IOSR Journal of Applied Chemistry (IOSR-JAC)
e-ISSN: 2278-5736. Volume 5, Issue 5 (Sep. – Oct. 2013), PP 01-04
www.iosrjournals.org

To Study The Viscometric Measurement Of Substituted-2-Diphenylbutanamide And Substituted-Spiro[1-Benzofuran2, 1'-Cychlohex-2-Ene]-3,4'-Dione In Ethanol–Water Mixture At Various Percentage Compositions.

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Abstract: *Recently in this laboratory the viscometric measurement of 4-[4-(4-chlorophenyl]-4-hydroxy piperidin-1-yl]-N, N-dimethyl-2, 2-diphenylbutanamide**[CPHDD]** and (2S, 6R)-7-chloro -2, 4, 6-trimethoxy-6'-methyl-3H, 4'H-spiro[1-benzofuran 2, 1'-] cychohex-2-ene]-3,4'-dione**[CTMBCD]** were carried out at different percentage compositions of solvent to investigate the solute-solvent interactions of drugs with solvent and the effect of dilution of the solvent. The effects of various substituents were also investigated. The results obtained during this investigation gave detail information about pharmacokinetics and pharmacodynamics of these drugs.*

Keywords: *4-[4-(4-chlorophenyl]-4-hydroxy piperidin-1-yl]-N, N-dimethyl-2, 2-diphenylbutanamide**[CPHDD]** and (2S, 6R)-7-chloro -2, 4, 6-trimethoxy-6'-methyl-3H, 4'H-spiro[1-benzofuran 2, 1'-] cychohex-2-ene]-3,4'-dione**[CTMBCD]** ethanol-water mixture, viscometric measurements, etc.*

I. Introduction:-

Viscosity is also called the internal friction of the liquid molecules. Measurement of viscosity plays an important role in pharmaceutical, medicinal, agricultural, industrial and drug chemistry[1-3]. In drug chemistry viscometric studies provides useful and important information regarding solute-solute, solute-solvent and solvent-solvent interactions. The activities of the drug like absorption, transmission and its effect will directly related to viscosity measurements of the drugs and solvent interactions in the human anatomy.

The pharmaceutical and medicinal literature survey reveals that these drugs which are the best for particular diseases became non-active for that disease due to rapid evolutionary phenomenon in pathogens. Hence it becomes challenge to chemist and researcher to synthesized new type of drug for such diseases. . Substituted diphenylbutanamide and substituted spiro[1-benzofuran 2, 1'- cychohex-2-ene]-3,4'-dione nucleus containing drug create their own identity and importance in drug and pharmaceutical chemistry[4-10]. Hence, taking all these things into consideration it was thought interesting to carry out the viscometric measurements of 4-[4-(4-chlorophenyl]-4-hydroxy piperidin-1-yl]-N, N-dimethyl-2, 2-diphenylbutanamide**[CPHDD]** and (2S, 6R)-7-chloro -2, 4, 6-trimethoxy-6'-methyl-3H, 4'H-spiro[1-benzofuran 2, 1'-] cychohex-2-ene]-3,4'-dione**[CTMBCD]** at various compositions. This study is helpful to predict the potency of drugs.

II. Experimental:-

All the chemicals used of A.R.grade. Double distilled water was used throughout the work. Weighing was made on Mechaniki Zaktady Precyzyjnej Gdansk balance (Poland make [±0.001gm]). Densities were determined by bicapillary having an internal diameter of 1mm. The viscosities were measured by Ostwald's viscometer. It was kept in Elite themostatics water bath and temperature variation was maintained at 23^0C (±0.1) for each measurements. Sufficient time was allowed to attain thermal equilibrium in between viscometer and water bath.

The present study deals with the viscosity investigation of **[CPHDD]** and **[CTMBCD]** drugs at 0.1M concentration in 60%, 70% and 80% ethanol-water system separately at 23^0C (296.15K) temperature. All solutions of the drugs were always used freshly in the present study. The viscometric readings were taken as described in literature[11].

Observations And Calculations:-

The data obtained in this study is used to compute molecular interactions in terms of β-coefficient of drugs. The result obtained was mentioned in **Table No. 1-6**. According to Jone's-Dole equation, $(\eta r-1)/\Gamma C = A+\beta\Gamma C$ at different concentration and different percentage. A and β-coefficient values calculated and are enlisted in **Table No.7-8**.

A] For Drug **[CPHDD]**

TABLE 1 - VISCOSITY MEASUREMENTS AT DIFFERENT OF LIGAND CONCENTRATION							
DETERMINATION OF RELATIVE AND SPECIFIC VISCOSITIES AT DIFFERENT CONCENTRATIONS AND TEMPERATURE							
SYSTEM:DRUG [CPHDD]			**MEDIUM - 60% ETHANOL-WATER**				
Temp T (°C)	**Conc. C (M)**	**√C**	**Time t (sec.)**	**Density ρx10^3 (kg.cm^{-3})**	**$\acute{\eta}_r$**	**$\acute{\eta}_{sp}=\acute{\eta}_r-1$**	**$(\acute{\eta}_r-1)/\sqrt{C}$ (pa˜s)**
23	0.100	0.31616	415.08	1.03405	1.7115	0.7115	2.25088
	0.075	0.27379	411.47	1.03094	1.6915	0.6915	2.52607
	0.050	0.23657	396.77	1.02394	1.6200	0.6200	2.62122
	0.025	0.20487	383.37	1.02264	1.5633	0.5633	2.75005

TABLE 2 - VISCOSITY MEASUREMENTS AT DIFFERENT CONCENTRATION OF DRUG							
DETERMINATION OF RELATIVE AND SPECIFIC VISCOSITIES AT DIFFERENT CONCENTRATIONS AND TEMPERATURE							
SYSTEM:DRUG [CPHDD]			**MEDIUM - 70% ETHANOL-WATER**				
Temp T (°C)	**Conc. C (M)**	**√C**	**Time t (sec.)**	**Density ρx10^3 (kg.cm^{-3})**	**$\acute{\eta}_r$**	**$\acute{\eta}_{sp}=\acute{\eta}_r-1$**	**$(\acute{\eta}_r-1)/\sqrt{C}$ (pa˜s)**
23	0.100	0.31616	496.54	1.0351	1.6684	0.6684	2.11459
	0.075	0.27379	482.81	1.0312	1.6162	0.6162	2.25111
	0.050	0.23657	463.01	1.0259	1.5418	0.5418	2.29076
	0.025	0.20487	445.72	1.0208	1.4770	0.4770	2.32896

TABLE 3 - VISCOSITY MEASUREMENTS AT DIFFERENT CONCENTRATION OF DRUG							
DETERMINATION OF RELATIVE AND SPECIFIC VISCOSITIES AT DIFFERENT CONCENTRATIONS AND TEMPERATURE							
SYSTEM:DRUG [CPHDD]			**MEDIUM - 80% ETHANOL-WATER**				
Temp T (°C)	**Conc. C (M)**	**√C**	**Time t (sec.)**	**Density ρx10^3 (kg.cm^{-3})**	**$\acute{\eta}_r$**	**$\acute{\eta}_{sp}=\acute{\eta}_r-1$**	**$(\acute{\eta}_r-1)/\sqrt{C}$ (pa˜s)**
23	0.100	0.31617	447.50	1.0366	1.4292	0.4292	1.35817
	0.075	0.27379	442.84	1.0338	1.4105	0.4105	1.50000
	0.050	0.23657	438.27	1.0309	1.3920	0.3920	1.65774
	0.025	0.20487	432.96	1.0295	1.3727	0.3727	1.82001

TABLE 4- VISCOSITY MEASUREMENTS AT DIFFERENT CONCENTRATION OF LIGAND							
DETERMINATION OF RELATIVE AND SPECIFIC VISCOSITIES AT DIFFERENT CONCENTRATIONS AND TEMPERATURE							
SYSTEM:LIGAND [CTMBCD]			**MEDIUM - 60% ETHANOL-WATER**				
Temp T (°C)	**Conc. C (M)**	**√C**	**Time t (sec.)**	**Density ρx10^3 (kg.cm^{-3})**	**$\acute{\eta}_r$**	**$\acute{\eta}_{sp}=\acute{\eta}_r-1$**	**$(\acute{\eta}_r-1)/\sqrt{C}$ (pa˜s)**
23	0.100	0.31617	527.36	1.03709	2.18097	1.18097	3.73462
	0.075	0.27379	510.06	1.03127	2.09762	1.09762	4.00802
	0.050	0.23657	485.22	1.02757	1.98832	0.98832	4.17651
	0.025	0.20487	462.83	1.02427	1.89048	0.89048	4.34521

TABLE 5 - VISCOSITY MEASUREMENTS AT DIFFERENT CONCENTRATION OF LIGAND							
DETERMINATION OF RELATIVE AND SPECIFIC VISCOSITIES AT DIFFERENT CONCENTRATIONS AND TEMPERATURE							
SYSTEM:LIGAND [CTMBCD]			**MEDIUM - 70% ETHANOL-WATER**				
Temp T (°C)	**Conc. C (M)**	**√C**	**Time t (sec.)**	**Density ρx10^3 (kg.cm^{-3}))**	**$\acute{\eta}_r$**	**$\acute{\eta}_{sp}=\acute{\eta}_r-1$**	**$(\acute{\eta}_r-1)/\sqrt{C}$ (pa˜s)**
23	0.100	0.31617	532.13	1.03939	1.79520	0.79520	2.51471
	0.075	0.27379	509.59	1.03237	1.70757	0.70757	2.58376
	0.050	0.23657	486.11	1.02927	1.62398	0.62398	2.63689
	0.025	0.20487	478.63	1.02607	1.59402	0.59404	2.89873

TABLE 6 - VISCOSITY MEASUREMENTS AT DIFFERENT CONCENTRATION OF LIGAND							
DETERMINATION OF RELATIVE AND SPECIFIC VISCOSITIES AT DIFFERENT CONCENTRATIONS AND TEMPERATURE							
SYSTEM:LIGAND [CTMBCD] MEDIUM - 80% ETHANOL-WATER							
Temp T (°C)	**Conc. C (M)**	**√C**	**Time t (sec.)**	**Density ρx10^3 (kg.cm^{-3}))**	**$\acute{\eta}_r$**	**$\acute{\eta}_{sp}=\acute{\eta}_r-1$**	**$(\acute{\eta}_r-1)/\sqrt{C}$ (pa$^-$s)**
23	0.100	0.31617	536.51	1.04018	1.71897	0.71897	2.27365
	0.075	0.27379	515.77	1.03707	1.64757	0.64757	2.36467
	0.050	0.23657	497.51	1.03317	1.58327	0.58327	2.46486
	0.025	0.20487	479.68	1.02997	1.52179	0.52179	2.54619

A and β Co-Efficient Value from Graphs at Different Temperatures for 60%, 70% and 80% Ethanol-Water Mixture for drugs [CPHDD].

TABLE – 7 - FOR [CPHDD]			
W-E Mixture %	**Temp °C**	**Mean "A"**	**β (Slope "m")**
60	23	3.045	-4.5197
70	23	2.35	-1.1897
80	23	2.17	-4.5397

A and β Co-Efficient Value from Graphs at Different Temperatures for 60%, 70% and 80% Ethanol-Water Mixture for drugs [CTMBCD].

TABLE – 8 - FOR [CTMBCD]			
W-E Mixture %	**Temp °C**	**Mean "A"**	**β (Slope "m")**
60	23	4.53	-5.5199
70	23	2.73	-1.6299
80	23	2.63	-2.7797

III. Result And Discussion

The relative viscosity was determined by using following formula

η_r = Ds x ts / Dw x tw

Where, η_r = Relative viscosity of drug solution, Ds and Dw are density of drug solution and density of water, ts and tw are the time flow for drug solution and water respectively.

The relative viscosities have been analyzed by Jone's-Doles equation as ,

$(\eta r-1)/\Gamma C = A+\beta\Gamma C$

Where, C is molar concentration of the drug solution, A is the Falkenhagen coefficient which is the measure of solute-solute interactions and β is the Jones-Dole coefficients which is the measure of solute-solvent interactions.

The graph are plotted between (ηr-1)/ΓC versus ΓC. The graph for each system gave linear straight line gave value of β-coefficient.

In the present study it was observed that when the concentration of drugs decreases, the density and relative viscosity also decreases for [CPHDD] and [CTMBCD] drugs at 23^{0}C temperature in ethanol-water mixture. This is due to the fact that when the concentration decreases the number of solute molecule decreases and at same time percentage of solvent molecules increases in the solution which is responsible to increases solvation effect.

At 23^{o}C for 60% ethanol-water mixture,

Drug	[CPHDD]	[CTMBCD]
ηr	1.8109	2.1807
Substitution	CON(-CH_3)$_2$ group	-CH_3 group

At 23^{o}C for 60% ethanol-water mixture, the relative viscosity (η_r) of [**CPHDD**] is found to be 1.8109 and for [**CTMBCD**] it is 2.1807. Generally, it was observed that, when the molecules are aromatic the relative viscosity is always greater. This trend was observed in [**CPHDD**]. Literature survey also reveals that, when there is a bulkier group, the relative viscosity is greater. But in this investigation, the value of relative viscosity of [**CTMBCD**] is greater than [**CPHDD**]. It means that, only the bulkiness of the group as a substituent not only interfere the values of relative viscosity but the reactivity and stability and tautomeric properties also interfere the values of relative viscosities. It is clear from the result that, in case of [**CPHDD**] the substituted amide group is present of adjacent carbon of benzene ring which is not directly attached to the benzene nucleus well as there

is chloro group present in the molecule which is strongly in electronegative character while in the case of [**CTMBCD**] there are methoxy, chloro as well as quinone groups present.

Such type of greater interference of methyl will not involved in [**CPHDD**] but when we compare, relative viscosity of [**CTMBCD**] as per the general norms, the relative viscosity of bulkier group must be greater but in this investigation, the relative viscosity of [**CTMBCD**] is greater than that of [**CPHDD**], this may be due to the donating capacity of $–CH_3$ group to the [**CTMBCD**] molecule. As the oxygen atoms in [**CTMBCD**] molecule is electron rich species and $–CH_3$ group is also electron donating group, hence in [**CTMBCD**] molecule there occurs compactness in the bond which is greater than [**CPHDD**] molecule. From this discussion, it is clear that bulky substituent on the molecule is not only factor in trend of relative viscosity but electron donating nature, electron clouds, nature of hetero atom present in drugs and the compactness in the molecule will directly hampered results and trends in the relative viscosity. Predictation of this factor's can be done by viscometric measurements. These two drugs showed good results hence this can be used as antibiotics. The potency of these two drugs can be increased by substituting different substituent on the parent drug.

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