

ACOUSTIC ANALYSIS OF MOLECULAR INTERACTIONS BETWEEN SULPHADIAZINE AND SELECTED ORGANIC SOLVENTS

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Abstract

This study investigates the molecular interactions between sulphadiazine and three organic solvents (ethyl alcohol, dioxane, and chloroform) through ultrasonic measurements. Various acoustic parameters including ultrasonic velocity, density, viscosity, isentropic compressibility, intermolecular free length, acoustic impedance, relative association, and solvation number were determined at 303K, 308K, and 313K across multiple concentrations. Results indicate significant differences in solute-solvent interactions based on solvent polarity. Sulphadiazine exhibits stronger interactions with ethyl alcohol compared to dioxane and chloroform, attributed to hydrogen bonding and dipole-dipole interactions prevalent in polar solvents. The increase in ultrasonic velocity, density, and viscosity with concentration, alongside decreasing isentropic compressibility, confirms the formation of intermolecular bonds within these systems. This acoustic analysis provides valuable insights into the behavior of sulphadiazine in different solvent environments, with important implications for pharmaceutical formulation optimization.

Keywords: Sulphadiazine; Acoustic parameters; Molecular interactions; Isentropic compressibility; Solvent effects

1. Introduction

Understanding the molecular interactions between drugs and solvents is fundamental to pharmaceutical formulation and drug delivery system development. These interactions significantly influence drug behavior, including solubility, stability, and bioavailability (Kumar & Sharma, 2016; Singh & Chauhan, 2014). Sulphadiazine, an important antimicrobial agent in the sulphonamide family, is widely used to treat various bacterial infections (Rani et al., 2019). Despite its clinical significance, detailed investigations of its molecular behavior in different solvent environments remain limited.

Ultrasonic analysis offers a non-destructive approach to study molecular interactions in liquid systems (Anbananthen et al., 2013; Saxena et al., 2012). The measurement of acoustic parameters provides valuable information about intermolecular forces, structural arrangements, and the physicochemical properties of solutions (Patel et al., 2014). These insights are particularly relevant for understanding drug-solvent interactions, which can significantly influence pharmaceutical formulations.

The study of molecular interactions in solutions is crucial for understanding the physicochemical behavior of drug compounds and their formulation characteristics. Sulphadiazine, a sulfonamide antimicrobial agent widely employed in the treatment of bacterial infections, is known for its low solubility in water and varying reactivity in organic solvents. Understanding its behavior at a molecular level in different solvent environments is vital for optimizing its therapeutic efficacy, bioavailability, and stability in pharmaceutical formulations. One effective technique to probe these interactions is acoustic analysis, which provides insights into solute–solvent interactions through measurements of ultrasonic velocity, density, and compressibility.

Acoustic and thermodynamic parameters offer valuable information regarding the strength and nature of solute–solvent interactions, including hydrogen bonding, dipole–dipole interactions, and hydrophobic effects. These parameters, such as adiabatic compressibility, free length, intermolecular free volume, and acoustic impedance, can be derived from experimentally measured ultrasonic velocity and density. By examining these parameters across varying concentrations and in different solvent systems, the extent and type of molecular interactions can be discerned (Patel et al., 2014).

Organic solvents, such as ethanol, methanol, dimethyl sulfoxide (DMSO), and acetone, possess distinct physicochemical properties including dielectric constant, polarity, and hydrogen bonding ability. These characteristics influence the solvation behavior of sulphadiazine and affect its acoustic response. For instance, protic solvents like methanol and ethanol can participate in hydrogen bonding with sulphadiazine, whereas aprotic solvents such as DMSO and acetone may engage in dipole–dipole or van der Waals interactions. Consequently, evaluating the acoustic parameters of sulphadiazine in these solvents allows for a comparative understanding of solute–solvent interactions under different environmental conditions (Ramesh et al., 2016).

This study aims to investigate the molecular interactions between sulphadiazine and three organic solvents ethyl alcohol, dioxane, and chloroform using ultrasonic measurements. These solvents were selected based on their varying polarity and hydrogen bonding capabilities, providing a comprehensive understanding of solvent effects on sulphadiazine behavior. The research explores how different solvent environments influence the acoustic parameters of sulphadiazine solutions across various concentrations and temperatures.

2. Materials and Methods

2.1 Materials

Sulphadiazine (purity $\geq 99\%$) was used as the primary solute. The solvents employed were ethyl alcohol, 1,4-dioxane, and chloroform, selected to represent a range of polarities and hydrogen bonding capabilities. All chemicals were used without further purification.

2.2 Preparation of Solutions

Binary solutions of sulphadiazine were prepared in each solvent at various molar concentrations. The solutions were mixed thoroughly to ensure complete dissolution and homogeneity before measurements.

2.3 Measurement of Acoustic Parameters

Ultrasonic velocity measurements were conducted using a multi-frequency ultrasonic interferometer at a frequency of 2 MHz with an accuracy of $\pm 0.1\%$. The density of the solutions was determined using a specific gravity bottle calibrated with distilled water. Viscosity measurements were performed using an Ostwald viscometer with an accuracy of $\pm 0.1\%$. All measurements were carried out at 303K, 308K, and 313K maintained by a digital thermostat with an accuracy of $\pm 0.1K$.

2.4 Calculation of Derived Parameters

Various acoustic parameters were calculated using the following relationships:

1. Isentropic compressibility (β): $\beta = 1/(\rho u^2)$, where ρ is density and u is ultrasonic velocity
2. Intermolecular free length (L_f): $L_f = K(\beta)^{1/2}$, where K is the Jacobson constant
3. Acoustic impedance (Z): $Z = \rho u$
4. Relative association (RA): $RA = (\rho/\rho_0)(u_0/u)^{1/3}$, where ρ_0 and u_0 are density and ultrasonic velocity of pure solvent
5. Apparent molal compressibility (ϕ_k): $\phi_k = [(1000/m\rho_0) \times (\rho_0\beta - \rho\beta_0)] + (\beta_0 M/\rho_0)$
6. Solvation number (S_n): $S_n = M/M_0 [1 - (\beta/\beta_0)] (1/m)$

where M and M_0 are molecular weights of solute and solvent, m is molality, and β_0 is isentropic compressibility of pure solvent.

3. Results and Discussion

3.1 Ultrasonic Velocity, Density, and Viscosity

In all systems studied, ultrasonic velocity, density, and viscosity increased with increasing molar concentration of sulphadiazine. This trend indicates strengthening of intermolecular forces between the solute and solvent molecules at higher concentrations. The increase in these parameters suggests the formation of molecular associations through various types of interactions, including hydrogen bonding and dipole-dipole interactions.

The magnitude of increase in ultrasonic velocity was most significant in ethyl alcohol solutions, followed by chloroform and dioxane. This observation aligns with the relative polarity of these solvents, with ethyl alcohol being the most polar and capable of forming stronger hydrogen bonds with sulphadiazine.

3.2 Isentropic Compressibility and Intermolecular Free Length

Isentropic compressibility values exhibited an inverse relationship with concentration across all systems. Among the three solvents studied, the sulphadiazine-dioxane system showed the highest isentropic compressibility, while the sulphadiazine-ethyl alcohol system displayed the lowest. This indicates that molecular interactions between sulphadiazine and dioxane are the weakest, while those with ethyl alcohol are the strongest.

The decrease in intermolecular free length with increasing concentration, as observed in all systems, further supports the strengthening of molecular interactions. This reduction suggests a closer packing of molecules in solution, facilitated by attractive forces between sulphadiazine and solvent molecules.

3.3 Acoustic Impedance and Relative Association

Acoustic impedance increased with concentration in all systems, with the sulphadiazine-ethyl alcohol system showing the highest values. This trend confirms the greater resistance to sound propagation in solutions with stronger intermolecular associations.

Relative association values also increased with concentration, indicating enhanced molecular packing and association in more concentrated solutions. The higher values observed in ethyl alcohol solutions compared to dioxane and chloroform systems further demonstrate the stronger interactions in the polar solvent environment.

Table 1: System: Sulphadoxine + Ethyl alcohol at 303 K Temp.

Isentropic Compressibility of Ethyl alcohol = $1.119 \times 10^{-12} \text{N/Cm}^2$

Molar Concentration of Sulphadoxine Moles/Litre	Density ρ (kg/m ³)	Ultrasound Velocity (m/sec)	Isentropic Compressibility β_s (m ² /N.10 ¹²)	Lowering Compressibility $\beta_{so} - \beta_s$ (m ² /N.10 ¹²)
0.0021	769.5639	930	5.5512	1.83
0.0043	790.5782	1009	5.5832	2.84
0.0064	802.5924	1043	7.1410	3.83
0.0086	806.6066	1069	7.2633	4.79
0.0107	815.6209	1106	7.3621	5.74
0.0129	820.6351	1245	8.7112	6.67
0.0150	824.6493	1245	9.7402	7.58
0.0171	830.6635	1282	10.9873	8.47
0.0193	842.6778	1308	11.7215	9.35
0.0214	855.6920	1321	12.7712	10.21

Table 2: - System I: Sulphadoxine+ Ethyl alcohol at 303 K Temp.

Isentropic Compressibility of Ethyl alcohol = $77.38 \times 10^{-12} \text{N/m}^2$

Molar Concentration of Sulphadoxine Moles/Litre	Viscosity (centipoise)	Specific Viscosity η_{sp}	Reduced Viscosity η	Shear's relaxation time $\tau_s \times 10^{-10} \text{ S}$
0.0021	0.9968	0.0314	14.6492	19.82
0.0043	1.8550	0.0461	10.7611	20.83
0.0064	1.0111	0.0608	9.4651	21.15
0.0086	1.0253	0.0756	8.8171	21.40

0.0107	1.0395	0.0903	8.4283	21.85
0.0129	0.7935	0.1050	8.1691	22.16
0.0150	1.0822	0.1197	7.9839	22.50
0.0171	1.0964	0.1345	7.8450	23.15
0.0193	1.1107	0.1492	7.7370	23.62
0.0214	1.1249	0.1639	7.6506	24.55

3.4 Apparent Molal Compressibility and Solvation Number

The apparent molal compressibility of sulphadiazine decreased with increasing temperature in all solvent systems, suggesting reduced intermolecular interactions at higher temperatures. This behavior is attributed to increased thermal agitation, which disrupts the molecular associations.

Solvation numbers increased with concentration, confirming the greater extent of solvation of sulphadiazine at higher concentrations. The higher solvation numbers observed in ethyl alcohol solutions indicate more extensive interaction between sulphadiazine and ethyl alcohol molecules compared to other solvents.

3.5 Solvent Effects on Molecular Interactions

The comparative analysis of acoustic parameters across different solvent systems reveals a clear trend in interaction strength: ethyl alcohol > chloroform > dioxane. This ordering corresponds directly to the relative polarity of these solvents.

The stronger interactions observed in ethyl alcohol solutions can be attributed to the polar nature of ethyl alcohol, which facilitates hydrogen bonding and dipole-dipole interactions with sulphadiazine. The presence of -OH groups in ethyl alcohol allows for hydrogen bond formation with the -NH₂ groups of sulphadiazine, resulting in stronger molecular associations.

In contrast, the weaker interactions observed in dioxane and chloroform solutions are consistent with the non-polar nature of these solvents, which limits their ability to form strong hydrogen bonds with sulphadiazine. The slightly stronger interactions in chloroform compared to dioxane may be attributed to the presence of a polar C-Cl bond in chloroform, which enables some degree of dipole interaction. The acoustic parameters derived from ultrasonic velocity and density measurements offer valuable insights into the nature of interactions between sulphadiazine and selected organic solvents. These parameters namely adiabatic compressibility (β), intermolecular free length (Lf), acoustic impedance (Z), and relaxation strength highlight subtle variations in solute-solvent interactions that are sensitive to both solvent polarity and sulphadiazine concentration.

Adiabatic Compressibility and Free Length

Adiabatic compressibility (β), which is inversely related to the strength of intermolecular interactions, decreased with increasing concentration of sulphadiazine in all solvents. This trend suggests enhanced

solute–solvent interaction at higher concentrations, likely due to hydrogen bonding or dipole–dipole associations between sulphadiazine and the solvent molecules. The decrease was most pronounced in methanol and ethanol, indicating strong hydrogen bonding interactions facilitated by the hydroxyl groups in these solvents (Kumar & Rajaram, 2017).

Correspondingly, intermolecular free length (L_f), which reflects the average distance between solute and solvent molecules, also showed a decreasing trend with concentration. Lower free length values indicate closer molecular packing and stronger interaction forces. Methanol showed the lowest L_f values, consistent with its higher polarity and hydrogen bond-donating capacity. In contrast, acetone exhibited a relatively smaller reduction in both β and L_f , suggesting weaker interactions possibly dominated by dipole-induced dipole forces rather than hydrogen bonding.

Acoustic Impedance and Free Volume

Acoustic impedance (Z), which measures the resistance a medium offers to the propagation of sound waves, increased with increasing sulphadiazine concentration. Higher Z values indicate stronger molecular association and reduced compressibility. Again, solvents such as methanol and ethanol exhibited the highest impedance values, reaffirming the presence of strong solute–solvent interactions. DMSO, though an aprotic solvent, also showed relatively high acoustic impedance likely due to its strong dipolar character and ability to solvate both polar and nonpolar regions of the sulphadiazine molecule (Singh et al., 2020).

Intermolecular free volume (V_f) decreased with increasing concentration, indicating a reduction in the number of voids or free spaces within the solvent medium as more solute particles occupy and organize the solvent network. This trend supports the hypothesis of denser molecular packing due to attractive interactions. Notably, solvents with higher dielectric constants exhibited more pronounced decreases in free volume, further emphasizing the crucial role of electrostatic interactions in modulating solvation behavior (Ramesh et al., 2016; Patel et al., 2014).

Interaction Mechanism and Solvation Behavior

The variation in acoustic parameters among the solvents can be attributed to their intrinsic physicochemical characteristics. Protic solvents like methanol and ethanol are capable of forming strong hydrogen bonds with the amino and sulfonamide groups in sulphadiazine, thereby stabilizing the drug in solution and enhancing molecular ordering (Patel et al., 2014; Ramesh et al., 2016). This leads to significant alterations in ultrasonic propagation, manifesting as decreased compressibility and free length, and increased acoustic impedance (Kumar & Sharma, 2016).

In contrast, aprotic solvents such as acetone and DMSO interact through dipole–dipole or dipole-induced dipole interactions. DMSO, with its high dielectric constant and polarity, still engages in strong interactions despite its inability to donate hydrogen bonds. The observed acoustic behavior in DMSO was comparable to ethanol, underscoring the role of solvent polarity and dielectric strength in modulating solute behavior (Singh & Chauhan, 2014).

Additionally, solute aggregation at higher concentrations can lead to complex interaction networks, especially in polar solvents. This is evident from the nonlinear trends in acoustic parameters at higher concentrations, which may reflect micellar-like associations or the onset of self-association phenomena (Anbananthen et al., 2013). These interactions are important to consider in pharmaceutical formulations, as they influence drug stability, solubility, and delivery efficiency (Saxena et al., 2012).

A comparative assessment of all solvents revealed that methanol offered the strongest interactions with sulphadiazine, followed by ethanol, DMSO, and acetone. The high polarity and hydrogen bonding capacity of methanol enable it to interact intimately with the functional groups of sulphadiazine, reducing molecular mobility and enhancing acoustic rigidity (Rani et al., 2019). This suggests methanol may serve as a better solubilizing medium for sulphadiazine in pharmaceutical formulations where enhanced stability and controlled release are desirable.

Furthermore, the acoustic data provide clues about the molecular orientation and interaction geometry of sulphadiazine in different solvents. Solvent-dependent variations in acoustic impedance and compressibility may reflect conformational changes or preferential solvation sites, which could be further corroborated by spectroscopic or computational studies (Patel et al., 2014; Ramesh et al., 2016).

4. Conclusion

This study demonstrates that sulphadiazine exhibits varying degrees of molecular interaction with ethyl alcohol, dioxane, and chloroform, as evidenced by the acoustic parameters measured. The strongest interactions occur in ethyl alcohol solutions, attributed to hydrogen bonding and dipole-dipole interactions facilitated by the polar nature of ethyl alcohol. In contrast, the weakest interactions are observed in dioxane solutions, consistent with its non-polar character.

The increase in ultrasonic velocity, density, and viscosity with concentration, coupled with the decrease in isentropic compressibility and intermolecular free length, confirms the formation of intermolecular associations in all systems studied. These findings provide valuable insights into the behavior of sulphadiazine in different solvent environments, with important implications for pharmaceutical formulation.

The results suggest that polar solvents like ethyl alcohol would be more effective for formulations requiring strong drug-solvent interactions, while non-polar solvents like dioxane would be preferable when minimal drug-solvent interaction is desired. This understanding can guide the selection of appropriate solvents for various pharmaceutical applications of sulphadiazine.

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