MICROMERITIC CHARACTERISTIC OF SPHERICAL AGGLOMERATED ACETAMINOPHEN CRYSTAL BY SPHERICAL NEUTRALIZATION METHOD

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ABSTRACT

Direct tableting method needs to increase compressibility and flowability of the bulk powder in order to maintain a steady supply of powder mixture to tableting machine and sufficient mechanical strength of compacted tablet. Acetaminophen exhibits poor water solubility and flow properties. Spherical agglomerates of acetaminophen were prepared by neutralization method. Spherical agglomerates were characterized by differential scanning calorimetry, Infrared spectroscopy and X-ray diffractometry. Micromeritic behavior of pure and spherical agglomerates of acetaminophen were carried out. Spherical agglomerates exhibited improved micromeritic properties compared with pure Acetaminophen.

Keywords: Spherical agglomeration, acetaminophen

INTRODUCTION

Conventional methods on manufacture of tablets is making granule (granulation) which is then compressed into tablets. The granulation process takes a lot of steps so that it required validation process. Recent year's pharmaceutical industry are more likely to adopt direct compress method. Direct compression is the favored method for preparation of tablet because it is involve small number of processing steps. In direct tableting method, it is necessary to increase flowability and compressibility of the bulk powder in order to retain a steady supply of powder mixture to the tableting machine and sufficient mechanical strength of the compacted tablets.(Kulkarni et all, 2010)

Spherical agglomeration process is a multiple unit process in which crystallization, agglomeration and spheronization can be carried out simultaneously in one step. (Kulkarni et all, 2010). Spherical agglomeration is a process of formation of aggregates of crystals held together by liquid bridges. The agglomerates are formed by agitating the crystals in a liquid suspension in presence of binding agent . (Yadav et all, 2010).

The properties of the particles so designed vary greatly as compared to the fine crystalline material. These agglomerates were found to have good flowability and compressibility. (Kulakmiet all, 2010) The object of this study is to improved micromeritic features using spherical agglomeration and develop agglomerates of Acetaminophen for direct compression.

MATERIAL AND METHODS

Acetaminophen was obtained from PT. Indofarma, Cikarang, Indonesia. All chemicals and buffers used were of analytical grade.

Preparation of spherical crystal of Acetaminophen

Acetaminophen 5 gram dissolved in 25 mL of NaOH 1 N maintained at 40°C solution of drug was quickly poured into 62,5 mL of HCl 0,3 N maintained at room temperature under continuous stirring at 300 rpm. When fine crystal of acetaminophen begin to form, added 12.5 mL of chloroform. Spherical crystals were separated from the solution by filtration and dried at 35°C for 8 hours.
Characterization of spherical crystal by FT-IR

The FT-IR spectral measurement were taken at ambient temperature using a Perkin Elmer.

Characterization of spherical crystal by X-Ray Powder Diffraction

Crystal X-ray scattering measurements were performed using Cu Kα. The data recorded over a range of 5° to 40°.

Characterization of spherical crystal by Differential Scanning Calorimetry

Sample weighed 5-7 mg placed in Al crucible then compressed. DSC measurements were made with empty Al crucible as the reference. Data recorded over in range of 40 °C to 250 °C. Scan speed was 10°C / min.

Micromeritic properties

Pure and agglomerates sample were evaluated for bulk density, tapped density and angle of repose measurement.

RESULT AND DISCUSSION

Spherical crystallization method involved three types of solvents, a good solvent, a poor solvent for a drug and bridging liquid. The selection of these solvents depends on miscibility of the solvents solubility of drug in each solvents. Acetaminophen provide free carboxyclic group to neutralize sodium hydroxide. Crystallization of Acetaminophen was induced by neutralizing the sodium hydroxide by adding excess of hydrochloric acid. Chloroform was added and stirred till the agglomerates of acetaminophen were obtained. Drug content was analyzed spectrophotometrically at 243 nm (Thermo) and calculated from calibration curve of acetaminophen. The drug contents was in 99.7%

FT-IR studies on pure and agglomerates acetaminophen have exhibited general characteristic peaks. IR spectra showed characteristic groups at 3326.1 cm⁻¹ and 3162.5 cm⁻¹ confirming the –NH and –OH groups in agglomerates sample. DSC studies were carried out for different crystal of acetaminophen. The thermogram DSC indicate no significant between value melting point onset of pure compared agglomerates sample indicating that no polymorphic conversion occurred during crystallization process.

In PXRD study, all the sample exhibited diffractiongram with similar peak position (2 theta value). Therefore, the presence of different polymorphs of acetaminophen in this samples was not exist.

FT-IR spectra A) pure acetaminophen, B) spherical acetaminophen

Flow rate, Bulk density and tapped density of agglomerates were 5g/s, 0.35g/cm³ and 0.42g/cm³ respectively when compared with pure sample.
Tuslinah: Micromeritic Characteristic Of Spherical Agglomerated Acetaminophen Crystal By Spherical Neutralization Method

(0.67g/s, 0.48 g/cm³ and 0.59 g/cm³ ). This showed that agglomerated Acetaminophen were more compact than pure one. Angle of repose measurement of agglomerates had of 29.05° whereas 33.11° for pure sampel. This decrease in angle of repose was refer to spherical shape of Acetaminophen after agglomeration.

**CONCLUSION**

Spherical Agglomeration method was successfully applied to acetaminophen. Agglomeration crystal prepared by neutralization method. FT-IR, DSC and PXRD analysis showed that there is no change in the chemical and crystal structure of acetaminophen during the crystallization process. Spherical crystal exhibited improved micromeric properties compared to untreated sample.

**REFERENCE**


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