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CONDUCTOMETRIC MEASURMENTS OF [DMPMDC] AND [CTMBCD] AT 28^0 C

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Abstract:-

Conductometric measurements of (4S,6S,12aS)-4-(dimethyl- amino)-1,4,4a,5,5a,6,11,12a-octa hydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-naphthacene-2-carboxamide **[DAOPMDC]** and (2S, 6R)-7-chloro -2, 4, 6-trimethoxy-6'-methyl-3H, 4'H-spiro[1-benzo- furan 2, 1'-] cyclohex-2-ene]-3,4'-dione[**CTMSBCD**] at different molar concentrations and at 28^{0}C were carried recently in this laboratory. This is an accurate technique for studding absorption, transmission and excretion of the drug in pharmaceutical sciences. The drug activity and drug effect were studied in pharmacokinetics. This study requires minimum percentage of chemicals as well as this study is easy and somewhat suitable. In this study we investigate the solute-solvent, ion-solvent interactions (Here solute means drug).

Key words:- Thermodynamic parameters; Walden Product, Ion association constants; (4S,6S,12aS)-4-(dimethyl-amino)-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo- naphthacene -2-carboxamide**[DMPMDC]**; (2S, 6R)-7-chloro -2, 4, 6-trimethoxy-6'-methyl-3H, 4'H-spiro[1-benzo- furan 2, 1'-] cyclohex-2-ene]-3,4'-dione[**CTMSBCD**].

Introduction:-

Solubility and permeability are the two keys which are responsible for biopharmaceutical parameters and the effective bioavailability good in vitro and in vivo correlation[1]. The results of measurement of electrolyte in the solution provides excellent information about this. Enhancement

of solubility and dissolution rate and oral bioavailability of poorly water soluble drugs are still the challenging aspects for the pharmaceutical technologists[2]. Hydrotropic solubilisation is considered as one of the safest methods of solubalisation[3]. Aqueous solubilisation of insoluble drugs can be achieved by the addition of hydrotropic agents. Many work highlighted the effect of the solubility enhancers (hydrotropic agents) [4,5] and hence improved stability of the drug but no detailed explanation is available relating to the improvement phenomena.

The conductance measurements provide valuable information regarding the ion-ion and ion-solvent interactions[6]. The conductometric studies of ionic association of divalent asymmetric electrolyte $Cu(NO_3)_2$ with Kryptofix-22 in mixed (MeOH-DMF) solvents at different temperatures were carried out by Gomaa and Al-Jahdalli[7]. Izonfuo and Obunwo[8] and Roy *et al*[9] studied the conductance of alkali metal in different mixtures mixed solvents. The Walden products and thermodynamic parameters of different complexes were studied by few researchers to determine the comparison of transition metal complexes among the halide groups by[10].

The present investigation focus on thermodynamic behaviour, conductometric properties and Walden product of (4S,6S,12aS)-4-(dimethyl- amino)-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-naphthacene-2-carboxamide **[DMPMDC]** and (2S, 6R)-7-chloro -2, 4, 6-trimethoxy-6'-methyl-3H, 4'H-spiro[1-benzo- furan 2, 1'-] cyclohex-2-ene]-3,4'-dione[**CTMSBCD**] in ethanol-water mixture at different concentration and at constant temperature i.e. 28^0C. The data were analyzed by Shedlovsky method.The thermodynamic parameters like ΔH^0; ΔS^0 and ΔG^0 for the formation have been studied from the values of ion association constant

at various temperatures. The computed values have been used to discuss qualitatively the nature of different interactions.

Experimental:-

The 0.1M solution of [**DMPMDC**] and **[CTMSBCD]** was prepared separately and then diluted to 0.075M, 0.050M and 0.025M by serial dilution method in 100% water and ethanol-water mixture respectively. Similar solutions were prepared for 80% and 70% water-ethanol mixture. All the solutions of drug were always used a fresh in the present investigation.

In 50 ml Borosil glass beaker drug solution was taken and it was kept inside the thermostat for 15-20 minutes to attain the thermal equilibrium (28^0C). After achieving the thermal equilibrium, the conductivity of that electrolyte was measured

Result and Discussion:-

In first set 0.1M solution of [DMPMDC] was prepared in conductivity water and by serial dilution method 0.075M, 0.050M and 0.025M. At 28^0C the conductance of each solution is measured by Conductivity Bridge. The result obtained are given in **Table-1 to Table-2**

From the data observed conductance (G), specific conductance (k) and molar conductance (μ) were determined by known literature method.

Table–1

CONDUCTOMETRIC MEASUREMENTS OF [DMPMDC]AT DIFFERENT CONCENTRATION				
DETERMINATION OF G, k and μ AT 28^0C IN DIFFERENT CONCENTRATIONS				
% of solution (**Water-ethanol**)	Concentration C (M)	Observed conductance (G)	Specific conductance (k)	Molar conductance (μ)
100%	0.1 M	$7.81X10^{-3}$	$7.41298\ X10^{-3}$	74.12966
	0.075 M	$6.34\ X10^{-3}$	$6.01413\ X10^{-3}$	80.18814

	0.050 M	4.63 X10^{-3}	4.38690 X10^{-3}	87.7378
	0.025 M	2.69 X10^{-3}	2.54079 X10^{-3}	101.6310
80%	0.1 M	4.68X10^{-3}	4.43448 X10^{-3}	44.3448
	0.075 M	4.01 X10^{-3}	3.79690 X10^{-3}	50.6254
	0.050 M	3.24 X10^{-3}	3.06417 X10^{-3}	61.286
	0.025 M	2.12 X10^{-3}	2.01741 X10^{-3}	80.6958
70%	0.1 M	4.120 X10^{-3}	3.97771 X10^{-3}	39.7771
	0.075 M	3.89X10^{-3}	3.68272 X10^{-3}	49.10258
	0.050 M	3.36 X10^{-3}	3.17836 X10^{-3}	63.56690
	0.025 M	2.28 X10^{-3}	2.15064 X10^{-3}	86.02466

TABLE – 2 -

CONDUCTOMETRIC MEASUREMENTS OF [CTMSBCD] AT DIFFERENTCONCENTRATION				
DETERMINATION OF G, k and μ AT 28^{0}C IN DIFFERENT CONCENTRATIONS				
% of solution (**Water-ethanol**)	Concentration C (M)	Observed conductance (G)	Specific conductance (k)	Molar conductance (μ)
100%	0.1 M	0.59X10^{-3}	0.54243 X10^{-3}	5.42414
	0.075 M	0.50 X10^{-3}	0.456770 X10^{-3}	6.09026
	0.050 M	0.36 X10^{-3}	0.323546X10^{-3}	6.47090
	0.025 M	0.21 X10^{-3}	0.180806X10^{-3}	7.23218
80%	0.1 M	0.73X10^{-3}	0.675638X10^{-3}	6.75638
	0.075 M	0.69 X10^{-3}	0.637574X10^{-3}	8.50098
	0.050 M	0.59 X10^{-3}	0.542414X10^{-3}	10.84826
	0.025 M	0.39 X10^{-3}	0.352094X10^{-3}	14.08370
70%	0.1 M	0.23 X10^{-3}	0.199838X10^{-3}	1.99838
	0.075 M	0.21 X10^{-3}	0.180806X10^{-3}	2.41074
	0.050 M	0.18 X10^{-3}	0.152258X10^{-3}	3.04516
	0.025 M	0.12 X10^{-3}	0.09518X10^{-3}	3.8066

From **Table-1 to Table-2**, it was observed that the observed conductance (G), specific conductance (k) and molar conductance (μ) were decreases from [DPMPCD] to [CTMSBCD] continuously. The decrease in all conductances is due to number of phenolic-OH groups present in the respective molecule. In [DPMPCD] electron donating groups are present in the molecule hence, the stability of carbanion increases which help to carry current easily in the solution. So, there is a increase in observed, specific and molar conductance in [DPMPCD], such types of functional groups are not present in [CTMSBCD] so these conductance decreases in [CTMSBCD].

In [DMPMDC] observed conductance continuously decreases from 0.1M concentration to 0.025M concentration continuously. This is due to the numbers of [CTMSBCD] present in these solutions were continuously decreases. Same pattern was observed in percentage compositions of the mixture. It is also observed that the observed conductance increases when the temperature of system increases. It means that the absorption, transformation and metabolism of [DMPMDC] are better than [CTMSBCD], so [DMPMDC] possesses best drug activity and drug effect than [CTMSBCD].

Specific conductance of [DMPMDC] decreases when the molar concentration and percentage composition of water decreases but the specific conductance increases at the same temperature. In [DMPMDC] it was also observed that molar conductance increases from 0.1M concentration to 0.025M concentration as well as it increases in all percentage compositions. In 100% water molar conductance is highest while it will decreases from 100% to 70% water-ethanol percentage compositions. As molar conductance in 100% water is highest in all molar concentrations hence, this drug is best drug which obey pharmokinetics and pharmodynamics of the standard drug. Same patterns of observed conductance, molar conductance and specific conductance were observed for [CTMSBCD].

The specific constant (Ksp), log (Ksp) and thermodynamics parameter viz. change in free energy (ΔG), change in entropy (ΔS) and change in enthalpy (ΔH) of [DMPMDC] and [CTMSBCD] were determined by known literature methods at

various molar concentration, percentage compositions and at same temperature. The results obtained were given in**Table-3 to Table-8.**

TABLE – 3 -

CONDUCTOMETRIC MEASUREMENTS OF [DMPMDC] AT DIFFERENT CONCENTRATION						
DETERMINATION OF Ksp, log Ksp, λG,λH and λS AT 28⁰C IN DIFFERENT CONCENTRATIONS						
SYSTEM: DMPMDC					MEDIUM - 100% WATER	
Temp T (°C)	Conc. C (M)	Ksp	Log Ksp	ΔG	ΔH	ΔS
28	0.100	0.099774997	-1.000978287	5673.098517	-425066.5526	-1455.20154
	0.075	0.074831248	-1.125917024	6381.195565	-425066.5526	-1457.59376
	0.050	0.049887499	-1.302008287	7379.202307	-425066.5526	-1460.96540
	0.025	0.024943750	-1.60303831	9085.306126	-425066.5526	-1466.72927

TABLE – 4 CONDUCTOMETRIC MEASUREMENTS [DMPMDC] AT DIFFERENT CONCENTRATION						
DETERMINATION OF Ksp, log Ksp, ΔG,ΔH and ΔS AT 28⁰C IN DIFFERENT CONCENTRATIONS						
SYSTEM:DRUG [DMPMDC]					MEDIUM - 80% WATER	
Temp T (°C)	Conc. C (M)	Ksp	Log Ksp	ΔG	ΔH	ΔS
28		0.079819998	-1.097888299	6222.34127	-425066.5526	-1457.057075
	0.075	0.059864998	-1.222827044	6930.438334	-425066.5526	-1459.449295
	0.050	0.039909999	-1.398918306	7928.44510	-425066.5526	-1462.820939
	0.025	0.019954999	-1.699948312	9634.548906	-425066.5526	-1468.584804

TABLE – 5 - CONDUCTOMETRIC MEASUREMENTS OF [DMPMDC] AT DIFFERENT CONCENTRATION						
DETERMINATION OF Ksp, log Ksp, ΔG,ΔH and ΔS AT 28⁰C IN DIFFERENT CONCENTRATIONS						
SYSTEM:DRUG [DMPMDC]					MEDIUM - 70% WATER	
Temp T (°C)	Conc. C (M)	Ksp	Log Ksp	ΔG	ΔH	ΔS
28	0.100	0.069842498	-1.155880250	6551.01378	-425066.5526	-1458.167455
	0.075	0.052381874	-1.280818987	7259.110805	-425066.5526	-1460.559675
	0.050	0.034921249	-1.456910259	8257.11763	-425066.5526	-1463.931320
	0.025	0.017460625	-1.757940267	9963.221439	-425066.5526	-1469.695184

TABLE – 6 - CONDUCTOMETRIC MEASUREMENTS OF [CTMSBCD]AT DIFFERENT CONCENTRATION						
DETERMINATION OF Ksp, log Ksp, ΔG,ΔH and ΔS AT 28⁰C IN DIFFERENT CONCENTRATIONS						
SYSTEM:DRUG [CTMSBCD]					MEDIUM - 100% WATER	
Temp T (°C)	**Conc. C (M)**	**Ksp**	**Log Ksp**	**ΔG**	**ΔH**	**ΔS**
28	0.100	0.099790374	-1.000911310	5672.719205	-425066.5526	-1455.200244
	0.075	0.074842779	-1.125850109	6380.816315	-425066.5526	-1457.592464
	0.050	0.049895187	-1.301941365	7378.823023	-425066.5526	-1460.964108
	0.025	0.024947594	-1.602971369	9084.926836	-425066.5526	-1466.72799

TABLE – 7 - CONDUCTOMETRIC MEASUREMENTS AT DIFFERENT CONCENTRATION OF DRUG [CTMSBCD]						
DETERMINATION OF Ksp, log Ksp, ΔG,ΔH and ΔS AT DIFFERENT CONCENTRATIONS AND AT SAME TEMPERATURE						
SYSTEM:LIGAND [CTMSBCD]				MEDIUM - 80% WATER		
Temp T (°C)	**Conc. C (M)**	**Ksp**	**Log Ksp**	**ΔG**	**ΔH**	**ΔS**
28	0.100	0.079832299	-1.097821377	6221.96198	-425066.5526	-1457.055794
	0.075	0.059874223	-1.222760126	6930.059073	-425066.5526	-1459.448013
	0.050	0.039916150	-1.398851378	7928.065758	-425066.5526	-1462.819658
	0.025	0.019958075	-1.699881395	9634.169645	-425066.5526	-1468.58354

TABLE – 8 - CONDUCTOMETRIC MEASUREMENTS AT DIFFERENT CONCENTRATION OF DRUG [CTMSBCD]						
DETERMINATION OF Ksp, log Ksp, ΔG,ΔH and ΔS AT DIFFERENT CONCENTRATIONS AND AT SAME TEMPERATURE						
SYSTEM:DRUG [CTMSBCD]				MEDIUM - 70% WATER		
Temp T (°C)	**Conc. C (M)**	**Ksp**	**Log Ksp**	**ΔG**	**ΔH**	**ΔS**
28	0.100	0.06985328	-1.155813323	6550.634450	-425066.5526	-1458.166174
	0.075	0.052389945	-1.280752076	7258.731583	-425066.5526	-1460.558394
	0.050	0.034926631	-1.456843325	8256.738251	-425066.5526	-1463.930037
	0.025	0.017463316	-1.757873329	9962.842064	-425066.5526	-1469.6941

From **Table-3** to **Table-8** it was observed for all three drugs Ksp, log Ksp, ΔH and ΔS decreases continuously while ΔG increases when we go from 0.1M concentration solution to 0.025M concentration. Same pattern was observed in percentage composition of the mixture i.e. these thermodynamic parameters are highest in 100% water while least in 70% water-ethanol solvent. In [CTMSBCD] the values of all thermodynamic parameter as well as Ksp and log Ksp are the greatest than [**DMPMDC**] possesses these thermodynamics values. From this study it is clear that various functional groups such as electron donating, electron withdrawing, acidic, basic and various functional groups present in the molecule directly affect conductance, specific conductance, molar conductance, Ksp, ΔH, ΔS and ΔG values of that drug. The structure of the drug as well as nature of that drug directly affects these parameters. The temperature, molar concentrations and percentage compositions are also responsible for changing the values of these parameters. The solute(drug)-solvent interactions, solvent-solvent interactions, solvent-solvent-solute interactions and –solute-solute-solvent interactions are another factors which directly hamper these parameters. The internal geometry as well as internal and intra hydrogen bonding affect these parameters.

During this investigation it was observed that the molar conductance of [**DMPMDC]** is highest than [CTMSBCD] which clearly indicates the drug effect of [**DMPMDC**] is comparatively [CTMSBCD].

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