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DILUTION EFFECT ON THE THERMODYNAMIC PARAMETERS OF PARACETAMOL BY CONDUCTIVITY METHOD

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ABSTRACT
The thermodynamic parameters viz., Gibbs free energy (ΔG), enthalpy (ΔH) and entropy (ΔS) of analgesic and antipyretic drug (paracetamol) were calculated form solubility value at different temperature in alcoholic medium. It was found that solubility and solubility product of paracetamol decreases with decreased concentration in ethanol. Also their solubility decreases with increase in temperature.

KEYWORD: Conductivity, Solubility, solubility product, thermodynamic parameters, etc.

INTRODUCTION
Human body contains many natural polymer such as protein and nucleic acid. Crystallization of drugs is takes place in alcoholic medium in presence of polymer.[1,2] It was found that yield of crystallization of drugs increases in the presence of polymer[3] Which decrease the action of drugs in a body. Because drugs action depends upon the rate of ionization and solubility of drug and their mobility.

Paracetamol is analgesic[4] and antipyretic[5] drugs, typically used as mild to moderate fever and pain control. In the present research work conductance measurement was used for the study of influence temperature on solute-solvent interaction in alcoholic medium.

Conductivity method is used for the study of the dissolution of compound in mixed solvent system.[6] Also it is an important tool to measure degree of disassociation of weak electrolyte, to measure degree of hydrolysis and for the analysis of the physicochemical properties of electrolyte in solution.[7] Conductometric measurement at different temperature gives idea of solubility product of drugs. Which is useful to explain the thermodynamic properties paracetamol in alcoholic medium.

Molar solubility "S", solubility product "Ksp" and Gibbs free energy "ΔG" is determined from the following equation.[8]

$$Ksp = [A+][B-] = S \times S = S^2 \quad ..(1)$$

$$\Delta G = -RT \ln (Ksp) \quad ..(2)$$

Where "R" is the universal gas constant, 'T" is the absolute temperature and "ΔG" is Standard Gibbs free energy is related to "ΔH" and "ΔS" by following relation.

$$\Delta G = \Delta H - T\Delta S \quad ..(3)$$

The value of thermodynamic parameters are calculated at two different temperature T_1=301K and T_2 = 308K by considering temperature range 301K to 318K.

MATERIAL AND METHOD[9]
In the present research work, conductivity method was used for the study of the influence of temperature on solute-solvent interaction in alcoholic medium. All reagents are used such as Paracetamol (E. Merck), Ethanol (E. Merck) each of these analytical grade reagent. These stock solutions were prepared in double distilled ethanol. Digital Conductivity meter ELICO (CM-180), JCE (LJ-101) magnetic stirrer, Thermostat (No.51633075, India) Pioneer Analytical Balance (SCPA64C) were used to carried out experiment.

0.01M paracetamol prepared by M/1000 molecular weight into 100ml of ethanol. Solution of different concentration (0.005M, 0.0025M, 0.00125M & 0.000625M) were prepared by considering 0.01M stock solution. And this solution was stirred for 30 minutes and then this solution was kept overnight to get maximum saturation. On next day the conductivity of different concentration solution were recorded at different temperature using digital conductivity meter. The solution was placed in water bath during the measurement of conductance and temperature was controlled by thermostat at a fixed temperature.

Calibration of Conductivity meter

At the given reading of the conductivity cell the knob of the conductivity meter was adjust and the conductivity cell was dipped in conductivity water so that the calibration was done.

Determination of cell constant

The 0.1 N KCl solution was prepared in 100 ml of distilled water then conductivity cell was immersed in a beaker which containing KCl solution and the conductance was recorded. that gives value specific conductance of KCl by considering following equation.

Cell Constant = Specific Conductance / Observed Conductance …(4)

Table 1:

Temp in K	Equivalence conductance(λ) of 0.1M KCl in x10^{-3} Scm^2eq^{-1}	Observed conductance(λ) of 0.1M KCl in x10^{-3} Scm^2equ^{-1}	Cell Constant (k) in cm^{-1}
301	13.24	14.78	0.8961
308	14.75	15.02	0.9820
318	17.02	17.24	0.9872

Determination Equivalent Conductance

It is defined as the conducting power of all the ions produced by dissolving one gram equivalent of an electrolyte in solution. It is expressed as Λ_e and is related to specific conductance as

$$\Lambda_e = \frac{\kappa \times 1000}{C} = \kappa \times \frac{1000}{M} \quad \ldots(5)$$

Where C is the concentration in gram equivalent per litre (or Normality) This term has earlier been quite frequently used. Now it is replaced by molar conductance. The units of equivalent conductance are $Ohm^{-1}\ cm^{2}(gm\ equiv)^{-1}$.

RESULT AND DISCUSSION

Solubility is the amount of substance dissolved into the solution. If the compound is soluble in major extent it means that its dissolution is in large amount, i.e form large numbers of ion in a solution. that's why solubility is directly related to conductance of solution.

The solubility and solubility product of the various solutions of paracetamol in alcoholic medium were calculated at 301K, 308K and 318K shown in the table no 2, 3 & 4 respectively.

In general solubility of substance increases with temperature but from table 2, 3 & 4 it is observed that solubility and solubility product decreases with temperature. This is because of association of paracetamol molecule takes place when temperature of solution increases.

The plot-1 between concentration of paracetamol and observed conductance tells that conductance decreases with decrease in concentration of solution this is because of less numbers of mobile ions present in a solution.

The plot-2 shows that solubility product is low when concentration is less but with increase in concentration solubility product increases sharply and at very high concentration Ksp try to attain some constant value.

Table 2: Conductance measurement of Paracetamol solution at different concentration and fixed Temperature 301K in Ethanol solvent.

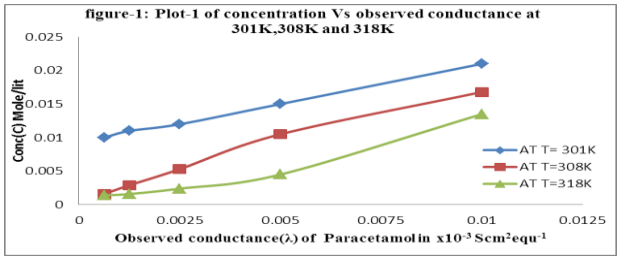
Concentration in Mole/lit	Observed conductance(λ) of Paracetamol in x10^{-3} Scm^2equ^{-1}	Specific conductance (k) of Paracetamol	Solubility (S)	Solubility Product (Ksp) x 10^6	Log Ksp
0.01	0.021	0.0188	1.454	84.602	18.2534718
0.005	0.015	0.01344	1.0388	43.164	17.5805174
0.0025	0.012	0.0107	0.831	27.625	17.1342317
0.00125	0.011	0.0098	0.761	23.213	16.960223
0.000625	0.01	0.0089	0.6925	19.184	16.7695872

Table 3: Conductance measurement of Paracetamol solution at different concentration and fixed Temperature 308K in Ethanol solvent.

Concentration in Mole/lit	Observed onductance(λ) of Paracetamol in x10^{-3} Scm^2equ^{-1}	Specific conductance (k) of Paracetamol	Solubility (S)	Solubility Product (Ksp) x 10^6	Log Ksp
0.01	0.0168	0.01649	1.2642	63.929	17.9732837
0.005	0.0105	0.0103	0.7901	24.972	17.0332658
0.0025	0.0053	0.0052	0.3988	6.3626	15.6659477
0.00125	0.0029	0.0028	0.218	1.9049	14.4599401
0.000625	0.0016	0.00157	0.1204	0.05798	10.9678534

Table 4: Conductance measurement of Paracetamol solution at different concentration and fixed Temperature 318K in Ethanol solvent.

Concentration in Mole/lit	Observed conductance(λ) of Paracetamol in $x10^{-3}$ Scm^2equ^{-1}	Specific conductance (k) of Paracetamol	Solubility (S)	Solubility Product (Ksp) x 10^6	logKsp
0.01	0.0135	0.013327	1.0112	40.9016	17.5266797
0.005	0.0045	0.0096	0.45	21.553	16.8860256
0.0025	0.0024	0.0023	0.179	1.2926	14.0721663
0.00125	0.0016	0.0015	0.119	0.5745	13.2612554
0.000625	0.0014	0.00138	0.1049	0.4398	12.9940754



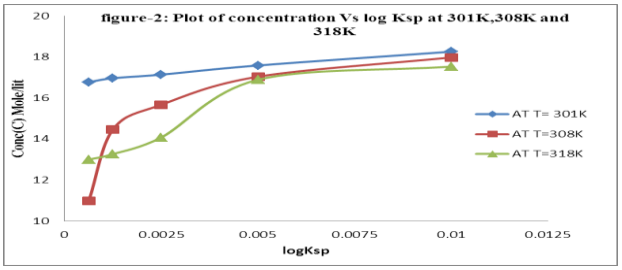


Table 5: Thermodynamic parameters of paracetamol drug at different concentration for temperature difference 301K-308K.

Concentration in Mole/lit	ΔG in Joule/mole	ΔH in Joule/mole	ΔS in Joule/mole
0.01	-45679.56	71051.43	387.81
0.005	-43995.49	138774.66	607.20
0.0025	-42878.65	372334.44	1379.44
0.00125	-42443.19	634033.62	2247.43
0.000625	-41966.12	1471231.2	5027.23

Table 6: Thermodynamic parameters of paracetamol drug at different concentration for temperature difference 308K-318K.

Concentration in Mole/lit	ΔG in Joule/mole	ΔH in Joule/mole	ΔS in Joule/mole
0.01	-46024.40	83753.76	421.35
0.005	-43617.28	27612.65	231.26
0.0025	-40115.98	298889.45	1100.66
0.00125	-37027.74	224795.05	850.07
0.000625	-28085.54	-379987.06	-1142.53

Form table no.5 and table no. 6 it is observed that value of ΔG is negative in all cases which indicate process of dissolution of paracetamol in alcohol is spontaneous and moving in forward direction. Spontaneity of reaction is depends upon magnitude of ΔG. If value of ΔG is higher greater is the spontaneity of reaction.

ΔH is positive at high concentration and it decreases with decrease in concentration. Positive value of ΔH indicate endothermic reaction and process of crystallization. Crystallization increases with increase in temperature.

$\Delta S^{[10]}$ is the measure of disorder or randomness. System is stable when value of ΔS is high. At high temperature molecule associate with energy which increase randomness of molecule, hence ΔS has greater value at high temperature.

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