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# Acoustical Characterization of Tramadol in Ethanol at Different Temperature

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**ABSTRACT**

This work is to find out the wide interactions of Tramadol molecules in ethanol at the different thermal environment, this research investigates the impact of temperature variations on the thermo-acoustic properties of tramadol drug in alcoholic solutions. The assessment and evaluation of molecular exchange interaction of alcoholic media and Tramadol drug at varied temperature have been observed under the ultrasonic mode within the range of frequency i.e. 2 MHz. The objective is to gain insights into molecular interactions and structural changes within the system by examining acoustic and thermal parameters. The peculiar deviation of these physical parameters confirms the structural change in the experimental solution so it is an appreciable sense shows the molecular interactions. Objective of study is crucial for understanding the potential effects of temperature on drug stability, solubility, and bioavailability, as well as the influence of alcohol on these properties. The findings of this research could have significant implications for drug formulation, storage, and administration, particularly in scenarios involving alcohol consumption.

**Keywords:** Ultrasonic velocity, Compressibility, Impedance, Thermo acoustic parameters, Tramadol, Alcohol.

## INTRODUCTION

Tramadol, a synthetic opioid analgesic, is widely used to treat moderate to severe pain. Understanding the behavior of tramadol in ethanol solutions at different temperatures is crucial for optimizing its therapeutic use and minimizing potential adverse effects. Thermo-acoustic properties, such as ultrasonic velocity, density, viscosity, and adiabatic compressibility, provide valuable insights into the molecular interactions and structural changes within a solution. By studying these properties, we can gain a deeper understanding of how temperature and alcohol concentration affect the behavior of tramadol molecules in solution. Ultrasonic information on thermos-acoustic properties of solutions is more crucial for their wide application in different industries like chemical, textile, and leather and also in nuclear. Various spectroscopic mode utilized to recognize molecular interactions[1-6]. The varied thermo-acoustic data direct pin out the structural re-arrangement term of different intermolecular forces[7-8].

Due to the associative and polar nature of alcohol provides interactive attractive sense within a specific group of compounds. Accurate knowledge

of thermo-dynamic mixing properties and their calculated excess data for the solution having protic, non-protic behaviors and it deals with theoretical and practical investigation. The difference between theoretical and practical data have been revealed the peculiar interactions. Aromatic nature compounds and alcohols[9] ensure as associative nature in liquid. One of the significant findings of the study is the associative behavior observed in tramadol-alcohol solutions. This behavior suggests that tramadol molecules interact with alcohol molecules through specific molecular forces, such as hydrogen bonding and ionic interactions. Hydrogen bonding, in particular, plays a crucial role in stabilizing the tramadol-alcohol complex, affecting its solubility and bioavailability. The nature of these interactions can vary with different types of alcohols, leading to unique thermo-acoustic profiles for each solvent.

Though, the absorption is measured as a function of frequency, relaxation process is observed by relaxation parameters are noticeably dependent on the structures of alcohol[10-15]. Thus, the potential of metabolic process, basically it happens due to nature and strength of the intermolecular interactions.

The inhibition of varied enzymes included in the biotransformation may causes the plasma concentration of tramadol or its active metabolite[16].

In this study, ultrasonic velocity and related parameters of tramadol and ethanol solution are stated at different thermal environment (T= 278.15K to 293.15K). The aim and objective of research to investigate the influence of temperature on the thermo-acoustic properties of tramadol in alcoholic media reveal valuable information on molecular interactions, solvation dynamics, and drug-solvent compatibility. By analyzing the experimental data, we can elucidate the underlying mechanisms responsible for the observed changes and their potential implications for drug formulation, storage, and administration.[17-22]

## METHODS

In the context of studying Tramadol in an ethanol medium, evaluating thermos-acoustic properties. To assess these parameters, an Ultrasonic Interferometer (Vi-Micro Systems Company, Chennai, Model VCT: 71) with a frequency of 2 MHz is utilized. The density of the liquid solutions is measured with a 10 mL specific gravity bottle, offering an accuracy of $\pm 2 \times 10^{-2}$ kg/m$^3$. For precise temperature control during these measurements, a temperature-controlled bath (Lab-Hosp Company, Mumbai) is used, maintaining an accuracy of ±1 K. The viscosity of each solution is determined at specific temperatures using an Ostwald Viscometer, with the timing for both pure water (double-distilled) and the experimental solutions recorded by a digital stop clock (Model: RACER-10W) with 0.01-second accuracy. Solution weights are measured using an electronic digital balance (Model: Contech CA-34) with an accuracy of 0.0001 g. This experimental setup is employed to measure the thermos- acoustic parameters of Tramadol solutions across a range of temperatures (278.15 K to 293.15 K) and varying concentrations (e.g., 0.01 M to 0.1 M).

### Thermo-acoustic parameters

Adiabatic Compressibility ($\beta$) = $1/U^2\rho$ (1)

Specific Acoustic Impendace (Z) = $U\rho$ (2)

Intermolecular Free Length ($L_f$) = $K_T\beta^{1/2}$ (3)

Relaxation Time ($\tau$) = $(4/3)*\beta*\eta$ (4)

Relative association (Ra) = $(\rho/\rho_0)(U_0/U)^{1/3}$ (5)

Classical Absorption ($a/f^2$) = $(8\pi^2\eta)/(3U\rho)$ (6)

Internal Pressure (P) = $bRT\,(K\eta/U)^{1/2} \times (\rho^{2/3}/M^{7/6}eff)$ (7)

Free Volume ($V_f$) = $(Meff\ U/\eta K)^{3/2}$ (8)

Molar Volume (Vm) = $Meff/\rho$ (9)

Molar Sound Velocity or Rao Constant (R) = $Meff/\rho(U)^{1/3}$ (10)

Molar Compressibility or Wada Constant (W) = $V\beta^{-1/7}$ (11)

Isothermal Compressibility ($\beta_i$) = $\gamma\beta$ (12)

Surface Tension ($\sigma$) = $(6.3 \times 10^{-4})\ \rho\ U^{3/2}$ (13)

Thermo-acoustic parameters such as adiabatic compressibility ($\beta$), intermolecular free length (Lf), specific acoustic impedance (Z), internal pressure (P), Rao's constant (R), and relative association (Ra) were derived from measurements of ultrasonic velocity (U), density ($\rho$), and viscosity ($\eta$). From such calculated and measured parameters molecular interaction, effectiveness of drug, drug properties for pharmaceutical science and drug release pattern will be obtained.

## MATERIALS

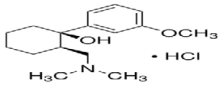
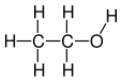
AR-grade Tramadol, a synthetic opioid analgesic, and ethanol (E-Merck chemicals, Germany) were used in this study. The purity of

these chemicals was verified through statistical analysis and cross-referenced with standard literature values[23].

**Interpretation of data by graph**

Graphs of thermo-acoustic parameters versus molar concentration tramadol.

**Table 1: Chemical and Physical information of Drugs material**

| Sr. No | Drug Name | Structure | Molecular Weight | Molecular Formula |
|---|---|---|---|---|
| 1 | Tramadol |  | 299.84 | $C_{16}H_{25}NO_2$ |
| 2 | Ethanol |  | 46.069 | $C_2H_6O$ |

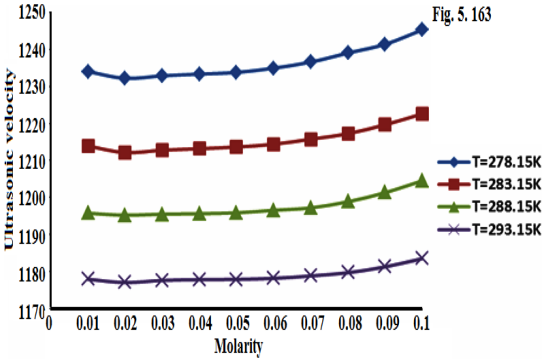



**Fig. 1. Plot of Ultrasonic Velocity and Molarity of Tramadol at T=278.15 K, 283.15K, 288.15K, 293.15K**

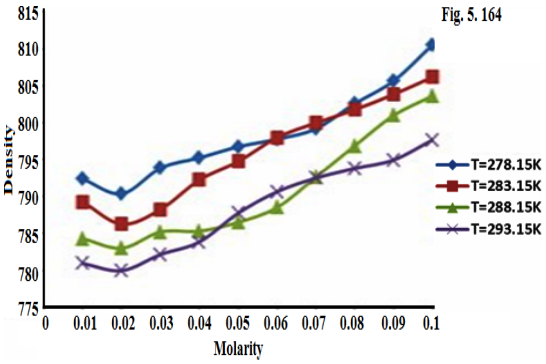



**Fig. 2. Plot of Density and Molarity of Tramadol at T=278.15 K, 283.15K, 288.15K, 293.15K**

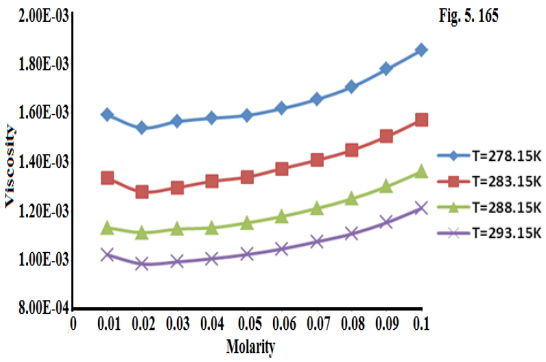



**Fig. 3. Plot of Viscosity and Molarity of Tramadol at T=278.15 K, 283.15K, 288.15K, 293.15K**

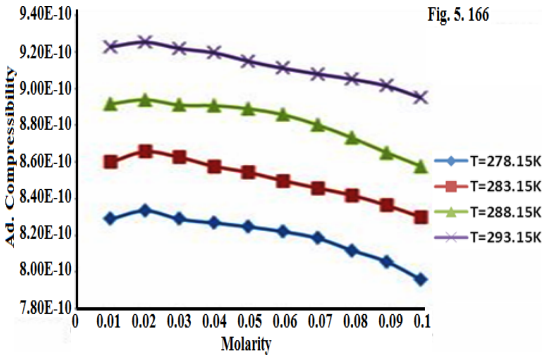



**Fig. 4. Plot of Adiabatic Compressibility and Molarity of Tramadol at T=278.15 K, 283.15K, 288.15K, 293.15K**

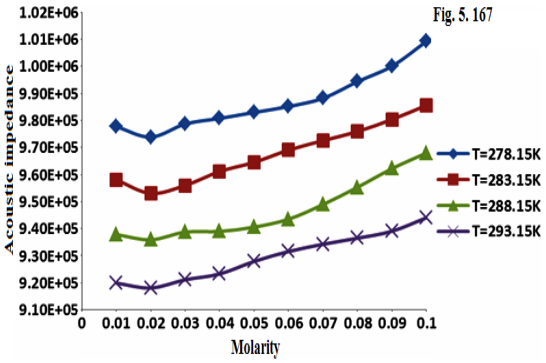



**Fig. 5. Plot of Acoustic Impedance and Molarity of Tramadol at T=278.15 K, 283.15K, 288.15K, 293.15K**

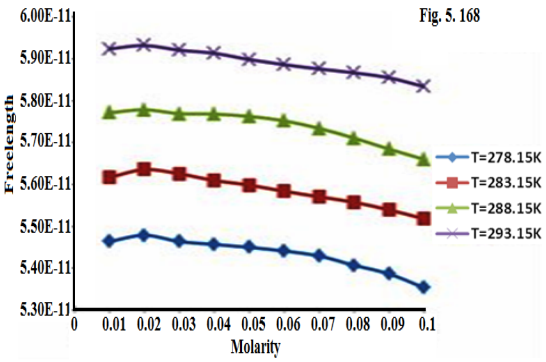



**Fig. 6. Plot of Free Length and Molarity of Tramadol at T=278.15 K, 283.15K, 288.15K, 293.15K**

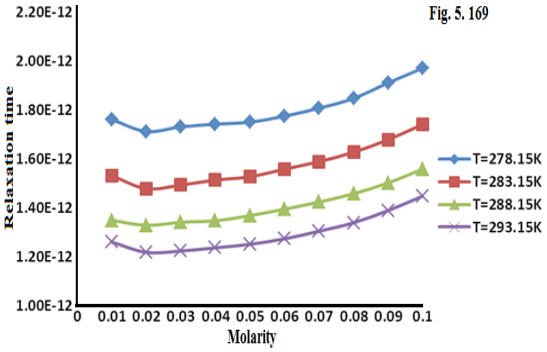



**Fig. 7. Plot of Relaxation Time and Molarity of Tramadol at T=278.15 K, 283.15K, 288.15K, 293.15K**

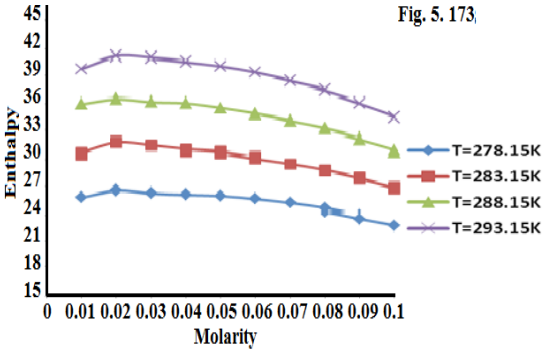



**Fig. 10. Plot of Enthalpy and Molarity of Tramadol at T=278.15 K, 283.15K, 288.15K, 293.15K**

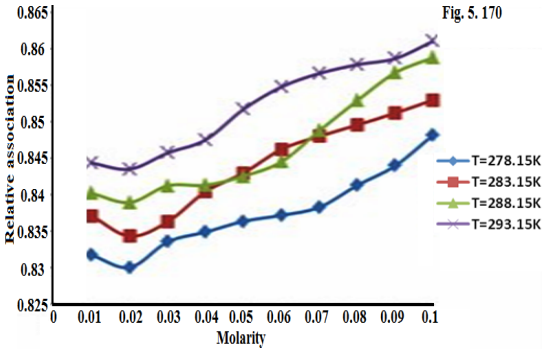



**Fig. 8. Plot of Relative Association and Molarity of Tramadol at T=278.15 K, 283.15K, 288.15K, 293.15K**

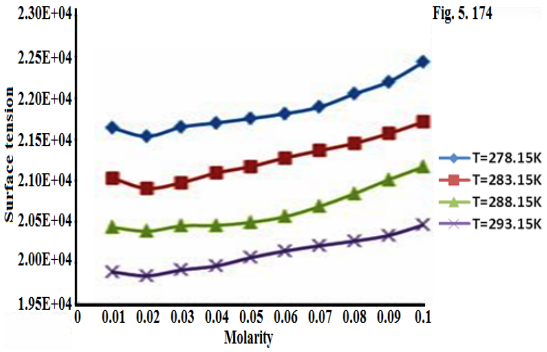



**Fig. 11. Plot of Surface Tension and Molarity of Tramadol at T=278.15 K, 283.15K, 288.15K, 293.15K**

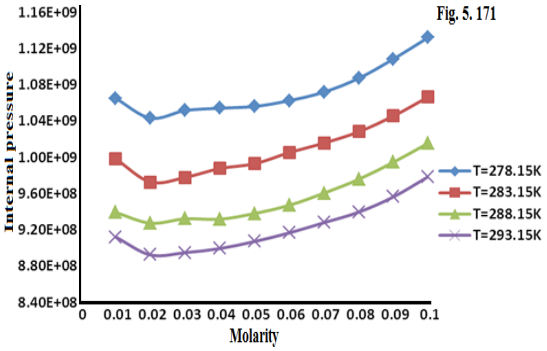



**Fig. 9. Plot of Internal Pressure and Molarity of Tramadol at T=278.15 K, 283.15K, 288.15K, 293.15K**

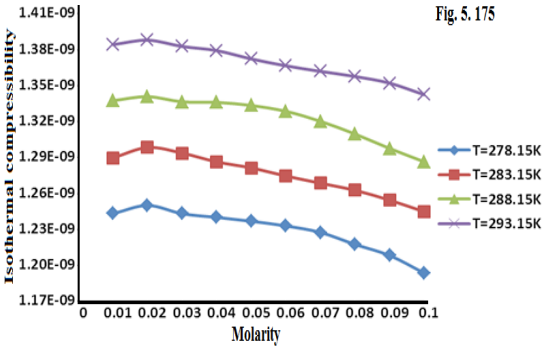



**Fig. 12. Plot of Isothermal Compressibility and Molarity of Tramadol at T=278.15 K, 283.15K, 288.15K, 293.15K**

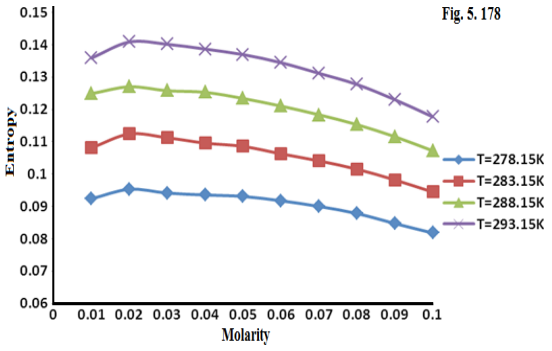



**Fig. 13. Plot of Entropy and Molarity of Tramadol at T=278.15 K, 283.15K, 288.15K, 293.15K**

## RESULTS AND DISCUSSIONS

By analyzing graphical tactics, the assessment of various thermos-acoustic factors of Tramadol with Ethanol at different temperature range at T=278.15K to 293.15K it has been concluded that associative behavior is primarily attributed to hydrogen bonding and ionic interactions between tramadol molecules and alcohol molecules. These interactions influence the solubility, stability, and bioavailability of tramadol in different alcoholic environments. The formation of hydrogen bonds stabilizes the tramadol-alcohol complexes, which can affect the drug's overall behavior in solution. Molecular interactions depend strongly upon temperature. It was found in the experiment that at lower temperatures (278.15 K) hydrogen bonds become more stable resulting in different acoustic properties. The lower temperatures stability of hydrogen bonds can affect the compressibility, density and sound velocity of the tramadol-alcohol solutions. It is important to understand these temperature dependent behaviors when designing and storing formulation for tramadol. In more concentrated mediums, the interaction of molecules get higher, resulting in the formation of aggregates or clusters that alter the solution as a whole.

Adiabatic compressibility was also affected by Tramadol concentration. This last indicates that the medium will become less compressible as the concentrations increase. This happens due to the fact that the increased intermolecular interaction of the solution limits its compression. In general, speed of sound decreased with increasing temperature. This implies that intermolecular interactions between Tramadol and solvent molecules are weakening. This means that the reduced velocity shows the speed of sound wave passing through the medium reduced. This suggests the strong significant interactions, and relative association varies linearly. The Tramadol concentration dependence of acoustic impedance usually increased. The effect of increasing density and ultrasonic velocity are combined. Nature and strength and involves pressure of this nature and force and greatly associative force. The outcome of the experiment has profound implications for pharmaceutical applications. Knowledge of molecular interplay of tramadol and alcoholic media can facilitate the development of more stable and better bioavailable drug formulations. These interactions can also tell us about the temperature dependent behaviors of these interactions and how this can inform the design of optimal storage and transportation conditions for tramadol so that it is effective and safe. Pharmaceutical companies can enhance the therapeutic outcomes of tramadol by tailoring the formulation conditions to accommodate these interactions.[24-30]

## CONCLUSION

Thermo-acoustic properties of tramadol in alcoholic media at varying thermal environments were useful for evaluating molecular interactions and thermal dependence together with their pharmaceutical implications. Ultrasonic techniques were exploited to elucidate the complex behaviours exhibited by tramadol in alcohol media, which has implications in the formulation of more effective and stable drug formulations. This research work deals with the molecular interaction of alcoholic tramadol drug solution using ultrasonic investigation technique which give additional information related to the physiology system and which may identify their metabolism in living organism. These various outcomes of the research work may be useful for pharmacological, pharmacokinetics, transport mechanism, drug delivery applications and wide physico-chemical behaviours. Displacement of drug molecules occurs in complex formation. The findings have important implications for the pharmaceutical industry and contribute to the development of better and more stable drug formulations.

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**Conflict of interest**

No conflict of interest.

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