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Original Article

SOLID STATE CHARACTERIZATION OF A NOVEL PHYSICAL INTERACTION (PARACETAMOL-CHLORPHENIRAMINE MALEATE)

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ABSTRACT

Objective: Interactions of active pharmaceutical ingredients (API) as well as pharmaceutical excipients don't occur in a pharmaceutical dosage form. Base on structures of paracetamol (PCT) and chlorphenamine maleate (CTM), its combination is possible to give a physical interaction in the solid state. This study was conducted to investigate the physical interaction of PCT and CTM in the solid state.

Methods: Characterization used the polarization microscope, solubility test, powder x-ray diffraction (PXRD) to observe peak shifting in 2Θ angle, and fourier transform infrared spectroscopy (FT-IR) to examine wavenumber shifting.

Results: Results of solubility exhibited an increased solubility percentage with increasing concentration. Polarization microscope analysis presented a combination of crystal morphology after the two substances were mixed in an equimolar ratio. The result of melting point determination of each pure substance was 172 °C for PCT, 132 °C for CTM, and 170 °C for the mixture of the two substances in various ratios. Diffractogram showed the shifting at angle 2Θ: 20.715, 19.355-23.500 and 21.840, 26.455-20.330 for concentration ratio of PCT: CTM in (132:0.5) and (330:1) respectively and any change in the functional group was observed from infrared spectrum.

Conclusion: All evaluation of PCT and CTM in the solid state has exhibited the interaction in solid condition.

Keywords*:* Paracetamol, Chlorphenamine maleate, Polarization microscope, X-Ray diffraction, FT-IR

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INTRODUCTION

In the process of drug manufacturing, drug interactions in a solid state are very likely to occur, but it analyzes need time and cost. In the drug industry, it is a difficult thing to do and other more disturbing features are chemical physics interactions that may emit a profile that affects biological availability such as drug solubility and dissolution. Pharmaceutical preparations in general consist of two or more active ingredients and an excipient. Since a number of ingredients are present, it is essential to understand their mutual compatibility. Ideally, the mixture should have no interaction or only minimal reaction between the ingredients when they are mixed. In some cases, a chemical reaction between materials can occur spontaneously and the change can be easily observed. However, the physical interaction between some materials do not produce visible changes; sometimes these interactions take place gradually to affect the performance of the active ingredient (medicine) or in other words reduce its stability before its time [1].

Theoretically, physics interactions can be occurred in two or more similar material [2], its similarity included in the molecular formula, internal structure, crystal lattice symmetry and the level of energy in the second of such material [3]. Physics interactions that occur can be either complex formation, molecular compounds (co-crystalline) [4], solid or aqueous dispersions and solid. In this study, the mixed raw materials will be studied from a drug that is already widely used as anti-influenza, namely PCT and CTM [5-6].

In drugs, both drugs (PCT and CTM), it is possible there is a physical interaction involving the merger of the two active ingredients. The areas where intermolecular interactions occur and where this interaction does not occur depending on the transfer of charge from the respective structure of paracetamol and CTM [7]. Furthermore, when seen from the perspective of bonding interactions, both structures formed hydrogen bonds and Van der Waals bonding. Of the bonding interactions that occur between paracetamol and CTM, bonding develops potentially during the occurrence of physical interaction [8-9]. Compounds that can form this type of interaction include compounds that have the potential to form clusters of non-covalent bonding, such as hydrogen bonding, ionic bonding, and van der Waals forces [8]. In this work, we attempted to characterize the physical interaction that occurs with PCT-CTM which may affect the pharmaceutical profile of a drug. Unexpected interactions may decrease the potential of drugs in ensuring the expected drug effects.

MATERIALS AND METHODS

Materials

Paracetamol purity>98 purchase from Changshu Huagang Pharmaceutical Co., Ltd China, Chlorpheniramine Maleate (Farma), Potassium Bromide (Merck), Methanol 95% (Merck).

Equipment

Polarization microscope (Olympus SC20 Cx31), melting point (biotech, UK), Spectrophotometry UV (Analytical Jena Specord 250), x-ray powder diffraction analysis (Pan Analytical), fourier transform infrared (R-Prestige Shimadzu®)

Methods

Observation on the morphology of crystal form of PCT, CTM, and mix both using polarization microscopes

PCT (1-3 mg) is dissolved in ethanol 95% saturated aqueous solution is then to be dripped on the glass objects, allowed to crystallize. Then for CTM is dissolved in ethanol 95% and then melted on the top area of recrystallization of PCT with comparison equimolar. The result of the crystallization observed in the areas of contact between the crystals of PCT with saturated aqueous CTM. Physical interaction is observed by polarization microscopy at 100 x magnification and recorded with a digital camera, using polarization microscope.

Determination of the melting point of CTM, PCT, and a mixture of both

Prepared samples of pure CTM, PCT, and a mixture of PCT and CTM sample by comparison mole (132:0.5), (9200:0.8), (330:1), (400:1.3), and (500:1.5). The mole comparison was prepared according to doses combination of PCT and CTM in the dosage form. After it crushed samples in advance to be smooth. Then the results of