INTRODUCTION

Microcrystalline cellulose (MCC) is a very popular pharmaceutical excipient used in direct compression. The compactibility of MCC mostly occurs through plastic deformation and mechanical interlocking between particles.[1,2] However, the irregular shape, which contributes to interlocking bonding, results in poor flowability of MCC. A previous study reported that a codried product of an MCC slurry with β-CD had better compactibility, powder flowability, and disintegration properties than did MCC alone.[3] Results in another study[4] showed that powder flowability and disintegration of codried product and Avicel significantly improved after wet granulation. However, the compactibility of codried product and Avicel decreased with increasing particle size. Nevertheless, the compactibility of the codried excipient after granulation was still better than those of non-granulated Avicel PH101 and 301. Preservation of compactibility of codried products seems to occur to a greater extent than for both grades of Avicel. On the other hand, both codried product and Avicel products were sensitive to lubrication which resulted in decreasing compactibility and increasing disintegration. It was concluded that because of the rounder shape of the particles, the codried excipient was more sensitive to magnesium stearate and produced weaker tablets than when using Avicel.

A better understanding of the influence of the amount of β-CD added and its size range on the characteristics of codried products is a prerequisite for the practical application of this material. In this study, the mechanical performance of tablets prepared from codried products of MCC with various amounts of β-CD in 2 different size ranges (37-61 and 61-149 um) was examined and compared with that prepared from 2 different grades of Avicel (PH101 and PH301) in 2 different size ranges (PH102 and PH302). Powder characteristics of these MCC samples were evaluated as well.

METHODS

Materials

Wood pulp, Temalfa 94®, was obtained from Tembec (Canada). Avicel PH101® (degree of polymerization [DP] ≒ 215-240; mean size: 40 μm), Avicel PH102® (DP ≒ 215-240; mean size: 120 μm), Avicel PH301® (DP ≒ 140-180; mean size: 40 μm), and Avicel PH302® (DP ≒ 140-180; mean size: 120 μm) were obtained from FMC (Philadelphia, PA, USA). Ringdex-B® (β-cyclodextrin, NF) was supplied by Sanraku (Japan). Magnesium stearate was obtained from Mallinckrodt (Raleigh, NC, USA).

Sample Preparation

Preparation of the MCC slurry

First, 400 g of wood pulp was hydrolyzed in 3 L of a 2.5-N HCl solution at 100 °C for 60 min. The hydrolyzed product was then washed with distilled water until the pH value of the washing solution was near neutral, and no white precipitation appeared with the addition of a 0.1-N $AgNO_3$ solution. The hydrolyzed product was next centrifuged to eliminate water. The final product which retained about 50.0% ± 0.1% w/w of moisture was designated the MCC slurry. The DP of this MCC slurry was about 220 and was measured according to NF 18.

Preparation of codried product of MCC with β-CD

The MCC slurry (DP ≒ 220) was blended with various amounts (0%, 5%, 10%, and 20% w/w) of β-CD and mixed well by hand in a plastic bag. The mixtures were then transferred to a planetary mixer (KitchenAid, Model K5SS, USA) and granulated with a fixed amount of water (54.5% w/w) at a speed set at no. 2 until homogeneous. The wet mass was next screened through a standard 30-mesh sieve, and the granules were dried at 60 ± 1 °C for 12 h. Dried granules were then milled and screened to retain 2 different size fractions of between 61 and 149 μm and between 37 and 61 μm, respectively. Since water content has been reported to influence both powder flowability and compactibility of MCC, the water content of all MCC samples and granules were controlled to about 3%~5%, which is the optimal range for MCC.[8]

Yield pressure

Flat-faced tablets of 8-mm diameter were pre-