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Sifting segregation of ideal blends in a two-hopper tester: Segregation profiles and segregation magnitudes

Mariagrazia Marucci [a,*], Banien Al-Saaigh [b], Catherine Boissier [a], Marie Wahlgren [b], Håkan Wikström [a]

[a] AstraZeneca Gothenburg, SE-431 83 Mölndal, Sweden
[b] Department of Food Technology, Lund University, P.O. Box 124, SE-221 00 Lund, Sweden

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ABSTRACT

The main aims of this work were: 1) to increase the understanding of the segregation process that occurs during a segregation test that follows the ASTM sifting segregation procedure, and 2) to understand the effect of powder load, fines mass fraction and particle diameter ratio on the segregation of ideal blends. Binary blends of microcrystalline cellulose particles (mean diameter ranging from 161 to 661 μm) were used. The segregation tendency of the blends was characterized with a tester built according to the ASTM D 6940 standard. Additional experiments were performed using only the upper or the lower hopper of the tester, to better understand the contribution of the set-up to segregation. The fines fraction in the samples collected during the segregation experiments was determined with a QicPic particle size analyser, and segregation profiles were obtained. Most of the segregation occurred when the upper hopper was discharged into the lower hopper. For most of the profiles, an initial phase presenting a significant oscillation in the fines mass fraction was followed by a second phase where the fines mass fraction was rather constant and, finally, by a third phase where the fines mass fraction decreased. Segregation was quantified calculating complementary coefficients: the standard deviation of the normalized fines mass fraction, the fines mass fraction ratio of the last to the first sample, the fines mass fraction ratio of the sample with the lowest fines fraction to the sample with the highest fines fraction. The segregation amount was rather constant reducing the powder load from 838 to 665 g, while segregation largely increased when the powder load was further reduced to 435 g. The segregation tendency largely increased when the fines mass fraction in the initial blend decreased from 75 to 25% w/w. Finally, the segregation tendency increased when the particle diameter ratio increased from 1.9 to 4.1. The generated data are useful also for comparison when blends of increased complexity are used.

1. Introduction

Particles segregation can have a very negative effect on the performance of processes that handle powders. During the processing of pharmaceutical powders, particles segregation may lead to poor content uniformity of the final dosage form. Particles segregation in powder flow is caused by differences in the particles physical properties, e.g. size, shape and density [1]. The segregation magnitude is a result of these differences, of the powder flowability [2], of the fines mass fraction [3] and of the process [4–6]. Several segregation mechanisms can contribute to the final segregation [4,7]. To address or prevent segregation issues by modifying the powder formulation and/or the process, it is important to understand: 1) the dominating segregation mechanism in the process; 2) how the powder segregation tendency is related to segregation in the process; 3) how the powder segregation tendency is related to the particles and blend properties. Different methods have been used to quantify the segregation tendency of powders [8–13]. In some studies, the effect of the particles properties on segregation was evaluated using ideal blends, i.e. binary blends that are free flowing and that are made of spherical particles with similar densities [9,12]. Although blends can be very complex in industrial situations, the use of ideal blends has the benefit that the data obtained are easy to be analyzed and can be used to better understand the results of complex blends.

Sifting segregation is one of the most common segregation mechanisms, caused primarily by a difference in the particles size [1]. During sifting segregation, fine particles sift through a grid of coarse particles. The ASTM D 6940 standard describes a bench-top segregation tester capable of characterizing the sifting segregation tendency of powder blends [8]. The tester was initially developed at Rutgers University [6,10]. During the past years, several studies using the ASTM D 6940 segregation tester, or modifications of the tester, have been reported in the scientific literature [6,14–19]. The ASTM tester consists of a mass flow hopper (upper hopper) on the top of a funnel flow hopper (lower hopper). A heap is created in the funnel flow hopper when the powder is discharged into it from the mass flow hopper. Although the tester can be used performing multiple fill-discharge cycles, it is usually used

* Corresponding author.
E-mail address: mariagrazia.marucci@astrazeneca.com (M. Marucci).

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performing one fill-discharge cycle. Samples are collected from the lower hopper. In tablet manufacturing and capsule filling processes, it is common that a powder blend initially well-mixed is discharged into a hopper creating a heap, and that formulation units are produced from the powder blend leaving the hopper. The tester mimics this type of set-up when only one fill-discharge cycle is used. It is relevant to mention that the segregation process that occurs during heap formation is complex and that several mechanisms in addition to sifting contribute to the resulting segregation pattern [7,20]. For particles with similar densities, the bigger particles move down the surface of the heap and accumulate around the bottom of the heap, while the finer particles built-up in the upper regions of the surface [21]. In this case, the periodic avalanching produces patches of fines within the coarse material [21]. Segregation profiles are obtained when all the samples collected from the lower hopper are characterized. Segregation profiles are not required by the ASTM procedure but are necessary to understand how the particles segregate during the test and to mechanistically relate segregation to the particles physical properties. Different segregation coefficients can be used to quantify segregation: e.g. the relative standard deviation of the fines mass fraction [6,14], the fines mass fraction ratio of the last to the first sample [15], the fines mass fraction ratio of the sample with the lowest fines fraction to the sample with the highest fines fraction [14]. Although each of the mentioned coefficients provides relevant information, its single use does dot depict completely the occurred segregation. Complementary segregation coefficients are required to quantify segregation accurately.

The studies with the ASTM tester, or with its modification, have shown that the segregation results depend on the particles properties [6,14,15] and also on the testing parameters [15]. Xie et al. have found increased segregation at increased particle diameter ratio [15]. Instead, He et al. have found that a higher segregation tendency corresponded to a smaller particle diameter ratio for a system of aspirin/lactose/microcrystalline cellulose [14]. Oka et al. have characterized several binary blends using 10 fill-discharging cycles but using only the mass flow hopper. They found increased segregation at increased ratio of the product particle-median-diameter times bulk-density [6]. Xie et al. have investigated the effect of powder load on segregation. Two loads have been used in their work, and a higher segregation tendency has been obtained increasing powder load [15]. Despite the diffusion of the tester and of the tester's modifications, and despite the complexity of the shape of the segregation profile in relation to the particles physical properties, only few complete segregation profiles have been characterized in the published works [6,14,17], and only few segregation profiles have been presented [14]. Segregation has been usually quantified using only one coefficient, and there are aspects that have not been considered (e.g. the effect of the fines mass fraction), or that need to be investigated in more details (e.g. the effect of the blend load). Moreover, to the best of our knowledge, the published data have been obtained on blends made of particles that differed in several physical properties and that in many cases contained several components, and segregation data on ideal blends have not been presented yet. This makes the results presented difficult to be used in a general way to predict the segregation tendency of other blends and/or to obtain an indication of the segregation that might occur during manufacturing. For the ASTM set-up, data on ideal blends and additional data on complex blends are required to better understand how the particles properties and the operating conditions affect the segregation results.

The aim of this work was to improve the understanding of the segregation that occurs in an ASTM D 6940 sifting standard tester by studying the effect of particle diameter ratio, fines mass fraction and powder load on the resulting segregation of ideal binary blends. Segregation profiles were obtained in a tester built according to the ASTM D 6940 standard, one fill-discharge cycle was performed and segregation was quantified calculating complementary segregation coefficients. Additional segregation experiments were performed using only the mass flow or the funnel flow hopper of the tester, to better understand the contribution of the set-up to segregation. The blends used in this work were prepared using microcrystalline cellulose particles with a mean particle diameter of 161 μm and microcrystalline cellulose particles with a mean particle diameter ranging from 307 to 661 μm. The blends could be considered ideal as the particles were spherical and had similar physical properties, and as the blends were free flowing.

2. Materials and methods

2.1. Materials

Microcrystalline cellulose (MCC) particles were used in this study. The MCC particles used were: Cellets 127 and Cellets 263 (iPc process-center GMBH & Co., Germany), as well as Celphere 305 and Celphere 507 (Asahi Kasei Chemicals Co., Japan). The particles are referred to as MCC 127, MCC 263, MCC 305 and MCC 507, respectively, in the following text.

2.2. Morphology of the microcrystalline cellulose particles

The MCC particles were imaged with a tabletop scanning electron microscope (Hitachi TM3030, Hitachi High-Technologies, Japan). The voltage applied for the measurements was 15 kV.

2.3. Bulk, tapped, compressed bulk and true density of the microcrystalline cellulose particles

Bulk and tapped density of the MCC particles was determined according to the European Pharmacopoeia [22]. Experiments were performed in triplicate. An Erweka SVM12 tester (Erweka, Germany) was used to determine the tapped density. A 100 mL graduated cylinder with a 1 mL precision was used for the measurements. The compressed bulk density was measured with a GeoPyc 1360 (Micromeritics, USA). A material sample (about 5.5 g) was placed in a cylinder (diameter equal to 1.9 cm). The cylinder was mounted horizontally into the instrument. The powder was compressed several times with a piston, while the cylinder rotated [23]. Experiments were performed in duplicate, and 3 measurements were obtained for each experiment.

The true density of the MCC particles was measured with a helium gas displacement pycnometer (AccuPyc 1330, Micromeritics, USA). Experiments were performed in duplicate. Ten measurements were obtained for each experiment.

2.4. Powder flow properties

The flow property of the individual materials was characterized by measuring the flow function coefficient (FFc) using a ring shear tester (Shulze Ring Shear Tester, RST-XS, Dr. Dietmar Schulze, Germany). A pre-shear normal load equal to 4 kPa was used in the experiments. Experiments were performed in duplicate.

2.5. Sifting segregation tester

The tester consists of three hoppers, one with a steep inner conical section and two with a non-steep inner conical section, of two slide gates, and of two aluminum stands. When assembled, the tester can be described as an upper hopper assembly (in this work simply called upper hopper), consisting of a steep hopper inside a non-steep hopper, in series with a non-steep hopper (in this work simply called lower hopper). A schematic representation of the assembled tester is reported in Fig. 1. The parts of the sifting segregation tester in contact with the powder were built according to the specifications of the ASTM D 6940 sifting segregation tester [8], with the main difference being the length of the collecting sample tube. The collecting sample tube was shorter in order to get more samples from each experiment (it was 52 mm long instead of 65 mm).