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Viscometric Studies of N-(3-Substituted) Phenyl-4-Methoxy Phenyl Schiff's Bases in Water-dioxane Mixture at Various Percentage Compositions

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ABSTRACT

Recently the viscometric measurements of N-phenyl-4-methoxyphenyl Schiff's base (PMPSB) and N-(3-nitro)phenyl-4-methoxyphenyl Schiff's base (NPMPSB) were carried out at different percentage compositions of dioxane-water solvent to investigate the solute-solvent interactions of drugs with mixture of solvent and the effect of dilution of the solvents. It is clear from the study that bulky substituent on the molecule is not only factor which affect 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. These properties are directly related with viscosity measurements. Absorption, transmission, metabolism and excretion are also depending on viscosity. Predication of these factors can be done by viscometric measurementsThe effects of various substituents were also investigated.

Keywords: N-Phenyl-4-methoxy phenyl Schiff's base (PMPSB) and N-(3-nitro)phenyl-4-methoxy phenyl Schiff's base (NPMPSB), dioxane-water mixture, viscometric measurements, etc.

INTRODUCTION

Viscosity measurements play an important role in pharmaceutical, medicinal, agriculturaland industrialand biochemical and drug sciences[1-3]. Viscosity is the internal friction of the liquid molecules. In pharmaceutical and medicinal chemistry viscometric studies make available useful and important information about solute-solute, solute-solvent and solvent-solvent interactions. The pharmaceutical results will directly related to viscometric measurements

of the drugs and solvent interactions in the human physiology and anatomy.

The literature survey tells that the drugs which are used for particular diseases became non-active for that disease after some time intervals 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 Schiff's bases containing –nitro and –methoxyphenyl groups created 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 N-phenyl-4-methoxy phenyl Schiff's base (PMPSB) and N-(3-nitro)phenyl-4-methoxy phenyl Schiff's base (NPMPSB),at various compositions. This study is helpful to predict the potency of drugs.

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 (Polandmake [±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 thermostatic water bath and temperature variation was maintained at 30^0C (±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 N-phenyl-4-methoxy phenyl Schiff's base (PMPSB) and N-(3-nitro)phenyl-4-methoxy phenyl Schiff's base (NPMPSB),drugs at 0.1M concentration in 60%, 70% and 80% dioxane-water system separately at 30^0C (330K) 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.**

RESULTS AND DISCUSSION

Relative viscosity was determined by using following formula[16],

$$\eta_r = Ds \times ts / Dw \times tw$$

Where, η_r = Relative viscosity of Schiff's base solutions, Ds and Dw are density of Schiff's base solution and density of water, ts and tw are the time flow for Schiff's base solution and water respectively.

The relative viscosities have been analyzed by Jone's-Doles[17] equation as,

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

Where, C is molar concentration of the Schiff's base 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 $(\eta r-1)/\Gamma C$ versus ΓC. The graph for each system gave linear straight line gave value of β-coefficient.

In the present work it was witnessed that when the concentration of drugs decreases, the density and relative viscosity similarly decreases for **(PMPSB)** and

(NPMPSB) drugs at 30^0C temperature in dioxane-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 30^oC For 60% Dioxane-Water Mixture,

Drug	[PMPSB]	[NPMPSB]
ηr	2.0599	2.0243
Substitution	-Phenyl group	-Nitrophenyl group

At 30^oC for 60% dioxane-water mixture, the relative viscosity (η_r) of **(PMPSB)** is found to be 2.0599 and for **(NPMPSB)** it is 2.0243. Generally, it was observed that, when the molecules are aromatic the relative viscosity is always greater. This trend was observed in **(PMPSB)** and **(NPMPSB).** Literature survey also reveals that, when there is a bulkier group, the relative viscosity is greater. 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[18]. It is clear from the result that, in **(PMPSB)** there is resonance stabilization in the benzene rings of **(PMPSB) but in** (**NPMPSB)** there is resonance stabilization of the benzene rings as well as in nitro group so there is a hyper conjugation. In the case of **(NPMPSB)** the substituted nitro group strongly shows electronegative character[19].

From this discussion , it is clear that bulky substituent on the molecule is not only factor which affect 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. These properties are directly related with viscosity measurements. Absorption, transmission, metabolism and excretion are also depending on viscosity. Predication of these factors can be done by viscometric measurements. The potency of these two drugs can be increased by substituting different substituent on the parent drug.

DISCUSSION

Considering the structural data, we could state that *Bombax ceiba* posses the immunostimulatory principles. Many of the presently available immunomodulators such as levamisole, glucans and teleronesz are not free from side effects, which include fever, neutropenia, leucopenia and allergic reactions. Hence, screening for new immunomodulators is an urgent need. Immunomodulatory agents of plant origin enhance the immune responsiveness of the organism against a pathogen by activating the immune system.

Bombax ceiba has ability to modulate humoral immune responses by acting at various levels in immune mechanism such as antibody production, release of mediators of hypersensitivity reactions, and tissue responses to these mediators in the target organs. In our study, foot volume was enhanced after *Bombax ceiba* treatment, suggesting cell-mediated immune enhancement. Cell-mediated immunity (CMI) involves effecter mechanisms carried out by T lymphocytes and their products (lymphokines). The CMI responses are critical to defend against infectious organisms, infection of foreign grafts, tumor immunity and delayed type hypersensitivity reactions. Humoral antibodies that are capable of killing free tumor cells in blood and in serosal cavities have been suggested to play a very important role in cancer. Both experimental and clinical results have demonstrated an apparently paradoxical effect of CP on the tumor-host immune response. The better anti-tumor effect of CP depends on the larger dose of CP administered. However,

along with a reduction of the tumor mass, large doses of CP usually bring an impairment of the host defense mechanisms, leading to immunosuppressive and cytotoxic effects.[27]

In the present study, *Bombax ceiba* exhibited beneficial actions on the specific and nonspecific immunity of immune-suppressed mice at the optimal dose. The actions of CP are primarily directed toward the depletion of T/B lymphocytes and the deficiency of macrophages.[27] A significant increase in white blood cell count was observed in methanol extract- treated mice as compared with cyclophosphamide treatment alone. Extract significantly ameliorated the RBC count, hemoglobin and also restored the suppressive effects induced by cyclo-phosphamide. Toxicities of cyclo-phosphamide include the suppression of white blood cells, RBC, Hb, nausea, vomiting, gonadal atrophy, liver, renal, and bladder injury. Significant improvements were found in relative organ weights of kidney, liver, and spleen; therefore, *Bombax ceiba* could be suggested for the drug-induced immunopathy in the organs.

The present study had shown that the administration of cyclophosphamide not only impair the immune responses but also produce oxidative stress in mice. In view of this, it appeared that cyclophosphamide which is a strong generator of superoxide radicals might impair the immune response through oxidative stress. It is further observed that administration of *B. ceiba* bark extract prevented the cyclophosphamide-induced changes of immunological and oxidative stress parameters. Hence, the immunomodulatory effect of *B. ceiba* bark extract may be subsequent to the antioxidant activity which it possesses.

The inflammatory response in the body is mediated by the proinflammatory cytokines such as tumor necrosis factor alpha (TNF-α) and interleukin-6 (IL-6). The level and persistence of TNF-α and IL-6 cytokines play an important role in determining the behavior of a given factor in immunomodulation. IL-6 plays a key role in host immune responses, such as acute protein synthesis, and the maintenance of homeostasis also acts as both a pro-inflammatory and anti-inflammatory cytokine.[28] Our result shows that test drugs induce cytokine production (including IL-6 and TNF-α) in a dose-dependent manner.

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(A) For Drug (PMPSB)

Table 1. Viscosity measurements at different concentration of drug

Determination of relative and specific viscosities at different concentrations and temperature							
System:drug (PMPSB)			Medium - 60% dioxane-water				
Temp T (°C)	Conc. C (M)	√C	Time t (sec.)	Density ρx10^3 (kg.cm^{-3})	η_r	$\eta_{sp}=\eta_r-1$	$(\eta_r-1)/\sqrt{C}$ (pa˙s)
30	0.100	0.31838	455.09	1.1671	2.8322	1.8322	3.66280
	0.075	0.27601	431.37	1.1668	2.7348	1.7348	3.72130
	0.050	0.23878	410.18	1.1666	2.6762	1.6762	3.90387
	0.025	0.20708	401.26	1.1664	2.6112	1.6112	4.03810

Table 2. Viscosity measurements at different concentration of ligand

Determination of relative and specific viscosities at different concentrations and temperature							
System:drug (PMPSB)			Medium - 70% dioxane-water				
Temp T (°C)	Conc. C (M)	√C	Time t (sec.)	Density ρx10^3 (kg.cm^{-3})	η_r	$\eta_{sp}=\eta_r-1$	$(\eta_r-1)/\sqrt{C}$ (pa˙s)
30	0.100	0.31842	515.37	1.0288	1.7212	0.7212	2.28155
	0.075	0.27604	490.13	1.0278	1.6353	0.6353	2.32085
	0.050	0.23882	470.30	1.0268	1.5676	0.5676	2.39979
	0.025	0.20712	452.42	1.0261	1.5070	0.5070	2.47534

Table 3. Viscosity measurements at different concentration of ligand

Determination of relative and specific viscosities at different concentrations and temperature							
System:drug (PMPSB)			Medium - 80% dioxane-water				
Temp T (°C)	Conc. C (M)	√C	Time t (sec.)	Density ρx10^3 (kg.cm^{-3})	η_r	$\eta_{sp}=\eta_r-1$	$(\eta_r-1)/\sqrt{C}$ (pa˙s)
30	0.100	0.31620	483.30	1.0389	1.5478	0.5469	1.73035
	0.075	0.27383	484.41	1.0353	1.5453	0.5451	1.99147
	0.050	0.23661	467.38	1.0314	1.4863	0.4863	2.05621
	0.025	0.20491	457.62	1.0289	1.4506	0.4506	2.20012

(B) For Drug(NPMPSB)

Table 4. Viscosity measurements at different of ligand concentration

Determination of relative and specific viscosities at different concentrations and temperature							
System:drug (NPMPSB)			Medium - 60% dioxane-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)
30	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 5. Viscosity measurements at different concentration of drug

Determination of relative and specific viscosities at different concentrations and temperature							
System:drug (NPMPSB)			Medium - 70% dioxane-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)
30	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 6. Viscosity measurements at different concentration of drug

Determination of relative and specific viscosities at different concentrations and temperature							
System:drug (NPMPSB)			Medium - 80% dioxane-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)
30	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

A and β Co-Efficient Value from Graphs at Different Temperatures for 60%, 70% and 80% DIOXANE-Water Mixture for drugs (PMPSB)

Table 7. Drug - (PMPSB)

W-E Mixture %	Temp °C	Mean "A"	β (Slope "m")
60	30	3.44	-2.9423
70	30	2.84	-2.0085
80	30	2.95	-7.4783

Aand β Co-Efficient Value from Graphs at Different Temperatures for 60%, 70% and 80% DIOXANE-Water Mixture for drugs (NPMPSB)

Table 8. Drug - (NPMPSB)

W-E Mixture %	Temp °C	Mean "A"	β (Slope "m")
60	30	3.2584	-4.3063
70	30	2.5634	-0.9763
80	30	2.3834	-4.3263