Acoustic studies of cefotaxime sodium in aqueous medium at different temperatures and at frequency 5 MHz under atmospheric pressure

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ABSTRACT: Ultrasonic velocity (U) and density (ρ) measurements have been performed for the antibiotic *Cefotaxime Sodium* in aqueous solution at five temperatures: 20°C, 25°C, 30°C, 35°C, and 40°C. These experimental values were employed to compute several thermodynamic and acoustic parameters, including adiabatic compressibility (β_a), change in adiabatic compressibility ($\Delta\beta$), relative adiabatic compressibility ($\Delta\beta/\beta°$), apparent molal volume (Φ_v), apparent molal compressibility (Φ_k), and their respective limiting values, $\Phi°_v$ and $\Phi°_k$. The variation of these parameters with temperature and concentration was analysed to explore the structure-making or structure-breaking behaviour of Cefotaxime Sodium in aqueous medium. The findings provide valuable insights into solute–solvent interactions and the molecular characteristics of this β-lactam antibiotic under thermal perturbation.

Keywords: Ultrasonic velocity, Interferometer, Cefotaxime Sodium, adiabatic compressibility, apparent molal volume, Aqueous medium.

INTRODUCTION

Understanding the molecular interactions between solutes and solvents in solution is critical for predicting the physicochemical behavior of pharmaceutical compounds, particularly antibiotics. Among various experimental techniques, ultrasonic velocity measurements have proven to be a powerful, non-invasive method for probing solute–solvent interactions, hydrogen bonding, and structural organization in liquids. These interactions significantly influence the stability, solubility, and bioavailability of drugs, and thus have direct implications for formulation science and therapeutic efficacy [1-2].

Cefotaxime sodium is a third-generation cephalosporin antibiotic known for its broad-spectrum antibacterial activity. It is commonly used to treat respiratory tract infections, urinary tract infections, meningitis, and is also administered prophylactically during surgical procedures to prevent postoperative infections. Despite its clinical importance, a deeper understanding of how this antibiotic behaves in aqueous media at the molecular level is essential for optimizing its formulation and delivery, especially under varying thermal and concentration conditions [3-6].

In recent years, researchers have employed acoustic, volumetric, and viscometric techniques to evaluate molecular interactions in aqueous solutions of various antibiotics such as vancomycin, doxycycline, and ampicillin. These studies utilize experimental measurements—ultrasonic velocity, density, and viscosity—to calculate acoustic and thermodynamic parameters such as adiabatic compressibility, apparent molal volume,

intermolecular free length, and others, which offer valuable insights into solute–solvent affinity, molecular packing, and structure-making or structure-breaking tendencies [7-10].

In the present investigation, the ultrasonic velocity, density, and viscosity of aqueous solutions of Cefotaxime sodium were measured at five temperatures (20°C, 25°C, 30°C, 35°C, and 40°C) and at varying molar concentrations, using a constant frequency of 5 MHz. From the experimental data, parameters such as adiabatic compressibility (β_a), apparent molal volume (Φ_v), apparent molal compressibility (Φ_k), and their limiting values were calculated. These parameters were then analyzed to interpret the nature and strength of molecular interactions, with particular attention to temperature-dependent structural modifications in the aqueous environment [7, 12-13].

MATERIALS AND METHODS

The antibiotic drug Cefotaxime sodium used in this study was procured from Laborate Pharmaceuticals India Limited. All solutions were prepared using double-distilled water to ensure purity and minimize ionic interference.

Density measurements were carried out using a Mettler Toledo handheld density meter, which offers high precision and is widely used for solution studies in pharmaceutical and chemical research [14-15]. To maintain consistent thermal conditions, a special thermostatic water bath was employed. The setup included continuous water circulation using an electric stirrer, and temperature control was achieved using an electronically operated digital constant temperature water bath with a precision of ±0.1°C [16-17].

Ultrasonic velocity measurements were conducted using a single crystal ultrasonic interferometer (Mittal type, Model F-83), operating in the frequency range of 1–10 MHz. For this investigation, measurements were made at a fixed frequency of 5 MHz, with a velocity accuracy of ±0.1 $m \cdot s^{-1}$. This technique is a standard and reliable method for probing molecular interactions in liquid systems [18-21].

The densities and ultrasonic velocities of pure water and aqueous solutions of Cefotaxime sodium were measured over a concentration range from 0.01 $mol \cdot kg^{-1}$ to 0.1 $mol \cdot kg^{-1}$, at five different temperatures: 20°C, 25°C, 30°C, 35°C, and 40°C. Each measurement was repeated at least three times to ensure reproducibility and reliability of the data.

RESULTS AND DISCUSSION

In the present investigation, experimental measurements of density (ρ), viscosity (η), and ultrasonic velocity (u) were carried out for Cefotaxime sodium solutions in water across various concentrations and temperatures. These fundamental measurements enabled the evaluation of several derived acoustic and thermodynamic parameters, which provide valuable insights into the solute–solvent interactions and structural behavior of the system.

1. Adiabatic Compressibility (β_a):

The adiabatic compressibility of the solution is a key parameter reflecting the ease with which a medium can be compressed under adiabatic conditions. It is calculated using the following relation:

$$\beta a = \frac{1}{u^2 \rho}$$

where u = ultrasonic velocity

ρ = density of the solution

2. Change in Adiabatic Compressibility (Δβ):

To evaluate the effect of solute on the compressibility of the medium, the change in adiabatic compressibility is calculated by:

$$\Delta\beta = \beta a - \beta^0$$

where β^0 is the compressibility of pure solvent (water).

3. Apparent Molal Volume (Φ_v):

The apparent molal volume, which provides information about the solute–solvent interactions and solvation behavior, is given by:

$$\Phi v = 1000 \frac{\rho^0 - \rho}{m\,\rho^0 \rho} + \frac{M}{\rho}$$

Where ρ^0 = density of pure solvent

M = molar mass of Cefotaxime sodium

m = molality

4. Apparent Molal Compressibility (Φ_k):

The apparent molal compressibility reflects the contribution of the solute to the compressibility of the solution and is calculated using:

$$\Phi_{k\,k} = 1000 \frac{(\beta a - \beta^0)}{m\,\rho^0} + \beta a \Phi v$$

5. Specific Acoustic Impedance (Z):

The specific acoustic impedance, representing the resistance to sound propagation in a medium, is determined from the product of ultrasonic velocity and density:

$$Z = u \cdot \rho$$

6. Relative Association (RA):

Relative association is a function of both ultrasonic velocity and density, and provides insight into solute–solvent molecular associations:

$$RA = \frac{\rho}{\rho 0}\left(\frac{u0}{u}\right)^{1/3}$$

Where u^0 and $\rho 0$ = velocity and density of the solvent

u and ρ = corresponding values for the solution

7. Relative Adiabatic Compressibility (RAC): The relative adiabatic compressibility, which quantifies the fractional change in compressibility upon solute addition, is expressed as:

$$RAC = \frac{\Delta\beta}{\beta^0}$$

These derived parameters were analyzed to assess the structure-making or structure-breaking tendencies of Cefotaxime sodium and to interpret the nature and extent of molecular interactions in the aqueous medium.

Table 1: Acoustic parameters of aqueous solution of Cefotaxime sodium at 20°C.

Conc.	Ultrasonic velocity u (cm/s)	Adiabatic Compressibility βa dyn-1.cm2	Acoustic Impedance Z dyn-1.cm2	App. Molar Volume Φv cm3.mol-1	App.Mol.Compr. Φk cm5. dyn-1mol-1
0.01	149200	4.49E-11	1.49E+05	259.02	-5.31E-08
0.02	150000	4.43E-11	1.50E+05	267.50	-4.89E-08
0.03	150700	4.39E-11	1.51E+05	273.31	-4.50E-08
0.04	151300	4.34E-11	1.52E+05	278.47	-4.13E-08
0.05	151800	4.31E-11	1.53E+05	279.33	-3.80E-08
0.06	152300	4.27E-11	1.54E+05	279.73	-3.58E-08
0.07	152800	4.23E-11	1.55E+05	281.31	-3.41E-08
0.08	153500	4.19E-11	1.56E+05	282.37	-3.42E-08
0.09	153700	4.17E-11	1.56E+05	283.07	-3.12E-08
0.1	154200	4.14E-11	1.57E+05	283.53	-3.04E-08

Table 2: Acoustic parameters of aqueous solution of Cefotaxime sodium at 25°C.

Conc.	Ultrasonic velocity u (cm/s)	Adiabatic Compressibility βa dyn-1.cm2	Acoustic Impedance Z dyn-1.cm2	App. Molar Volume Φv cm3.mol-1	App.Mol.Compr. Φk cm5. dyn-1mol-1
0.01	150600	4.48E-11	1.49E+05	262.07	-5.15E-08
0.02	151300	4.41E-11	1.50E+05	269.06	-4.46E-08
0.03	151900	4.36E-11	1.51E+05	276.06	-3.98E-08
0.04	152500	4.32E-11	1.52E+05	278.54	-3.74E-08
0.05	152900	4.28E-11	1.53E+05	279.00	-3.37E-08
0.06	153400	4.25E-11	1.54E+05	281.66	-3.20E-08
0.07	153800	4.21E-11	1.55E+05	282.98	-2.99E-08
0.08	154200	4.18E-11	1.55E+05	284.73	-2.83E-08
0.09	154700	4.15E-11	1.56E+05	285.86	-2.77E-08
0.1	155300	4.12E-11	1.57E+05	286.97	-2.77E-08

Table 3: Acoustic parameters of aqueous solution of Cefotaxime sodium at 30°C.

Conc.	Ultrasonic velocity u (cm/s)	Adiabatic Compressibility βa dyn-1.cm2	Acoustic Impedance Z dyn-1.cm2	App. Molar Volume Φv cm3.mol-1	App.Mol.Compr. Φk cm5. dyn-1mol-1
0.01	151600	4.36E-11	1.51E+05	266.18	-4.44E-08
0.02	152300	4.31E-11	1.52E+05	274.20	-4.05E-08
0.03	152900	4.27E-11	1.53E+05	280.55	-3.68E-08
0.04	153400	4.24E-11	1.54E+05	282.71	-3.35E-08
0.05	153900	4.20E-11	1.55E+05	283.79	-3.16E-08
0.06	154400	4.17E-11	1.55E+05	285.51	-3.01E-08
0.07	154800	4.14E-11	1.56E+05	287.47	-2.82E-08
0.08	155200	4.11E-11	1.57E+05	288.04	-2.69E-08
0.09	155700	4.08E-11	1.58E+05	288.26	-2.64E-08
0.1	156200	4.04E-11	1.58E+05	288.24	-2.60E-08

Table 4: Acoustic parameters of aqueous solution of Cefotaxime sodium at 35°C.

Conc.	Ultrasonic velocity u (cm/s)	Adiabatic Compressibility βa dyn-1.cm2	Acoustic Impedance Z dyn-1.cm2	App. Molar Volume Φv cm3.mol-1	App.Mol.Compr. Φk cm5. dyn-1mol-1
0.01	152800	4.30E-11	1.52E+05	274.36	-4.28E-08
0.02	153500	4.25E-11	1.53E+05	281.91	-3.90E-08
0.03	154100	4.21E-11	1.54E+05	286.10	-3.56E-08
0.04	154500	4.18E-11	1.55E+05	289.95	-3.09E-08
0.05	154900	4.15E-11	1.55E+05	290.23	-2.82E-08
0.06	155400	4.12E-11	1.56E+05	291.09	-2.73E-08
0.07	155700	4.10E-11	1.57E+05	291.11	-2.51E-08
0.08	156000	4.07E-11	1.57E+05	290.88	-2.34E-08
0.09	156500	4.04E-11	1.58E+05	290.69	-2.33E-08
0.1	156800	4.02E-11	1.59E+05	292.59	-2.20E-08

Table 5: Acoustic parameters of aqueous solution of Cefotaxime sodium at 40°C.

Conc.	Ultrasonic velocity u (cm/s)	Adiabatic Compressibility βa dyn-1.cm2	Acoustic Impedance Z dyn-1.cm2	App. Molar Volume Φv cm3.mol-1	App.Mol.Compr. Φk cm5. dyn-1mol-1
0.01	153500	4.27E-11	1.53E+05	278.55	-3.63E-08
0.02	154100	4.23E-11	1.53E+05	287.66	-3.25E-08
0.03	154600	4.19E-11	1.54E+05	291.70	-2.92E-08
0.04	155000	4.16E-11	1.55E+05	293.71	-2.61E-08
0.05	155500	4.13E-11	1.56E+05	294.91	-2.54E-08
0.06	155800	4.11E-11	1.56E+05	295.88	-2.30E-08
0.07	156300	4.07E-11	1.57E+05	296.57	-2.28E-08
0.08	156800	4.04E-11	1.58E+05	297.86	-2.26E-08
0.09	157200	4.01E-11	1.58E+05	298.06	-2.19E-08
0.1	157500	3.99E-11	1.59E+05	299.26	-2.07E-08

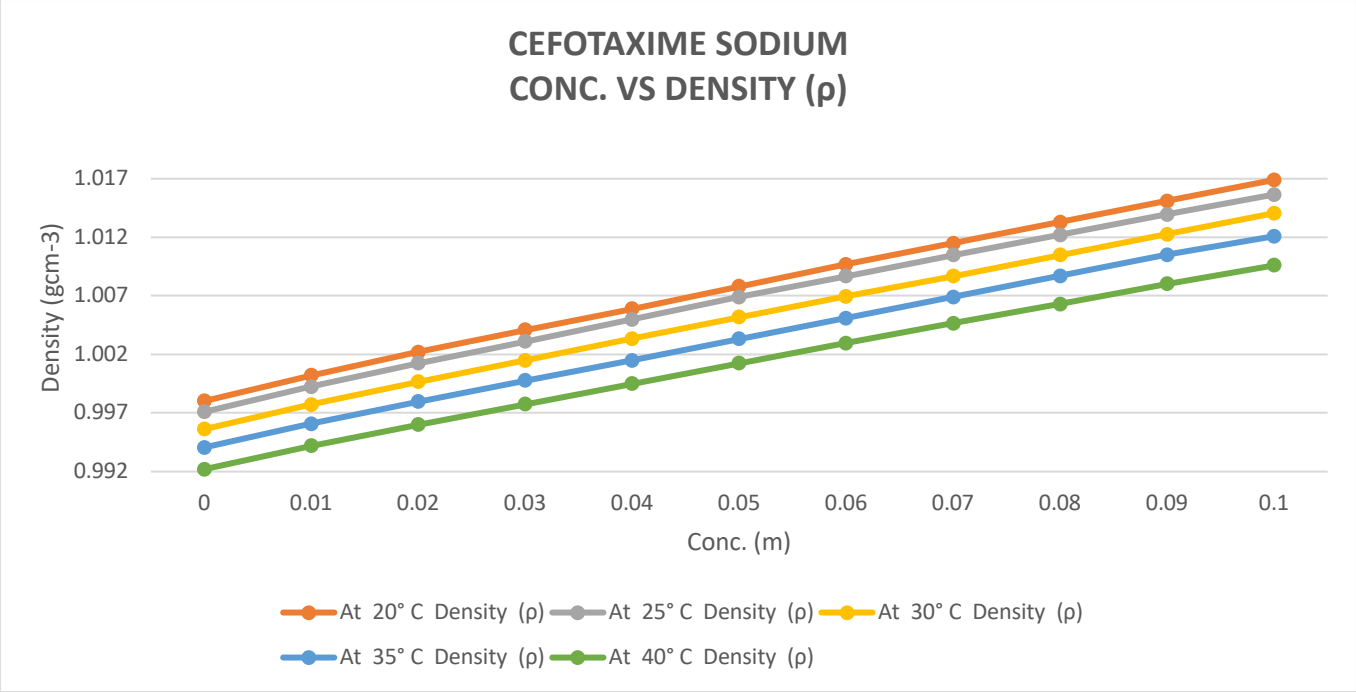

Fig 1: Concentration vs. Density

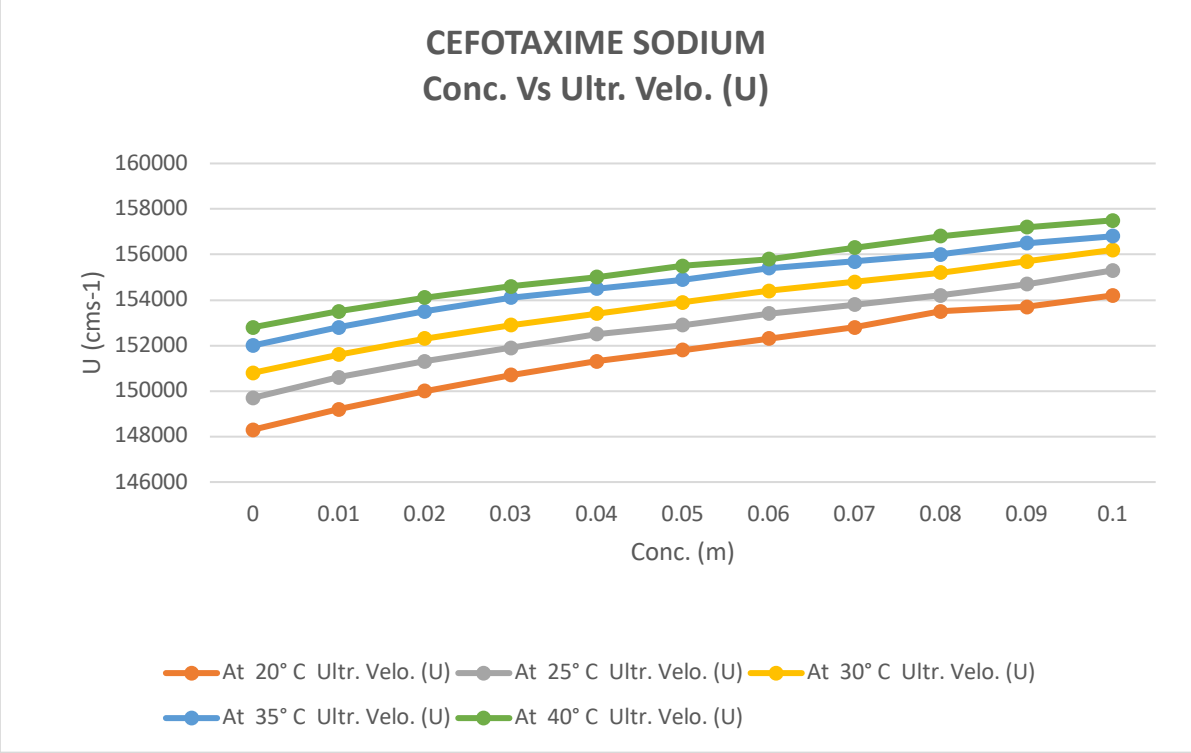

Fig. 2: Concentration vs. Ultrasonic Velocity

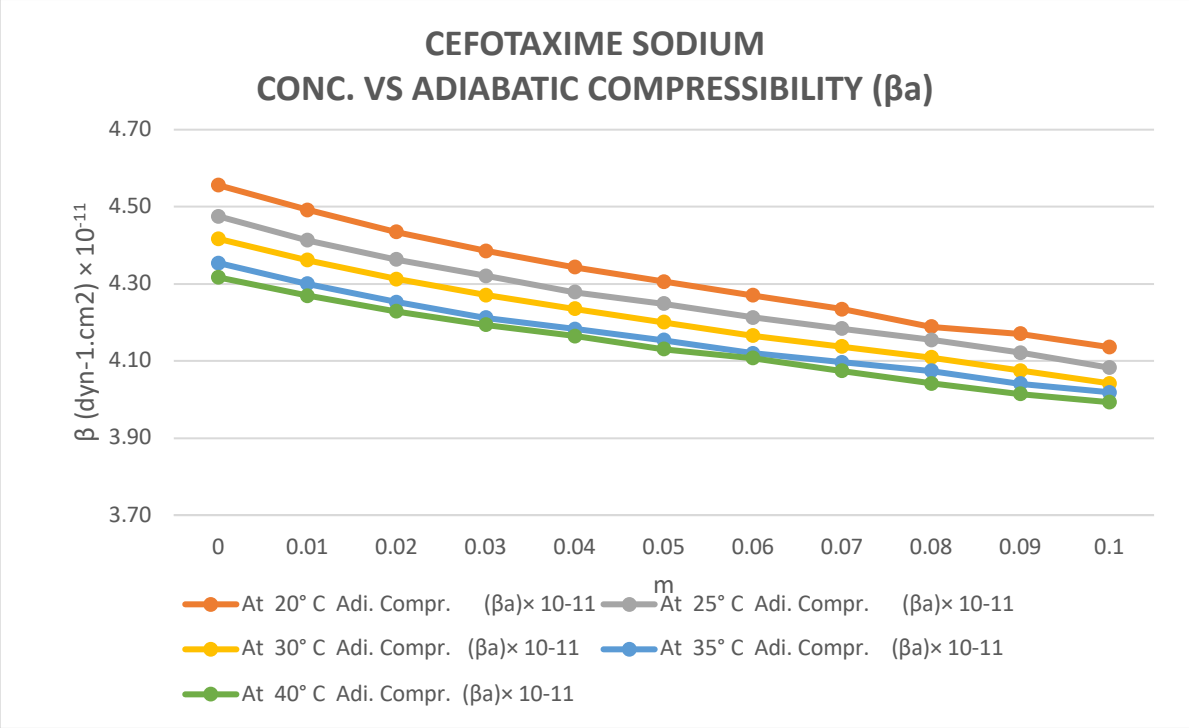

Fig. 3: Concentration vs. Adiabatic Compressibility

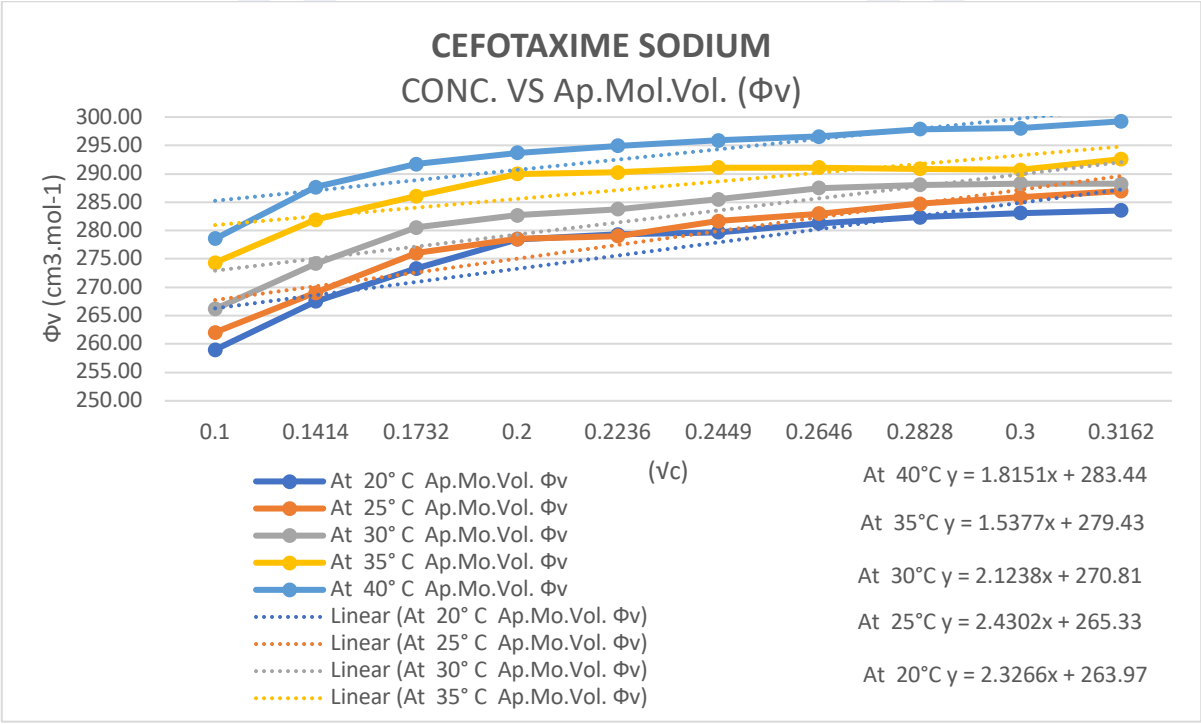

Fig. 4: Concentration vs. Apparent molal volume

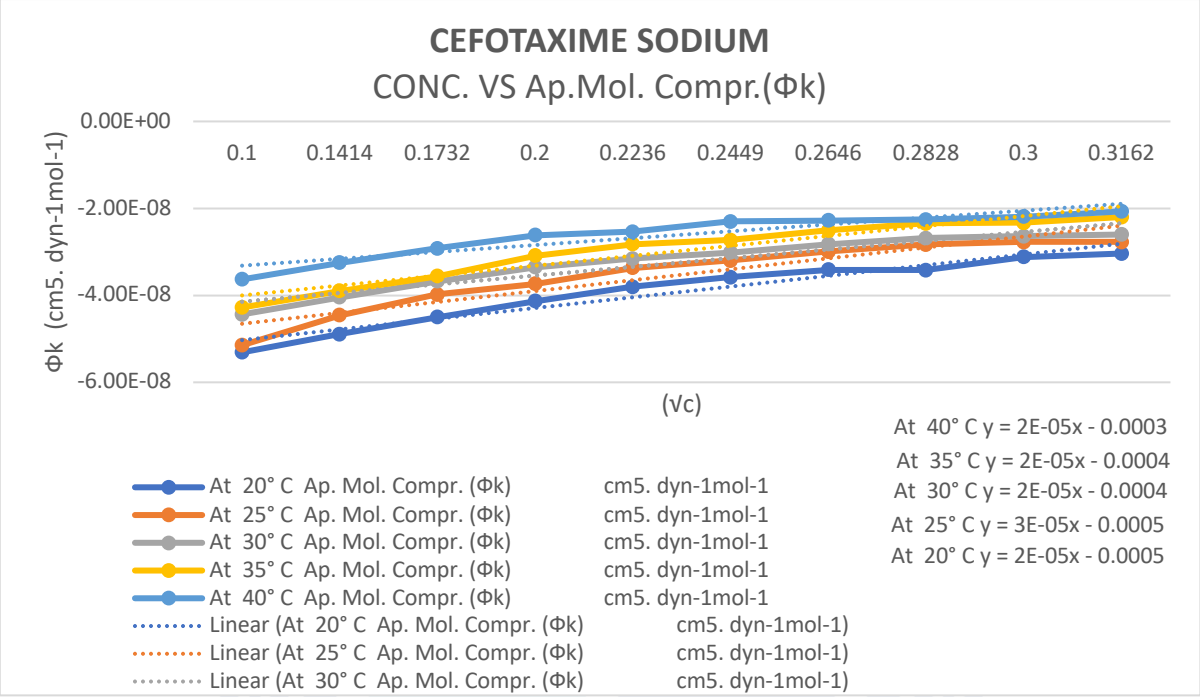

Fig. 5: Concentration vs. Apparent molal compressibility

The acoustic parameters of Cefotaxime sodium solutions were evaluated over a concentration range of 0.01–0.10 M at five different temperatures (20°C, 25°C, 30°C, 35°C, and 40°C) using a 5 MHz ultrasonic frequency. The variation in ultrasonic velocity (u), adiabatic compressibility (β_a), acoustic impedance (Z), apparent molar volume (Φ_v), and apparent molar compressibility (Φ_k) reveals valuable insights into the solute–solvent and solute–solute interactions in the solution medium. The key observations and their implications are discussed below:

The observed increase in ultrasonic velocity with both concentration and temperature reflects enhanced molecular interactions between Cefotaxime sodium and water molecules, primarily through hydrogen bonding and ion–dipole forces. This behavior, coupled with the consistent decrease in adiabatic compressibility (β_a), indicates increased molecular cohesion and reduced free volume, signifying the solute's structure-making propensity.

The slight rise in acoustic impedance (Z) with increasing concentration and temperature is attributed to the combined effects of elevated density and velocity, suggesting greater resistance to sound propagation due to reinforced intermolecular interactions. Apparent molar volume (Φ_v) exhibits a positive trend, indicating solute expansion through hydration shell formation and thermal effects. Concurrently, the apparent molar compressibility (Φ_k) becomes progressively less negative, signifying a reduction in solute–solvent interactions at higher concentrations and temperatures, alongside a transition toward solute–solute dominance.

Overall, the acoustic and volumetric data consistently support the classification of Cefotaxime sodium as a structure-making solute in aqueous media. These findings offer valuable insights into its solvation behavior

and molecular interaction dynamics, with significant implications for pharmaceutical formulation, stability, and transport mechanisms in biological systems.

CONCLUSION:

Density and sound velocity data was used to study the volumetric behavior of antibiotics cefotaxime sodium in water at different concentrations and temperatures. Density and sound velocity of antibiotic solutions cefotaxime sodium are measured which decreases and increases respectively with temperature due to increase in vibrations and kinetic energy. It is concluded that the values of apparent molar volume (Φ_v) calculated using density and sound velocity for all concentrations of solution at all temperatures are found positive which indicates the presence of strong ion-solvent interactions. Decrease in value of (Φ_v) with rise in temperature suggests that increase in temperature causes strong ion-solvent interactions. The values of slope of line of apparent molar volume (Sv), which is a measure of ion pair interactions, are negative, showing the presence of weak solute-solute interactions. Higher negative values of apparent molar isentropic compressibility (Φ_k) indicate a closed-packed structure in both antibiotic solutions owing to ion-solvent interactions. The higher negative values of partial molal isentropic compressibility (Φ_k) and positive values of slope of line of apparent molal isentropic compressibility (Sk) indicate weak solute-solute interactions.

The study reveals that Cefotaxime sodium acts as a structure-making solute in aqueous solutions, as indicated by increasing density, ultrasonic velocity, and apparent molar volume, and decreasing compressibility with concentration. These trends reflect strong solute-solvent interactions, especially at lower concentrations, which weaken with rising temperature and shift toward solute-solute interactions at higher concentrations. Apparent molar volume data further confirm enhanced hydration around the drug. These insights are valuable for optimizing drug formulation and understanding β-lactam behavior in solution.

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