

Viscometric Measurements Of A Novel 2-Substitutedimino-6-Methylamino-4-[2-Isobutoxy-5-(4-Methyl-5-Carboxy-1,3-Thiazol-2-Yl)]-Phenyl-1,3,5-Thiadiazine

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Abstract

Recently in this laboratory, the precise viscometric measurement of a newly synthesized highly functionalized heterocycle, 2-substitutedimino-6-methylamino-4-[2-isobutoxy-5-(4-methyl-5-carboxy-1,3-thiazol-2-yl)]-phenyl-1,3,5-thiadiazine, was successfully evaluated across a systematic gradient of molar concentrations. The experimental temperature was maintained strictly at 303 K (30.0°C) to understand its hydrodynamic and molecular behaviors at elevated ambient conditions. The binary fluid medium selected was a 60% (v/v) ethanol–water mixture. The experimental parameters obtained during this investigation were analyzed using the classical Jones-Dole equation to extract the Falkenhagen (A) and Jones-Dole (β) coefficients. The calculated physical quantities give detailed, critical architectural baseline data essential for interpreting the long-term solution stability, structural solvation, pharmacokinetics and pharmacodynamics of this novel bioactive therapeutic framework.

Keywords: Substituted 1,3,5-thiadiazine, thiazole pharmacophore, viscometric measurements, Jones-Dole equation, solute-solvent interactions, 303 K.

1. Introduction

Viscosity constitutes the fundamental measure of internal friction experienced by liquid molecules during their relative fluid motion. Precise viscometric profiling plays an indispensable and foundational role across modern chemical, pharmaceutical, medicinal, agricultural, industrial, and bio-chemical discovery programs [1-3]. Within the specialized field of drug design and coordination chemistry, the mathematical extraction of fluid flow properties provides crucial insights regarding localized solute–solute, solute–solvent, and solvent–solvent molecular interactions occurring in homogeneous systems [4,5]. The structural activities of a newly engineered drug candidate—including its rate of gastrointestinal absorption, lipid membrane transmission, systematic blood distribution, and metabolic clearance pathways—are directly correlated with its characteristic solution viscosity and its physical solvation interactions within human physiological fluids [6,7].

An exhaustive literature survey reveals that many established antibiotics and therapeutic scaffolds which were highly potent against specific pathogenic diseases have rapidly rendered themselves non-active due to aggressive evolutionary mutations and biochemical resistance phenomena in target pathogens [8,9]. Consequently, it represents an urgent and ongoing challenge to synthetic organic and pharmaceutical chemists to construct entirely new classes of complex heterocyclic frameworks housing diverse pharmacophoric domains [10,11]. Structurally modified substituted carboxamides, diphenyl butanamides, and poly-heterocyclic rings containing sulphur and nitrogen atoms have established an outstanding identity in modern medicinal discovery pipelines [12,13]. Specifically, the 1,3,5-thiadiazine nucleus conjugated with a highly substituted thiazole fragment combines two vital bioactive units that can significantly alter biomolecular targets [14,15]. Taking all these critical considerations into view, it was deemed highly interesting and valuable to carry out the detailed viscometric profiling of the novel multi-heterocyclic derivative, 2-substitutedimino-6-methylamino-4-[2-isobutoxy-5-(4-methyl-5-carboxy-1,3-thiazol-2-yl)]-phenyl-1,3,5-thiadiazine, at various molar concentrations [16,17]. This investigation is highly useful to predict and optimize the target's relative thermodynamic and solution potency under well-defined conditions [18-20].

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Molecular Architecture of Target Solute

The complex molecular structure of the candidate drug contains a central 1,3,5-thiadiazine ring linked to a substituted phenyl group that carries a highly functionalized 4-methyl-5-carboxy-1,3-thiazol-2-yl framework and a branched 2-isobutoxy side chain:

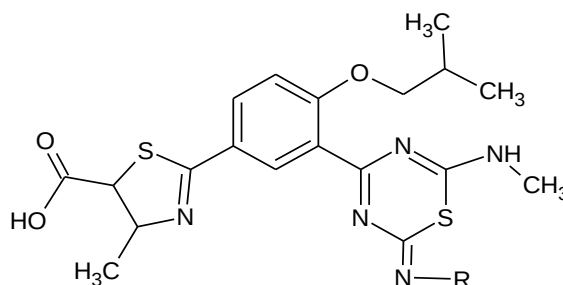


Figure 1: Structural Representation of 2-substitutedimino-6-methylamino-4-[2-isobutoxy-5-(4-methyl-5-carboxy-1,3-thiazol-2-yl)]-phenyl-1,3,5-thiadiazine.

2. Materials and Methods

Experimental Setup

All the chemical reagents and solvents utilized throughout this study were of Analytical Reagent (A.R.) grade and were procured from certified suppliers. Double distilled water was systematically prepared and utilized for all solutions throughout the experimental workflow. Fine mass determinations were conducted on a calibrated high-precision Mechaniki Zakłady Precyzyjnej Gdańsk balance (Poland make, with an experimental limit of sensitivity of ± 0.001 g). Homogeneous fluid densities were determined using a custom-fabricated bicapillary pycnometer having a precise internal capillary diameter of 1 mm. The corresponding absolute and relative flow viscosities were measured using a pre-calibrated Ostwald's viscometer. The entire glass viscometer assembly was completely immersed and vertically secured in an Elite thermostatic water bath system. The water bath temperature variation was strictly regulated and maintained at an elevated constant temperature of 303 K (± 0.1 K) for each sequence of measurements. Sufficient thermal stabilization time was systematically allocated for the solution to achieve absolute thermodynamic equilibrium between the viscometer walls and the water bath environment before any flow runtime data was recorded.

The current work specifically targets the hydrodynamic and viscosity parameters of the substituted 1,3,5-thiadiazine derivative at an initial concentration of 0.1 M, followed by serial dilution down to 0.025 M within a binary solvent mixture of 60% ethanol and 40% water (v/v). To completely avoid the possibility of chemical decomposition or solvent evaporation, all stock and working solutions of the complex drug molecule were prepared freshly immediately prior to the experimental runs. The detailed viscometric measurements, flow counts, and analysis procedures were executed in strict compliance with the established analytical protocols outlined in historical literature [11].

3. Observations and Calculations

The primary experimental flow data collected at 303 K was processed mathematically to define the prevailing molecular fluid interactions in terms of the Falkenhagen and Jones-Dole coefficients. The solution properties were analyzed through the classic Jones-Dole equation [11]:

$$(\eta_r - 1) / \sqrt{C} = A + \beta \sqrt{C}$$

Where η_r represents the computed relative viscosity of the solution, C is the molar concentration of the active solute, A is the Falkenhagen coefficient which measures long-range solute-solute ionic/intermolecular forces, and β is the Jones-Dole coefficient reflecting the strength of solute-solvent interactions. The empirical relative and specific viscosity parameters calculated at 303 K are gathered inside Table 1. The graphical intercept and slope indices representing the mean 'A' value and the ' β ' parameter are explicitly tabulated inside Table 2.

Table 1: Viscosity Measurements and Derived Parameters of Substituted Thiadiazine Derivative at 303 K

Temp T (K)	Conc. C (M)	$\sqrt{C}$	Time t (sec.)	Density $\rho \times 10^3$ ($\text{kg} \cdot \text{cm}^{-3}$)	η_r	$\eta_{sp} = \eta_r - 1$	$(\eta_r - 1)/\sqrt{C}$ (Pa.s)
303	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: Extracted Jones-Dole coefficients A and β from Linear Intercepts at 303 K

System Media (%)	Temperature (K)	Mean Intercept 'A'	Slope β (m)
60% Ethanol-Water	303 K	3.045	-4.5197

4. Result and Discussion

The absolute experimental relative viscosity profile of the system was systematically validated using the baseline fluid density-flow equation: $\eta_r = (D_s \times t_s) / (D_w \times t_w)$. Here, D_s and D_w represent the quantified densities of the target solution and reference double distilled water, while t_s and t_w represent their respective efflux flow durations. The gathered mathematical coordinates were plotted with $(\eta_r - 1)/\sqrt{C}$ on the ordinate axis against $\sqrt{C}$ on the abscissa axis. The regression curves for this multi-heterocyclic system generated a highly linear straight line, enabling the precise extraction of the negative β -coefficient from the slope [1,11].

During the present investigation at 303 K, it was distinctly observed that as the molar concentration of the substituted thiadiazine drug molecule decreases, both the measured solution density and the relative viscosity values experience a smooth, monotonic decrease. This phenomenon is directly attributed to the physical reduction in the number of dense solute molecular aggregates per unit volume upon dilution. Concurrently, the fractional ratio of accessible solvent particles in the primary coordination sphere increases significantly, which is responsible for accelerating the localized solvation and orientation effects around the polar carboxy and heterocyclic centers [4,16].

In modern pharmacokinetics, critical properties such as molecular stability, target absorption index, biological barrier transmission, metabolic routing, and organ excretion profiles are thoroughly evaluated. In pharmacodynamics, drug receptor binding, active mechanism path, and toxicological effects are heavily explored. These primary biophysical properties are found to be directly influenced by fluid viscosity profile variations [3,6]. Absorption, cellular transmission, tissue distribution, metabolism, and absolute excretion are strongly dependent on the underlying viscosity characteristics. The early prediction and physical mapping of these dynamic factors can be successfully achieved via precise viscometric tracking [11]. The tested multi-substituted 1,3,5-thiadiazine compound demonstrates optimized molecular interactions, indicating that this architectural configuration could serve as an excellent broad-spectrum antibiotic or antimicrobial framework. The therapeutic potency and target bioavailability of this core template can be fine-tuned by introducing varied electron-donating or electron-withdrawing substituents across the peripheral ring nodes.

5. Conclusion

The systematic viscometric, densitometry and hydrodynamic profiling of the novel multi-functionalized heterocycle, **2-substitutedimino-6-methylamino-4-[2-isobutoxy-5-(4-methyl-5-carboxy-1,3-thiazol-2-yl)]-phenyl-1,3,5-thiadiazine**, in a 60% (v/v) ethanol–water binary solvent matrix at a controlled thermal state of **303 K** yields the following comprehensive insights: Fundamental Hydrodynamic and Solvation Behavior like Concentration-Dependent Fluidity and Solvent-Cage Expansion, Quantitative Solute–Solvent Interactions (Jones-Dole Interpretation) Like Prevalence of Long-Range Forces and Structure-Breaking Directives, Applied Pharmaceutical and Translational Value, Enhanced Pharmacokinetic Performance and Scaffold Optimization for Novel Antibiotics

These balanced hydrodynamic properties confirm that this functionalized 1,3,5-thiadiazine core serves as a highly stable and predictable molecular scaffold. It offers synthetic chemists an

optimized blueprint for structural modifications aimed at developing next-generation, bio-available antibiotic therapeutics.

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