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Thermo Physical Behaviour of Curcumin using Acoustic Spectroscopy

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Abstract

Effect of temperature on the structural and dynamical properties of curcumin in polar protic and aprotic solvents such as ethanol and DMSO (Dimethyl sulphoxide) having dielectric constant 25 and 47 & dipole moment 1.6 D and 3.96 D respectively has been investigated in the temperature region $35^0C - 70^0C$. Ultrasonic pulse echo technique at 5 MHz frequency has been employed for this purpose. Acoustic parameters such as ultrasonic velocity (ν), Compressibility (β), Free length (L_f), Acoustic Impedance (Z), Rao's constant (R) and Wada's constant (W) has been calculated and discussed in terms of structural dynamics, inter and intramolecular H-bonding & intermolecular forces between solute and solvent molecules. Results from all the measured acoustic parameters show that curcumin in polar aprotic solvent show clatrates-like structure at specific concentration along with the general solvent effect. A sharp ultrasonic velocity maximum and compressibility minimum at 0.0032 concentration observed for curcumin-DMSO mixture at all the measured temperatures indicates the formation of clathrate-like structures which seems to be more towards high temperatures. In polar protic solvent such as ethanol, clathrates –like structure seems to be both temperature as well as concentration dependence giving a sharp maximum at 0.0012 concentrations which on increasing the temperature shifts towards lower concentration. This shift towards lower concentration and higher temperature may be attributed to the domination of hydrophobic interaction between phenyl-phenyl rings of curcumin and formation of aggregations. Such kind of interactions will find a variety of applications in pharmaceutical and biological research with reference to bioavailability and to understand target oriented mode of action of curcumin.

Key words: Curcumin, Ultrasonic velocity, Dimethyl Sulphoxide, Ethanol, Acoustic parameters.

Introduction

Properties of substances are directly related to the structural changes in it. These structural changes may occur due to various factors such as change in dipole moment of solute and solvents, change in polarity, concentration, pressure, temperature, magnetic field etc. Acoustic spectroscopy is very important and powerful tool for the investigation of structural and dynamical properties not only for the pure or binary mixtures but also extended its application to herbal, organic, bioactive and other systems [1-3]. The interaction of molecules can be predicted by measuring their concentration and temperature dependent acoustic parameters such as velocity, density, compressibility, free length etc. The variation of these parameters provides vital information about the molecular interaction between solute and solvents.

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Curcumin, is a bioactive compound extensively used for the prevention and treatment of several diseases like cancer[4]. Many studies have suggested a wide range of potential therapeutic or preventive effects associated with curcumin like antitumor, antioxidant, antiarthritic, antiamvloid and antiinflametory [5-10]. Only hurdle, curcumin finds in its wideband applications is its poor solubility in water. It is practically insoluble in water at neutral and medium acidic pH due to strong hydrophobicity of the conjugated alkene chain and unavailability of strong polar group renders the molecule insoluble or sparingly soluble in polar solvent [11]. However, it is found more soluble in alkaline solvents and in extremely acidic solvents, due to the ionization of phenolic or enolic groups or due to the degradation or change in dissociated form. There are two kinds of acidic hydrogen in the curcumin molecules, one is phenolic hydrogen and the other is acive methylene hydrogen of β- deketones [12]. Apart from the functional groups the absorption of curcumin strongly depends upon the solvent nature and polarity [12]. Therefore, an attempt has been made to study temperature dependent acoustic properties of curcumin in polar protic and aprotic solvent environment such as ethanol having dielectric constant 25 and low dipole moment (1.69 D) which is less polar as compared to DMSO having dielectric constant 47 and dipole moment 3.97 D.

A number of investigators have studied the solvent dependent structural properties of curcumin previously. D. Patra et al. [12] studied the behaviour of curcumin in different solvents using synchronous fluorescence spectroscopy and compared the results with conventional fluorescence measurements and concluded that spectral properties of curcumin is solvent polarity dependence.

Modasia et al [13] studied the water solubility of curcumin by soid dispersion process. temperature dependent spectroscopic study of curcumin in aqueous medium has been investigated by Ramya Jagannathan et al.[11] and discussed the mechanism of solubility of curcumin in water at different temperatures in terms of intermolecular H-bonding, intermolecular forces and aggregation-disaggregation. Wing-Hin Lee et al [14], described the historical use of curcumin in medicine, its chemistry, stability and biological activities, including curcumin's anti-cancer, anti-microbial, anti-oxidant, and anti-inflammatory properties. They further discussed the pharmacology of curcumin and provided new perspectives on its therapeutic potential and limitations. The study also focused in detail on the effectiveness of curcumin and its mechanism of actions in treating neurodegenerative diseases such as Alzheimer's and Parkinson's diseases and brain malignancies.

However, temperature dependence of curcumin in varying polar protic and aprotic solvent environment using acoustic spectroscopy is not yet reported. Therefore, an attempt has been made in order to study thermophysical behaviour of curcumin through structural dynamics and molecular interaction under polar protic and aprotic environment.

Material and Methods

Materials

Curcumin (M.W. 368.38 g mol $^{-1}$), purchased from local market was grinded in a fine powder and was further filtered through cotton clothes so as to make it again fine (nano sized) and uniform particles. DMSO (Dimethyl sulphoxide) (M.W. 78.13 g mol-1) purchased from sd fine chemicals limited was used as a solvent for making binary solution.

Measurements

Ultrasonic pulse-echo method was used for the measurement of acoustic parameters. Ultrasonic flaw detector (Model MV 4400) supplied by Roop telsonix ultrasonix limited, Mumbai has been employed for this purpose. Ultrasonic transducer of 5 MHz frequency has been used for the detection of ultrasonic velocity in the mixture with the uncertainty in the measurement of velocity is ±0.02 m s^{-1}. For the temperature measurement, system is placed on automated hot plate having automatic temperature controlled facility with the accuracy of ± 1^0 C. Gravity bottle has been used for the measurement of density of the mixture at different temperatures.

Theory

Employing the velocity and density at the measured temperatures, some acoustical and allied parameters can be calculated through the following expressions.

The Adiabatic Compressibility (β) has been calculated using the equation,

$$\beta = (v^2\rho)^{-1} \quad \text{------------------------------- (1)}$$

Where, ρ is density of the solution is the Ultrasonic velocity of solution.

The Inter molecular free length has been calculated by,

$$L_f = k\,\beta^{1/2} \quad \text{------------------------------ (2)}$$

Where, k is a constant known as Jacobson constant ($k=2*10^{-6}$).

Acoustic impedance calculated by

$$Z = \rho v \quad \text{-------------------------------- (3)}$$

Rao's constant calculated by using the formula

$$R = v^{1/3} M/\rho \quad \text{---------------------------- (4)}$$

Where, M is molar mass.

Wada's constant calculated using

$$W = \beta^{1/7} M/\rho \quad \text{------------------------- (5)}$$

Results and Discussion

Structural arrangement of curcumin with its different forms alongwith DMSO (Dimethyl sulphoxide) and ethanol has been shown in fig. 1. Whereas, experimentally observed values of ultrasonic velocity (v), Acoustic impedance (Z), Rao's constant (R), adiabatic compressibility(β),Free length (L_F) and Wada's constant (W) for curcumin in DMSO (Dimethyl sulphoxide) and ethanol as a function of temperature and concentration has been depicted in fig. 2-7 respectively.

For the studied two systems, the variations in ultrasonic velocity (v), Acoustic impedance (Z) and Rao's constant (R) as a function of both temperature and concentration are found similar. Whereas, for the other studied parameters like adiabatic compressibility, Free length (L_F) and Wada's constant (W) it show reverse trend.

Effect of temperature

It has been observed that the acoustical parameters such as Ultrasonic velocity (v), acoustic impedance (Z) and Rao's constant (R) for curcumin-DMSO system were found to be increasing non-linearly with increase in temperature for all the measured concentrations. This indicates increases in molecular interaction through hydrogen bonding between various hydrogen bonding cites of curcumin and polar aprotic solvent (DMSO). This increase in the values of sound velocity with temperature will certainly increase the acoustic impedance (Z) (fig. 3a) and Rao's Constant (R) (fig.4 a) of the studied systems. This is because, at higher temperatures, there may be a possibility of breaking of intramolecular hydrogen bonding which leads to exposure of polar groups and hence responsible for the molecular interaction to take place [11]. In most of the moderately polar and non polar solvents, enol form is more stabilized than keto form. Therefore, there may be a strong possibility of molecular interactions between active hydrogen cites of curcumin and DMSO.

In case of polar protic ethanol, ultrasonic velocity (v), acoustic impedance (Z) and Rao's constant (R) were also observed to be temperature dependent which increases non-linearly with increasing temperature for all the measured concentrations. But, these variations were found to be totally different than that observed in DMSO and appear to be deviated from the normal solvent effect. This may be due to the fact that at high temperature, curcumin is likely to exist in the keto form, which appears to favour H-atom transfer reactions in the surrounding of protic polar ethanol, thus, may play a crucial role in the antioxidant action of curcumin [11].

This may boost the possibility of strong specific interaction through hydrogen bonding between hydroxyl group of ethanol and various hydrogen bonding cites available in curcumin.

Acoustic impedance (Z) is one of the important parameters which offer impedance to the sound velocity. Non-linear variation of acoustic impedance with increasing temperature for both the systems curcumin-DMSO and curcumin-ethanol (fig. 3) suggests the strengthening of molecular interaction between solute and solvent molecules towards higher temperature.

Molar compressibility or Rao's constant (R) is one more parameters studied for the two systems is shown (fig. 4) for curcumin in DMSO and ethanol respectively. As, density of both the systems decreases with increasing temperatures (table 1) therefore; molar compressibility must behave as sound velocity. Thus, non-linear variations in the molar compressibility with temperature boost the possibility of formation of hydrogen bonding between solute and solvent molecules towards higher temperature.

The structural geometry of the mixture depends upon adiabatic compressibility. Non linear decrease in the values of adiabatic compressibility for curcumin-DMSO (fig. 5a) and curcumin-ethanol (fig. 5b) with increasing temperature has been observed. This supports for denser packing of molecules and progressive molecular interaction between different possible OH groups of curcumin and solvent molecules.

The variation of sound velocity in a mixture depends upon the increase or decrease of intermolecular free length. Fig.6 show the dependence of free length on temperature and concentrations for curcumin-DMSO and curcumin-ethanol mixtures respectively. Since, the free length L_f is proportional to the adiabatic compressibility β, the same trend of variation similar to the variation of adiabatic compressibility for the studied systems has been observed in the graphs. Non linear variations and decrease in the values of free length with increasing temperature supports for the strong interaction between solute and solvent molecules.

Temperature dependence of molar compressibility or Wada's constant (W) for curcumin-DMSO and curcumin-ethanol is shown in fig. 7. Molar compressibility for curcumin in DMSO was found to be decreasing non-linearly with increase in temperature. This suggests strong possibility of formation of hydrogen bonding between curcumin and DMSO molecules towards higher temperatures.

Effect of concentration

Concentration dependence of ultrasonic velocity for curcumin has also been carried out over the concentration region 0.001 to 0.0054 for DMSO and 0.0004 to 0.0021 for ethanol in order to understand the molecular behaviour of curcumin in polar aprotic and polar protic environment. Sound velocity was observed to be increasing with concentrations of curcumin, reaching maximum at 0.0032 mole fraction and then decreases for further increase in the concentration for all the measured temperatures. This indicates the formation of clathrate-like structures of curcumin and high polar aprotic DMSO molecules which seems to be more towards higher temperatures. Similar concentration dependence of velocity has been observed for aqueous 2- butoxyethanol studied in the temperature region 25 to 70^0 C by N.P Rao et al [15]. At temperature 35 and 40^0 C, velocity was found to be increasing with concentration, becomes maximum at 0.0032 mol fraction. This may be due to increased molecular interaction and hydrogen bonding between curcumin and DMSO molecules. At, higher concentration, the interaction seems to be decreasing which results in reduction of sound velocity. This decrease in velocity at higher concentration may be due to saturation of possible cites of hydrogen bonding and formation of aggregation- disaggregation of the molecules [11]. Towards higher temperature i.e. above 45^0C, velocity was found to be decreasing around 0.002 mol fraction. This may be due to breaking of hydrogen bonding which leads to dissociation between curcumin-DMSO.

For curcumin ethanol mixture, clathrates–like structure seems to be formed at lower temperatures (35 and $40)^0$ C, giving a sharp maximum at the concentration 0.0012 mol fractions. The peak in the ultrasonic velocity was observed to be shifted towards lower concentrations as temperature of the system increases [15]. At higher temperatures hydrophobic interaction between phenyl-phenyl rings of curcumin was more dominant and forms aggregations at the same concentration [16]. However, the clathrates-like structure appears to be more dominant towards lower concentration and higher temperature, as the peaks in the sound velocity were observed to be shifted towards lower concentration.

At the high concentration end, sound velocity increases rapidly with rise in temperature. This is because at higher temperature and higher concentrations more hydrogen bonding cites may be available for hydrogen bonding between solute and protic solvent molecules.

Conclusion

The studied acoustical parameters of curcumin in aprotic and protic polar solvent i.e. in DMSO and ethanol show both temperature and concentration dependence. The overall study apart from molecular interaction between solute and solvent molecules, concludes that

- curcumin in polar aprotic solvent DMSO show that the formation of clathrates-like structure is both concentration and temperature dependent. However, the effect seems to be more at higher temperatures.
- Under the polar protic solvent (ethanol) environment, clathrate-like structure forms at all the measured temperatures but at higher temperatures the peak shifts towards lower concentrations.

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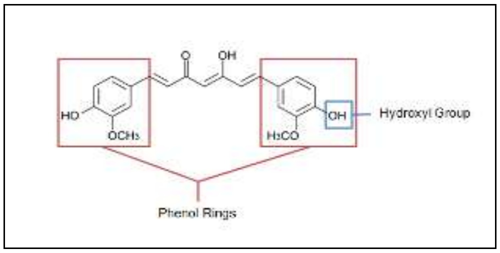
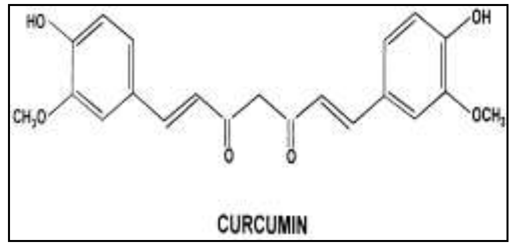
References

1. Manjunath M S & J Sannappa. (2012). Molecular Interaction study of Curcumin with 1-Propanol binary mixture *Research Journal Of Pharmaceutical, Biological And Chemical Sciences*, 3 191.
2. Richa Saxena & S C Bhatt. (2010). Molecular Interactions in Mixture of Polymethylmethacrylate with Acetic Acid *Interna Journal Of Chemistry* 2 164-172.
3. Mustafa Vatandas , Ali Bulent Koc & Caner Koc.(2007). Ultrasonic velocity measurements in ethanol–water and methanol–water mixtures *Eur Food Res Technol*, 225 525–532
4. Aggarwal B B, Kumar A, Bharti A C. (2003).Anticancer potential of curcumin: preclinical and clinical studies *anticancer research*, 23(1A) 363-98.
5. Hatcher H, Planalp R, Cho J, Torti F M & Torti S V.(2008). Curcumin: From ancient medicine to current clinical trials *Cell Mol Life Sci*, 65 (11) 1631–1652.
6. Strofer M, Jelkmann W & Depping R. (2006). Curcumin decreases survical of Hep3B liver and MCF-7 breast cancer cells:the role HIF *Strahlentherapie und Onkologie.* 187 (7) 393–400.
7. Aggarwal B B & Shishodia S. (2011). Molecular targets of dietary agents for prevention and therapy of cancer *Biochemical Pharmacology*, 71 (10) 1397–1421.
8. Choi H, Chun Y S, Kim S W, Kim M S & Park J W. (2006). Curcumin inhibits hypoxia-inducible factor-1 by degrading aryl hydrocarbon receptor nuclear translocator: a mechanism of tumor growth inhibition *Molecular Pharmacology*, 70 (5) 1664–1671.
9. Shukla P K, Khanna V K, Ali M M, Khan M Y & Srimal R C. (2008). Anti-ischemic effect of curcumin in rat brain. *Neurochem Res*,33 (6) 1036–1043.
10. Stix G.(2007). Spice Healer *Sci Am*, 296 (2) 54-7.
11. R Jagganathan, P M Abraham & P Poddar. (2012). Temperature-dependent spectroscopic evidences of curcumin in aqueous medium: a mechanistic study of its solubility and stability *J. Phys. Chem. B*, 116 14533-14540.
12. D Patra & C Barakat. (2011).Synchronous fluorescence spectroscopic study of solvatochromic curcumin dye *spectrochimica Acta part A*, 79 1034-1041.
13. M K Modasia and V M Patel. (2012). studies on solubility of curcumin, *International J. of Pharm. And life sciences*, 3(3) 1490-1497.
14. C Y Loo, M Bebawy, F Luk, R S Mason and R Rohanizadeh.(2013). Curcumin and its derivatives: their application in neuropharmacology and neuroscience in the

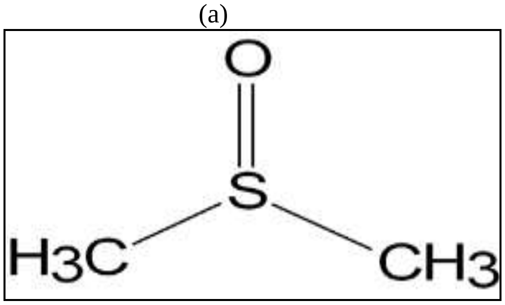
21st century *Curr Neuropharmacol*. 11(4) 338–378.
15. N P Rao and R E Verrall. (1987), Ultrasonic velocity, excess adiabatic compressibility, apparent molar volume, and apparent molar compressibility properties of binary liquid mixtures containing 2-butoxyethanol, *Can. J. chem.* 65 810-816.
16. M K Hazra, S Roy and B Bagchi. (2014). Hydrophobic hydration driven self-assembly of curcumin in water: Similarities to nucleation and growth under large metastability, and an analysis of water dynamics at heterogeneous surfaces *J. Chem. Phys.* 141 18C501.



(a)



(b)



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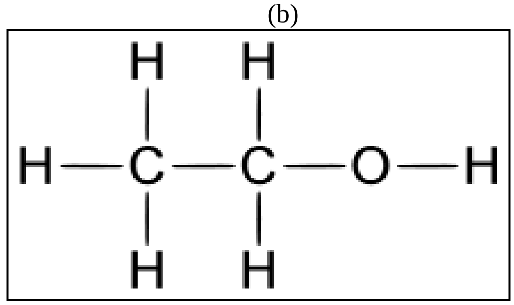
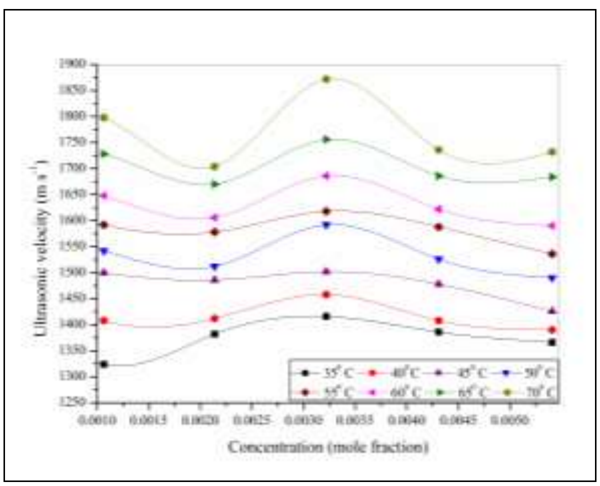


(d)

Fig. 1 Structure of curcumin (a) Enol form (b) Keto form and solvents (c) DMSO (d) Ethanol



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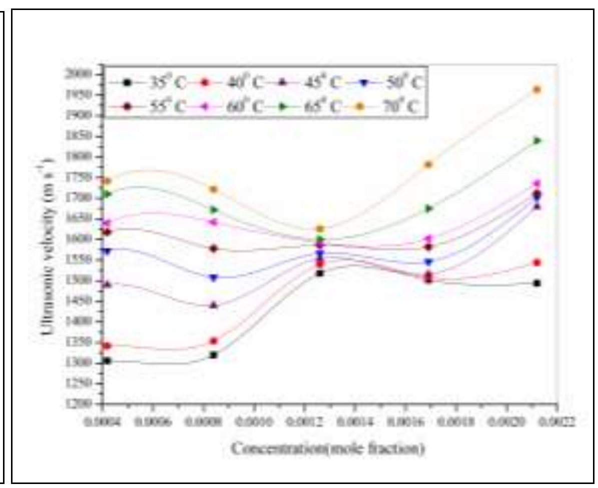
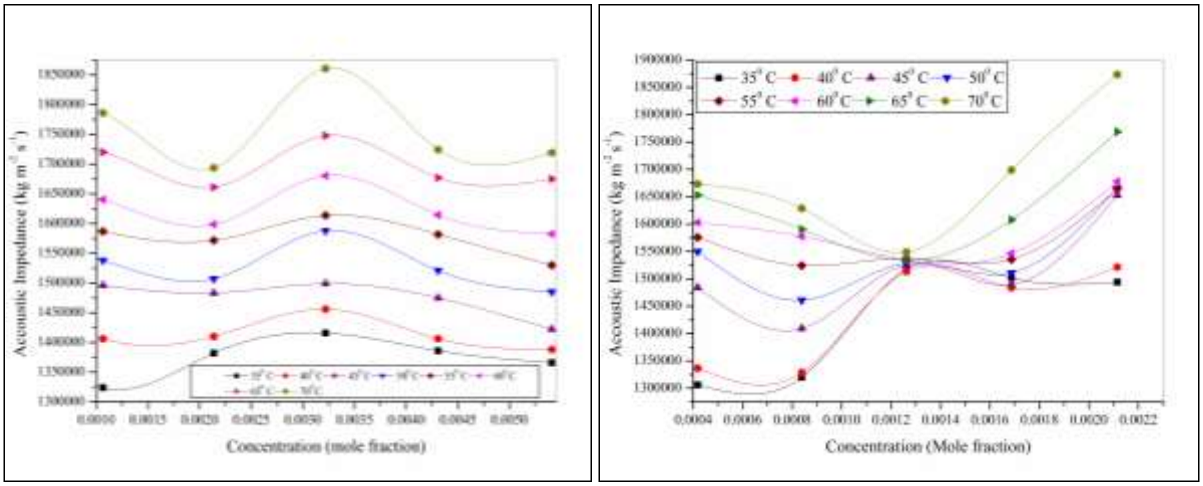


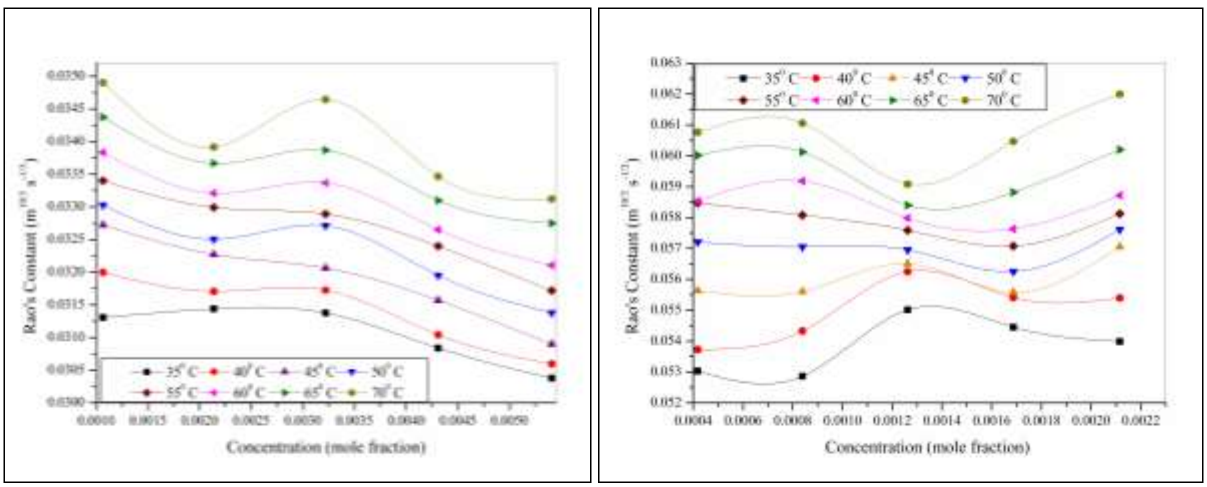
b

Fig. 2 Variation of ultrasonic velocity as a function of temperature and concentration of curcumin in (a) DMSO and (b) ethanol



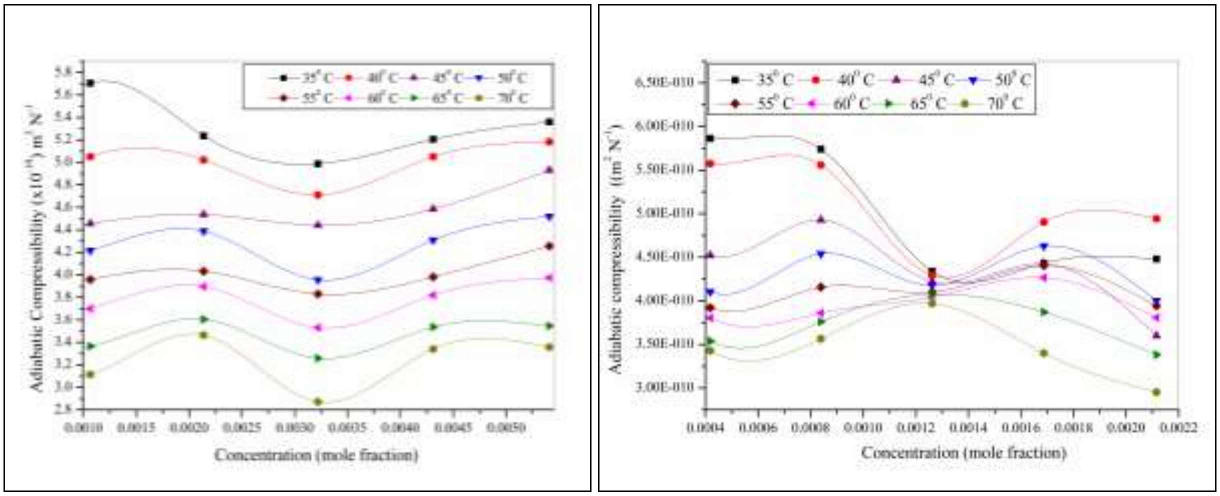
a b

Fig. 3 Variation of acoustic impedance as a function of temperature and concentration of curcumin in (a) DMSO and (b) Ethanol



a b

Fig. 4 Variation of Rao's constant as a function of temperature and concentration of curcumin in (a) DMSO and (b) ethanol



a b

Fig. 5 Variation of adiabatic compressibility as a function of temperature and concentration of curcumin in (a) DMSO and (b) ethanol

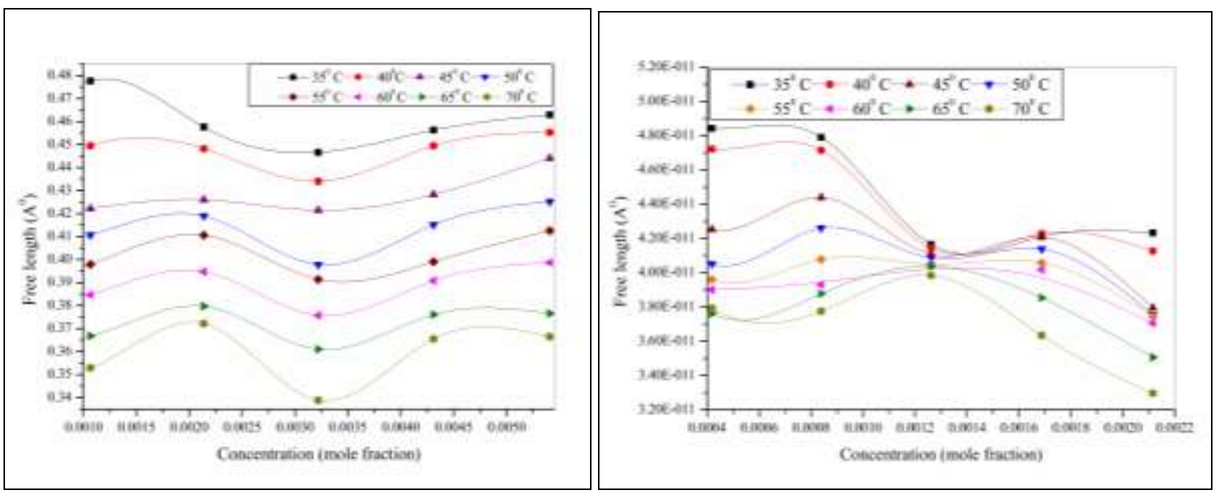


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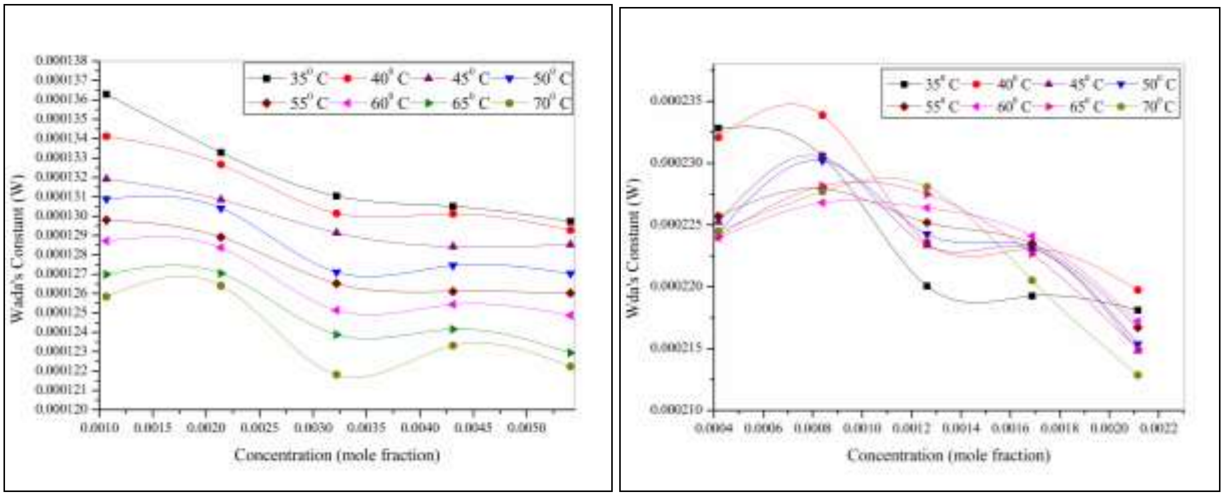
Fig. 6 Variation of Free length as a function of temperature and concentration of curcumin in (a) DMSO and (b) ethanol



a b

Fig. 7 Variation of Wada's constant as a function of temperature and concentration of curcumin in (a) DMSO and (b) ethanol

Table 1. Densities of curcumin in ethanol and DMSO at various temperatures

Solvent (mole fraction)	Density (kg /m3)							
Ethanol	35^0 C	40^0 C	45^0 C	50^0 C	55^0 C	60^0 C	65^0 C	70^0 C
0.000418075	997.980	996.000	996.000	986.000	974.000	977.340	966.670	960.670
0.000838604	983.860	981.340	978.670	968.670	966.000	960.670	951.340	946.000
0.001261607	984.780	982.670	981.340	976.000	969.340	964.000	958.670	952.670
0.001687106	985.560	984.000	982.670	977.340	970.670	965.340	960.000	953.340
0.002115124	986.350	985.340	984.000	978.670	972.000	966.670	961.340	954.000
DMSO								
0.001064648	998.460	998.667	997.333	997.333	996.667	995.333	995.333	993.333
0.002137751	997.970	998.667	998.000	996.667	996.000	995.333	994.667	994.000
0.003219411	998.860	998.667	998.000	997.333	997.333	996.667	995.333	994.000
0.004309729	998.830	998.667	998.000	996.667	996.000	995.333	994.667	993.333
0.005408811	998.750	998.667	997.333	996.667	996.000	995.333	994.667	992.667

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