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Effect of particle shape on powder flowability of microcrystalline cellulose as determined using the vibration shear tube method

Takehiko Horio [a], Masatoshi Yasuda [a,b], Shuji Matsusaka [a,*]

[a] Department of Chemical Engineering, Kyoto University, Kyoto 615-8510, Japan
[b] IMP, 67-20 Ichibu-cho, Ikoma-shi, Nara 630-0222, Japan

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ABSTRACT

Powder flowability of microcrystalline cellulose particles having different particle shapes, whose aspect ratios ranged from 1.8 to 6.4, was measured using the vibration shear tube method. Particles lubricated with magnesium stearate were also investigated in order to evaluate the effect of surface modification on powder flowability. Particles were discharged through a narrow gap between a vibrating tube edge and a flat bottom surface, where each particle experienced high shear forces, thus, overcoming adhesion and friction forces. Vibration amplitude was increased at a constant rate during measurement and the masses of the discharged particles were measured at consistent time intervals. Flowability profiles, i.e., the relationships between the mass flow rates of the discharged particles and their vibration accelerations, were obtained from these measurements. Critical vibration accelerations and characteristic mass flow rates were then determined from flowability profiles in order to evaluate static and dynamic friction properties. The results were compared with those obtained using conventional methods. It was found that angle of repose and compressibility were related to static and dynamic friction properties. Furthermore, it was found that particle aspect ratio more significantly affects powder flowability than does lubrication with magnesium stearate.

1. Introduction

Microcrystalline cellulose (MCC) is widely used in the pharmaceutical industry because of its excellent compressibility (York et al., 1990; Doelker, 1993; Doelker et al., 1995; Hancock et al., 2000; Inman et al., 2008). One of the reasons for its widespread use is that MCC can perform diverse functions; applicability for a particular function is determined by the shape and internal structure of the MCC particles (Obae et al., 1999). In pharmaceutical manufacturing processes, appropriate excipients must be selected by considering such factors as tablet hardness, disintegration time, dissolution profile, and powder flowability. Furthermore, to improve medication compliance and persistence, formulations with appropriately sized tablets must be designed. To make smaller tablets and capsules, smaller quantities of more highly-functional excipients must be used in formulations.

In recent years, several grades of highly-functional MCC have been developed. For example, spherical MCC particles with a porous structure exhibit higher compressibility and improved powder flowability. On the other hand, elongated fibrous MCC, in a tight packing state, has been developed to increase tablet hardness. The effect of particle shape on powder flowability was studied by Ridgway and Rupp (1969); Podczeck and Miah (1996); Fu et al. (2012); Mellmann et al. (2013). Evaluation of the flowability of fibrous MCC has been carried out by measuring its angle of repose, and/or compressibility (Landín et al., 1993; Patel and Podczeck, 1996; Mohammadi and Harnby, 1997; Gamble et al., 2011). However, measurements of angles of repose of cohesive and fibrous powders are not easy (Wouters and Geldart, 1996; Schulze, 2008; Krantz et al., 2009). Powder flowability can also be measured by other methods (Schwedes, 2003; Lumay et al., 2012), e.g., using a shear cell (Jenike, 1962; Antequera et al., 1994; Shi et al., 2011; Yu et al., 2011; Nalluri et al., 2013), rotary rheometer (Freeman et al., 2009; Freeman, 2007), and revolutionary drum (Lavoie et al., 2002; Bhattachar et al., 2004; Hancock et al., 2004), or by employing Carr's method (Carr, 1965a,b). However, these methods require large amounts of sample powder and significant technical knowledge and skill. Hassanpour and Ghadiri (2007); Wang et al. (2008) developed the ball indentation method, enabling the evaluation of powder flowability of small samples. Jiang et al. (2006, 2009) invented the vibrating tube method for evaluating powder flowability, which is inspired from the micro-feeding of

* Corresponding author. Tel.: +81 75 383 3054; fax: +81 75 383 3054.
E-mail address: matsu@cheme.kyoto-u.ac.jp (S. Matsusaka).

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fine powders (Matsusaka et al., 1995, 1996). The method enables high-sensitivity measurement of powder flowability of small samples and the evaluation of both static and dynamic friction properties of various powders (Ishii et al., 2009, 2011a,b). Applying the vibrating tube method, Horio et al. (2013) evaluated the powder flowability of pharmaceutical powders. However, this method cannot be used for the evaluation of extremely cohesive powders or fibrous powders that do not flow through the narrow tube.

Zainuddin et al. (2012a,b) have developed the vibration shear tube method to evaluate static and dynamic friction properties of nanoparticles and micron-sized particles. This method measures the mass flow rate of particles discharged through a narrow gap between a vibrating tube edge and a flat bottom surface, where each particle experiences high shear forces, thus, overcoming adhesion and friction forces. However, comparisons of results obtained from the vibration shear tube method and those of conventional methods have not been performed.

In the present study, the powder flowability of MCC particles having different particle shapes is evaluated using the vibration shear tube method. From the perspective of static and dynamic friction properties, the results obtained using conventional methods, i.e., angle of repose and compressibility, are analyzed. Furthermore, the effects of particle aspect ratio and lubrication with magnesium stearate (MgSt) on powder flowability are investigated.

2. Materials

2.1. Sample preparation

Different types of Ceolus® MCC particles, PH-101, PH-102, PH-200, PH-301, PH-302, UF-702, KG-802, and KG-1000 (Asahi Kasei Chemicals Corporation, Japan) were used. Scanning electron microscopy (SEM) images of the MCC particles are shown in Fig. 1. PH-101 was a powder consisting of both fibrous and elongated particles. The particles of PH-102 had a longer minor axis, width, than those of PH-101. Some particles of PH-200 were over 200 μm. The particle size of PH-301 was similar to that of PH-101; however, the major axis lengths of PH-301 particles were smaller than those of PH-101 particles. PH-302 had larger particles than PH-301. UF-702 had elongated particles compared to PH-302. KG-802 had even more elongated particles and KG-1000 had the most elongated particles.

Fig. 2 shows the cumulative distribution functions (F), of the major axis lengths (L), of the MCC particles. More than 200 values for each sample were measured by SEM image analysis. The particle lengths of PH-301 were short, with a median value of approximately 50 μm. The median values of the particle lengths of KG-802 and KG-1000 were both approximately 100 μm. The median value of the particle lengths of PH-200 was as large as 120 μm. Table 1 summarizes the powder properties, including nominal mass median diameter, median value of major axis length, minor axis length, width, and aspect ratio (A_r), i.e., ratio of the major axis to the minor axis. The values of nominal mass median diameter can be classified into three categories corresponding to 50, 90, and 170 μm. The maximum value of the aspect ratio was 6.4, for KG-1000, and the second highest value was 3.6, for KG-802. The particles of the other samples all had an aspect ratio of approximately 2. In the pharmaceutical industry, MCC particles with aspect ratios of approximately 2 are often used for direct compression excipients because of their superior flowability. MCC particles with higher aspect ratios are used, in a tight packing state, to increase tablet hardness. In general, such MCC particles are lubricated with MgSt before tableting; however, the effect of lubrication of MCC particles having different particle shapes on powder flowability is still unclear. In this experiment, 0.5 mass% of MgSt that was sieved through a 500 μm mesh was added to MCC particles. The MCC and MgSt were mixed in a tumbling blender (Bohle bin blender LM-20; Kotobuki Industries Co., Ltd., Japan) at 20 rpm for 5 min. The effective volume of the blender is between 25–85% of the total container volume. The container had a volume of 2.5 L and was filled with the mixture to 50% capacity. The sample preparation and flowability measurements were performed at a temperature of 21 ± 2 °C and relative humidity of 45 ± 5%.

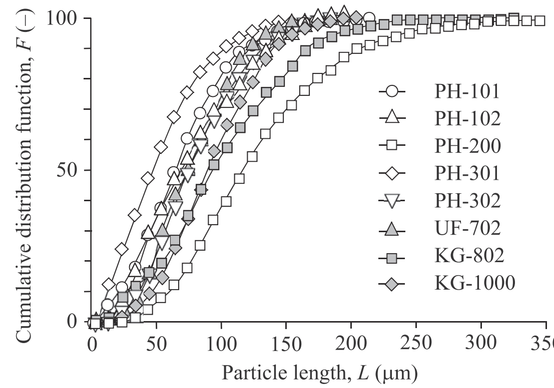

Fig. 2. Cumulative distribution functions (F), of the major axis lengths (L), of the MCC particles.

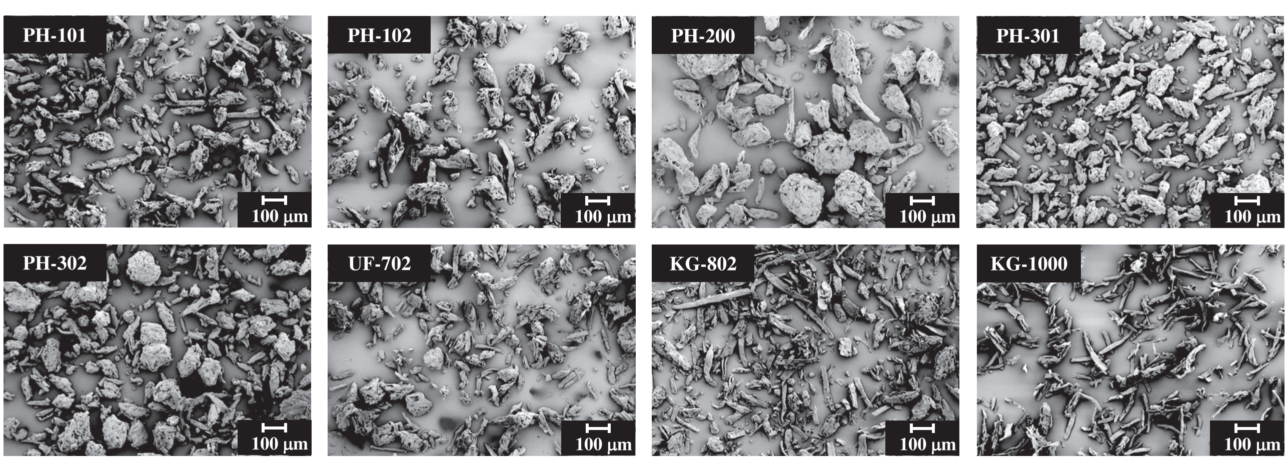

Fig. 1. SEM images of the different types of MCC particles.