Determination of molecular interactions of Nimesulide and Aceclofenac in different solvent by using ultrasonic interferometer

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Abstract:

Nimesulide and Aceclofenac drugs were selected for study looking at their medicinal importance in treatment. Ultrasonic interferometer was used for measurement of ultrasonic velocity of 0.01M solution of these drugs in Acetone and a binary mixture i.e. (Water: Acetone 1:1) as a solvent at 303.15 K at 2 MHz, 4 MHz and 6 MHz frequency. This experimental data is used to explore the acoustic properties like adiabatic compressibility, specific acoustic impedance and intermolecular free length. From these thermodynamic and acoustic properties, the molecular interactions like solute-solute and solute-solvent interaction occurring in solution have been interpreted with respect to change in solvent at different frequencies.

Key words: Ultrasonic interferometer, adiabatic compressibility, specific acoustic impedance and intermolecular free length.

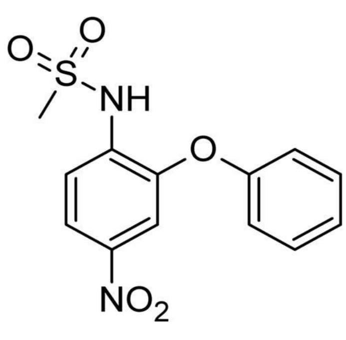
Introduction:

Nimesulide is non-steroidal anti inflammatory drug (NSAID) with analgesic and antipyretic properties. It is used to treat acute pain. Nimesulide blocks the production of prostaglandin (a chemical associated with pain) thereby relieving pain and inflammation. Aceclofenac is also a non-steroidal anti-inflammatory agent (NSAID) with antipyretic and analgesic actions. Ultrasonic wave is useful in understanding physico-chemical behavior of liquid mixture. Ultrasonic velocity and density of binary liquid mixture has been studied by C.Rambabu[1]. Ultrasonic velocity measurements can be employed to detect and assess weak and strong molecular interactions present in all type of liquid mixtures (binary and ternary)[2]. In view of the medicinal and pharmaceutical significance of Nimesulide and Aceclofenac we intended to study the intermolecular interactions by ultrasonic interferometer.

Comparative study of molecular interaction by acoustic properties of α-bromoacetophenone and coumaran-3-ones in ethanol and dioxane solvent was studied by Aswale S. S. etal[3-6]. Ultrasonic velocity measurements are helpful to interpret solute-solvent, ion-solvent and solvent-solvent interaction in aqueous and non aqueous medium. Ultrasonic interferometer is non destructive technique which is particularly used for liquid mixture to determine molecular interactions in solute and solvent. According to Baskarana R[7], Herfeld[8] and Kannapan[9], the molecular interactions are mostly studied by ultrasonic interferometer. In recent years measurement of ultrasonic investigation finds extensive application in determining the physiochemical behavior of liquid mixture. To study the liquid theory, the acoustic properties such as ultrasonic velocity, apparent molar compressibility and relative association are very useful.

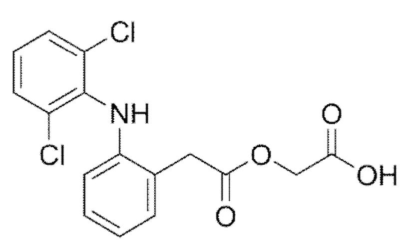
Selection of drugs:-

1. **Nimesulide:-**



N-(4-nitro-2-phenoxyphenyl) methane sulfonamide

2. **Aceclofenac:-**



2-[2-[(2, 6-Dichlorophenyl) amino] phenyl] acetoxy acetic acid.

An attempt in this investigation is made to study the intermolecular interactions of 0.01M concentration of Nimesulide and Aceclofenac in Acetone and Mixture of solvent (i.e. Water: Acetone 1:1) at different frequencies like 2 MHz, 4 MHz and 6 MHz, keeping the temperature constant i.e. 303.15K. The acoustic properties like adiabatic compressibility, specific acoustic impedance and intermolecular free length are determined from the ultrasonic velocity and density measurements of the solution. From the observations of these properties the molecular interactions between solute, solvent are predicted.

Experimental:

Nimesulide and Aceclofenac API samples were provided by Ramdev Chemicals. Advanced electronic densitometer Anton Paar-35 having accuracy of ± 0.1 kg/m3 was used to measure the density which directly shows the temperature and density of solutions. Multi frequency interferometer (Mittal Enterprises, Model F-83) with accuracy of ±0.03% at frequency 2, 4 and 6 MHz was used in the present work.

AR grade Acetone and double distilled water were used as a solvent. Weighing of sample was done on digital balance Model CB/CA/CT-Series, Contech, having accuracy 0.0001g. Calibration of interferometer instrument was done by measuring the ultrasonic velocity of pure water at 303.15K.The measured value 1511 ms-1 is very close to theoretical[10] value 1515 ms-1 and thus confirms the accuracy of instrument. A 0.01M solution of Nimesulide and Aceclofenac were prepared in pure Acetone and mixture of acetone and distilled water in ratio 1:1 separately. The densities and ultrasonic velocities of all solutions were measured at 303.15K. Similar measurements were carried out in both solvents i.e. Acetone and mixture of water and Acetone in ratio 1:1 for 0.01 M solutions of Nimesulide and Aceclofenac. Constant temperature was maintained by thermostat.

Results and discussion:

In the present investigation, measurements of densities and ultrasonic velocity of Nimesulide and Aceclofenac API in solvent Acetone and mixture of Acetone and distilled water in ratio 1:1 having concentration 0.01M at 303.15 K at 2MHz, 4MHz and 6 MHz frequency have been made, and given in Table 1 and 2 respectively.

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

$$\beta = 1 / v2.\, \varrho \qquad \ldots\ldots (1)$$

Where, v = velocity and ϱ = density

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

$$Z = vs.\, \varrho s \qquad \ldots\ldots (2)$$

The solute-solvent interactions may be interpreted in terms of acoustic impedance.

Intermolecular free length (Lf) is one of the important acoustic properties to study the intermolecular interactions. Intermolecular free length has been evaluated from adiabatic compressibility (β) by Jacobson's[11-13] formula,

$$Lf = K.\sqrt{\beta s} \qquad \ldots\ldots (3)$$

Where, K is the temperature dependent constant known as Jacobson's constant and is independent of the nature of liquid, (At 303.15 K, K=627).

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

MHz	Solvents	Density of Solution (Kg/m3) (ϱ)	Ultrasonic velocity of Solution m/s (v)	Adiabatic compressibility (β)	Specific acoustic impendence (Kgm-2sec-1) (Z×105)	Intermolecular free length (A0) (Lf)
2	Acetone	775.88	3.7600	9.1167E-11	29.1728	0.0060
	Water: Acetone 1:1	926.15	2. 4036	1.8689E-10	22.2612	0.0086
4	Acetone	775.88	8.3996	1.8268E-11	65.1711	0.0027
	Water: Acetone 1:1	926.15	4.7921	4.7018E-11	44.3820	0.0043
6	Acetone	775.88	12.5900	8.1312E-12	97.6831	0.0018
	Water: Acetone 1:1	926.15	5.7195	3.3007E-11	52.9710	0.0036

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

MHz	Solvents	Density of Solution (Kg/m3) (ϱ)	Ultrasonic velocity of Solution m/s (v)	Adiabatic compressibility (β)	Specific acoustic impendence (Kgm-2sec-1) (Z×105)	Intermolecular free length (Lf)
2	Acetone	782.50	4.0044	7.9698E-11	31.3342	0.0056
	Water: Acetone 1:1	925.55	3.5221	8.7094E-11	32.5992	0.0059
4	Acetone	782.50	7.8019	2.0995E-11	61.0497	0.0029
	Water: Acetone 1:1	925.55	4.3852	5.6185E-11	40.5872	0.0047
6	Acetone	782.50	11.3855	9.8585E-12	89.0913	0.0020
	Water: Acetone 1:1	925.55	7.8257	1.7642E-11	72.4305	0.0027

These acoustic parameters are directly reflecting the structural interaction of solvents with solute and explore valuable and important information regarding internal structure and molecular association.

In Nimesulide, Ultrasonic velocity increases from 2 to 6 MHz in both solvents i.e. pure acetone as well as water: acetone 1:1. But ultrasonic velocity slightly decreases in water: acetone 1:1 at 6 MHz. As frequency increases ultrasonic velocity increases fastly in pure acetone as compared to water: acetone from 2 to 6 MHz (figure 1). Eyring and Kincaid proposed a model for sound propagation which state that variation of ultrasonic velocity in solution depends upon the increase or decrease of molecular free length after mixing the component.

In Aceclofenac same kind of trend was observed. Ultrasonic velocity increases with increase in frequency. Ultrasonic velocity continuously increases in Acetone whereas it slowly increases in mixture of acetone: water (1:1) from 2 MHz to 4 MHz but it suddenly increases at 6 MHz in binary mixture. It may be because of nature of solute in that particular solvent. (Figure 1)

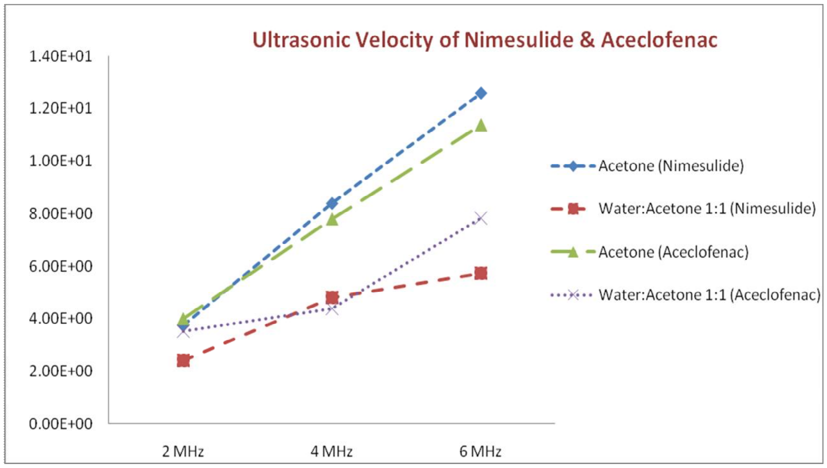


Figure 1: Ultrasonic Velocity of Nimesulide and Aceclofenac at 0.01M and 303.15K

From table no 1 and 2 and fig 2, it is observed that adiabatic compressibility decreases from 2 to 6 MHz. Kiyohara and Benson14 clarify that adiabatic compressibility is a result of several opposing effects. Strong hydrogen bonding between the molecules leads to more compact structure which decreases adiabatic compressibility. This decrease of adiabatic compressibility is may be due to collection of solvent molecule around ions which is supported by weak ion-solvent interaction. This indicates that there is significant solute-solvent interaction. The decrease in adiabatic compressibility followed by decrease in ultrasonic velocity shows strong intermolecular interaction.

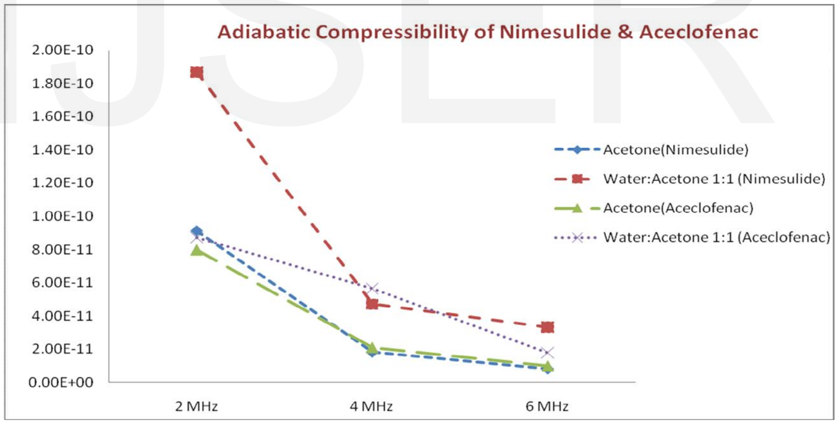


Figure 2: Adiabatic Compressibility of Nimesulide and Aceclofenac at 0.01M and 303.15K

Specific acoustic impedance makes the contribution in explaining molecular interactions. Specific acoustic impedance is the complex ratio of the effective sound pressure at a point to the effective particle velocity at that point to effective particle at that point15. It is also defined as the impedance offered to the sound wave by the components of mixture. Specific acoustic impedance increases in proportion to the density of the medium and the velocity of ultrasound in the medium. In both Nimesulide and Aceclofenac specific acoustic impendence linearity increases in Acetone from 2 MHz to 6 MHz. Whereas in mixture of acetone-water, in case of Nimesulide, specific acoustic impedance increases up to 4 MHz and from there it increases slowly up to 6 MHz (figure 3). On other hand in Aceclofenac reverse trend was observed, where specific acoustic impendence increases slowly up to 4 MHz and suddenly at 6 MHz (figure 3). This change in mixture of acetone-water may be due to the structural changes occurring in the mixtures resulting in weakening of intermolecular forces.

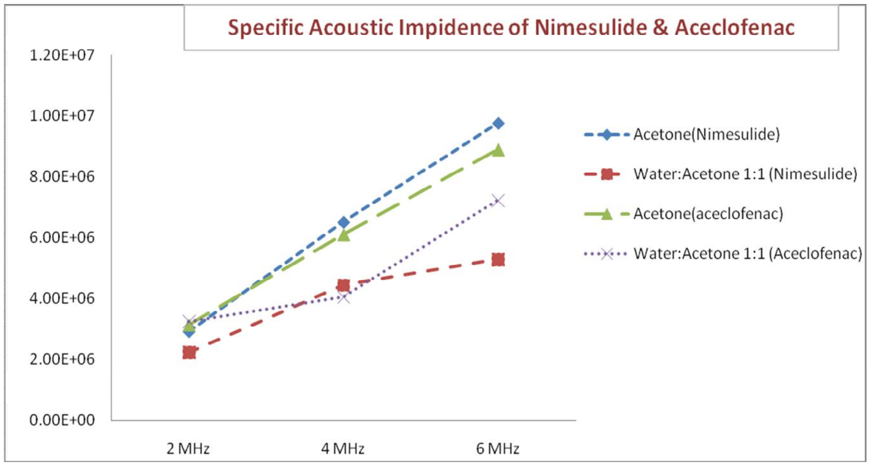


Figure 3: Specific acoustic impendence of Nimesulide and Aceclofenac at 0.01M and 303.15K

Intermolecular free length is the distance between surfaces of the neighboring molecules. Eyring and Kincaid16 have proposed that free length is dominant factor in determining the variation of ultrasonic velocity of solution. Ultrasonic velocity depends on intermolecular free length Lf, with decrease in free length velocity increases or vice versa17. Mathematically intermolecular free length is inversely proportional to ultrasonic velocity and directly proportional to adiabatic compressibility shows similar behavior to that of adiabatic compressibility and opposite to that of Ultrasonic velocity. It was found that in both Nimesulide and Aceclofenac, intermolecular free length decreases in both solvents i.e. Acetone as well as mixture of acetone and water (1:1). It was observed that intermolecular free length decrease from 2 MHz to 6 MHz in both solvents (figure 4). It may happen due to smaller force of interaction between solute and solvent because of hydrogen bonding. This happened because there is significant interaction between ions and solvent molecules suggesting destructive nature of the added electrolyte .This may also indicates that decrease in number of free ions showing the occurrence of ionic association due to weak ion-ion interaction. As per D. T. Tayade and A. M. Kshirsagar[18], the intermolecular free length goes on decreasing with increase in concentration of solute which indicates decrease in free space between the molecules because of stronger solute-solvent interactions which is in agreement with on observed value of β.

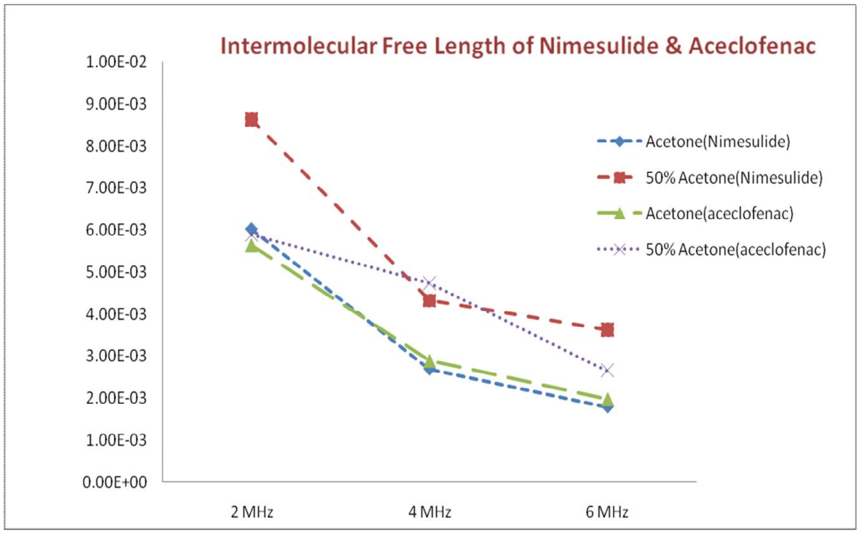


Figure 4: Intermolecular Free Length of Nimesulide and Aceclofenac at 0.01M and 303.15K

Conclusion:

In present investigation, physical and acoustic parameters were determined for Nimesulide and Aceclofenac in solvents like Acetone and Acetone: distilled water mixture at 2, 4 and 6 MHz at constant temperature i.e. 303.15K.

Adiabatic compressibility decreases from 2 MHz to 6 MHz in Nimesulide as well as in Aceclofenac. Decrease in adiabatic compressibility is supported by decrease in ultrasonic velocity.

Specific acoustic impedance value increases from 2 to 6 MHz in both i.e. Nimesulide as well as Aceclofenac may be because of effective particle velocity. When effective particle velocity increases then dispersion forces should get active inside the solution.

Decrease in intermolecular free length clearly indicates that there is decrease in free space between the molecules because of strong solute solvent interaction and solvent suggests structure promoting behavior of solute.

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