NOTE

Tabletability Modulation Through Surface Engineering

FREDERICK OSEI-YEBOAH, CHANGQUAN CALVIN SUN

Pharmaceutical Materials Science and Engineering Laboratory, Department of Pharmaceutics, College of Pharmacy, University of Minnesota, Minneapolis, Minnesota, 55455

Received 19 March 2015; revised 1 May 2015; accepted 15 May 2015

Published online 8 May 2015 in Wiley Online Library (wileyonlinelibrary.com). DOI 10.1002/jps.24532

ABSTRACT: Poor powder tabletability is a common problem that challenges the successful development of high-quality tablet products. Using noncompressible microcrystalline cellulose beads, we demonstrate that surface coating is an effective strategy for modulating tabletability, almost at will, through judicious selection of coating material. This strategy has broad applicability as tabletability of such particles is dictated by the properties of the outermost layer coat regardless the nature of the core. © 2015 Wiley Periodicals, Inc. and the American Pharmacists Association J Pharm Sci 104:2645–2648, 2015

Keywords: compaction; compression; fluid-bed; hardness; materials science; polymers; powder technology; polyvinylpyrrolidone; tablet

Poor powder tabletability is a common problem that challenges the successful development of high-quality tablet products. A symptom of this problem is that sufficient tablet mechanical strength cannot be attained within the accessible compaction pressure range (typically 50–350 MPa).[1] This problem occurs more frequently when a high dose of a poorly compressible drug must be delivered or when the powder is inappropriately granulated, by an either dry or wet process, before compression.[2,3]

The problem of poor tabletability has been traditionally addressed during formulation development through the use of tablet excipients with superior tableting properties, such as microcrystalline cellulose (MCC).[4] In that case, a large amount of excipient is required to afford sufficient tablet mechanical strength. For example, in a mixture with noncompressible silica and a compressible polymer, 40% of the polymer is required to form intact, but weak (~0.25 MPa tensile strength) tablets, and 60% of the polymer is required to form reasonably strong tablets (1.3 MPa tensile strength) at 250 MPa compaction pressure.[5] In another example, 40% of another highly compressible polymer is insufficient for forming an intact tablet with poorly compressible acetaminophen.[6] A tablet, however, cannot be too big (usually less than 1 g) for easy swallowing and compliance by patients.[7] Consequently, this strategy of simply adding highly compressible excipients to a formulation is unfit for drugs that must be delivered in a high dose.

We previously showed that coating particles with a layer of highly bonding polymer is effective in improving powder tabletability of extremely poorly compressible powders.[5,6] When coated with a layer of plastic and highly bonding material, large bonding area can develop irrespective of the deformation mechanism of the original particles. Surface coating delivers highly bonding excipients where they are most needed in the tablet, that is, at the particle–particle contact points (Fig. 1). Such coating controls the nature of particle–particle bonding, regardless of the mechanical properties of the core particles. Therefore, tabletability of the coated powder can be effectively controlled by judiciously selecting coating material. If the coating material is highly bonding, a strong tablet tensile strength develops even at a low compaction pressure. On the contrary, tabletability is expected to be poor when bonding property of the coating layer is poor. The effectiveness of coating on tabletability is in contrast to the physical mixtures between a bonding excipient and a nonbonding drug, where a three-dimensional bonding network forms only when the amount of bonding excipient exceeds the critical threshold, as predicted by the percolation theory.[8,9] Therefore, a strong tablet cannot be obtained unless the three-dimensional strongly bonding network permeates the entire volume of the tablet, which requires the use of a large amount of bonding excipients. Otherwise, the tablet will fail at the weakest point. However, a uniform three-dimensional bonding network is formed, even at a low pressure, to afford a strong tablet if coating of highly bonding material is applied to all particles in the powder.

Using 350–500 μm diameter MCC beads (Cellets 350; Glatt Air Techniques Inc., Ramsey, New Jersey), we have demonstrated the ability of modulating tabletability, almost at will, through judicious selection of surface coating materials. We used polyvinylpyrrolidone (PVP, K30; BASF, Geismar, Germany), poly(methacrylate-ethylacrylate) 1:1 copolymer (Kollicoat® MAE 30DP; BASF, Ludwigshafen, Germany), a 1:1 mixture of PVP and caffeine, and nanosized silica as coating materials in this study. Caffeine was used as a model drug to represent drug layering onto beads, a process commonly employed during the development of controlled release beads. Continuous film coating was achieved using a fluid bed (Unilab, Bosch, Germany). Discrete dry coating by silica was carried out in a twin shell blender (Patterson–Kelley, East Stroudsburg, Pennsylvania). Cylindrical tablets (8 mm in diameter) were compressed on a Materials Testing Instrument (Zwick-Roell 1485, Ulm, Germany). Tablets were broken diametrically and tensile strength was calculated from the breaking force and tablet dimensions following the standard procedure.[10] Figure 2 shows that the tablet tensile strength oscillates wildly as the beads are sequentially coated by bonding and nonbonding materials. The data show that the outermost layer dictates tableting performance of beads regardless of the structure of beads underneath. It should be noted that the ability to modulate powder tabletability by surface coating cannot be effectively shown by simply comparing tableting performance of beads

Correspondence to: Changquan Calvin Sun (Telephone: +612-624-3722; Fax: +612-626-2125; E-mail: sunx0053@umn.edu)

Journal of Pharmaceutical Sciences, Vol. 104, 2645–2648 (2015)

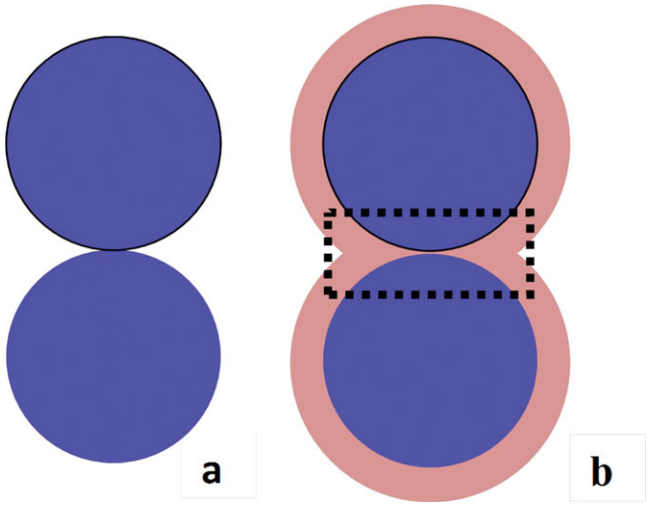

Figure 1. Schematic of bonding between poorly compressible beads in a compressed tablet. (a) Without coating, only a small bonding area is developed. (b) With coating by a layer of highly bonding material, a large bonding area is developed. A thicker coating layer leads to a larger bonding area.

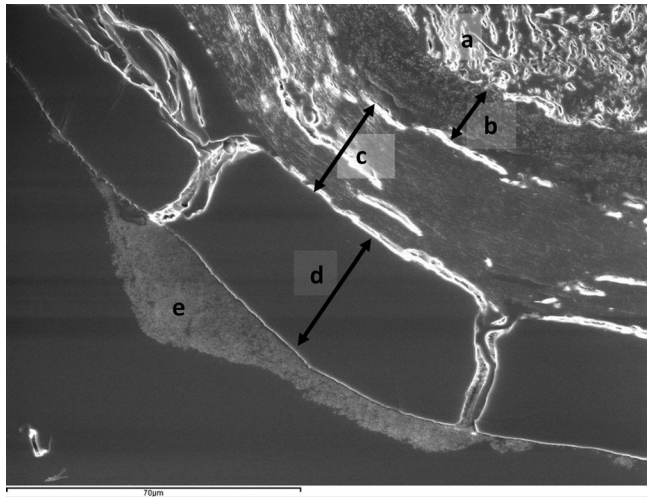

Figure 3. Back scattered electron SEM image of a cross-section of a coated bead showing core and various coating layers. (a) MCC core. (b) 1:1 caffeine–PVP layer. (c) Kollicoat MAE layer. (d) PVP layer. (e) Nanosilica.

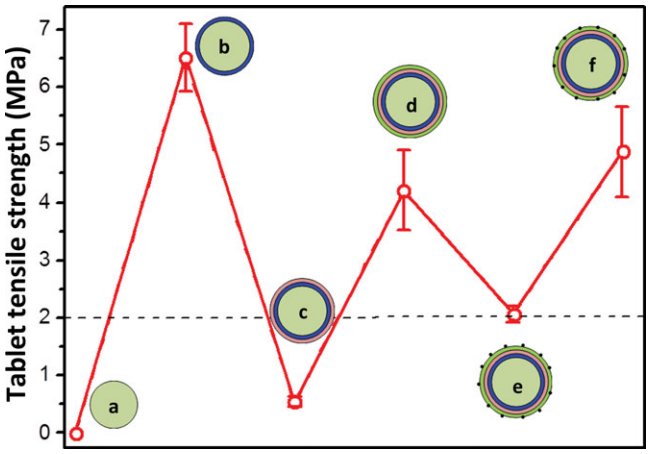

Figure 2. Effect of surface coating on tablet tensile strength of beads compressed at 150 MPa. Beads were exposed to 75% RH for 4 days. Layered structures of beads are illustrated. (a) MCC core bead. (b) Bead (a) coated with caffeine–PVP (1:1). (c) Bead (b) coated with Kollicoat MAE. (d) Bead (c) coated with PVP. (e) Bead (d) coated with nanosilica. (f) Bead (e) after 8 days of exposure to 75% RH. The broken line indicates the desired tablet tensile strength for successful processing and handling of tablets.

individually coated with different materials. Figure 3 is back scattered electrons image of the cross-section of a bead obtained using a field emission scanning electron microscope (Sigma FE-SEM; Carl Zeiss, Oberkochen, Germany), showing the layered bead structure.

Nearly spherical MCC beads exhibit very poor tabletability. In fact, no intact tablet could be prepared by compaction up to 350 MPa. This is similar to dense MCC granules that are prepared by high shear wet granulation or dry granulation because they do not undergo sufficient amount of plastic deformation or fragment during compaction.[11] Consequently, a significant amount of elastic deformation is developed during compression.[12] The elastic recovery of particles upon the release of compaction pressure results in the survival of only a relatively small area of contact between adjacent particles (Fig. 1a) and, therefore, low tablet tensile strength results.[13]

When exposed to 75% relative humidity (RH), the beads coated with 10% (wt % of beads) of caffeine–PVP (1:1) are visually free flowing and they form tablets with tensile strength of 7.0 MPa at 300 MPa compaction pressure, which is significantly higher than 2 MPa, a tensile strength target for successful handling of tablets.[14] At lower RHs, tablet tensile strength improvement is marginal for the same beads (0.4 and 1.0 MPa at 32% and 52% RH, respectively). This highlights the importance of plastic deformation of the outer layer on the tablet mechanical strength. Polymer equilibrated at a higher RH is more plastic because of the higher amount of moisture.[15,16] Hence, larger bonding area between particles is developed under identical compaction conditions (Fig. 1b).

When the beads further coated with a layer of Kollicoat (40%, wt %) are compressed, tablet tensile strength is significantly reduced to be nearly negligible even at 75% RH (Fig. 2). The nearly complete loss of tabletability indicates that Kollicoat does not develop sufficient bonding area between adjacent beads, which is necessary for achieving a high tablet tensile strength.[17] Further top coating with 5%–25% (wt %) PVP significantly restores the tabletability of beads. However, the highly plasticized PVP coating causes the problem of caking at 75% RH, which is the worst with 25% PVP coating. Beads form large and strong agglomerates over time because of the interdiffusion of polymer chains at contact points.[18] This problem is solved by blending the PVP-coated beads with 1% (wt %) nanosized silica to form a discrete coating layer of nanoparticles, which form a physical barrier to prevent sticky PVP layers from coming to contact. With silica coating, beads coated with 25% PVP remain visually free flowing even after exposure to 75% RH for 6 days. The nanocoating is possible by a simple blending process because these free-flowing beads can come to frequent contact with silica to facilitate their spreading onto the beads.[19] For cohesive powders, successful coating by nanoparticles would require the application of external stresses to

DOI 10.1002/jps.24532