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Hafsa, Asfa, Nuha Rasheed, Abdul Saleem Mohammad

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Safa Mohammed Sadiq, Amtul Kareem, Nuha Rasheed, Abdul Saleem Mohammad

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Solid State Characterization of Acyclovir-Nicotinamide Binary Systems using Solvent Evaporation Technique (AbstractView.aspx?PID=2017-7-1-6)

Agnes Nuniek Winantari1, Dwi Setyawan, Siswandono, Sundani Nurono Soewandhi

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Formulation and Characterization of fast Dissolving tablets of Perindopril (AbstractView.aspx?PID=2017-7-1-8)

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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 cocrystallization was solvent evaporation in equimolar ratio between acyclovir an 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 cocrystallization are different from pure components which specific peak was found on $2\theta = 11.27^0$ (AN in ethanol); 21.05^0 (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 activ 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 suc physical properties as solubility, dissolution, hygroscopicity, physical stability, and chemical stability. Attempting to find a solid with the desired properties and manufacturability, companie spend significant effort looking for polymorphs, salts and cocrystal of their API's (Active Pharmaceutical Ingredient)[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 tha the coformers have GRAS status. The physicochemical properties of API's can be modified while the intrinsic activities of these drug molecules remain the same. From the thermodynamic poir of view, pharmaceutical cocrystals are stable and high energy forms. Therefore, they can have impact on solubility and dissolution rate of the drug. The strategy involves drug-coforme combinations that have the potential of forming energetically and structurally robust interactions[3,5,6,7]. Pharmaceutical cocrystals often rely on hydrogen bonded assemblies between an API an 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 AP Common functional groups, such as carboxylic acids, amides and alcohols are typically found to interact with one another in cocrystals[3,8,9].

Acyclovir, a guanosine 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% [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, solutio 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 compound was dissolved in solvent separately. The two solutions were mixed and stirred for a few minutes. Equimolar solutio of both components was evaporated at room temperature for 48 hours. The obtained of solid binary system stored in a dessicator under vacuum.

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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 t recrystallize. Recrystallization process was observed under a polarizing microscope. The microscopic images were recorded with an Olympus SC-30 digital color camera attached to th Olympus BX-50 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 pan. The sample was heated from 30^0 to 300^0C at heating rate of 10^0C/min under nitrogen purged.

Characterization by PXRD:

Powder X-ray diffraction (Phillips X'Pert diffractometer) analysis was performed at room temperature. Condition of measurement was set as follows : Cu metal target, Kα filter, voltage c 40kV, 40 mA. The analysis was performed on the range of 2 theta of $5\text{-}40^0$. Sample was placed on the sample holder and flatted to prevent particle orientation during preparation.

RESULTS AND DISCUSSION:

The cocrystallization process of AN binary systems observed under polarized microscope. Polarizing light microscopy is particularly useful for studying the optical properties of crystals. Whe crossed polarized light passes through an anisotropic crystal, the crystal will show bright interference colors, as long as it is not in an extiction position or aligned on an optic axis [16]. As show in Fig. 1, AN binary systems have unique crystal habit.

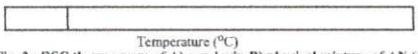
A

B

C

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 b independent of the DSC heating rate[16].



Temperature (°C)

Fig. 2 : DSC thermogram of A) acyclovir, B) physical mixture of AN (1:1), C) nicotinamide , D) AN binary systems (1:1) in ethanol, E) AN binary systems (1:1) in methanol

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

Since every 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 an fundamental tool for a specification of the polymorphic identity of an analyte[17].

Figure 3 shows the X-ray powder difractogram of AN binary systems, compared to the single component and physical mixture of both components without treatment. PXRD pattern of cocryst different from the pattern of acyclovir, nicotinamide, and physical mixture of AN. AN binary systems pattern showed interference peaks typical at 2θ : 11.27° (in ethanol) and 21.05°(i methanol).

(a) (b)

Fig. 3 : PXRD difractogram of AN binary systems (a) in ethanol and (b) in methanol : A) AN binary systems (1:1), B) physical mixture of AN (1:1), C) nicotinamide , D) acyclovir

CONCLUSION:

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

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RESEARCH ARTICLE

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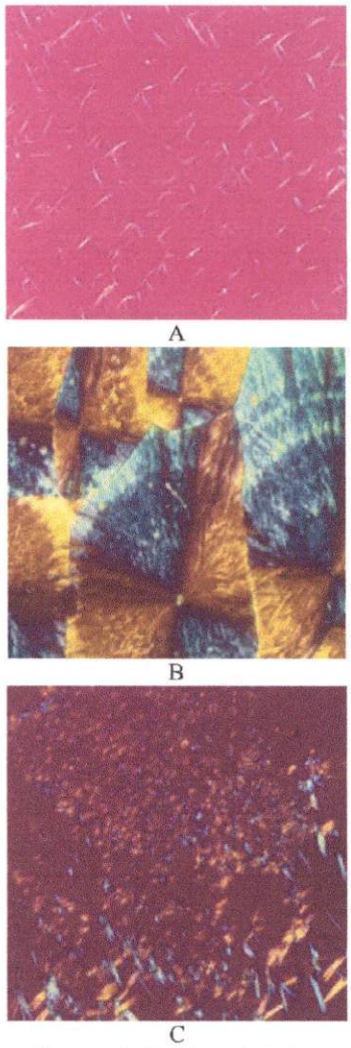

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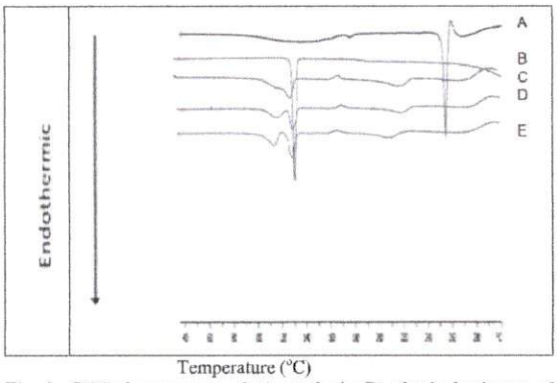

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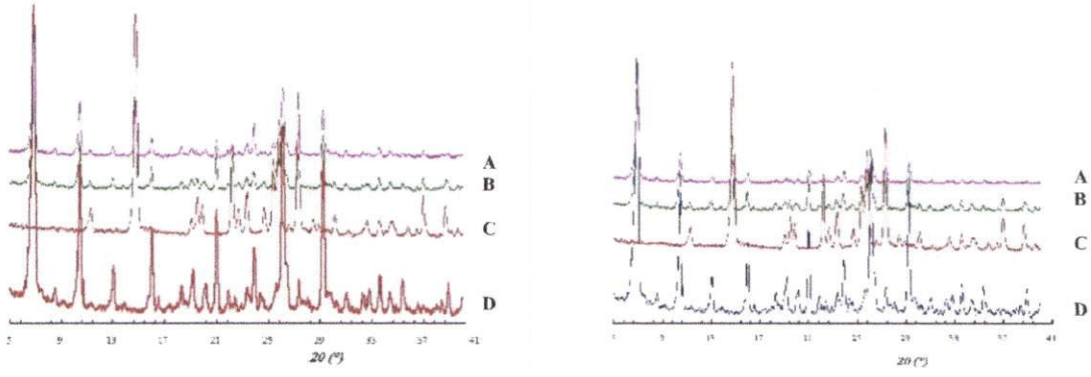

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