Gurukul International Multidisciplinary Research Journal (GIMRJ)*with* International Impact Factor 8.357
Peer Reviewed Journal
https://doi.org/10.69758/GIMRJ/2504I5VXIIIP0031

e-ISSN No. 2394-8426
Monthly Issue
APR-2025
Issue–IV, Volume–XIII

SOLVENT EFFECTS ON THE PHYSICO-CHEMICAL BEHAVIOR OF 1-((4-METHOXY-3, 5-DIMETHYLPYRIDIN-2-YL) METHYL)-3-PHENYLTHIOUREA IN 40% ETHANOL-WATER SOLUTIONS

R.D. More[1], P.R. Kute[2*], A.O.Dhokte[2], G.B. Andhale[3], N.D.Chaudhari[4], S.U Shinde[4] R.D.Pathrikar[5]

[1]Department of Chemistry, Siddharth Arts, Commerce and Science College, Jafrabad, Dist. Jalna (MS), India.
[2*]Department of Chemistry, Pratishthan Mahavidyalaya, Paithan, Dist.-Chh. Sambhajinagar, (MS), India.
[3]Department of Chemistry, Shri Shivaji Arts, Commerce and Science College Akot,Maharashtra, India
[4]Department of Chemistry, Pratishthan Mahavidyalaya, Paithan, Dist.-Chh. Sambhajinagar, (MS), India.
[4]Department of Chemistry, Rajaeshi Shahu College Pathri. Dist.-Chh. Sambhajinagar, (MS), India.
[2*]**Email: -** ***kuteprabhakar@gmail.com***

ABSTRACT

Heterocyclic molecules play a crucial role in medicinal chemistry, serving as the structural backbone for many pharmaceutical drugs. Pyridine, a six-membered heteroaromatic ring, is an essential component of various natural compounds, such as vitamins and alkaloids, and its derivatives are widely recognized for their adaptability in drug design. In a recent study conducted in our laboratory, we investigated the viscosity and density of 1-((4-methoxy-3,5-dimethylpyridin-2-yl)methyl)-3-phenylthiourea across different concentrations and temperature conditions. The experimental results provided significant insights into solute-solvent interactions and the influence of solvent dilution. The findings revealed that as temperature increases, relative viscosity decreases, indicating enhanced solvation effects. This research enhances the understanding of the physicochemical properties of pyridine derivatives, supporting the development of more efficient pharmaceutical compounds.

Keywords: Heterocyclic, pyridine, Viscosity, Density, Medicinal, Solute-solvent interactions, 1-((4-methoxy-3,5-dimethylpyridin-2-yl)methyl)-3-phenylthiourea,etc.

INTRODUCTION

Sulfur- and nitrogen-containing heterocyclic compounds are vital for life, playing a key role in numerous biological systems and processes. These molecules exist in various ring structures, with nitrogen and sulfur atoms contributing to their unique chemical properties, reactivity, and biological activity[1,2].The most prevalent heterocyclic compounds feature five- or six-membered rings that include nitrogen (N), oxygen (O), or sulfur (S) as heteroatoms. Among the most well-known simple heterocycles are pyridine, pyrrole, furan, and thiophene. Pyridine consists of a six-membered ring with five carbon atoms and one nitrogen atom. In contrast, pyrrole, furan, and thiophene each have a five-membered ring structure containing four carbon atoms and one heteroatom—nitrogen in pyridine, oxygen in furan, and sulfur in thiophene[3].Their primary commercial significance stems from their transformation into various compounds, particularly dyes and pharmaceuticals. Additionally, pyridine serves as a solvent, a waterproofing agent, a rubber additive, an alcohol denaturant, and a dyeing aid[4].

Pyridine derivatives exhibit a wide range of biological applications. Due to its pharmacological properties, the pyridine heterocycle is extensively utilized in the development of new drugs. Pyridine-based compounds are employed in the formulation of anti-inflammatory, antibacterial, antiviral, anticancer, antioxidant, antihypertensive, antidiabetic, and antimalarial medications. Additionally, their strong affinity for various ions and neutral species makes pyridine derivatives highly effective as chemosensors for detecting different substances[5]. Pyridine nucleus substitutions target a wide spectrum of biological concerns, including microbial infections, viral diseases, and various cancer cells. Pyridine derivatives interact with enzymes, proteins, and DNA, playing a crucial role in addressing diverse biological challenges[6]. The compounds that contain the nucleus of 2-(Chloromethyl)-4-Methoxy-3,5- Dimethylpyridine have gained their own relevance and importance in organic chemistry because of their numerous applications in pharmaceutical, industrial, biological, agricultural, and industrial science[7-9].

The chemistry of substituted thiourea derivatives has attracted attention because of their potential use as reagents for the separation of metal ions and in medicinal chemistry. Thioureas are versatile ligands, able to co-ordinate to metal centers either as neutral ligands, monoanions or dianions. O, N and S donor atoms of thiourea derivatives provide a multitude of bonding possibilities[10-11].

Measurements of viscosity are important. Viscosity is a fundamental property of liquids that defines their resistance to flow. It measures how resistant a liquid is to its layers shifting relative to one another. This resistance is brought on by internal friction that develops as the liquid's molecules move and interact with one another[12].Solute-solvent interactions occur in both aqueous and non-aqueous solutions, and valuable insights into these interactions can be gained through viscometric measurements. The viscosity and solvent interactions of a drug play a crucial role in determining its absorption, distribution, and effects within the human body[13]. These physical parameters are used to understand molecular interactions between the components of the mixture[14].

Considering these aspects, evaluating the viscometric concentration of 1-Ethyl-3-((4-Methoxy-3,5-Dimethylpyridin-2-yl)Methyl)Thiourea across different temperatures is highly significant[10]. Numerous pharmacological and biochemical properties of pyridine derivatives, including antiviral, antibacterial, anti-inflammatory, anesthetic, and mydriatic effects, have been documented in the literature. Additionally, the heterocyclic compound featuring a 1,3,5-dithiazino core is widely utilized in medicine, biochemistry, biotechnology, and pharmaceutical sciences[1,2,]. One of the most important applications of thiourea derivatives is their anti-cancer properties[16-21]. All things considered, this kindof research advances the field of drug science and helps create pharmaceutical goods that are more dependable and effective, which eventually improves patient outcomes[1,2,22].

Water-alcohol mixtures are intriguing systems due to their complex dynamics, influenced by hydrogen bonding and hydrophobic interactions. These mixtures are extensively studied both theoretically and experimentally because of their broad applications as solvents. Various factors, including temperature, molecular size, weight, intermolecular forces, and impurities, can impact

Gurukul International Multidisciplinary Research Journal (GIMRJ)*with* International Impact Factor 8.357
Peer Reviewed Journal
https://doi.org/10.69758/GIMRJ/2504I5VXIIIP0031

e-ISSN No. 2394-8426
Monthly Issue
APR-2025
Issue–IV, Volume–XIII

a liquid's viscosity. Analyzing viscosity helps in understanding the molecular interactions and characteristics of binary and ternary liquid systems, where favorable interactions can lead to increased viscosity. Density plays a crucial role in determining whether a substance will float or sink in a liquid, with materials floating if their density is lower than that of the liquid. Moreover, density is a fundamental physical property used to evaluate various acoustic and physical characteristics, such as surface tension, molar refraction, dipole moment, and boiling point[23].

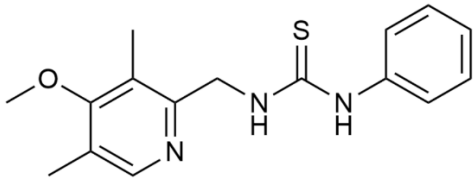

Fig.1. Structure of 1-((4-methoxy-3,5-dimethylpyridin-2-yl)methyl)-3-phenylthiourea

Informati
on is also provided about solute–solute and solute-solvent interactions and structural insight of micelles. Present work generates new hopes in the pharmacological field[24].

EXPERIMENTAL

In this research, all experiments were conducted using double-distilled water and analytical-grade (A.R.) chemicals. The compound weights were accurately measured with a MechanikiZektadyPrecyzyjnej Gdansk balance, ensuring a precision of ±0.001 grams. Liquid viscosity was assessed using anOstwald viscometer, while temperature was maintained at 29°C (±0.1°C) with the help of an Elite thermostatic water bath. Density measurements were performed using a bicapillary tube with an internal diameter of 1 mm. To ensure accuracy, sufficient time was given for both the viscometer and water bath to stabilize thermally before taking measurements.

The viscosity of 1-((4-Methoxy-3,5-Dimethylpyridin-2-yl)Methyl)-3-Phenylthiourea was examined at a 0.1 M concentration in a 40% ethanol-water mixture across different temperatures. Freshly prepared solutions were used for the analysis, and viscometric readings were recorded following standard literature methodologies.

OBSERVATIONS AND CALCULATIONS

Molecular interactions were assessed through the solute's β-coefficient, which was calculated from the experimental data shown in Table 1. The Jones-Dole equation, $C(\eta r - 1) = A + BC$, was utilized to determine values at various temperatures for a 0.1 M concentration. The resulting A and β-coefficients are presented in Table 2.

TABLE No.1

The determination of relative and specific viscosities at different temperatures for a 0.1 m concentration, along with viscosity measurements at constant concentrations.

MEDIUM - 40% ETHANOL-WATER							
Conc.	**Temp. (°C)**	**√C**	**Time (sec.)**	**Density ρx10^3 (kg.cm^{-3})**	**$\acute{\eta}_r$**	**$\acute{\eta}_{sp}=\acute{\eta}_r-1$**	**$(\acute{\eta}_r1)/\sqrt{C}$ (pa$^-$s)**

0.1 M	22	0.314	72	0.8751	0.069642	-0.930358	-2.9629
	25	0.314	64	0.8125	0.064642	-0.935358	-2.9788
	28	0.314	51	0.7943	0.053631	-0.946369	-3.0139
	32	0.314	40	0.7514	0.051694	-0.948306	-3.0200

The results indicate that as the temperature increases, the solution's movement time decreases, along with its density. The lowest relative viscosity was recorded at 32°C, while the highest was observed at 22°C. Between 22°C and 32°C, both relative viscosity and specific viscosity showed a decreasing trend.

TABLE No. – 2

The a and β values for the 40% coefficient are presented with references to 1-((4-methoxy-3, 5-dimethylpyridin-2-yl)methyl)-3-phenylthiourea.

W-E Mixture (%)	Temp° C	Mean "A"	β (Slope "m")
40	27	-2.9939	0.0068

RESULT AND DISCUSSION

The relative viscosity was calculated using the following formula.

η_r= Ds x ts / Dw x tw.

The Jones-Dole equation was utilized to evaluate the relative viscosities,

$(\eta r-1)/\sqrt{C} = A+B\sqrt{C}$

Were,

A = Falkenhagen coefficient

B = Jones-Dole coefficient

C = concentration of solutions

The Jones-Dole coefficient (B) was employed to evaluate the interaction between the solute and solvent, whereas the Falkenhagen coefficient (A) was used to assess the solute-solute interaction. A graph was created plotting $\sqrt{C}$ against $(\eta r-1)/\sqrt{C}$. For each system, the graph showed a straight-line correlation, which allowed for the determination of the β-coefficient value.

CONCLUSIONS

In this study, both density and relative viscosity decrease as temperature rises. This is because the solvation effect strengthens with increased temperature, enhancing the interaction between solute and solvent. Pharmacodynamic and pharmacokinetic studies are essential in scientific research and public health understanding.

A positive β-coefficient of viscosity indicates a strong solute-solvent interaction, often referred to as a "structure former." When hydrogen bonding occurs in a solution, structure formation or breakdown depends on whether the solute-solvent interactions increase or decrease. These changes, driven by variations in density or viscosity, lead to either hydrophilic (structure-breaking) or hydrophobic (structure-forming) characteristics of the solute.

As temperature increases, intermolecular interactions weaken, causing molecules to move more rapidly, which reduces viscosity. This lower viscosity helps molecules or drug particles to move more freely, facilitating their transport and diffusion. This is important for enhancing pharmacodynamics and pharmacokinetics. After drug metabolism, ions move more efficiently toward the target, and solutions with lower viscosity promote better diffusion.

REFERENCES

1. Solanki, A. and Thakur, I. (2007). Indian Journal of Chemistry. 45(B): 517.
2. Saleem, F. (2008). Eur. Pot., CHAPPL. 87: 19.
3. Kunied, T., &Mutsanga, H. (2002). The chemistry of heterocyclic compounds. Palmer (B), 175.
4. Foye, W. O. (2008). Foye's principles of medicinal chemistry. Lippincott williams&wilkins.
5. Mohammad Abu-Taweel G, Ibrahim MM, Khan S, Al-Saidi HM, Alshamrani M, Alhumaydhi FA, Alharthi SS. Medicinal Importance and Chemosensing Applications of Pyridine Derivatives: A Review. Crit Rev Anal Chem. 2022 Jun 20:1-18.
6. Ataf Ali Altaf, Adnan Shahzad, ZarifGul, Nasir Rasool, Amin Badshah, BhajanLal, Ezzat Khan. A Review on the Medicinal Importance of Pyridine Derivatives. Journal of Drug Design and Medicinal Chemistry. Vol. 1, No. 1, 2015, pp. 1-11.
7. Mainil, J. (2013). Escherichia coli virulence factors. Veterinary immunology and immunopathology, 152(1-2), 2-12.
8. Kubicki, M., Dutkiewicz, G., Jasinski, J. P., Butcher, R. J., Siddegowda, M. S., Yathirajan, H. S., &Narayana, B. (2012). Ordering of the Water Molecule in the Crystal Structure of 2-[3-Methyl-4-(2, 2, 2-Trifluoroethoxy)-2-Pyridinyl] Methylthio-1H-Benzimidazole Hydrate (LansoprazoleSulphide Hydrate). Journal of Chemical Crystallography, 42, 245-250.
9. Vakil, N. B., Shaker, R., Johnson, D. A., Kovacs, T., Baerg, R. D., Hwang, C., ...& Hamelin, B. (2001). The new proton pump inhibitor esomeprazole is effective as a maintenance therapy in GERD patients with healed erosive oesophagitis: a 6-month, randomized, double-blind, placebo-controlled study of efficacy and safety. Alimentary pharmacology & therapeutics, 15(7), 927-935.
10. Kapoor, P.; Fahmi, N.; Singh, R.V. Microwave assisted synthesis, spectroscopic, electrochemical and DNA cleavage studies of lanthanide(III) complexes with coumarin based imines. Spectrochim. ActaA Mol. Biomol. Spectrosc., 2011, 83(1), 74-81. [http://dx.doi.org/10.1016/j.saa.2011.07.054] [PMID: 21903455]
11. Mathur, N.; Dobhal, M.P.; Jain, N. A comparative antibacterial analysis of substituted benzothiazole and substituted phenylthiourea complexes with copper metal. Int. J. Green Herb. Chem., 2017, 7(1), 1-6.
12. Bhat, B.A. Dhar, K.L. Saxena, A.K. and Shanmugavel, M. (2005). Bio org. and Med. Chem. 15(3): 177-180.
13. Vibhute, Y.B. and Basser, M.A. (2003). Ind. J. of Chem. 42(B): 202-205.
14. Mathur, N.; Bargotya, S. Evaluation of novel N/S containing heterocyclic metal complexes as biologically potent agents. Res. J. Chem. Sci., 2018, 8(4), 30-34.

15. Jakhar A. and Makrand J.K., J. Chem. Res., 4(3), 2010, 238-240.
16. Sanmartín, C., Echeverría, M., Mendívil, B., Cordeu, L., Cubedo, E., García-Foncillas, J., ...&Palop, J. A. (2005). Synthesis and biological evaluation of new symmetrical derivatives as cytotoxic agents and apoptosis inducers. Bioorganic & medicinal chemistry, 13(6), 2031-2044.
17. Hallur, G., Jimeno, A., Dalrymple, S., Zhu, T., Jung, M. K., Hidalgo, M., ...& Khan, S. R. (2006). Benzoylphenylurea sulfur analogues with potent antitumor activity. Journal of medicinal chemistry, 49(7), 2357-2360.
18. Moreau, E., Fortin, S., Desjardins, M., Rousseau, J. L., Petitclerc, É.,& René, C. (2005). Optimized N-phenyl-N′-(2-chloroethyl) ureas as potential antineoplastic agents: Synthesis and growth inhibition activity. Bioorganic & medicinal chemistry, 13(24), 6703-6712.
19. Manjula, S. N., Noolvi, N. M., Parihar, K. V., Reddy, S. M., Ramani, V., Gadad, A. K., ...& Rao, C. M. (2009). Synthesis and antitumor activity of optically active thiourea and their 2-aminobenzothiazole derivatives: A novel class of anticancer agents. European Journal of Medicinal Chemistry, 44(7), 2923-2929.
20. Esteves-Souza, A., Pissinate, K., da GraçaNascimento, M., Grynberg, N. F., &Echevarria, A. (2006). Synthesis, cytotoxicity, and DNA-topoisomerase inhibitory activity of new asymmetric ureas and thioureas. Bioorganic & medicinal chemistry, 14(2), 492-499.
21. Choi, S. J., Park, H. J., Lee, S. K., Kim, S. W., Han, G., &Choo, H. Y. P. (2006). Solid phase combinatorial synthesis of benzothiazoles and evaluation of topoisomerase II inhibitory activity. Bioorganic & medicinal chemistry, 14(4), 1229-1235.
22. Zhang, L.X. Zhang, A.J. Hu, M.L. and Lei, X.X. (2003). ActaChim.Sinica. 61(6): 917.
23. Padmanaban, R.; Gayathri, A.; Gopalan, A.I.; Lee, D.-E.; Venkatramanan, K. Comparative Evaluation of Viscosity, Density and Ultrasonic Velocity Using Deviation Modelling for Ethyl-Alcohol Based Binary Mixtures. Appl. Sci. 2023, 13, 7475.
24. Bargotya, S.; Mathur, N.; Sharma, A.K. Antimicrobial & DNA cleavage studies of heterocyclic metal complexes"ISBN978-613-8-34627-2; LAP LAMBERT Academic Publishing: Germany, 2018.