnidazole, ronidazole and azomycin, is a well-established group of antiprotozoal and antibacterial agents. These antibiotics have many other biological uses of therapeutic importance like radio sensitizers in cancer treatment, control of fertility and as anti-tubercular agent [5–7]. Chemical nature of drugs is essential to study their behavior in living cells.



Metronidazole (MNZ)



Dimetridazole (DMZ)

Aqueous solution of antibiotics is of biologically and chemically importance as to enhance the solubility of drugs, aqueous mixtures is used [8–12]. Therefore, in the present study, through density and sound velocity measurements, solute-solvent and solute-solute interactions in aqueous solutions of antibiotics (DMZ and MNZ) have been studied at different temperatures (293.15 K, 298.15 K, 303.15 K, 308.15 K and 313.15 K).

## 2. Experimental

### 2.1. Materials

The Drugs (Metronidazole and Dimetridazole) (Fluka product; CAS No. 7681-76-7 and 551-92-8) of 98% and 99% used in this work. Double distilled de-ionized water with a conductivity of $1.5 \times 10^{-4}\ \Omega^{-1}\ m^{-1}$ for the preparation of aqueous antibiotic solutions.

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**Table 1**
Ultrasonic velocity ($u_o$) and density ($d_o$) data of water at different temperatures.

| Temperature/(K) | Sound velocity ($u_o$)/$ms^{-1}$ | Density ($d_o$)/$g \cdot cm^{-3}$ | Sound velocity/($ms^{-1}$) | Density/($g \cdot cm^{-3}$) |
|---|---|---|---|---|
| | This work | | Literature values | |
| 293.15 | 1481.63 | 0.999458 | 1482.32 [15] | 0.998220 [16] |
| 298.15 | 1499.66 | 0.999170 | 1497.00 [16] | 0.997100 [16] |
| 303.15 | 1509.57 | 0.997748 | 1509.40 [16] | 0.996071 [3] |
| 308.15 | 1517.15 | 0.995645 | 1519.83 [16] | 0.994058 [16] |
| 313.15 | 1529.63 | 0.994258 | 1529.30 [3] | 0.992210 [16] |

### 2.2. Methods

Doubly distilled de-ionized water has been used to prepare the solutions of drugs at different molal concentrations 0.01, 0.02, 0.03, 0.04 and 0.05 M (by w/w method). Weighing of solute was done by Wiggen Hauser electronic balance with a precision of ±0.001 mg. At least three readings of each composition were reproducible to ±0.005 mg and the obtained values were averaged. Density and speed of sound measurements of solutions of different concentrations at different temperature were carried out by using DSA 5000 M. Calibration of density sound analyzer (DSA 5000) was done using density of the standard materials such as; $H_2O$ and air at each temperature. The accuracy and repeatability of DSA 5000 M for density are $5 \times 10^{-6}$ g/cm$^3$ and $1 \times 10^{-6}$ g/cm$^3$ and that of temperature is 0.01 °C and 0.001 °C respectively. In the same way sound velocity is also measured by the instrument up to 0.5 m/s accuracy and 0.1 m/s repeatability.

## 3. Results and discussion

Behavior of liquids undertakes many physical properties like density, viscosity and speed of sound etc. Density variations are of major importance. Density (d) and sound velocity (u) data has been used for the calculations of apparent molar volume ($V_\phi$), adiabatic compressibility ($\beta$) and apparent molar compressibility ($V_\phi$) for antibiotics (DMZ and MNZ) in aqueous solutions at different temperatures (293.15, 298.15, 303.15, 308.15 and 313.15 K).

**Table 2a**
Molality (m), density (d) and sound velocity ($u_s$) data of DMZ in aqueous solution at different temperatures.

| Molality (m)/($mol \cdot kg^{-1}$) | Density (d)/($g \cdot cm^{-3}$) | Sound velocity ($\mu_s$)/($ms^{-1}$) |
|---|---|---|
| 293.15 K | | |
| 0.00 | 0.999458 | 1481.63 |
| 0.01 | 0.999465 | 1485.43 |
| 0.02 | 0.999504 | 1488.47 |
| 0.03 | 0.999623 | 1490.73 |
| 0.04 | 0.999728 | 1493.07 |
| 0.05 | 0.999849 | 1494.58 |
| 298.15 K | | |
| 0.00 | 0.999170 | 1499.66 |
| 0.01 | 0.999185 | 1504.09 |
| 0.02 | 0.999225 | 1507.65 |
| 0.03 | 0.999342 | 1510.36 |
| 0.04 | 0.999486 | 1512.83 |
| 0.05 | 0.999617 | 1514.23 |
| 303.15 K | | |
| 0.00 | 0.997748 | 1509.57 |
| 0.01 | 0.997778 | 1515.17 |
| 0.02 | 0.997832 | 1518.87 |
| 0.03 | 0.997958 | 1521.43 |
| 0.04 | 0.998081 | 1524.03 |
| 0.05 | 0.998212 | 1526.16 |
| 308.15 K | | |
| 0.00 | 0.995645 | 1517.15 |
| 0.01 | 0.995689 | 1522.51 |
| 0.02 | 0.995753 | 1526.11 |
| 0.03 | 0.995874 | 1529.31 |
| 0.04 | 0.995995 | 1532.09 |
| 0.05 | 0.996131 | 1534.55 |
| 313.15 K | | |
| 0.00 | 0.994258 | 1529.63 |
| 0.01 | 0.994314 | 1535.34 |
| 0.02 | 0.994393 | 1539.29 |
| 0.03 | 0.994502 | 1543.16 |
| 0.04 | 0.994653 | 1545.71 |
| 0.05 | 0.994839 | 1547.84 |

**Table 2b**
Molality (m), density (d) and sound velocity ($u_s$) data of MNZ in aqueous solution at different temperatures.

| Molality (m)/($mol \cdot kg^{-1}$) | Density (d)/($g \cdot cm^{-3}$) | Sound velocity ($\mu_s$)/($ms^{-1}$) |
|---|---|---|
| 293.15 K | | |
| 0.00 | 0.999458 | 1481.63 |
| 0.01 | 0.999460 | 1484.76 |
| 0.02 | 0.999475 | 1487.81 |
| 0.03 | 0.999509 | 1490.61 |
| 0.04 | 0.999650 | 1493.06 |
| 0.05 | 0.999710 | 1494.01 |
| 298.15 K | | |
| 0.00 | 0.999170 | 1499.66 |
| 0.01 | 0.999181 | 1502.81 |
| 0.02 | 0.999210 | 1505.89 |
| 0.03 | 0.999291 | 1508.77 |
| 0.04 | 0.999370 | 1511.31 |
| 0.05 | 0.999509 | 1512.11 |
| 303.15 K | | |
| 0.00 | 0.997748 | 1509.57 |
| 0.01 | 0.997769 | 1512.67 |
| 0.02 | 0.997795 | 1515.67 |
| 0.03 | 0.997882 | 1518.61 |
| 0.04 | 0.997991 | 1520.77 |
| 0.05 | 0.998147 | 1522.03 |
| 308.15 K | | |
| 0.00 | 0.995645 | 1517.15 |
| 0.01 | 0.995671 | 1520.23 |
| 0.02 | 0.995701 | 1523.32 |
| 0.03 | 0.995819 | 1526.16 |
| 0.04 | 0.995961 | 1528.12 |
| 0.05 | 0.996095 | 1529.56 |
| 313.15 K | | |
| 0.00 | 0.994258 | 1529.63 |
| 0.01 | 0.994291 | 1532.73 |
| 0.02 | 0.994353 | 1535.76 |
| 0.03 | 0.994477 | 1538.68 |
| 0.04 | 0.994597 | 1540.65 |
| 0.05 | 0.994751 | 1542.11 |