Microwave Frequency Dielectric Spectroscopy of Paracetamol and its Aqueous Solutions at Different Temperatures

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ABSTRACT

*The study of pharmaceutical drug compounds benefits greatly from the use of frequency domain dielectric relaxation spectroscopy. Using the Agilent precision LCR meter E4980A and the Agilent 16452A four-terminal liquid test fixture, the complex relative dielectric permittivity *() ='- j " of aqueous solutions of paracetamol is measured across the frequency range of 20 Hz to 2 MHz at a temperature of 293.15 K. Loss tangent is determined for each paracetamol concentration in pure water by using complicated relative permittivity data. All solutions' electrode polarization relaxation times have been computed. Changes in these dielectric properties as a result of varying paracetamol concentrations in distilled water are described.*

Keywords: *Microwave Frequency; Dielectric Spectroscopy; Paracetamol; Temperatures*

INTRODUCTION

Dielectric spectroscopy at microwave frequencies is a strong method for studying molecular dynamics and interactions in a wide range of materials, including medicinal drugs and their solutions. Paracetamol (or acetaminophen) is a common painkiller and antipyretic, and its action in aqueous solutions at various temperatures is the subject of this investigation. Due to its effectiveness, safety, and low toxicity when taken in the approved quantities, paracetamol is an often prescribed medicine. Temperature, concentration, and hydrogen bonding interactions are just a few of the variables that might affect its behavior in aqueous solutions. Paracetamol's formulation, stability, and bioavailability may all be improved by a deeper understanding of its molecular dynamics in solution.[1]

Measurements of the material's dielectric characteristics as a function of frequency and temperature form the basis of dielectric spectroscopy. The dielectric characteristics provide information about the molecular interactions and dynamics of the system under investigation since they are influenced by the polarization of molecules in response to an applied electric field. Dielectric spectroscopy shines as a method for studying molecule rotations and movements at microwave frequencies. In order to evaluate dielectric properties, a high-frequency microwave spectrometer will be used. The sample, which might be in the form of a solid or a liquid, will be sandwiched between the electrodes. The sample will be subjected to a microwave electromagnetic field, resulting in the polarization of molecules and the induction of rotational and vibrational vibrations. The sample's molecular reaction to the applied field and molecular dynamics may be characterized by measuring its dielectric constant and dielectric loss.[2]

The influence of temperature on the dielectric behavior of paracetamol will be investigated by conducting the investigation at several temperatures. Molecular mobility and hydrogen bonding interactions, both of which may affect dielectric characteristics, are strongly temperature dependent. To provide a full picture of the system's behavior, the experiment will be repeated at different temperatures. Paracetamol and its aqueous solutions' dielectric spectroscopic data will be compared and studied. Hydrogen bonding, molecule rotations, and vibrational movements, among others, will be elucidated by interpreting the temperature- and concentration-dependent changes in the dielectric properties. Activation energies, relaxation periods, and correlation lengths, among other useful molecular properties, will be extracted from the collected data via analysis using the appropriate theoretical models and equations. Paracetamol and water dynamics may be better understood using these values, since they give information on energy barriers and molecule cooperativity.[3]

Explanation of microwave frequency dielectric spectroscopy

Dielectric characteristics of materials are studied as a function of frequency in the microwave region using a method called Microwave Frequency Dielectric Spectroscopy (MFDS), sometimes known as Time Domain Dielectric Spectroscopy (TDDS). The response of a substance to an electric field is referred to as its dielectric characteristics. This method shines when applied to soft matter and biological systems, where it may provide light on their molecular dynamics and relaxation processes.[4]

Microwave frequency dielectric spectroscopy is explained in detail here:

- **Principle of Dielectric Spectroscopy:** When a material is placed in an electric field, its dipoles will often line up with the direction of the field. The material is polarized as a result of this process of alignment. Dielectric spectroscopy is a technique that quantifies the polarization response of a material to an alternating electric field.
- **Setup:** An MFDS experiment begins with a sample cell containing the target substance. To create a time-varying electric field at microwave frequencies, this sample cell is put in a special device. Several MHz to several GHz is the typical frequency range for MFDS.
- **Electromagnetic Waves:** Electromagnetic waves having wavelengths in the millimeter to centimeter range are equivalent to microwave frequencies. The oscillating electric and magnetic fields of these waves allow them to permeate most materials; as a result, they may be used to investigate the dielectric characteristics of a broad variety of substances.
- **Time Domain Analysis:** The sample is subjected to a brief microwave pulse in MFDS. The material is polarized as a consequence of the electromagnetic wave's interaction with the sample. The sample's dielectric characteristics at various frequencies may be determined by timing the lapse between an incident pulse and the sample's response.
- **Dielectric Relaxation:** The capacity of dipoles to realign in response to an applied electric field is called dielectric relaxation, and it is seen in a wide variety of materials. The molecular structure of the material and the frequency of the applied electric field both play a role in this relaxing process. The molecular dynamics and interactions inside a material might be better understood by investigating the relaxation times at various frequencies.[5]

Dielectric properties and their relevance in materials science

The field of materials science and engineering relies heavily on dielectric characteristics, notably in the creation and implementation of new electronic devices and methods. A "dielectric" is a substance that, in contrast to metals, does not readily allow the flow of electric current through it. The insulating properties of dielectrics make them useful in a wide variety of electronic applications, including capacitors, transformers, and ICs. It is crucial to optimize device performance and guarantee their dependability by learning the dielectric characteristics of materials.[6]

The importance of dielectric characteristics in materials research is discussed below:

- **Dielectric Constant (Permittivity):** A material's dielectric constant indicates how well it can hold an electric charge in an applied field. It measures how much an object will become electrically polarized in a given electric field. When designing capacitors, it is preferable to use materials with high dielectric constants since this enhances their capacitance and therefore their usefulness. For insulating purposes, low-dielectric-constant materials are favoured because of their lower capacitance and crosstalk in electronic circuits.

- **Dielectric Loss:** When an electric field is applied to a material, the amount of energy dissipated as heat is measured by a quantity called dielectric loss. In order to avoid overheating and energy waste, it is crucial to reduce dielectric loss in applications like power transformers and high-frequency electronic equipment.
- **Breakdown Strength:** The breakdown threshold is the electric field strength over which a dielectric substance begins to conduct electricity. Particularly in high-voltage settings, the dependability and safety of electrical components depend on their high breakdown strength.
- **Dielectric Strength:** The voltage needed to break down an electrical barrier in a substance is its dielectric strength. To prevent electrical failure and associated dangers, proper insulation of electrical equipment and wires is essential.
- **Polarization:** When a dielectric substance is put through an electric field, electric dipoles may occur. Capacitors and other energy storage devices may be made more efficient if their polarization behavior is understood.[7]

LITERATURE REVIEW

P. W. Khirade and S. C. Mehrotra (2019) Paracetamol and its aqueous solutions are studied here employing microwave frequency dielectric spectroscopy to examine their dielectric relaxation behavior. When polar molecules, like water or paracetamol, are subjected to an external electric field, a phenomena known as dielectric relaxation occurs. Temperature has a role in how these compounds act in solution. The authors performed tests at several temperatures to examine the effects of temperature on the dielectric characteristics of paracetamol and its solutions. Paracetamol and its aqueous solutions were discovered to have temperature-dependent behavior in terms of their dielectric relaxation durations. The findings showed that the relaxation durations reduced with increasing temperature, indicating a change in the dynamics of the molecular interactions. Understanding the pharmacological and biological behavior of paracetamol requires knowledge of its molecular dynamics and hydrogen bonding interactions in various settings, which are shown by these results.[8]

G. Dewey and A. Majumdar (2015) Microwave dielectric spectroscopy is a useful tool for investigating solid pharmaceuticals such as paracetamol. By analyzing the frequency and temperature dependence of the dielectric characteristics of materials, dielectric spectroscopy sheds light on molecular motion and interaction. Paracetamol and its aqueous solutions have interesting physicochemical features, and the authors cover the many experimental procedures and data processing approaches used to obtain this information. Advantages of microwave frequency dielectric spectroscopy are discussed in this article. These include the technique's versatility, non-destructive character, and sensitivity to molecular dynamics. The authors stress that this method may provide light on the crystal structure, phase transitions, and intermolecular interactions of paracetamol in its solid form. For the purposes of drug discovery, formulation, and stability testing, an awareness of these features is crucial.[9]

Elangovan, S. (2017) Using microwave frequency dielectric spectroscopy, this work examines the effect of dielectric relaxation on both temperature and concentration in aqueous paracetamol solutions. Because of its sensitivity to both temperature and solution composition, dielectric relaxation behavior is a great tool for investigating molecular dynamics and intermolecular interactions in aqueous systems. Paracetamol solutions' dielectric behavior as a function of concentration and temperature. They found that the dielectric relaxation durations shortened with increasing paracetamol content, revealing altered molecular interactions and dynamics in the solution. In addition, they were able to investigate how temperature affected the dielectric characteristics of paracetamol solutions by doing temperature-dependent measurements.[10]

Forest, E. and C. P. Smyth (2020) Methyl methacrylate (MMA) and butyl methacrylate (BMA) H-bonded complexes with p-cresol, p-chlorophenol, 2,4-dichlorophenol, and p-bromophenol in the dilute solutions of carbon tetrachloride were investigated for dielectric absorption and their dielectric parameters (0,, ', '') were determined at a constant microwave frequency of 9. They found that the length of the phenolic chain had a significant impact on the relaxation durations of methacrylate. The larger effective radius of the spinning unit might be to blame for this. The carbon tetrachloride molecule's propensity for hydrogen bonding makes this a distinct possibility. They also observed that the phenols in these mixes break intermolecular hydrogen bonds more readily than the other compounds. In comparison to other mole ratios (1:2, 1:3, 2:1, and 3:1), the 1:1 complex is dominant in the system because it yields the highest relaxation durations.[11]

P. Jeevanandham and S. Kumar (2016) At a fixed microwave frequency and 300K room temperature, Gedam and Suryavanshi studied the dielectric loss and dielectric constant of polar liquids in a benzene dilution. They discovered that both dielectric properties change in a linear fashion with increasing concentration. The values of and were computed for all three polar liquids when dissolved in the non polar medium benzene. The polar liquids tested were acetone, pyridine, and nitrobenzene. The wavelength of the microwave radiation in the liquid dielectric cell, as well as its dielectric loss and dielectric constant, were determined using an X-band microwave bench. In the diluted benzene solution, they prepared solutions of varying concentrations of all polar liquids. They were stored in a well volumetric flask for 12 hours to ensure thermal equilibrium. They used extremely dilute solutions to reduce the likelihood of solute-solute interactions.[12]

METHODOLOGY

Paracetamol powder from "Farmson Pharmaceuticals Gujarat Pvt. Ltd." and distilled water from "High Purity Laboratory Chemicals (HPLC), Mumbai" were used to make aqueous solutions of different PCM weight fractions. The solubility of PCM in water was used to determine the concentration of the solutions. Then, an equation is used to convert the PCM weight fractions to molarity (M) for all solutions. Following open and short calibrations, dielectric parameters were obtained from prepared solutions using an Agilent precision LCR meter E4980A and an Agilent 16452A four terminal liquid test fixture. Figure 3.1 depicts the experimental setup. This apparatus was used to measure parallel capacitance (Cp) and parallel resistance (Rp), two fundamental dielectric characteristics from which others (such as dielectric constant, dielectric loss, etc.) may be derived. Table-3.1 displays the molarity of solutions with varying PCM concentrations.

Table 3.1: Concentrations of PCM and respective molarity of solutions

Concentrations of PCM (mg)	**Molarity (M)**
0	0
20	0.013
40	0.026
60	0.039
80	0.052
100	0.065
120	0.079
140	0.092

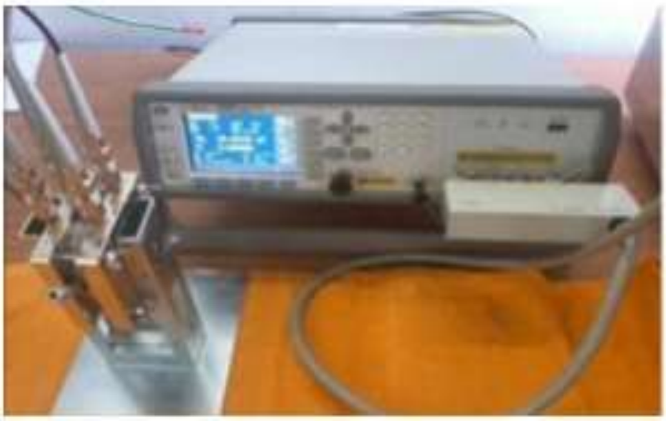

Figure 3.1: E4980A, a precision LCR meter from Agilent, with four liquid test fixtures. 16452A by Agilent

RESULTS

Figure 4.1 (a) displays, for all PCM concentrations in water, the frequency dependence of the real component of complex permittivity, also known as the dielectric constant ('). The dielectric constant of water (0 M) solution is the lowest of all PCM solution concentrations. The $' value of the 0.065 M solution is greatest across the board. For all solutions, the dielectric constant drops fast up to a frequency of 1 kHz, and thereafter it declines slowly. The higher frequency expansion seen in the inset of Figure 4.1 (a) demonstrates a discernible range in the value of the dielectric constant across all solutions. Since the ability of oscillating dissociated ions decreases with increasing frequency of alternating fields, the decreasing dielectric constant value with rising frequency may be explained in the case of water. Figure 4.1(b) displays the non-linear relationship between the dielectric constant and PCM concentrations. Electrode polarization (EP) effect, which symbolizes the creation of electric double layers (EDL) capacitance at the interface of dielectric material (aqueous solutions) and the metallic electrode surface of liquid test fixture, causes the value of e' to rise as the frequency decreases.

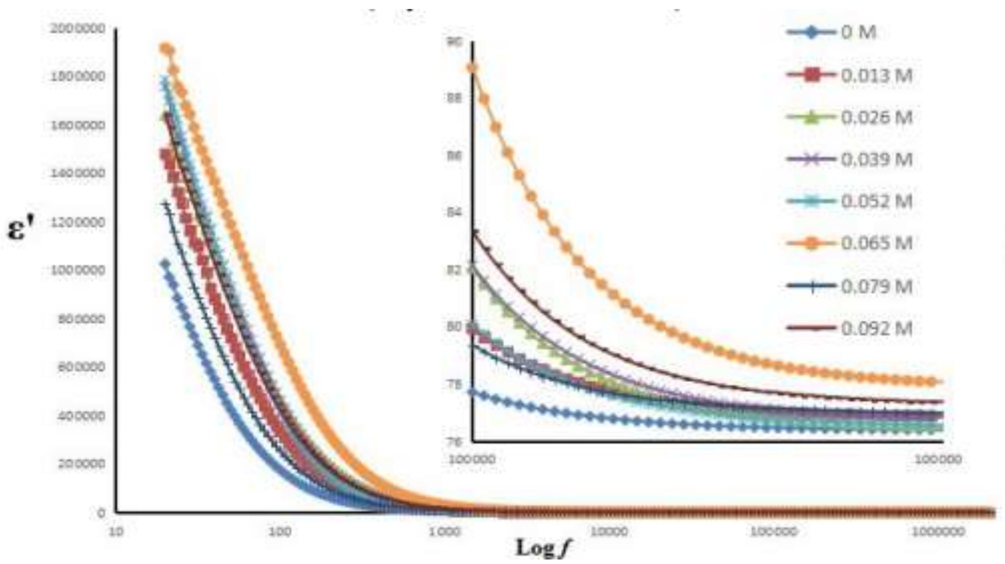

Figure 4.1 (a): Plot of dielectric constant (ε') as a function of frequency for all concentrations of PCM

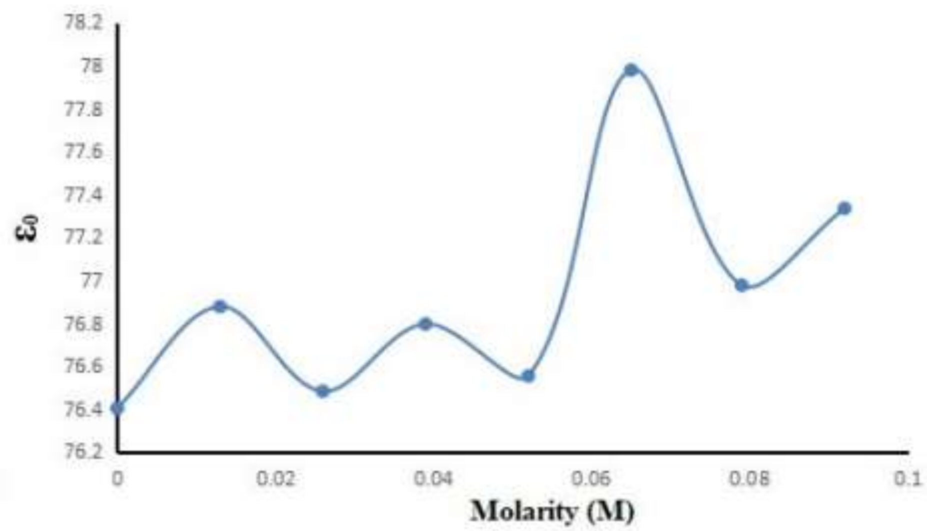

Figure 4.1 (b): Plot of static permittivity (ε0) for different concentrations of PCM

In Figure - 4.2, we see the frequency-dependent spectra of dielectric loss ('') at varying PCM concentrations. At all frequencies, dielectric loss is greatest for a 0.065 M solution and lowest for water (0 M). Since the values of dielectric constant (') have decreased, the values of dielectric loss (''') have also decreased. Above 100 Hz, all solutions exhibited a sharp decrease in dielectric loss. The results once again demonstrate the existence of free charge carriers in all solutions, confirming the role of the EP effect. Figure 4.2's inset indicates that the ionic current in these solutions satisfies Ohm's law, as seen by the linear reduction in dielectric loss '' with log of frequency, with slope greater than unity.

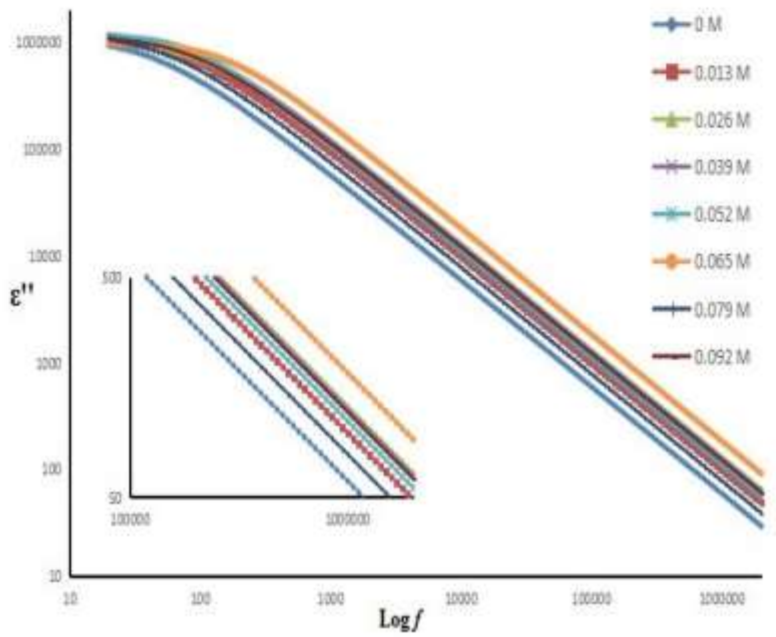

Figure 4.2: Plot of dielectric loss (ε") as a function of frequency for all concentrations of PCM

A significant capacitance is created in series with the conducting bulk of PCM aqueous solutions because the ions present in the solution migrate towards the electrode, generating an ionic double layer at the interface. Electrode polarization (EP) is the name given to this phenomena. Figure 4.3 (a) displays the loss tangent (tan 8 = ''/'') spectra as a function of frequency for varying PCM concentrations. The only PCM solution (0.065 M) with a higher peak value than water is water itself. The EP relaxation time for each solution was calculated using the following equation, where each peak value represents the EP relaxation frequency fEP.

$$\tau_{EP} = (2\pi f_{EP})^{-1} \text{ - - - } (1)$$

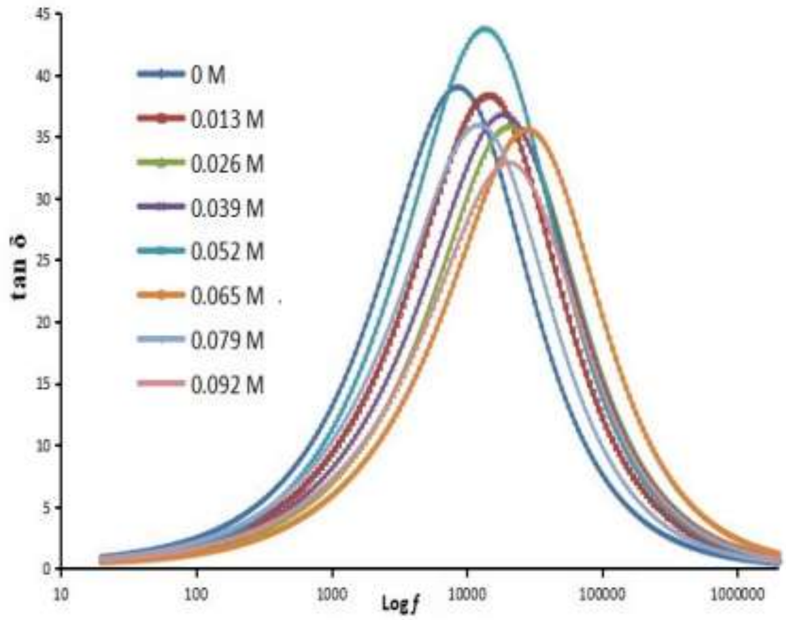

Figure 4.3 (a): Plot shows the loss tangent for all PCM concentrations as a function of frequency

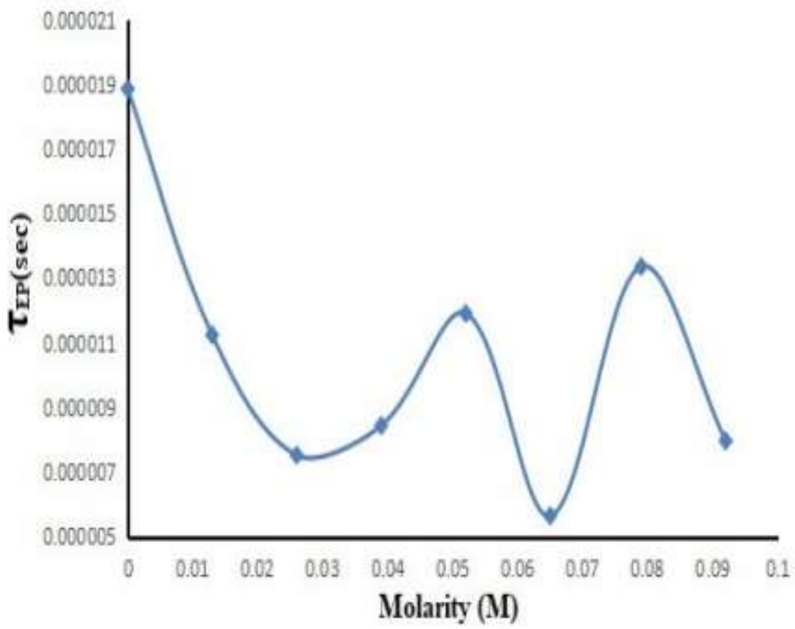

Figure 4.3 (b): Plot showing the EP relaxation time (EP) at various PCM concentrations

Figure 4.3(b) shows a plot of the relaxation time of electrode polarization vs PCM concentrations in water. It is noteworthy to notice that when 20 mg PCM is added to water, the EP value lowers dramatically from 0.18 s for water to 0.11 s for a 0.013 M solution. Value of EP relaxation time demonstrates non-linear change with increasing PCM concentrations.

CONCLUSION

The E4980A from Agilent is a precision LCR meter that has a liquid test fixture with four terminals. The dielectric constants of paracetamol aqueous solutions were measured using an Agilent 16452A at 293.15 K, from 20 Hz to 2 MHz. The findings of the dielectric constant and the dielectric loss indicate the existence of free charge carriers in solutions and the electrode polarization effect. The dielectric constant varies non-linearly with PCM concentration, as seen by a plot of static permittivity against PCM concentration. The 0.065 M solution is the only one of them that behaves unusually across the board for dielectric constant. We have determined the non-linear relationship between PCM content in water and the relaxation duration of electrode polarization for all solutions.

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