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Therapeutic Deep Eutectic Solvents As Solubility Enhancers For Different Active Pharmaceutical Ingredients

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Abstract:

In recent years, deep eutectic solvents (DES) have emerged as a sustainable alternative to ionic liquids mainly due to their lower production costs and higher biodegradability/ biocompatibility. DES are defined as a mixture of organic compounds with a melting point significantly lower than that of either individual component. DES constituted by bioactive substances or active pharmaceutical ingredients (APIs), which we define as therapeutic deep eutectic solvents (THEDES), are a promising source for several pharmaceutical and biomedical applications due to their increased ability to dissolve model drugs by increasing their solubility, permeation and absorption. In this work, we synthesized several THEDES based in choline chloride (ChCl) or menthol conjugated with three different APIs: acetylsalicylic acid (AA), benzoic acid (BA) and phenylacetic acid (PA) with different molar ratios (ChCl:AA 1:1, ChCl:PA 1:1, Menthol:AA 3:1, Menthol:BA 3:1, Menthol:PA 2:1, Menthol:PA 3:1). All THEDES produced were characterized by differential scanning calorimetry and polarized optical microscopy. Dissolution studies performed in PBS for 24 hours shown that THEDES increased significantly the dissolution of all APIs studied compared to the control (APIs only). This increased solubility was even more noticeable for the cases of THEDES with menthol in their composition. Antibacterial activity was assessed using *E. coli* and *B. subtilis* as gram negative and gram positive model organisms. Results show that all the THEDES had antibacterial activity. In overall, our results suggest the great promise of using THEDES as solubility enhancers in the development of novel and more effective drug delivery systems.

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