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Title : SOLUBILITY ENHANCEMENT OF STATIN-BASED MOLECULES BY ARGININE: THERMODYNAMICS, SOLUTE-SOLVENT INTERACTION AND SOLID STATE CHARACTERIZATION

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Categorized as a Biopharmaceutics Classification System (BCS) Class II drugs, statins exhibit low aqueous solubility and bioavailability thus presenting an obstacle and great challenge to formulation researchers. As a consequence, abundant studies are available in regard to the solubility enhancement of statins but very few actually describe this phenomenon in terms of thermodynamics and the solute solvent interaction. The present study aimed to elucidate the solute-solvent and solute-cosolute interactions, solid state characteristics, wetting behaviour, surface energy and thermodynamic parameters that bolstered the solubility of simvastatin (SMV) and atorvastatin (ATV) in the presence of ARG. First, the solubility of SMV and ATV in 0.01, 0.02, 0.04, 0.09, 0.18, 0.36 and 0.73 mol dm^{-3} arginine (ARG) in water solutions was determined. These solutions were subjected to conductometric, volumetric, viscometric, acoustic and refractometric measurements at temperatures (T) of 298.15, 303.15, 308.15 and 313.15 K. Results indicated that there was a massive increase of SMV and ATV solubility in the presence of ARG as a cosolute. Based on physical characteristics, a strong solute-solvent and solute-cosolute interaction has occurred in the SMV-ARG and ATV-ARG binary solution mixture. Furthermore, results of spectral analysis complemented the thermophysical findings which proved that SMV-ARG and ATV-ARG complexes were formed as a result of an interaction between the molecules. The second part of the study looked at how easy SMV and ATV formed a complex with ARG. The complexes were characterized based on their physicochemical properties and subjected to solubility and *in vitro* dissolution study. SMV-ARG and ATV-ARG complexes enhanced solubility by 12,000 and 25-fold respectively, as compared to the pure drug. Additionally, an increase in the dissolution rate for both acidic and alkaline dissolution media was also observed. Results from physicochemical properties revealed molecular interaction between SMV or ATV and ARG during the complexation formation. Finally, the study on the influence of various ratios of statin-arginine complexes on the surface wettability and energy was carried out. Results from this study indicate that a high ratio of ARG in the statin arginine complexes leads to a reduction in the contact angle and an increase in the work of adhesion and surface energy values.