UNIVERSITI TEKNOLOGI MARA

CENTRIFUGAL AIR-ASSISTED MELT AGGLOMERATION FOR FAST-RELEASE "GRANULET" DESIGN: DEVELOPMENT OF A BLADELESS PROTOTYPE

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ABSTRACT

Conventional melt pelletization and granulation processes produce round and dense, and irregularly shaped but porous agglomerates respectively. This study aimed to design centrifugal air-assisted melt agglomeration technology for manufacture of spherical and yet porous "granulets" for ease of downstream manufacturing and enhancing drug release. A bladeless agglomerator, which utilized shear-free air stream to mass the powder mixture of lactose filler, polyethylene glycol binder and poorly water-soluble tolbutamide drug into "granulets", was developed. The inclination angle and number of vane, air-impermeable surface area of air guide, processing temperature, binder content and molecular weight were investigated with reference to "granulet" size, shape, texture and drug release properties. Unlike fluid-bed melt agglomeration with vertical processing air flow, the air stream in the present technology moved centrifugally to roll the processing mass into spherical but porous "granulets" with a drug release propensity higher than physical powder mixture, unprocessed drug and dense pellets prepared using high shear mixer. The fast-release attribute of "granulets" was ascribed to porous matrix formed with a high level of polyethylene glycol as solubilizer. The agglomeration and drug release outcomes of centrifugal air-assisted technology are unmet by the existing high shear and fluid-bed melt agglomeration techniques.

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CHAPTER ONE
INTRODUCTION

1.1 OVERVIEW

1.1.1 Agglomeration

Agglomeration is a size enlargement technique where fine powder are agglomerated together to form agglomerates of certain sizes and shapes. Practically, an ideal agglomeration should be able to produce agglomerates with spherical shape, homogeneous size and uniform distribution of ingredients in a formulation [1]. The final product of agglomeration is called granules when the process results in irregularly shaped agglomerates of a rather wide size of distribution, typically within the range about 0.1 to 2.0 mm. If the final agglomerates are spherical and of a narrow size distribution, typically with size range of 0.5 to 2.0 mm, the agglomerates are called pellets [2, 3]. For pharmaceutical purposes, agglomerates range from 0.5 to 1.5 mm are intended fractions for oral administration [4].

Agglomerates offer many advantages as drug carrier. Drugs encapsulated in agglomerates are more stable than liquid preparations physically and chemically [5]. Agglomerates are a convenient form to dispense drugs with a large dose. Orally administered agglomerates have a faster drug dissolution rate than tablets, as the latter requires to be first disintegrated before having the drug dissolved.

The use of agglomerates as drug carrier has its inherent weaknesses. Agglomerates are far less convenient for the patients to carry than a small container of tablets. The masking of unpleasant tastes of drugs may be less achievable with the concept of agglomerates owing to its large specific surface area in contact with the taste buds of tongue. Besides, agglomerates are not an ideal form of administering potent drugs with a low dose and require a higher level of process modification in formulation of drugs which are potentially being inactivated in the stomach [5].