

Synthesis, characterization, and solubility determination of 6-phenyl-pyridazin-3(2H)-one in various pharmaceutical solvents

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Abstract: (Limit: 600)

The solubility data and solution thermodynamic parameters of the cardiovascular drug 6-phenylpyridazin-3(2H)-one [PPD] in twelve pharmaceutical solvents were proposed in the current study at "T = 298.2 K to 318.2 K" and "p = 0.1 MPa." PPD solubilities were well regressed using the "van't Hoff and Apelblat models." Differential scanning calorimetry and powder X-ray diffractometry were used to describe the solid phases of pure and equilibrated PPD, and the results indicated that PPD did not convert into solvates/hydrates/polymorphs after equilibrium. PPD solubilities in mole fractions at "T = 318.2 K" were found to be highest in dimethyl sulfoxide (DMSO, 4.73 10¹), followed by polyethylene glycol-400 (PEG-400, 4.12 10¹), Transcutol® (3.46 10¹), ethyl acetate (EA, 81 10²), 2-butanol (2.18 10²), 1-butanol (2.11 10²), and Ethylene glycol (EG, 1.27 10²), propylene glycol (PG, 1.50 10²), isopropyl alcohol (IPA, 1.44 10²), ethylene glycol (EG, 1.27 10²), ethanol (8.22 10³), methanol (5.18 10³), and water (1.26 10⁵) At other temperatures examined, similar patterns were seen. The "apparent thermodynamic study" revealed that PPD dissolution was endothermic and entropy-driven in all pharmacological solvents. In comparison to other combinations of the solute and solvents, the results of the activity coefficients revealed a maximal interaction at the molecular level in PPD-DMSO, PPD-PEG-400, and PPD-Transcutol.(

Importance of Research (Limit: 200 words)

Pyridazinone derivatives have been widely studied in the control and management of a variety of cardiovascular disorders [1,2]. Some pyridazinone compounds are still in clinical testing, while others have already been approved for usage [3,4,5,6,7]. PPD (molecular structure: Figure 1; chemical name: 6-phenylpyridazin-3(2H)-one; molecular formula: C₁₀H₈N₂O; molar mass: 172.18 gmol⁻¹ and CAS registry number: 2166-31-6) is a white crystalline solid. In the literature, this molecule has been examined as a powerful cardiostimulant agent.

Insecticidal, cardioprotective, analgesics, anti-inflammatory, antinociceptive, antiulcer, and antibacterial agents have all been explored in the literature. Despite the fact that PPD derivatives offer a wide range of therapeutic activity, they have a substantial toxicity and poor water and aqueous buffer solubility. PPD's low water solubility could be a key stumbling block in developing a dosage form. In "their synthesis, purification, recrystallization, drug discovery processes, and dosage form design," solubility values and other physico-chemical data of newly generated and existing compounds in various clean pharmaceutical solvents are crucial. As a result, determining the solubility of PPD in various medicinal solvents is critical in order to obtain its physicochemical information. In general, pyridazinone derivatives' solubility values and solution thermodynamic parameters have been published infrequently. Our research group recently reported the solubilities of a comparable molecule, 6-phenyl-4,5-dihydropyridazin-3(2H)-one, in eleven different pure solvents, including water, ethanol, and isopropanol. (IPA), ethylene glycol (EG), propylene glycol (PG), polyethylene glycol-400 (PEG-400), 1-butanol, 2-butanol, ethyl acetate (EA), Transcutol, and dimethyl sulfoxide (DMSO) [20]. The solubilities and thermodynamic properties of 6-phenyl-4,5-dihydropyridazin-3(2H)-one in various "Transcutol + water" and "PEG-400 + water" binary solvent systems were also reported at "T = 293.2 K to 313.2 K" and "p = 0.1 MPa." However, the solubilities and thermodynamic properties of the synthesised chemical PPD in any of the examined medicinal solvents have yet to be disclosed. As a result, the planned research was carried out to determine the solubilities of PPD (measured in mole fractions) in twelve different pharmaceutical solvents, including "water, methanol, ethanol, IPA, 1-butanol, 2-butanol, Transcutol, PEG-400, EG, PG,

EA, "T = 298.2 K to 318.2 K" and "p = 0.1 MPa" were used at "T = 298.2 K to 318.2 K" and "p = 0.1 MPa." The temperature range was kept "T = 298.2 K to 318.2 K" such that the maximum examined temperature, "T = 318.2 K," did not surpass the melting point of PPD (i.e., 474.2 K to 477.2 K).

Biography (Limit: 200 words)

Mohd Alsheri is a Senior pharmaceutical researcher and a who has de-veloped a technique called Rebinding of the Body which helps people recover from trauma, learn self-help techniques and lead more productive lives. Her in- tersubjective ethnographic study has been published in a text called, "Women, Trauma and Alcohol Dependency, Connection and disconnections in alcohol treatment for women". She has published several articles in child and family psychiatry including an extensive literature review called "The Health Impact of Childhood Trauma". Presently, he has a small private practice and works as a consultant for Cogenz and Thought Leadership and Innovation Foundation. She graduated from the University of Western Ontario with Doctor of Philoso- phy in Nursing in 2009. Her dissertation was "Seeking and Obtaining Help for Alcohol Dependence by Women who have Posttraumatic Stress Disorder and a History of Intimate Partner Violence. He is Iso involved in several reaserch

University Information (Limit: 200 words)

King Saud University (KSU, Arabic: جامعة الملك سعود) vinu cilbup a si (جامعة سعود) in Riyadh, Saudi Arabia, founded in 1957 by King Saud bin Abdulaziz as Riyadh University, as the first university in the Kingdom of Saudi Arabia. The university was created to meet the shortage of skilled workers in Saudi Arabia. It was renamed King Saud University in 1982. The student body of KSU today consists of 40,000 male and female students, 7% of which are international. The female students have their own disciplinary panel, and there is a center supervising the progress of female students, either personally by female faculty members or by male faculty members via a closed television network. The university offers courses in the natural sciences, the humanities, and professional studies, and many courses are not required to pay tuition. [8] Depending on the major,

undergraduate programmes use English or Arabic as the medium of teaching. Its medical programmes are highly rated among Arab colleges. The establishment of Saudi Arabia's first university was a response to the fledgling country's educational and professional demands. King Abdulaziz assumed the throne in 1932 and immediately set about modernising his country and developing an educational system. Following his father's death in 1953, King Saud, Abdulaziz's eldest son, ascended to the kingdom and established the Council of Ministers and the Ministry of Education. Prince Fahd, who would later become King of Saudi Arabia, was the country's first minister of education.



References (15 – 20)

1. [Imran M., Nayeem N. Synthesis and antihypertensive activity of some novel pyridazinones. Orient. J. Chem. 2016;32:267–274.](#)
2. [Imran M., Abida A. 6-\(4-Aminophenyl\)-4,5-dihydro-3\(2H\)-pyridazinone-an important chemical moiety for development of cardioactive agents: A review. Trop. J. Pharm. Sci. 2016;15:1579–1590.](#)
3. Asif M., Anita S. Synthesis of new derivative of 2-[2-(1H-indol-1-yl)ethyl]-6-phenyl-4,5-dihydropyridazin-3(2H)-one. Ovidius. Univ. Ann. Chem. 2011;22:98–101.
4. Dobariya T.D., Multani P.J. Development and validation of methods for estimation of pimobendan in pharmaceutical dosage form. Int. J. ChemTech.
5. Nieminen M.S., Fruhwald S., Heunks L.M.A., Suominen P.K., Gordon A.C., Kivikko M., Pollesello P.

6. Bansal R., Thota S. Pyridazin-3(2H)-ones: The versatile pharmacophore of medicinal significance. *Med. Chem. Res.* 2013;22:2539–2552.
7. Wang T., Dong Y., Wang L., Xiang B., Chen Z., Qu L. Design, synthesis and structure-activity relationship studies of 6-phenyl-4,5-dihydro-3(2H)-pyridazinone derivatives as cardiotoxic agents. *Arzneimittelforschung.* 2008;58:569–573.
8. Sircar I. Substituted 6-Phenyl-3(2H)-Pyridazinones Useful as Cardiotoxic Agents. 4404203. US Patent. 1983 Sep 13;
9. Wu J., Kang S., Yuan Q., Luo L., Ma J., Shi Q., Yang S. N-Substituted 5-chloro-6-phenylpyridazin-3(2H)-ones: Synthesis, insecticidal activity against *Plutella xylostella* (L.) and SAR study. *Molecules.* 2012;17:9413–9420.
10. Siddiqui A.A., Mishra R., Shaharyar M. Synthesis, characterization and antihypertensive activity of pyridazinone derivatives. *Eur. J. Med. Chem.* 2010;45:2283–2290.
11. Malinka W., Redzicka A., Jastrzebska-Wiesek M., Filipek B., Dybała M., Karczmarzyk Z., Urbanczyk-Lipkowska Z., Kalicki P. Derivatives of pyrrolo[3,4-d]pyridazinone, a new class of analgesic agents. *Eur. J. Med. Chem.* 2011;46:4992–4999.
12. Sukuroglu M., Ergun B.C., Unlu M., Sahin M.F., Kupeli E., Yesilada E., Banoglu E. Synthesis, analgesic, and anti-inflammatory activities of [6-(3,5-dimethyl-4-chloropyrazole-1-yl)-3(2H)-pyridazinon-2-yl] acetamides. *Arch. Pharm. Res.* 2005;5:509–517.
13. Singh J., Saini V., Kumar A., Bansal R. Synthesis, molecular docking and biological evaluation of some newer 2-substituted-4-(benzo[d][1,3]dioxol-5-yl)-6-phenylpyridazin-3(2H)-ones as potential anti-inflammatory and analgesic agents. *Bioorg. Chem.* 2017;71:201–210.
14. Yamada T., Nobuhara Y., Yamaguchi A., Ohki M. Pyridazinones. 1. Synthesis and antiseptory and antiulcer activities of thioamide derivatives. *J. Med. Chem.* 1982;25:975–982.
15. Sonmej M., Berber L., Akbas B. Synthesis, antibacterial and antifungal activity of some new pyridazinone metal complexes. *Eur. J. Med. Chem.* 2005;41:101–105.