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THERMODYNAMIC STUDIES OF PARACETAMOL AND ASPIRIN IN ALCOHOLIC SOLUTION AT DIFFERENT TEMPERATURE.

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ABSTRACT
Density and viscosity measurements are reported for alcoholic solutions of the drugs like paracetamol & aspirin at different temperatures T = (300.15, 310.15 and 320.15) K within the concentration range ($1x10^{-2}$ M to $6x10^{-4}$ M). The density and viscosity data are used to obtain specific viscosity and relative viscosity of different concentrated alcoholic solutions at different temperatures. Jones–Dole equation for viscosity is used to calculate A and B coefficients. The results obtained have been interpreted in terms of solute–solvent and solute–solute interactions and structure making/breaking ability of solute in the aqueous solution. The thermodynamic properties such as free energy change(ΔG), enthalpy change(ΔH) and entropy change (ΔS) of paracetamol & aspirin drugs have been investigated in pure alcoholic medium at different temperature such as (300.15,310.15 and 320.15) K. The experimental data gives the idea about effect of temperature on the molecular interaction and structural changes in solute.

KEYWORDS: Density, relative viscosity, specific viscosity, thermodynamic parameters, solute-solvent interaction.

INTRODUCTION
Paracetamol and Aspirin herein referred to collectively as mild analgesics[1] and antipyretic[2], are among the most sold pharmaceutical drugs worldwide. These molecules have excellent reputations within the general population and are widely used for self-medication and prophylaxis and are also present in the environment.[3] However, they are often mis- or over-consumed, including in populatio subgroups, such as elite athletes, to prevent pain and treat injuries.[4,5]

Physicochemical and thermodynamic investigation attract the inquisitive minds of researchers owing to the important role that drugs play. Physicochemical and thermodynamic investigations play an important role in understanding the nature and the extent of the patterns of molecular aggregation that exist in binary liquid mixtures and their sensitivities to variations in composition and the molecular structure of the pure components.[6] In biophysical chemistry, drug–macromolecular interaction is an important phenomenon involving a complex mechanism.[7] Since most of the biochemical processes occur in aqueous and alcoholic media, the studies on the thermodynamic and transport properties of drugs in the alcoholic phase provide useful information in pharmaceutical and medicinal chemistry. The drug-solvent molecular interaction and their temperature dependence play an important role in the understanding of drug action. Viscometric properties provide valuable clues for solute–solvent interactions in the solution phase. Such results can be helpful in predicting the absorption of drugs and transport of drugs across the biological membranes. Therefore, it may be interesting to investigate variation of their properties with temperature for understanding the mechanism of drug action.

The present work represents the continuation of a systematic investigation of the viscometric properties of paracetamol and aspirin drugs in binary solutions at various temperatures. Viscosity is one of the important physical property owned by the liquid. The study of molecular interaction of an electrolyte in liquids by viscometrically plays an important role.[8,9] Many researcher study the biologically important drug at different temperature.[10,11,12] The Jones-Doles equation[13] helps to evaluate the observed viscosity concentration dependence of dilute electrolyte solutions.

MATERIAL AND METHOD
The compounds paracetamol and aspirin used in this study have been procured from Pharmaceutical Company. All the compounds were of 0.999 mass fraction purity. The purity was checked by mass spectral analysis (LC–MS). The above compounds were dried in a vacuum oven and then stored in desiccator under vacuum over fused calcium chloride before use. They

were used without any further purification. All the solutions were prepared in freshly prepared doubly distilled ethanol on molarity scale when required, using density data at different temperatures. A Mettler balance having a precision of 0.1 mg was used for weighing. The temperatures T = (300.15, 310.15 and 320.15) K of experimental water bath were maintained constant up to ±0.002 K by circulating the coolant liquid. The densities of the solutions were measured at different temperatures using density bottle. Viscosities of the solutions were determined with the help of calibrated Ostwald viscometer (± 0.1% $Kgm^{-1}s^{-1}$). The flow time of solutions were measured by using digital clock of racer company having error (±0.01sec).

CALCULATION

To determine the relative and specific viscosity, in the different concentration of the paracetamol and aspirin solution were prepared and there viscosities are measured with help of the following mathematical relation.

$(\eta_r) = (ds \times ts/dw \times tw) \times \eta_w$.....(1)

Where

η_r = Relative viscosity,
η_w = Viscosity of water
ds = Density of solution,
dw = Density of water
ts = Flow time for solution,
tw = Flow time for water.

From the calculated values of relative viscosities (η_r) and the temperature (T), the graph between log (η_r) vs 1/T are plotted.

The relative viscosities of solution at different concentration are presented in table 1. The viscosity data have been analyzed by Jones –Dole equation,

$(\eta_r - 1)/\sqrt{C} = \eta_{sp}/\sqrt{C} = A + B\sqrt{C}$ ----------2

Where

A = Falkenhagen coefficient
B= Jones-Dole coefficient
C = concentration of solutions

The Falkenhagen coefficient (A) measures the solute-solute interation while Jones-Dole coefficient (B) measures the solute-solvent interaction.

The thermodynamic parameters i.e. free energy change(ΔG), enthalpy change(ΔH) and entropy change (ΔS) are determined by using following relation,

$\Delta G = -2.303 \times R \times$ slope……3

$\log \eta_{r1} - \log \eta_{r2} = (\Delta H/2.303) \times (1/T1 - 1/T2)$ ……4

$\Delta S = (\Delta G - \Delta H)/T$……5

Table-1: Densities (d) gm/cc and relative viscosities (η_r) of paracetamol and aspirin at different concentration in ethanol solvent at 300.15K.

Conc. mole/lit	Paracetamol		Aspirin	
	Density (d) (Kgm^{-3})	Rel. Viscosity η_r	Density (d) (Kgm^{-3})	Rel. Viscosity η_r
0.01	0.804	1.8301	0.996	2.8544
0.005	0.798	1.7458	0.990	2.5127
0.0025	0.789	1.6510	0.994	2.1730
0.00125	0.798	1.5304	0.996	1.9006
0.000625	0.798	1.4066	0.994	1.6758

Table-2: Densities (d) gm/cc and relative viscosities (η_r) of paracetamol and aspirin at different concentration in ethanol solvent at 310.15K.

Conc. mole/lit	Paracetamol		Aspirin	
	Density (d) (Kgm^{-3})	Rel. Viscosity η_r	Density (d) (Kgm^{-3})	Rel. Viscosity η_r
0.01	0.797	1.9159	0.994	2.8818
0.005	0.795	1.8368	0.992	2.5712
0.0025	0.792	1.7104	0.992	2.1994
0.00125	0.793	1.5688	0.993	1.9133
0.000625	0.794	1.4364	0.991	1.6755

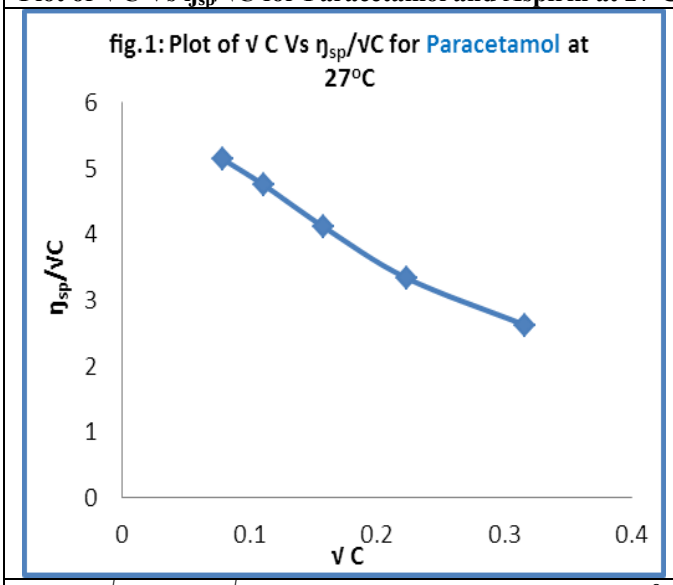
Table-3: Densities (d) gm/cc and relative viscosities (η_r) of paracetamol and aspirin at different concentration in ethanol solvent at 320.15K.

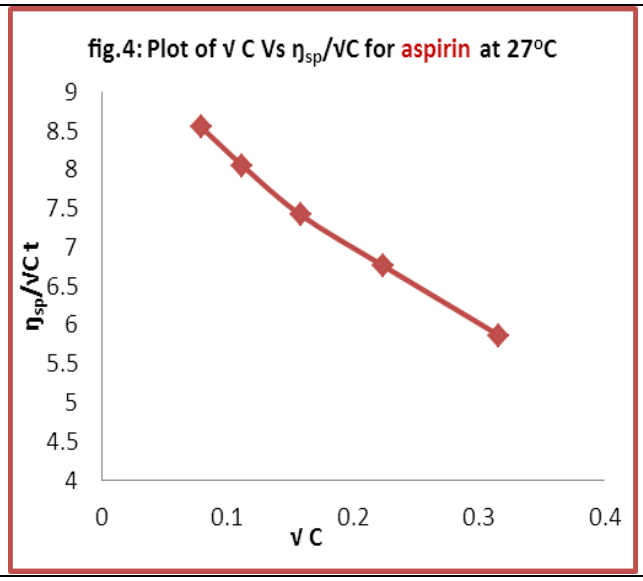
Conc. mole/lit	Paracetamol		Aspirin	
	Density (d) (Kgm^{-3})	Rel. Viscosity η_r	Density (d) (Kgm^{-3})	Rel. Viscosity η_r
0.01	0.792	1.9159	0.993	2.9263
0.005	0.790	1.8368	0.989	2..5561
0.0025	0.788	1.7104	0.989	2.2784
0.00125	0.786	1.5688	0.994	2.0026
0.000625	0.785	1.4364	0.992	1.7083

Table-4: The value of A = Falkenhagen coefficient, B= Jones-Dole coefficient is calculated by plotting the graph between of √ C V/S ηsp/√C of paracetamol and aspirin at 300.15K, 310.15K & 320.15K.

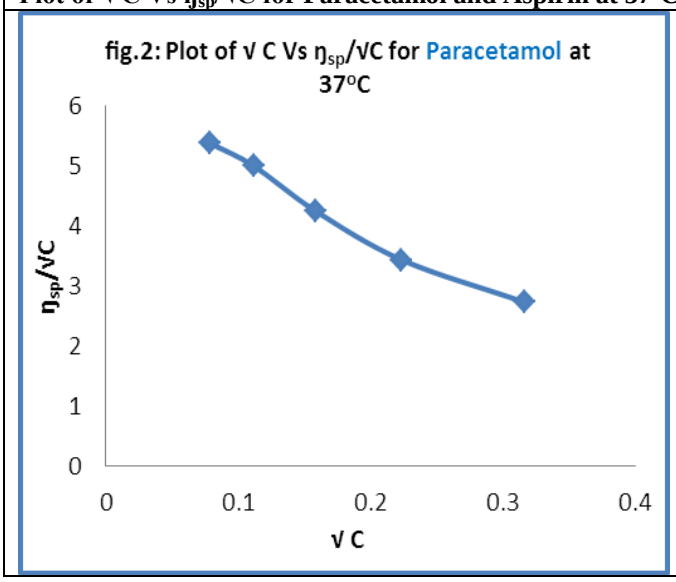
Temp in K	Paracetamol		Aspirin	
	A	B (Lit/mol)	A	B (Lit/mol)
300.15	5.9082	-10.777	9.3133	-11.154
310.15	6.1886	-11.412	9.3706	-10.772
320.15	6.3176	-11.079	10.161	-13.208

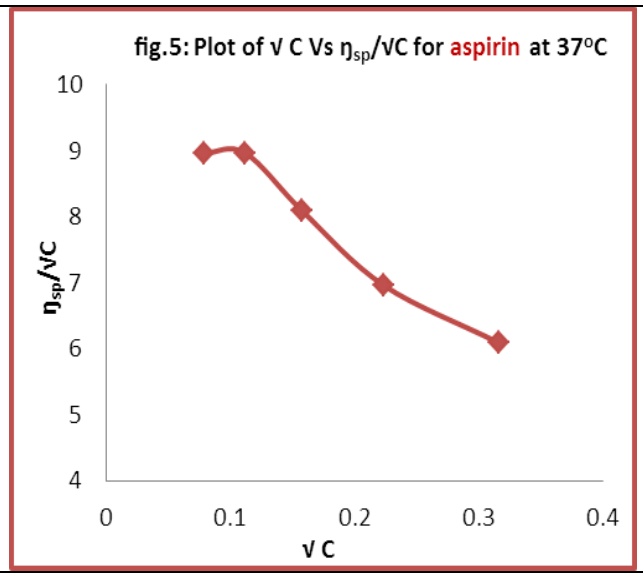
Plot of √ C Vs $\eta_{sp}/\sqrt{C}$ for Paracetamol and Aspirin at 27°C



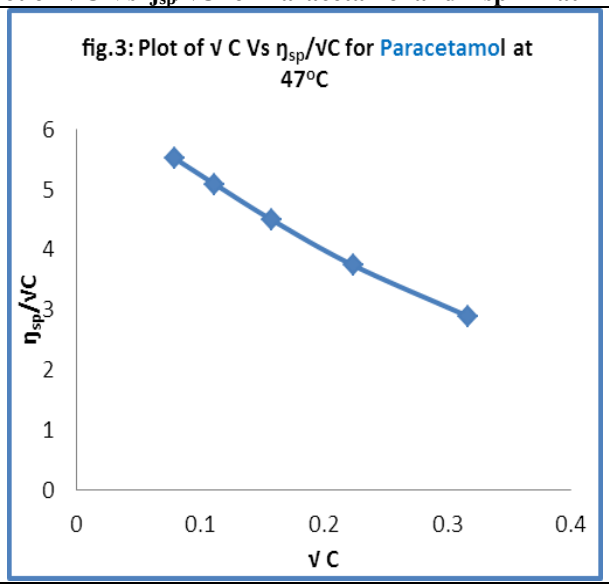


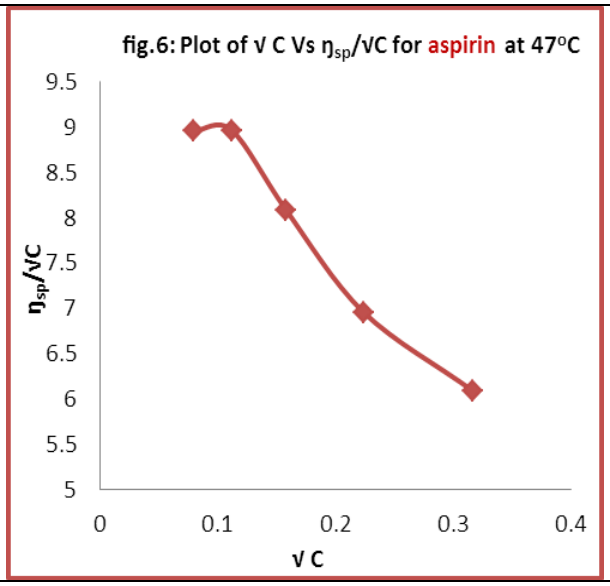
Plot of √ C Vs $\eta_{sp}/\sqrt{C}$ for Paracetamol and Aspirin at 37°C



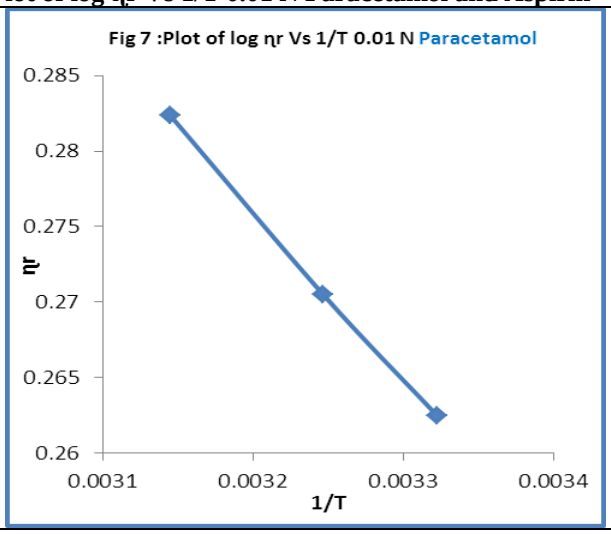


Plot of √ C Vs $\eta_{sp}/\sqrt{C}$ for Paracetamol and Aspirin at 47°C





Plot of log ηr Vs 1/T 0.01 N Paracetamol and Aspirin



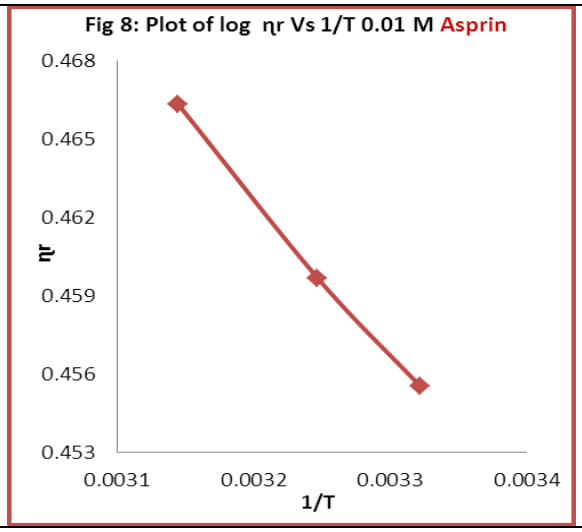


Table 5: Values of Thermodynamic Parameters for temperature difference (300.15– 310.15)K.

System	ΔG (J mol^{-1} K^{-1})	ΔH (J mol^{-1} K^{-1})	ΔS (J mol^{-1} K^{-1})
Paracetamol	-360529	-1465.89	1177.24
Aspirin	-662057	-2025.73	2164.04

Table 6: Values of Thermodynamic Parameters for temperature difference (310.15– 320.15)K.

System	ΔG (J mol^{-1} K^{-1})	ΔH (J mol^{-1} K^{-1})	ΔS (J mol^{-1} K^{-1})
Paracetamol	-372228	-1937.36	1190.65
Aspirin	-683552	-3563.91	2186.46

RESULT AND DISCUSSION

Figure-1, 2 & 3 for paracetamol and figure- 4, 5 & 6 for aspirin shows the variation of specific viscosity of solution at (27, 37 & 47)°C as a function of concentration of drugs in ethanol solvent for all the systems studied in this work. It is seen that the density of the solution increases with increase concentration of drugs.

The solution properties of solutes provide information about the sizes they adopt and their compatibility with the structure.[14] In the present investigation, the relative viscosity of paracetamol and aspirin solutions decreases with decrease in concentration of solutions. The increase in viscosity with increase in concentration may be ascribed to the increase in the interactions of solute-solvent. Aspirin has more value of density than

paracetamol and value is decreases with increase in temperature of solution which is shown in table no. 1, 2 & 3. The relation between viscosity ($\eta_{sp}/\sqrt{}$ C) and concentration of solution (√C) represented by plotting the graph (fig.1-6). The plotted graphs prove the validity of Jones-Dole equation for all systems giving linear straight line. The values of Jones-Dole coefficients especially β -coefficients are the slope of graph ($\eta_{sp}/\sqrt{C}$) Vs (√C) while A-Coefficient are the intercept of graph. The order or disorder introduced by solute in solvent is measured by the values of β coefficient which shows either positive or negative values. β coefficient is in turn measures the effective hydrodynamic volume of solute, which accounts for the ion-solvent interaction.

In this work, the values of β -coefficients for all systems are negative at all temperature. It is apparent from table-4 that, β -coefficient is measure the effective thermodynamic volume of solute which accounts for solute-solvent interaction. It is known as a measure of disorder introduced by a solute in to the solvent. So aspirin has more disorder than paracetamol in ethanol solvent. Falkenhagen coefficient (A) represent the solute-solute interaction. Large value of A in case of aspirin indicate it has strong solute-solute interaction.

Figure-7 & 8 represents the plot between logarithmic value of relative viscosity and reciprocal of temperature at which viscosity of solution studied for paracetamol and aspirin having concentration 0.01M respectively. Graph has a straight line nature in both the cases, slope of that line gives free energy change(ΔG) by using equation-3. Enthalpy change(ΔH) and entropy change (ΔS) of drugs calculated from equation 4 and 5 respectively. Table no 5 & 6 represent thermodynamic parameters for a temperature difference of 10^{o}C. in both the cases of temperature range value of ΔG, ΔH & ΔS are in good agreement for paracetamol and aspirin. The negative value free energy change (ΔG) shows interaction is feasible in all cases. Large negative value of aspirin than paracetamol gives supporting proof to Jones-Dole coefficients-β, aspirin has strong solute-solvent interaction in solution with ethanol. Enthalpy change (ΔH) interpreted that interaction of drugs and ethanol solvent are spontaneous and exothermic. Positive value of entropy change (ΔS) interpreted that, molecules of paracetamol and aspirin are in disperse form in ethanol solvent.

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