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VISCOMETRIC STUDY OF SYNTHESIZED DILTIAZEM-VANADIUM (V) COMPLEX IN NON-AQUEOUS SOLVENTS

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ABSTRACT: In the present research work, measurement of viscometric parameters - Density, Molar Volume, Apparent Molar Volume, Viscosity, Specific Viscosity, and Fluidity of synthesized Vanadium (V) complex of commercial antihypertensive drug, Diltiazem has been reported in non-aqueous solvents of varying compositions. Composition of non-aqueous solvents selected for study is 20% and 40% methanol-water mixture. Experimental results showed the effect of Concentration of solute (Diltiazem drug) on density and viscosity in a methanol-water mixture. The density of Diltiazem-V (V) complex showed an irregular pattern in 20% methanol-water mixture, whereas an increase was observed in 40% methanol-water mixture. The molar volume value for the complex solution in both 20% & 40% methanol-water mixture showed rapid increase with the increase in complex Concentration. The apparent molar volumes (φ_v) decreased with an increase in Concentration of complex and same trend was followed in both 20% and 40 % methanol-water solvent system. Study of the viscous behavior of complex molecules in solution gives an understanding of the transport process mechanism and information about the shape and size of molecules. Specific viscosity 'ηsp' values of diltiazem-V(V) in 20% and 40% methanol-water mixture show that it raises with a rise in complex Concentration. This in turn gives a picture of molecular interactions taking place in different solutions. Information about molecular interactions between a metal complex of drug and various solvent compositions helps in the formulation of the stable, effective, and safe dosage form. It also helps in the understanding of their oral absorption by increasing the solubility or dissolution rate.

INTRODUCTION: Biophysical chemistry, study of physicochemical parameters, is an important tool to study the interactive behavior of drugs and also to study about the complex mechanism of their action [1-4].

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Once injected, drug actions take place in a fluid medium inside the body, and hence study of viscometric parameters give valuable information about transport properties and molecular interaction pattern [5-9].

Detail analysis of solute-solvent interaction during the solution phase of the drug helps in understanding the transport mechanism and absorption of the drug within cells [10-16]. Diltiazem, which is chemically 1, 5-benzothiazepin - 4(5H)-one, 3- (acetyloxy)-5 [2-(dimethyl amino) ethyl]- 2,

- 3 – dihydro – 2 (4-methoxyphenyl) -, mono hydrochloride, (+)-cis] is a significant calcium channel blocker coronary vasodilator antihypertensive drug [17-19]. Diltiazem forms 1:1 complex with transition metal Vanadium (V). In this research work, various compositions have been reported viscometric investigation of the drug diltiazem– vanadium (V) metal complex in binary solution (water-methanol). Parameters investigated for the complex include density, molar volume, apparent molar volume, viscosity, specific viscosity and fluidity. This is helpful in understanding the formulation of stable, effective, and safe dosage form. It helps in the understanding of their oral absorption by increasing the solubility or dissolution rate.

EXPERIMENTAL:

Purification of Solvents: Water and Methanol mixture were used as solvents in various compositions. A Distillatory column is used for the double distillation of water. The distillate so obtained was refluxed over sodium metal, and it was again distilled. For the methanol purification, it was kept over potassium hydroxide for twenty-four hours and then distilled. The distillate obtained was refluxed with one percent of calcium metal for about eight hours and then distilled again. The fraction was collected at 65^{o}C for experimental purposes.

Solute Diltiazem-Vanadium (V) Complex Preparation: For synthesis of diltiazem–Vanadium (V) Complex, a standard solution of Diltiazem was prepared by dissolving a tablet (brand name Tizac-90mg diltiazem per tablet) in 100 ml distilled water. 0.01 M solution of vanadium pentoxide was prepared by dissolving 0.181 gm of vanadium pentoxide in 100 ml double distilled water. Solutions of lower concentrations were prepared by diluting aliquots of standard stock solution.

On mixing both the solutions at 35 ^{o}C and pH 2.6, the diltaizem –Vanadium (V) complex was synthesized with λ_{max} 290 nm. The synthesized complex was then solidified and used as a solute for viscometric analysis. For accurate density measurements, the calculated amount of solid diltiazem-Vanadium (V) complex was weighed on a watch glass and dissolved in the required amount of water and methanol to prepare the solution.

In this way, solutions containing different concentrations of complex Diltiazem-V (V) in water-methanol solvent system at varying compositions were prepared.

Procedure: For the study of Diltiazem-Vanadium (V) metal complex density, a simple instrument Pycnometer, was used **Fig. 1.**

FIG. 1: PYCNOMETER WITH THERMOMETER V11204

For calculation of density'd' of complex solution, the relationship used was:

$$d = W/W_o \text{---------- (1)}$$

Where *W* and W_0 are the weights of the same sample solution and water volume, respectively, the calculated density of the complex solution was then used further to determine the molar volume and apparent molar volume. Molar volume calculation involves the relationship

$$V = X_1M_1 + X_2M_2 + X_3M_3 / d \text{ ---------- (2)}$$

Where X_1= Mole fraction of the complex of molecular weight M_1, 'X_2' and 'X_3' are the mole fraction of the water and methanol of molecular weight M_2 and M_3, respectively, d = density of the solution.

Apparent molar Volume was calculated by using the formula:

$$\Phi_v = M/d_0 + 1000(d_0-d)/ C.d_0 \text{ ---------- (3)}$$

Where d_o= density of the solvent, d=Density of complex solution, M= Molecular weight of the complex, and C= Concentration of the solution in $gmolL^{-1}$.

For measurement of viscosity, Ostwald's viscometer was used **Fig. 2**.

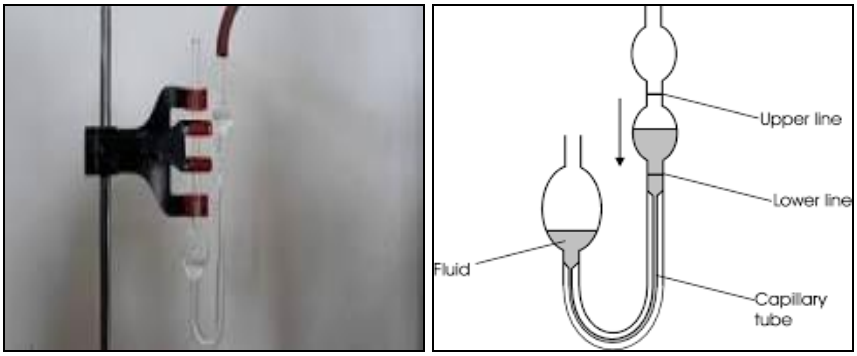

FIG. 2: OSTWALD VISCOMETER

The viscosities, specific viscosity, and fluidity of the complex solutions were calculated using relationships (4), (5), and (6), respectively.

$$\eta_0/\eta = d_0t_0/dt \quad \text{---------- (4)}$$

$$\eta_{sp} = \eta\text{-}\eta_0/\eta_0 \quad \text{---------- (5)}$$

$$\text{Fluidity } (\varphi) = 1/\text{Viscosity } (\eta) \text{---------- (6)}$$

RESULTS AND DISCUSSION:

Density Measurement: As per the experimental results, the density of Diltiazem-V (V) in 20% methanol-water mixture initially showed a slight increase with the increase in the Concentration of complex, then decreased and then again increased.

Whereas in the 40% methanol-water mixture, density variations of the complex were different. It showed a decrease followed by a very slight increase in the volume percent of methanol solvent **Fig. 3**.

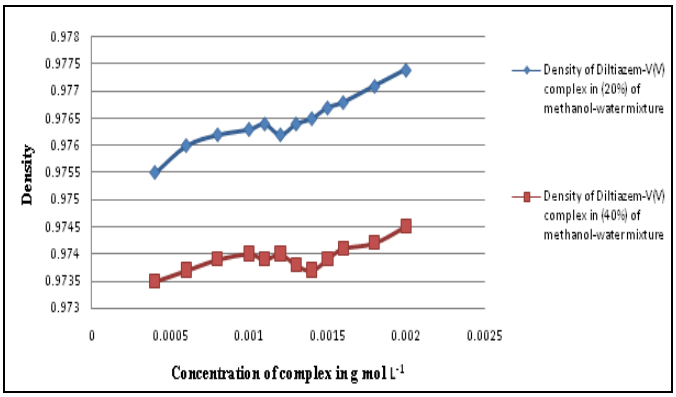

FIG. 3: DENSITY OF DILTIAZEM-V (V)COMPLEX IN DIFFERENT % VOLUMES OF METHANOL-WATER MIXTURE

Molar Volume Measurement: The value of molar volume for the complex solution in 20% methanol-water mixture showed a rapid increase with the increase in complex Concentration. The same pattern of variation was visible in 40% methanol-water mixture but with lower values **Fig. 4**.

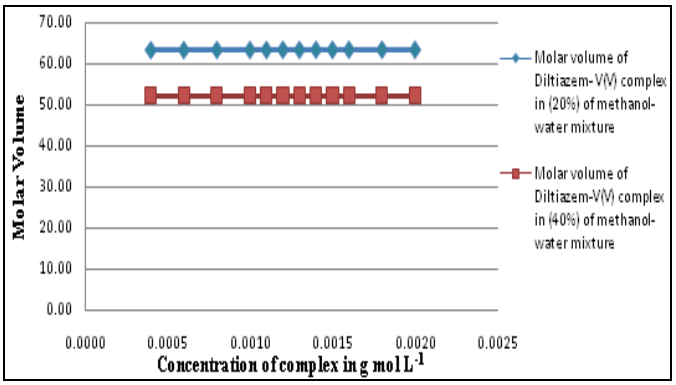

FIG. 4: MOLAR VOLUME OF DILTIAZEM-V (V) COMPLEX IN DIFFERENT % VOLUMES OF METHANOL-WATER MIXTURE

Apparent Molar Volume: Apparent molar volume provides valuable information about different types of interaction occurring in solutions. Thus the interaction of the V (V) complex of diltiazem with solvents having different polarity is worth to be analyzed. On plotting the value of apparent molar volume with Concentration of complex, the trend showed a decrease in the value of apparent molar volume with the increase in Concentration of complex molecule, with a sharp peak in between. The apparent molar volumes (φ_v) followed the same trend in the 20% and 40 % methanol-water solvent systems **Fig. 5**.

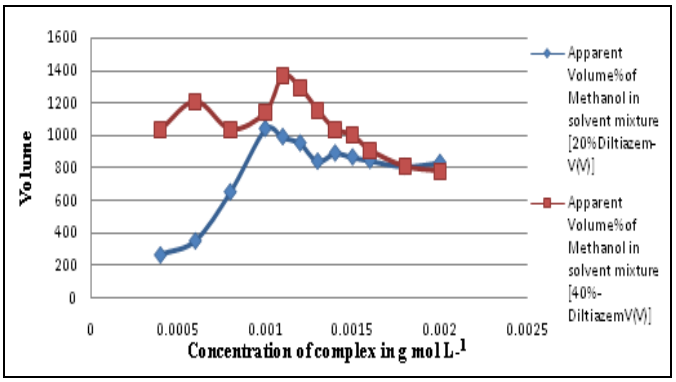

FIG. 5: APPARENT MOLAR VOLUME OF DILTIAZEM V(V) COMPLEX IN DIFFERENT % VOLUME OF METHANOL-WATER SYSTEM

Viscosity: The viscous behavior of complex molecules in solution is important to understanding the transport process mechanism. The viscosity variable provides valuable information about the shape and size of these molecules. The effect of complex Concentration on viscosity of Diltiazem-V (V) solution in 40% methanol-water mixture of varying composition is almost the same as that of 20% methanol-water mixture. The viscosity of the complex increased with the increase in complex Concentration and then decreased after a definite concentration as was visible in the viscosity-concentration plot. The viscosity pattern observed with the increase in Concentration of complex solution may be due to the increasing tendency of complex molecules to associate **Fig. 6**.

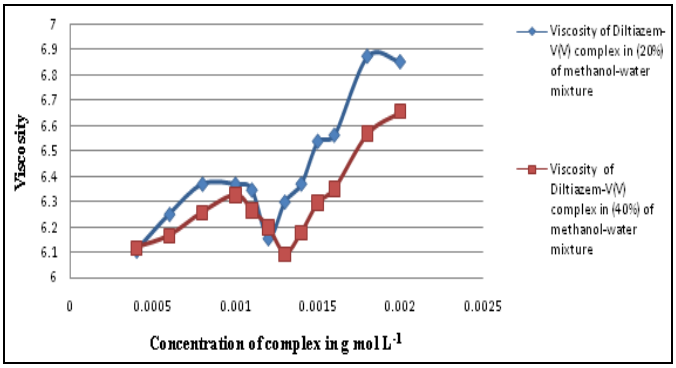

FIG. 6: VISCOSITY OF DILTIAZEM V (V) COMPLEX INDIFFERENT % VOLUME OF METHANOL-WATER SYSTEM

Specific Viscosity: Specific viscosity 'ηsp' values of diltiazem-V (V) in 20% and 40% methanol-water mixture were recorded. The outcomes showed that the specific viscosity (ηsp) of Diltiazem-V (V) rose in complex Concentration. This rise might be due to the rising trend of the complex solution molecules to form aggregates with increasing complex Concentration **Fig. 7**.

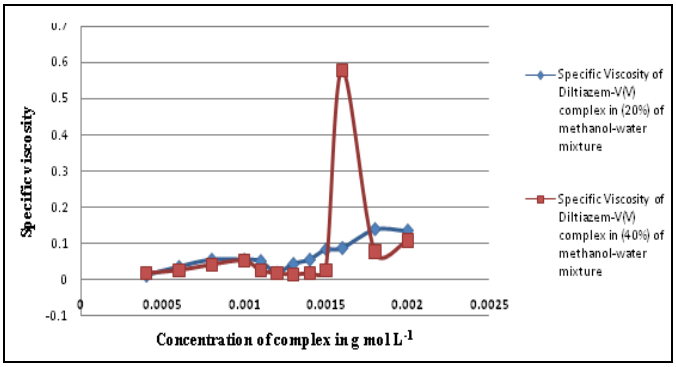

FIG. 7: SPECIFIC VISCOSITY OF DILTIAZEMV (V) COMPLEX IN DIFFERENT % VOLUMES OF METHANOL-WATER SYSTEM

Fluidity: The fluidity 'φ' of Diltiazem-V (V)in 40% methanol-water mixture is similar to that of 20% methanol-water mixture. The value of fluidity initially decreased with an increase in complex Concentration and ended up at a peak **Fig. 8.**

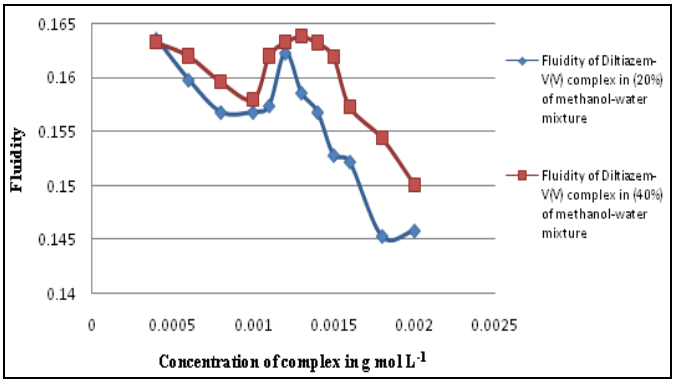

FIG. 8: FLUIDITY OF DILTIAZEMV (V) COMPLEXIN DIFFERENT % VOLUMES OF METHANOL-WATER SYSTEM

CONCLUSION: The present research work reports the viscometric measurements of the Diltiazem-V (V) complex at different solvent compositions of the methanol-water solvent mixture. Density, molar volume, viscosity, and fluidity values of the complex's 20% methanol water solvent system are higher than the 40% methanol-water system. Density and molar volume values are directly proportional to the Concentration of complex; this shows strong solute-solute interaction. The increase in viscosity and specific viscosity with the increase in complex Concentration might be due to the increased solute-solvent interactions.

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CONFLICTS OF INTEREST: The authors declare that the research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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