

Studies on the Interactions of Paracetamol in Water and Binary Solvent Mixtures at T = (298.15–313.15) K: Viscometric and Surface Tension Approach

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Abstract: Temperature, concentration, and solvent conditions have consequences on the formation and dissolution of the drug. Viscometric measurements of paracetamol solutions of different concentrations in 5, 10, and 15% methanol have been made at 298.15, 303.15, 308.15, and 313.15K. Surface tension values (γ) of the solutions were obtained experimentally by using a stalagmometer as well as were derived from the ultrasonic velocity (U) and density (d) values at 298.15 K. The surface tension data have been analyzed using the Gibbs equation to evaluate surface excess (Γ_2). The surface tension and surface excess data obtained by the two different methods are well in accordance. The viscosity (η) data were used to calculate relative viscosity (η_r), Falkenhagen coefficients (A_F), Jones-Dole's coefficients (B_J) and chemical potential (μ). The obtained data have been analyzed based on the Jones-Dole equation to know the molecular interactions.

Keywords: molecular interactions; paracetamol; viscometric parameters; stalagmometer; surface tension.

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1. Introduction

Specific forms of a drug have different physicochemical properties that significantly impact how it is processed into a drug product. Recent research shows that overdose of paracetamol is hepatotoxic for alcoholics [1-3]. The bioavailability of a drug is a function of its solubility. The aqueous solubility of paracetamol is poor at room temperature. However, it is relatively higher in boiling water. Solubility of paracetamol increases effectively in polar organic solvents like methanol, ethanol, dimethylformamide, ethylene dichloride, acetone, and ethyl acetate. Several scientists have carried out solubility studies on paracetamol in organic solvents [4-6]. It is very important to remember that methanol is not utilized to prepare liquid medicines considering its substantial toxicity at the pharmaceutical level, but in some illustrations, it is taken in the process of drug purification [7]. On the other hand, methanol has immense utility in some microencapsulation techniques and is also used as the most common solvent in high-performance liquid chromatography [8, 9]. Hence, methanol, a commonly used organic solvent, is considered an important carbon and energy feedstock in the chemical industry [10, 11].

A whole range of paracetamol solutions of different concentrations in 5, 10, and 15% methanol were prepared at 298.15, 303.15, 308.15, and 313.15K. Viscometric studies were performed by using an Ostwald viscometer, respectively. The viscosity (η) data were used to

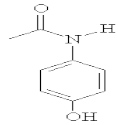

calculate relative viscosity (η_r), Jones-Dole's coefficients (B_J), Falkenhagen coefficients (A_F) and chemical potential (μ). The obtained data have been analyzed based on the Jones-Dole equation to know the molecular interactions. The surface tension values (γ) of the solutions were measured by using a stalagmometer. The values can also be derived from the ultrasonic velocity (U) and density (d) values. The surface tension data have been analyzed using the Gibbs equation to evaluate surface excess (Γ). The surface tension, including surface excess data obtained by the two different methods, is well in accordance. The complete analysis of this study presents solute-solvent and solvent-solvent interactions existing in the paracetamol solution at different temperatures, which provide a much more informed idea about the type of molecular interactions of paracetamol in the investigated binary solvent mixtures.

2. Materials and Methods

2.1. Reagents.

All chemical reagents as given in Table 1 are of GR, BDH, or AnalaR grades. Required solutions were made with Conductivity water (Sp. cond. $\sim 10^{-6} \text{Scm}^{-1}$).

Table 1. Chemical samples used with their provenance and purity.

| Chemical name with formula | Molar mass (g. mol^{-1}) | Provenance | Mass fraction purity | Purification method | Chemical structure |
|---|-------------------------------------|--|----------------------|---------------------|---|
| Paracetamol ($\text{C}_8\text{H}_9\text{NO}_2$) | 151.163 | Orissa Drugs & Chemicals Ltd (ODCL). Bhubaneswar, Odisha | >0.99 | Used as such |  |
| Methanol (CH_3OH) | 32.04 | Laboratory Chemicals Bhubaneswar, Odisha | >0.9999 | Used as such |  |

2.2. Methods.

2.2.1. Preparation of solutions.

In the present study, paracetamol is the solute, and aqueous methanol is the solvent. Methanol solutions were prepared in three different weight % (5, 10, 15 wt %) in purified water with the help of a measuring flask. For the experimental process, paracetamol solutions were prepared by weighing the paracetamol on a digital weighing machine with a precision of ± 0.001 mg and dissolved in methanol solutions to get the stock solution. The solutions were prepared on a molality basis. The conversion of molality into molarity was done using the standard expression.

$$c = md (1 + 0.001m M^{-1})$$

where c = concentration expressed in molarity; m = concentration expressed in molality; d = density; M = Molecular mass of the solute;

2.2.2. Measurement of viscosity.

A calibrated Ostwald viscometer of 25mL capacity was used to measure the viscosity of the solutions at the experimental temperatures controlled to ± 0.05 K by keeping it in a water thermostat. The viscosity values were calculated from the flow time of the solutions. The

reference values of viscosity of water at different experimental temperatures are collected from the literature [12].

2.2.3. Measurement of surface tension.

The surface tension of paracetamol in aqueous and aqueous methanol media was measured with the use of a Stalagmometer by drop count method [14] at 298.15K. Surface tension values (γ) can also be determined using the experimentally measured density and ultrasonic velocity values. The experimentally obtained surface tension values were matched with the derived values. The study of surface tension and surface excess are important tools for interpreting different intermolecular interactions in the solutions.

3. Results and Discussion

3.1. From viscometric analysis.

3.1.1. Viscosity calculation.

The viscosity, η of paracetamol solutions in pure water as well as aqueous methanol at four different temperatures (298.15, 303.15, 308.15, and 313.15 K) are listed in Table 2. The flow time and density of the paracetamol solutions were measured at different temperatures. Density and coefficient of viscosity values of water were obtained from the literature for the experimental temperatures. The viscosity of the paracetamol solutions was evaluated with reference to water at all experimental temperatures by the following relation,

$$\frac{\eta_1}{\eta_2} = \frac{d_1 t_1}{d_2 t_2}$$

where η_1 = coefficient of viscosity of water; η_2 = coefficient of viscosity of solution = η ; d_1 = density of water; d_2 = density of solution; t_1 = flow time of water; t_2 = flow time of solution;

Relative viscosity η_r of a solution can be obtained as $\eta_r = (\eta/\eta_0)$, where η = viscosity coefficient of solution and η_0 = viscosity coefficient of solvent.

Table 2. Values of η ($\text{kg. m.}^{-1} \text{s}^{-1}$) for paracetamol in water and different weight % of methanol at different temperatures.

| Solvent (wt % of methanol) | Conc. of paracetamol (mol. m.^{-3}) | $\eta \times 10^3$ ($\text{kg. m.}^{-1} \text{s}^{-1}$) | | | |
|----------------------------|--|---|---------|---------|---------|
| | | 298.15K | 303.15K | 308.15K | 313.15K |
| 0 wt % (water) | 10 | 0.909 | 0.810 | 0.744 | 0.665 |
| | 30 | 0.921 | 0.822 | 0.750 | 0.671 |
| | 50 | 0.927 | 0.834 | 0.755 | 0.676 |
| | 70 | 0.932 | 0.840 | 0.761 | 0.682 |
| | 90 | 0.939 | 0.845 | 0.767 | 0.688 |
| 5 wt % | 10 | 1.056 | 0.940 | 0.857 | 0.773 |
| | 30 | 1.068 | 0.948 | 0.864 | 0.779 |
| | 50 | 1.084 | 0.958 | 0.873 | 0.783 |
| | 70 | 1.101 | 0.968 | 0.880 | 0.789 |
| | 90 | 1.112 | 0.979 | 0.887 | 0.794 |
| 10 wt % | 10 | 1.208 | 1.073 | 0.984 | 0.865 |
| | 30 | 1.191 | 1.054 | 0.960 | 0.846 |
| | 50 | 1.166 | 1.033 | 0.942 | 0.827 |
| | 70 | 1.141 | 1.009 | 0.915 | 0.805 |
| | 90 | 1.119 | 0.988 | 0.887 | 0.783 |
| 15 wt % | 10 | 1.326 | 1.139 | 1.068 | 0.960 |

| Solvent (wt % of methanol) | Conc. of paracetamol (mol. m. ⁻³) | $\eta \times 10^3$ (kg. m. ⁻¹ s. ⁻¹) | | | |
|----------------------------|---|---|---------|---------|---------|
| | | 298.15K | 303.15K | 308.15K | 313.15K |
| 30 | | 1.346 | 1.169 | 1.086 | 0.976 |
| 50 | | 1.357 | 1.193 | 1.104 | 0.990 |
| 70 | | 1.372 | 1.216 | 1.123 | 1.003 |
| 90 | | 1.384 | 1.235 | 1.149 | 1.021 |

Standard uncertainties $u(c) = 0.01(\text{mol. m}^{-3})$, $u(T) = 0.05 \text{ K}$, $u(\eta) = 0.022 \times 10^{-3} (\text{kg. m}^{-1} \text{ s}^{-1})$. $u(p) = 0.01 \text{ M Pa}$.

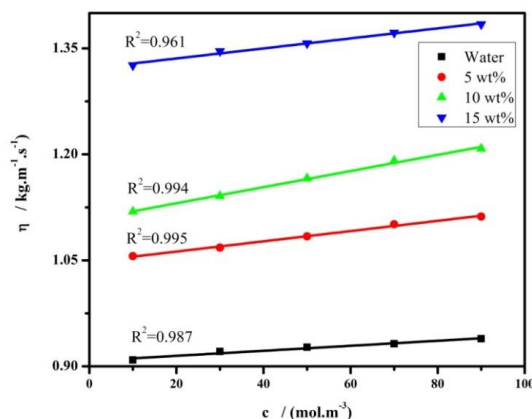


Figure 1. Plot of η vs. c for paracetamol in water and different weight percent of methanol solutions at 298.15.

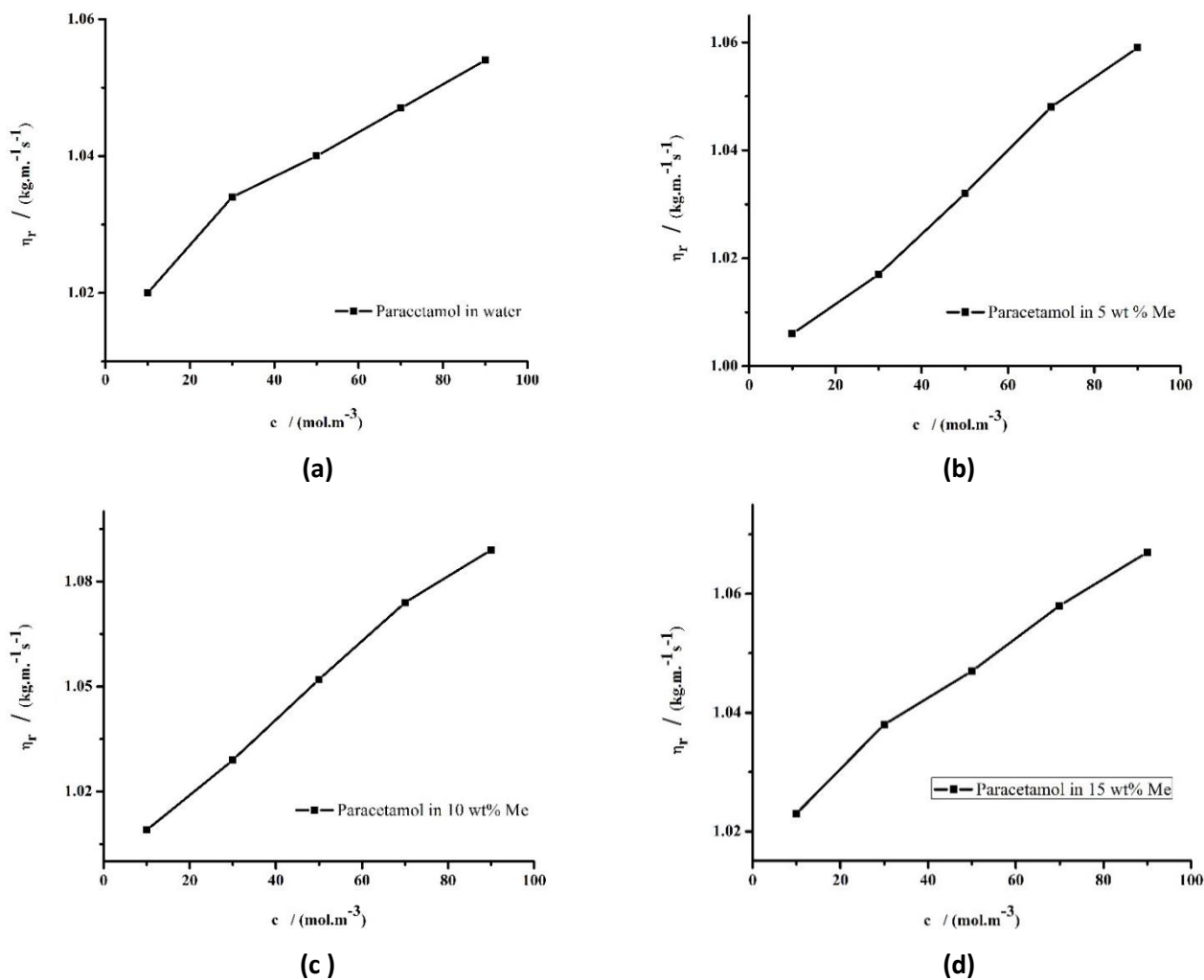


Figure 2. Plot of η_r vs c for paracetamol in (a) water; (b) 5%; (c) 10%; (d) 15% methanol solutions at 298.15K.

Viscosity, we can say, is one of the most structural sensitive properties of solutions. The measurements of concentration and temperature dependencies of viscosity in liquid are often taken as an important method for studying their structural features as well as analyzing various intermolecular interactions in them. As observed from Table 2, the viscosity values decreased with an increase in temperature, which can be ascribed to the fact that due to the intervention of thermal energy, an increase in temperature weakens the attraction between molecules [15]. It is also found that with the increase in the concentration of solute (paracetamol), there is an increase in viscosity (as well as relative viscosity) of the solutions both in water and aqueous methanol medium. This may be due to an increase in solute-solute or solute-solvent interactions. Also, as noticed from Table 2 viscosity of paracetamol in water is less than that in aqueous methanol, and with an increase in wt % of methanol, viscosity has increased. The increased viscosity in aqueous methanol and its higher wt % may be due to strong hydrogen bonding in aqueous methanol, which solvates the solute molecules together, thereby increasing its viscosity. The variations of viscosity and relative viscosity with a concentration of paracetamol in water and different weight percentages of methanol are presented in Figure 1 and Figure 2, respectively.

3.1.2. Viscosity coefficients (A_F and B_J).

These reliable experimental data on the viscosity and relative viscosity of paracetamol solutions are related to its concentration and important for the calculation of Falken-Hagen and Jones-Dole coefficient by Jones-Dole equation [16] as

$$\eta_r = \frac{\eta}{\eta_0} = 1 + A_F c^{1/2} + B_J + c$$

where η_r = relative viscosity (η/η_0); η = viscosity coefficient of solution; η_0 = viscosity coefficient of solvent A_F = Falken-Hagen coefficient; B_J = Jones-Dole coefficient; and c = molar concentration [17];

Ion-ion or solute-solute interactions can be understood in terms of the Falken-Hagen coefficient A_F [17]. Jones-Dole coefficient B_J helps in calculating the solvodynamic radii, hence decides structure making/ breaking properties of a solute in a solution [18].

A plot of $(\eta/\eta_0 - 1)/c^{1/2}$ vs $c^{1/2}$ (Figure 3), the values of A_F and B_J (listed in Table 3) can be obtained [19]. As observed from Table 3, positive values of A_F indicate solute-solute interaction at all tested temperatures (except a few).

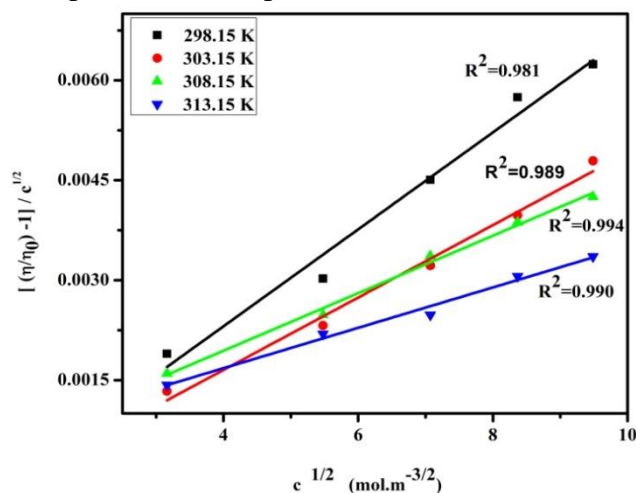


Figure 3. Plot of $(\eta/\eta_0 - 1)/c^{1/2}$ vs $c^{1/2}$ for paracetamol in 5% methanol at different temperatures.

As we know, in the kinetic process of dissolution, when a solute goes to the solvent either the solute or its ions get surrounded by the solvent molecules increasing the viscosity of the solution. Since the co-efficient B_j supervises the solute-solvent interactions; its positive values state an increase in viscosity and structure was breaking property of the solute in solution because of the solute-solvent interactions.

3.1.3. Free energy of activation.

Transition state theory is applied to analyze the viscosity data as suggested by Feakins *et al.* [20] by the equation:

$$\Delta\mu_2^{0*} = \Delta\mu_1^{0*} + \left(RT/\bar{V}_1^0 \right) \left[1000B_j - \left(\bar{V}_1^0 - \bar{V}_2^0 \right) \right]$$

Where, \bar{V}_1^0 = partial molar volume of the solvent; \bar{V}_2^0 = partial molar volume of the solute; B_j = Jones-Dole parameter; $\Delta\mu_2^{0*}$ = free energy of activation per mole of solvent for the viscous flow of the solution; $\Delta\mu_1^{0*}$ = free energy of activation per mole of solute for the viscous flow of the solvent [21];

It can be calculated by equation:

$$\Delta\mu_1^{0*} = 2.303 RT \log \left(\frac{\eta_0 \bar{V}_1^0}{hN} \right)$$

$$\bar{V}_1^0 = M_{\text{solvent}}/d$$

and

$$V_2^0 = V_\phi^0$$

Where, h = Planck's constant; N = Avogadro number;

Thus for paracetamol solutions, the values of \bar{V}_1^0 , \bar{V}_2^0 , $\Delta\mu_1^0$ and $\Delta\mu_2^0$ are also given in Table 3 at different temperatures.

Table 3. Values of parameters A_F ($\text{m}^{3/2} \cdot \text{mol}^{-1/2}$), B_j ($\text{m}^{3/2} \cdot \text{mol}^{-1/2}$), \bar{V}_1^0 ($\text{m}^3 \cdot \text{mol}^{-1}$), \bar{V}_2^0 ($\text{m}^3 \cdot \text{mol}^{-1}$), $\Delta\mu_1^0$ ($\text{kJ} \cdot \text{mol}^{-1}$) and $\Delta\mu_2^0$ ($\text{kJ} \cdot \text{mol}^{-1}$) for paracetamol in water and different weight % of methanol at different temperatures.

| Solvent (in wt% of methanol) | T (K) | $A_F \times 10^2$ | $B_j \times 10^2$ | $\bar{V}_1^0 \times 10^3$ | $\bar{V}_2^0 \times 10^{-1}$ | $\Delta\mu_1^0 \times 10^{-3}$ | $\Delta\mu_2^0 \times 10^{-5}$ |
|------------------------------|--------|-------------------|-------------------|---------------------------|------------------------------|--------------------------------|--------------------------------|
| 0 wt% (water) | 298.15 | 0.000067 | 0.013 | 18.15 | -0.192 | 3.167 | 0.030 |
| | 303.15 | 0.000039 | 0.027 | | -0.149 | 3.218 | 0.036 |
| | 308.15 | 0.000080 | -0.028 | | -0.160 | 3.268 | 0.029 |
| | 313.15 | 0.000051 | 0.000 | | -0.159 | 3.318 | 0.033 |
| 5 wt% | 298.15 | -0.060 | 0.073 | 23.49 | 0.040 | 2.782 | 7.636 |
| | 303.15 | -0.052 | 0.054 | | 0.043 | 2.826 | 5.790 |
| | 308.15 | 0.022 | 0.043 | | 0.053 | 2.870 | 4.674 |
| | 313.15 | 0.047 | 0.030 | | 0.056 | 2.914 | 3.333 |
| 10 wt% | 298.15 | 3.935 | 0.428 | 23.72 | 0.182 | 2.784 | -44.262 |
| | 303.15 | 4.433 | 0.477 | | 0.181 | 2.827 | -50.125 |
| | 308.15 | 5.140 | 0.562 | | 0.197 | 2.871 | -59.857 |
| | 313.15 | 4.751 | 0.524 | | 0.193 | 2.915 | -56.501 |
| 15 wt% | 298.15 | 0.709 | 0.002 | 23.95 | 0.266 | 2.788 | -0.188 |
| | 303.15 | 0.509 | 0.069 | | 0.275 | 2.831 | 7.183 |
| | 308.15 | -0.156 | 0.104 | | 0.293 | 2.876 | 11.032 |
| | 313.15 | -0.052 | 0.083 | | 0.311 | 2.920 | 8.918 |

Standard uncertainties $u(T) = 0.05 \text{ K}$, $u(A_F) = 0.003 \times 10^{-2} (\text{m}^{3/2} \cdot \text{mol}^{-1/2})$, $u(B_j) = 0.004 \times 10^{-2} (\text{m}^{3/2} \cdot \text{mol}^{-1/2})$, $u(\bar{V}_1^0) = 0.14 \times 10^{-3} (\text{m}^3 \cdot \text{mol}^{-1})$, $u(\bar{V}_2^0) = 0.001 \times 10^1 (\text{m}^3 \cdot \text{mol}^{-1})$, $u(\Delta\mu_1^0) = 0.170 \times 10^3 (\text{kJ} \cdot \text{mol}^{-1})$, $u(\Delta\mu_2^0) = 0.081 \times 10^5 (\text{kJ} \cdot \text{mol}^{-1})$. $u(p) = 0.01 \text{ M Pa}$.

A view of Table 3 also indicates that $\Delta\mu_1^0$ and $\Delta\mu_2^0$ values are positive. $\Delta\mu_1^0$ increases with the increase in temperature in all the solvents taken. As compared to $\Delta\mu_1^0$ the values of $\Delta\mu_2^0$ are larger which indicates the stronger solute-solvent interactions and such behavior is in fact similar to that of B_j .

3.2. Surface tension studies.

3.2.1 Surface tension and excess surface calculation.

Surface tension is the result of the attractive forces existing between the liquid molecules (cohesion) and the layers of a liquid (adhesion) in bulk.

Two methods were adopted to compute the surface tension (γ) values for different concentrations of the drug in water and (water+methanol) mixtures, (i) Derived from density and ultrasonic velocity values and (ii) Measured experimentally by drop number method using Stalagmometer.

(i) Surface tension is derived from sound velocity and density measurements.

The following equation is used to evaluate surface tension values γ at 298.15K,
$$\gamma = 6.3 \times 10^{-4} \times d \times U^{3/2}$$

Debye-Huckel limiting law [22] is applied to convert molality (m) to mean ionic activities (a_{\pm}) using the mean ionic activity coefficients (γ_{\pm}) given in the following equations,

$$a_{\pm} = (Q\alpha m \gamma_{\pm})$$

$$Q = (v_+^{v_+} v_-^{v_-})^{1/v},$$

$$\log \gamma_{\pm} = -A |z^+| |z^-| I^{1/2}$$

$$A = 1.823 \times 10^6 / (\epsilon T^{3/2})$$

v_+ and v_- are the number of moles and Z_+ and Z_- are the valences of positive and negative ion respectively; v is the total number of moles of ions [23] produced per mole of solute; A is the Debye-Huckel constant and ϵ is the dielectric constant.

I is the ionic strength of the solution and can be calculated by the equation,

$$I = \frac{1}{2} \sum m_i Z_i^2, \text{ where } m_i \text{ is } m_+ \text{ or } m_-$$

The surface excess Γ_2 can be obtained from the Gibbs equation [24]

$$\Gamma_2 = -(a_{\pm}/2RT) \times (d\gamma/da_{\pm})$$

The slope of the plot of γ vs. a_{\pm} gives $(d\gamma/da_{\pm})$.

(ii) Surface tension from drop number method using Stalagmometer.

Traube's Stalagmometer [25] is one of the most important tools to measure the surface tension of a liquid. The exact number of drops of a given quantity of liquid falling from the Stalagmometer at the experimental temperature is counted in this method.

The surface tension (γ) of the solution then can be calculated by using the following equation, $\gamma_1/\gamma_2 = (n_2/n_1) \times (d_1/d_2)$

γ_1 and γ_2 are surface tension of water and solution, respectively

d_1 and d_2 are density of water and solution, respectively

n_1 and n_2 are number of drops of water and solution falling, respectively.

For a given volume of liquid, surface tension is proportional to the density and inversely proportional to the number of drops of the solution falling.

Table 4. Values of mean ionic activity (a_{\pm}), surface tension (γ) and surface excess (Γ_2) (derived from ultrasonic velocity (U) and drop number method) at different concentrations for paracetamol in various solvent systems at 298.15 K.

| Solvent (wt % of methanol) | Conc. of paracetamol (mol.m ⁻³) | $a_{\pm} \times 10^3$ | Derived values | | Measured values | |
|----------------------------|---|-----------------------|-------------------------|------------------------|-------------------------|------------------------|
| | | | $\gamma \times 10^{-1}$ | $\Gamma_2 \times 10^4$ | $\gamma \times 10^{-1}$ | $\Gamma_2 \times 10^4$ |
| 0 wt% (Water) | 10.0 | 191.80 | 3662.65 | 805.88 | 3663.83 | 803.56 |
| | 30.0 | 11.29 | 3679.36 | 47.44 | 3679.44 | 47.30 |
| | 50.0 | 0.59 | 3694.10 | 2.47 | 3695.22 | 2.46 |
| | 70.0 | 0.11 | 3706.38 | 0.47 | 3707.42 | 0.44 |
| | 90.0 | 0.02 | 3722.18 | 0.10 | 3723.21 | 0.07 |
| 5 wt% | 10.0 | 158.46 | 3667.18 | 934.57 | 3667.26 | 937.50 |
| | 30.0 | 7.49 | 3682.80 | 44.17 | 3682.97 | 44.30 |
| | 50.0 | 0.77 | 3700.62 | 4.54 | 3700.81 | 4.55 |
| | 70.0 | 0.09 | 3721.46 | 0.54 | 3721.58 | 0.57 |
| | 90.0 | 0.00 | 3740.10 | 0.02 | 3740.46 | 0.04 |
| 10 wt% | 10.0 | 137.20 | 3743.53 | 316.05 | 3743.71 | 316.68 |
| | 30.0 | 4.70 | 3749.98 | 10.82 | 3750.23 | 10.84 |
| | 50.0 | 0.54 | 3755.13 | 1.25 | 3755.42 | 1.29 |
| | 70.0 | 0.08 | 3761.52 | 0.19 | 3762.66 | 0.21 |
| | 90.0 | 0.01 | 3768.06 | 0.01 | 3769.23 | 0.06 |
| 15 wt% | 10.0 | 92.81 | 3755.27 | 611.32 | 3755.13 | 610.50 |
| | 30.0 | 3.19 | 3766.29 | 20.98 | 3766.06 | 20.95 |
| | 50.0 | 0.29 | 3777.61 | 1.93 | 3777.56 | 1.91 |
| | 70.0 | 0.04 | 3790.53 | 0.26 | 3790.35 | 0.22 |
| | 90.0 | 0.01 | 3803.59 | 0.04 | 3803.34 | 0.01 |

Surface tension is one of the important fundamental properties among all other physico-chemical properties, which are very much essential to investigate different molecular interactions among the components of mixtures. Surface tension reveals the information not only on the intermolecular interactions but also interfacial behavior [26]. That's why surface tension shows an important outstanding role in most scientific and technological areas, like distillation, separation, liquid-liquid extraction and absorption processes, and enhancement of drug formulation [27]. Surface tension data of paracetamol in water and water + methanol is given in Table 4.

Normally surface tension is found to be increased linearly with concentration. This is clearly seen from the representative plot of surface tension (γ) vs. concentration for paracetamol in water and different weight percent of methanol (Figure 4). This is also found that the same trend is followed by the data obtained from the drop number method using the Stalagmometer.

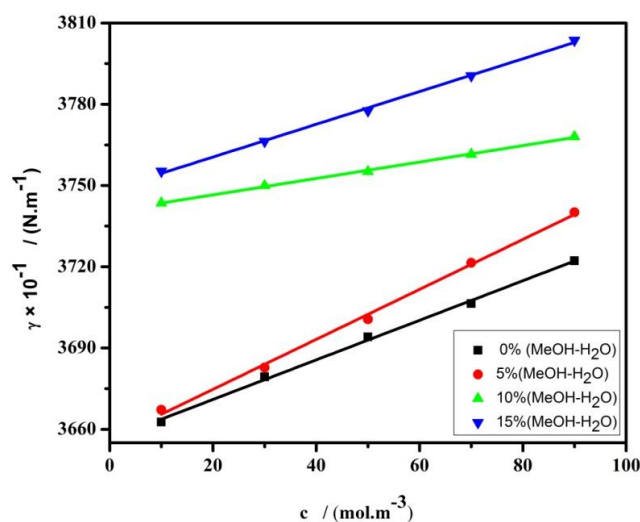


Figure 4. Plot of surface tension (γ) vs. concentration (c) for paracetamol in water and different weight percent of methanol solutions at 298.15K.

The excess surface data were estimated from the Gibbs equation and are presented in Table 4. It is seen that surface excess concentration is positive in all cases. It is known as positive adsorption. The positive values indicate the solute has more concentration at the surface than that in bulk. This may be due to the additional pull already existing between the water molecules other than H-bonding responsible for the additional surface tension. It is also observed that there is a general decreasing trend in excess surface concentration with the increase in concentration in all the cases. Probably for such a trend, one possible reason may be with the increase in concentration. The holding capacity of the solute particles increases beneath the surface layer of solvent, decreasing the surface excess concentration and increasing the surface tension [28].

4. Conclusions

Intermolecular interactions existing between paracetamol and binary mixed solvents of methanol and water within a temperature range of 298.15K to 313.15K have been examined using the experimental data of viscosity. An increment in the viscosity values is observed with increasing paracetamol concentrations due to the weak solute–solute interaction. The values of A_F and B_j coefficients are found to be positive, indicating solute-solute and solute-solvent interactions, respectively, which is also supported by the positive values of free energy of activation per mole of the solute ($\Delta\mu_1^0$) and solvent ($\Delta\mu_2^0$) between paracetamol and mixed solvent systems. The surface tension of the solution has increased with the concentration of the paracetamol. It can be concluded that surface tension and surface excess values derived from ultrasonic velocity and density measurements and determined experimentally by the drop count method with a stalagmometer resemble each other closely. The results explained their relevancy in the ground of pharmaceutical sciences of numerous stages involving dosage selection, drug formulation designing, etc.

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Conflicts of Interest

The author declares no conflict of interest.

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