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Solid State Characterization of Acyclovir-Nicotinamide Binary Systems using Solvent Evaporation Technique

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ABSTRACT:
Objective of the study is to characterize acyclovir-nicotinamide binary systems (AN). Methods of recrystallization was solvent evaporation in equimolar ratio between acyclovir and nicotinamide using ethanol and methanol. The binary systems were characterized by polarization microscope, Differential Scanning Calorimetry (DSC) and Powder X-Ray Diffraction (PXRD). Physical characterization showed that AN binary systems have unique crystal habit in microscopic. A new endothermic peak appears at 123.69°C. The PXRD patterns of AN binary system after recrystallization are different from pure components which specific peak was found on 2θ = 11.27° (AN in ethanol); 21.05° (AN in methanol).

KEY WORDS: Acyclovir, nicotinamide, binary systems, solvent evaporation, ethanol, methanol.

INTRODUCTION:
On average, about a decade of research and development is expended in the discovery and commercialization of a new pharmaceutical product. The molecular structure of the active pharmaceutical ingredient (API) of a drug substance is selected to optimize therapeutic properties, selecting the physical form of an API represents a strategic opportunity for optimizing its physical properties as solubility, dissolution, hygroscopicity, physical stability, and chemical stability. Attempting to find a solid with the desired properties and manufacturability, companies spend significant effort looking for polymorphs, salts and cocrystal of their APIs (Active Pharmaceutical Ingredients)1-2,3,4.
Cocrystal is a homogenous crystalline materials composed of a neutral target and a neutral coformer held together through non covalent bonds. For pharmaceutical applications it is essential that the coformers have GRAS status. The physicochemical properties of API can be modified while the intrinsic activities of these drug molecules remain the same. From the thermodynamic point of view, pharmaceutical cocrystals are stable and high energy forms. Therefore, they can be effective on solubility and dissolution rate of the drug. The strategy involves drug-coformer combinations that have the potential of forming energetically and structurally robust interactions3,5-7. Pharmaceutical cocrystals often rely on hydrogen bonded assemblies between an API and coformer with well-defined stoichiometries. For a target API, we are interested in coformers with functional groups that can interact (i.e., form H-bonds) with the functional groups on the API. Common functional groups, such as carboxylic acids, amines and alcohols are typically found to interact with one another in cocrystals3,6,7.
Acyclovir, a guanines analogue antiviral drug with a solubility of 1.62 mg/mL. Due to its poor solubility and permeability, the oral bioavailability of acyclovir attains just 15-30%.8,9,10,11,12,13
Different methods have been used to produce cocrystals: solution crystallization, solid state and solvent drop grinding, and crystallization from melt. For scale up purposes, solid state crystallization is the most popular.3,14,15

MATERIALS AND METHOD:
Materials:
Acyclovir and nicotinamide was obtained from Sigma-Aldrich (USA). Ethanol and methanol were purchased from Merck Chemicals (Germany) without any purification.

Preparation of binary system of AN using solvent evaporation technique:
Acyclovir and nicotinamide carefully weighed equimolar. Each component was dissolved in solvent separately. The two solutions were mixed and stirred for a few minutes. Equimolar solution of both components was evaporated at room temperature for 48 hours. The obtained of solid binary system stored in a desiccator under vacuum.

Characterization by polarized microscope:
One to two mg of physical mixture between acyclovir and nicotinamide was placed on object glass. A drop of ethanol was added to each physical mixture until dissolved and allowed to recrystallize. Recrystallization process was observed under a polarizing microscope. The microscopic images were recorded with an Olympus BX-51 digital color camera attached to the Olympus BX-51 polarized microscope.

Thermal Analysis by DSC:
Differential Scanning Calorimetry (DSC) was performed using Mettler Toledo. About four mg of each sample was placed in crimped sample pans. The sample was heated from 30°C to 300°C at heating rate of 10°C/min under nitrogen purged.

Characterization by PXRD:
Powder X-ray diffractometer (Philips X'Pert diffractometer) analysis was performed at room temperature. Condition of measurement was set as follows : Cu metal target, Ka filter, voltage 40kV, 40 mA. The analysis was performed on the range of 2θ of 5-45°. Sample was placed on the sample holder and flated to prevent particle orientation during preparation.
RESULTS AND DISCUSSION:
The eutectic crystallization process of AN binary systems observed under polarized microscope. Polarizing light microscopy is particularly useful for studying the optical properties of crystals. When crossed polarized light passes through an anisotropic crystal, the crystal will show bright interference colors, as long as it is in an extinction position or aligned on an optic axis. As shown in Fig. 1, AN binary systems have unique crystal habit.

![Diagram](image)

Melting is a first order process that can be observed in the form of an endothermic peak in DSC curves. Recall that unlike the peak temperature, the onset temperature of melting will be independent of the DSC heating rate.

![Diagram](image)

DSC thermogram showed endothermic peak of acetylsalicylic solids at 251.08°C, while the nicotinamide at 128.13°C (Fig. 2). DSC thermogram of physical mixture equivalent of AN showed endothermic peak at 122.01°C. While DSC thermogram of AN binary systems exhibited endothermic peak at 123.69°C. This indicated that both the solid components transform into new crystalline phase of acetylsalicylic-nicotinamide. The difference of melting point of AN binary systems from starting component is indicated that eutectic was formed.

Since each compound produces its own characteristic powder pattern owing to the unique crystallography of its structure, powder x-ray diffraction (PXRD) is clearly the most powerful and fundamental tool for a specification of the polymorphic identity of an analyte.

Figure 3 shows the X-ray powder diffractogram of AN binary systems, compared to the single component and physical mixture of both components without treatment. PXRD pattern of co-crystall from the pattern of acetylsalicylic, nicotinamide, and physical mixture of AN. AN binary systems pattern showed interference peaks typical at 20 : 11.27° (in ethanol) and 21.05°(in methanol).

![Diagram](image)

CONCLUSION:
Binary systems of acetylsalicylic-nicotinamide were formed using solvent evaporation technique in ethanol and methanol as solvent. The system have been characterized by polarized microscopy DSC and PXRD.

REFERENCES:

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Fig. 1 : Crystal images obtained by polarized microscope of A) acyclovir, B) nicotinamide, C) Contact zone of AN binary systems

Melting is a first order process that can be observed in the form of an endothermic peak in DSC curves. Recall that unlike the peak temperature, the onset temperature of melting will be independent of the DSC heating rate[16].
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