REPORT OF THE PROJECT PROPOSAL SANCTIONED UNDER RUSA 2.0

TITLE: Physicochemical studies of some drugs with deep eutectic solvents (DESs) in aqueous medium

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My seed grant assistance for formulation of research project proposals under RUSA 2.0 titled **"Physicochemical studies of some drugs with deep eutectic solvents (DESs) in aqueous medium"** amounting to Rs. 1 lakh has the following impact outcomes:

1) The RUSA 2.0 seed proposal was the primary research proposal, which helped me to prepare a complete Major DST Research Proposal.
2) The Research Methodology used in the above titled project has helped me a lot in preparing the DST Proposal titled, **"Effect of deep eutectic solvents on the thermodynamics and DFT properties of some drugs in aqueous media"**, which was submitted to the DST EMR Scheme last year. But, unfortunately the project was not recommended for funding.
3) Now, again I have modified the not recommended DST Proposal and whenever next DST Research Project notification comes, I will submit the Research Proposal for funding.
4) The details of work done and published work under RUSA 2.0 are given below:
   (a) Physicochemical properties of non-steroidal anti-inflammatory drugs (NSAIDs), salicylic acid and salicylamide, in choline chloride and urea based deep eutectic solvent (DES), reline, have been determined at temperature range from 288.15 to 313.15 K. In this work, physicochemical parameters such as apparent molar volume apparent molar isentropic compressibility and relative viscosities are studied for the said NSAIDs in water and aqueous reline solutions. The results indicate that in all cases, the solute–solvent interactions increases with increasing concentration of DES as well as temperature. In addition, the values of viscosity B-coefficient are determined by analyzing Jones-Dole equation. Hepler's constant and limiting apparent molar expansivity are deduced as well. Finally, the intermolecular interactions are evaluated by making plots among various

parameters and discussed in terms of competing interactions present in the ternary systems **(Journal of Molecular Liquids, 2021, 334, Article No. 116500, ISSN: 0167-7322 (Print) 1873-3166 (Online), Peer Reviewed, Abstracted, Indexed, Impact factor: 6.165).**

(b) A comprehensive examination of thermophysical properties of semicarbazide hydrochloride and domiphen bromide in water and aqueous maline solutions, (maline; a deep eutectic solvent (DES) made by mixing choline chloride and malonic acid in 1:2 mol ratio), have been done by the combination of ultrasonic, volumetric, viscometric and thermodynamic methods at the temperature range from 293.15 to 318.15 K. Exploration of molecular interactions through the procured thermophysical properties is very important because it provides an insight into the forces that are operating in the liquid mixtures. In the present study, thermophysical parameters such as apparent molar volume (V_ϕ), apparent molar isentropic compressibility ($K_{\phi,s}$), viscosity coefficients, hepler's constant etc are studied for the above drugs in water and aqueous maline solutions. The results revealed the dominance of solute-solvent interactions in the studied systems which were found to escalate with elevation in temperature and with the concentration of maline. The results are discussed in terms of hydrophilic-hydrophilic and hydrophilic-hydrophobic interactions in these systems along with the structure breaking/making ability of the drugs. The co-sphere overlap model has been used to interpret the positive transfer values **(Under Review in Journal of Chemical and Engineering Data, 2022).**

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Effect of choline chloride and urea based deep eutectic solvent on the physicochemical properties of salicylic acid and salicylamide at T = (288.15 to 313.15) K

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ABSTRACT

Physicochemical properties of non-steroidal anti-inflammatory drugs (NSAIDs), salicylic acid and salicylamide, in choline chloride and urea based deep eutectic solvent (DES), reline, have been determined at temperature range from 288.15 to 313.15 K. In this work, physicochemical parameters such as apparent molar volume (V_ϕ), apparent molar isentropic compressibility ($K_{\phi,s}$) and relative viscosities (η_r) are studied for the said NSAIDs in water and aqueous reline solutions. The results indicate that in all cases, the solute–solvent interactions increases with increasing concentration of DES as well as temperature. In addition, the values of viscosity *B*-coefficient are determined by analyzing Jones-Dole equation. Hepler's constant ($\partial^2 V_\phi^0/\partial T^2$) and limiting apparent molar expansivity (E_ϕ^0) are deduced as well. Finally, the intermolecular interactions are evaluated by making plots among various parameters and discussed in terms of competing interactions present in the ternary systems.

1. Introduction

Drug solubility and permeability has been a major reason for inadequate pharmacokinetics of the active pharmaceutical ingredient (API) [1,2]. So developing a system to overcome this with simultaneously least environmental effect has been a challenge from decades. In this pursuit, deep eutectic solvents (DESs) came as potent and alternative green solvents as compared to conventional ionic liquids (ILs) and organic solvents [3–5]. There have been some concerns with the use of ILs like their high cost, synthesis, purification requirements and toxicity. These limitations reduced to some extent by DESs, which are prepared from a mixture of hydrogen bond acceptor and hydrogen bond donor components whereas, a particular cast of anion and cation is responsible for the formation of ionic liquids [6,7]. Decrease in lattice energy by hydrogen bonding and charge delocalization are the sole reasons for the depression in the melting point of the DES mixture as compared to that of individual components [8,9]. DESs contain large, non-symmetric ions that have low lattice energy and therefore have lesser melting point. This work is preceded with reline (a DES composed of choline chloride and urea in the mol ratio of 1:2). Both the constituent components are cheap, biodegradable and nonpoisonous. Choline chloride is an essential component of B-vitamin and is found in many plant and animal sources, eggs, liver, fish, soybeans, and wheat germ [10]. It is used at large scale as nutritional additives in animal feed [11,12]. Whereas, urea is the most commonly used nitrogenous fertilizer and is vital for the metabolism of nitrogen-containing compounds in living beings.

Interaction of drugs with water and aqueous reline solutions as a function of temperature gives crucial information about absorption and transportation of these NSAIDs across biological membrane. Besides, physicochemical parameters and configuration of drugs molecules plays vital role in predicting binding trends between drugs and solvent systems. Both the NSAIDs (salicylic acid and salicylamide) have two polar functional groups; however, the hydrophobic characters of the aromatic ring lower their polarity and hence are less soluble in water. And that's why; the impact of hydrophobic part becomes important in analyzing the relationship between molecular structure and thermodynamic properties.

In this work, the physicochemical parameters of two NSAIDs (salicylic acid and salicylamide) have been determined. Both these NSAIDs exhibit various anodyne, anti-inflammatory, febrifuge and platelet cessation properties [13]. However; these have severe implications like gastrointestinal toxicities and hemorrhage due to suppression of prostaglandin production. Since, it has been reported that DESs can be used in medicinal fields thereby increasing their solubility, skin permeation and absorption of drugs, the said NSAIDs are interacted with DES [14,15]. Also, both the NSAIDs

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