Experimental Investigation of Molecular Interactions of Piroxicam and Tenoxicam in mixture of solvents by Ultrasonic Studies

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Abstract:
Ultrasonic velocity and density of binary liquid mixture is useful in understanding physico-chemical behavior of liquid mixture. The ultrasonic velocity and other related acoustical parameters provide useful information regarding the structure of molecules, molecular order, molecular packing, inter and intra molecular interactions. The study of molecular interaction in liquids provides valuable information regarding internal structure, molecular association and complex formation etc. Ultrasonic velocity and density measurement of Piroxicam and Tenoxicam were carried out by using mixture of water-Acetone in ratio 1:1 and pure Acetone at different frequencies for investigating solute-solvent interactions. The data obtained during this study is used for determining the most significant acoustic parameters like adiabatic compressibility (βs), apparent molar compressibility (ϕk) and specific acoustic impedance (Z). These parameters have been used to explore the interactions between Piroxicam and Tenoxicam in acetone and in mixture of Acetone:water (1:1). The present studies investigated that there is presence of molecular interaction in binary liquid system. It may be due to hydrogen bonding through highly polar lone pair oxygen atom. From experimental data acoustical parameters are calculated and studied to explain solute-solvent interaction exist between drugs and organic solvents mixture.

Key words: Ultrasonic interferometer, adiabatic compressibility, apparent molar compressibility, Specific Acoustic impedance.

Introduction:

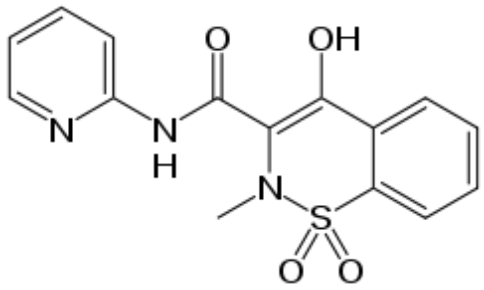
The ultrasonic velocity and other related acoustical parameters provide useful information regarding the structure of molecules, molecular order, molecular packing, inter and intra molecular interactions[1-4]. Ultrasonic properties of binary liquid mixtures have been studied by number of researchers[5-9]. The structural arrangements are influenced by the shape of the molecules as well as by their mutual interactions. The activation energy of the metabolic processes and biological activity of drug molecules basically depend on the type and strength of intermolecular interactions[10-12].

Piroxicam is a non steroidal anti inflammatory drug (NSAID). It helps to reduce pain in human body. It is also used to reduce the inflammation and stiffness caused by rheumatoid arthritis and osteoarthritis.

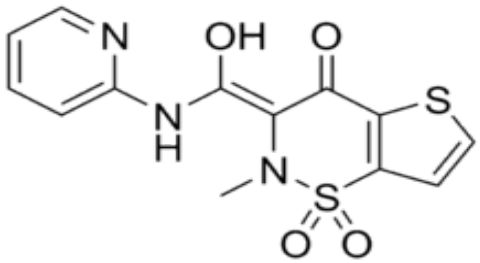
Tenoxicam is also a non steroidal anti inflammatory drug (NSAID). Both are of same category. Tenoxicam is manufactured under the trade name Mobiflex. It is used to relieve inflammation, swelling, stiffness, and pain associated with rheumatoid arthritis, osteoarthritis any losing spondylitis.

Experimental:

Piroxicam and Tenoxicam were obtained from Ramdev Chemical as a gift sample. The density of Acetone and Acetone: Water (1:1) mixture was measured at 303K. Sample weighing was done on Roy CCB-4 Balance having an accuracy of ±0.001g. Single crystal interferometer (Mittal Enterprises, Model F-81) with accuracy of ± 0.03% and frequency 2, 4, 6 MHz, were used in the present work. 0.01M solution of Piroxicam and Tenoxicam was prepared in Acetone and in water: Acetone mixture at 303K. The densities and ultrasonic velocities of all solutions were measured at 2, 4, 6 MHz.



(3E)-3-[hydroxy-(pyridine-2-ylamino) methylidene]-2-methyl-1,1dioxobenzo[e]thiazin-4-one **(Piroxicam)**



(3E)-3-[hydroxy(pyridin-2-ylamino)methylene]-2-methyl-2,3-dihydro-4H-thieno[2,3-e] [1,2] thiazin-4-one 1,1-dioxide
(Tenoxicam)

The adiabatic compressibility (β) is evaluated by using equation.

$$\beta = 1 / v^2.\square\square \quad \ldots\ldots (1)$$

Apparent molar compressibility depends upon the molality of solution and molecular weight of the solute by the relation,

$$\square K = [1000 (\beta_s \square_0 - \beta_0 \square_s) / m \square_s \square_0] + (\beta_s M / \square_s) \quad \ldots\ldots (2)$$

Where, $\square_0$ = density of pure solvent, $\square_s$ = density of solution, m = molality of solution, M = molecular weight of solute, β_0 = adiabatic compressibility of pure solvent, and βs = adiabatic compressibility of solution.

Specific acoustic impedance is determined from the measurement of ultrasonic velocity and density by formula,

$$Z = vs. \square s \quad \ldots\ldots (3)$$

Results and discussion:

Table 1: 0.01M solution of Piroxicam at temperature 303.15 K

MHz	Solvents	Density of Solution (Kg/m³)	Ultrasonic velocity of Solution m/s	Adiabatic compressibility	Specific acoustic impendence	Apparent molar compressibility
2	Acetone	779.00	1.8393	3.7947E^{-10}	1432780.42	4.8E^{-08}
	Water: Acetone 1:1	924.41	2.5418	1.6744E^{-10}	2349623.27	1.8 E^{-08}
4	Acetone	779.00	3.7045	9.3543E^{-11}	2885778.58	1.2 E^{-08}
	Water: Acetone 1:1	924.41	3.7985	7.4973E^{-11}	3511382.27	8.1 E^{-08}
6	Acetone	779.00	11.0934	1.0431E^{-11}	8641758.60	1.3 E^{-09}
	Water: Acetone 1:1	924.41	5.4064	3.7011E^{-11}	4997682.43	4.0 E^{-09}

Table 2: 0.01M solution of Tenoxicam at temperature 303.15 K

MHz	Solvents	Density of Solution (Kg/m³)	Ultrasonic velocity of Solution m/s	Adiabatic compressibility	Specific acoustic impendence	Apparent molar compressibility
2	Acetone	779.76	3.7013	9.3614E^{-11}	2886094.49	1.2 E^{-08}
	Water: Acetone 1:1	926.15	1.5184	4.6643E^{-10}	1411916.72	5.0 E^{-08}
4	Acetone	779.76	6.8802	2.7092E^{-11}	5364873.56	3.4 E^{-09}
	Water: Acetone 1:1	926.15	3.0442	1.1605E^{-10}	2830647.33	1.2 E^{-08}
6	Acetone	779.76	11.6902	9.3842E^{-12}	9115519.16	1.2 E^{-09}
	Water: Acetone 1:1	926.15	7.7783	1.7776E^{-11}	7232571.43	1.9 E^{-09}

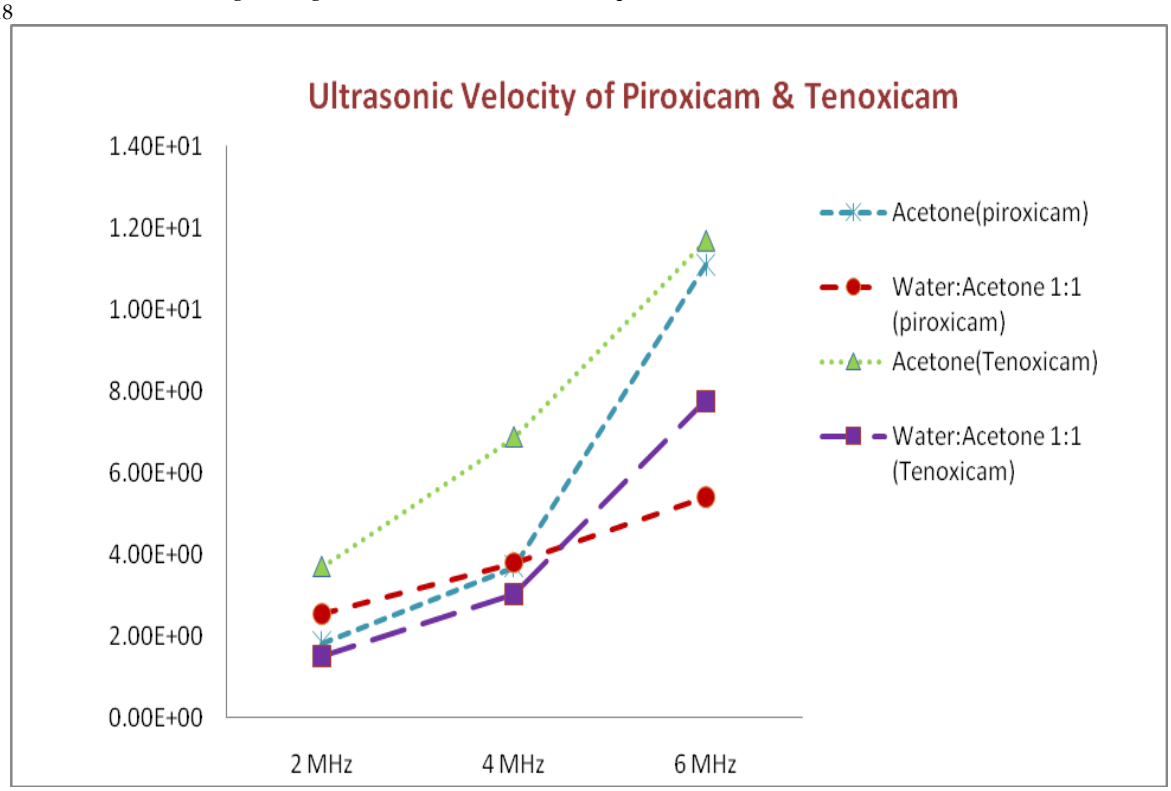


Figure 1: Ultrasonic Velocity of Piroxicam & Tenoxicam at 0.01M & 303.15K

A.Sadashivrao[14] studied the existence of molecular association between the components of the liquid mixtures from increase in ultrasonic velocity (U) with increasing percentage of dioxane.

Ultrasonic velocity increases steadily with increase in frequency up to 4 MHz. But at 6MHz ultrasonic velocity increases drastically in acetone while in mixture of acetone: water 1:1 it increases linearly (fig 1).

It may be due to the structural changes occurring in the mixtures resulting in strong intermolecular forces. The increase in ultrasonic velocity brings molecules to a closer packing which is attributed to strong intermolecular association resulting in formation of H-bonds between solute and solvent molecules.

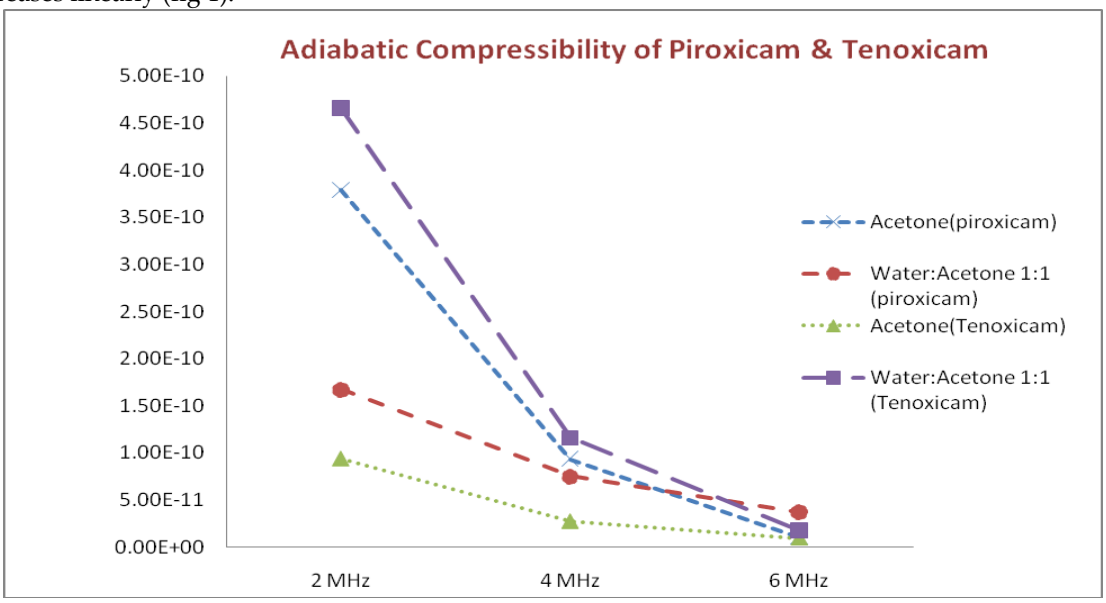


Figure 2: Adiabatic Compressibility of Piroxicam & Tenoxicam at 0.01M & 303.15K

The adiabatic compressibility is nothing but fractional decrease of volume per unit increase of pressure at constant temperature. As concentration increases number of molecules in the medium increases, making the

medium to be denser, this leads to greater compressibility resulting in slow transfer of sound waves and hence ultrasonic velocity decreases with increase of concentration.

Adiabatic compressibility decreases gradually with increase in concentration, temperature and frequency because this depends on electron donor and acceptor capacity or nature. Water is polar solvent when Piroxicam and Tenoxicam is added the association of solute and solvent molecules occur resulting in close packing and clinging of molecules. Because of this, solution becomes less compressible and hence values of adiabatic compressibility decrease.

The decreased values of adiabatic compressibility indicate strong intermolecular association between Tenoxicam and Acetone molecules. It is also observed that the values of adiabatic compressibility of piroxicam are greater in organic solvent i.e. in acetone.

As the percentage of organic solvent increases it decreases the number of free ions due to aggregation of solvent molecules around the ions[15] showing the occurrence of ionic association due to strong ion-ion interaction.

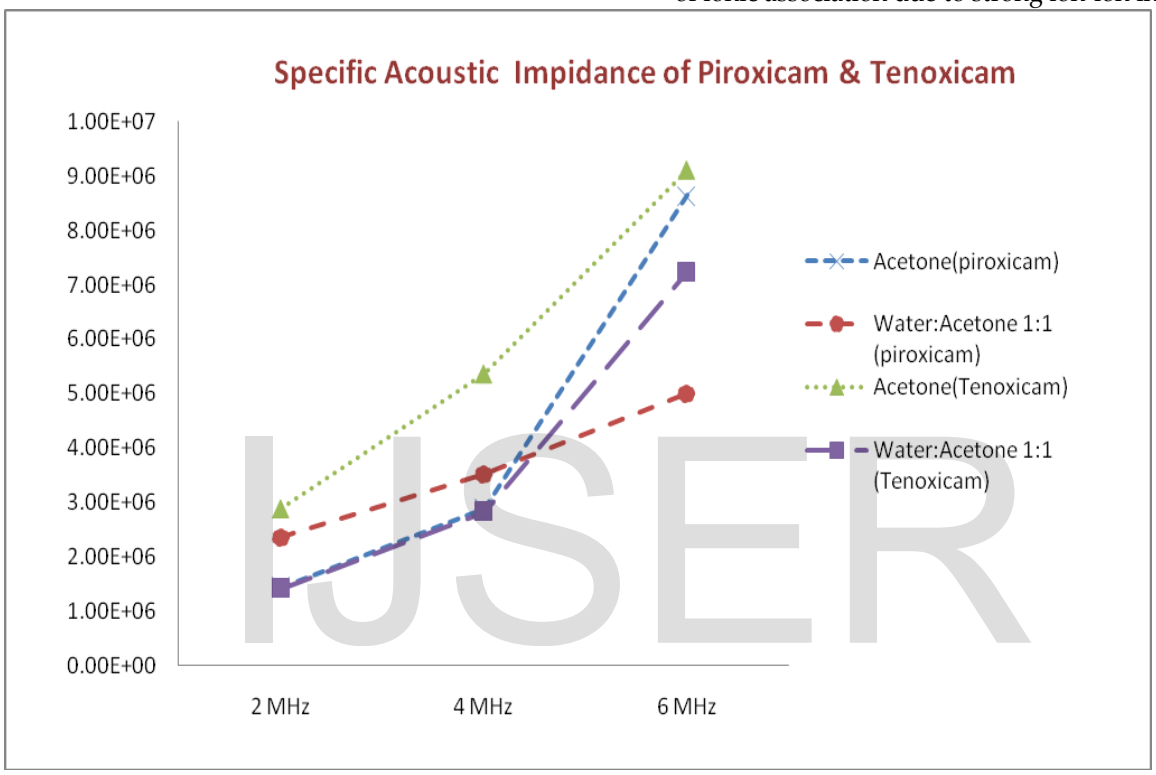


Figure 3: Specific acoustic impendence of Piroxicam & Tenoxicam at 0.01M 303.15K

Specific acoustic impedance is the complex ratio of the effective sound pressure at a point to the effective particle velocity at that point[16]. Specific acoustic impedance increases in proportion to the density of the medium and the velocity of ultrasound in the medium. From table no 1 and figure 3; it was observed that specific acoustic impendence value increases from 2 MHz to 6 MHz in both the solution of Piroxicam. In case of acetone: water (1:1) solvent, specific acoustic impendence value increases as compared to acetone. This may happen because of density effect as well as weak hydrogen bonding effect in acetone-water system. This increase in specific acoustic impendence can be explained on the basis of lyophobic interaction between solute and solvent molecule which increases the intermolecular distance by making relatively wider gap between the molecules. In case of Tenoxicam, somewhat parallel increasing trend observed in both solvents, it may be because; when effective particle velocity increases then dispersion force get active inside the solution .A result anticipated in the absence of specific interaction.

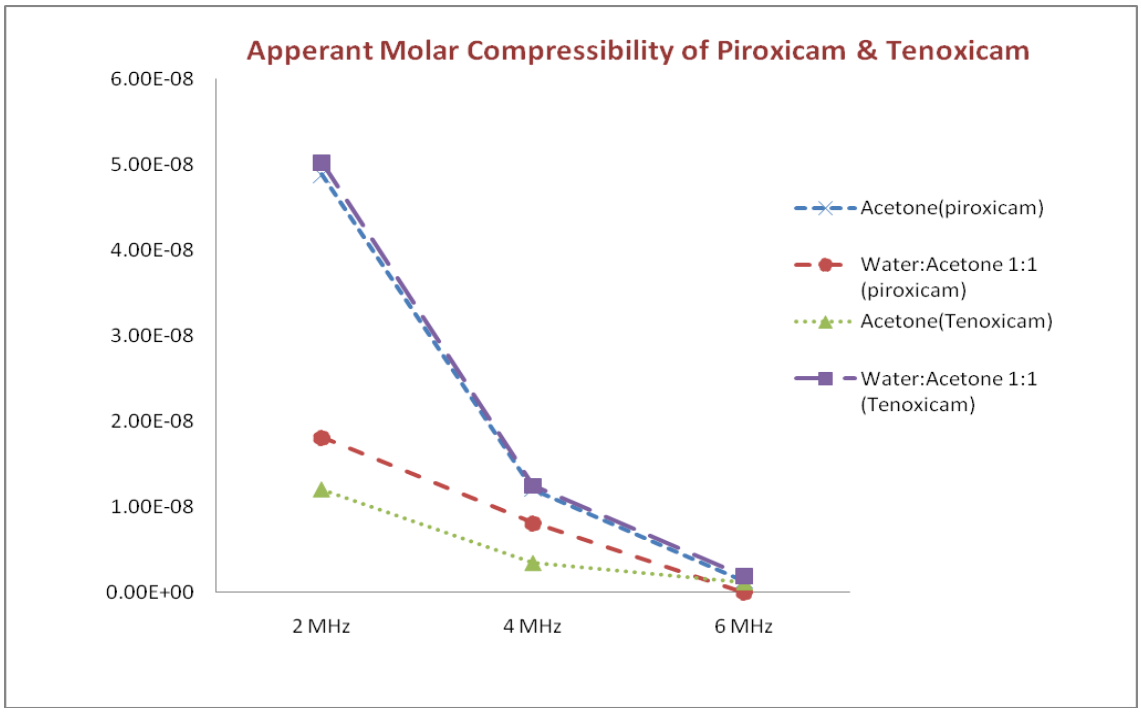


Figure 4: Apparent molar compressibility of Piroxicam & Tenoxicam at 0.01M & 303.15K

Apparent Molar Compressibility (ϕk) explains the solute-solvent and solute-solute interactions in solutions. Apparent molar compressibility property is fairly sensitive to structure changes especially in highly structured solvent and is hence expected to throw interesting light[17]. The structure of solute and the number of atoms present in it will have direct effect on ϕk values. Landge[18] studied the change in apparent molar compressibility with glucose concentration and found linear observation. Aapparent molar compressibility explains the molecular interactions like structure making and structure breaking nature of solute. Minute changes due to change in structure may only be noticed by apparent molar compressibility. Piroxicam and Tenoxicam shows same trend as seen from Table 1 and 2 and Fig. 4. ϕk values decrease in both the medium at 300K. An addition of solute in acetone solvent may produce weak interaction of the Vander Wall forces, which is expected to introduce structuredness in the solution. That is specific arrangement of acetone molecule may be occurring due to attached solute molecules. It decreases from 2 to 6 MHz from the trend it was concluded that there is minimum difference between values of apparent molar compressibility on 4 MHz and 6 MHz but at 2 MHz shows large difference in apparent molar compressibility.

The apparent molar compressibility values are lower in acetone rather than acetone: water mixture in both drugs from this it was observed that apparent molar compressibility gets decreased with increase in concentration of acetone. This observed difference may be because of ketone group in solvent. It shows weak electrostatic attractive force in the vicinity of ions. It can be concluded that weak molecular association is found in all systems. It is found that there is weak interaction between solute and solvent.

Conclusion:

The present studies investigated that there is presence of molecular interaction in binary liquid system. It may be due to hydrogen bonding through highly polar lone pair oxygen atom. From experimental data acoustical parameters are calculated and studied to explain solute-solvent interactions which exist between drugs and organic solvents mixture. From experimental data it can be conclude that there is presence of solute-solvent interaction of drugs in both the solvents.

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