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The phenomenon of tablet flashing — Its impact on tableting data analysis and a method to eliminate it

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ABSTRACT

Flashing at tablet edges, an inevitable phenomenon when tableting a plastically deforming material under a high pressure, can introduce significant errors to tablet density and porosity determinations due to overestimated tablet thickness when tablet were measured out-of-die. Errors in tablet density determination also lead to errors in true density obtained by the Sun method, which is suitable for water-containing solids. Errors in true density and tablet porosity propagate to fundamental parameters, derived from common equations, for quantifying mechanical properties of compacts. In this work, we have developed and validated a method to eliminate tablet flashing using sand paper. Using binary mixtures of water-containing plastic materials, we have further demonstrated the impressive improvement in powder deformability assessment by using accurate density of tablets free from flashing.

1. Introduction

A number of mechanical properties of compacts, such as tensile strength, elastic modulus, and hardness, strongly depend on tablet porosity [1]. Commonly employed methods, such as the Heckel and Kuentz-Leuenberger analyses, for assessing the plasticity of powders are based on the relationship between tablet porosity and pressure [2–3]. Thus, accurate determination of tablet porosity is critical for reliable characterization of powder compaction behaviors. Accurate tablet porosity requires accuracy in both powder true density and tablet density, from which tablet porosity is calculated. Impact of erroneous true density on these analyses has been well recognized [4–5]. Helium pycnometry is a routinely used method for determining true density of powders, either single components or mixtures, at room temperature. However, one inherent problem with helium pycnometry is its sensitivity to the moisture released from water-containing solids during measurement [6]. Helium pycnometry measurements are based on the Boyle's law of pressure-volume relationship, which assumes constant number of gas molecules in a sealed system at a constant temperature. Thus, the release of water from the powder violates one of the assumptions and results in erroneous true densities. Drying may transform a hydrate to an anhydrate, which has a different true density as well as mechanical properties than corresponding hydrate [7–9]. Even when no phase change is involved, a dry powder can exhibit significantly different true density and mechanical properties than its water-containing counterpart [10–11]. Therefore, true density must be determined using powders in its native state instead of being completely dried for the purpose of avoiding the impact of moisture release on accuracy of measured true density. Hence, accurate true density of powders containing volatile components, such as water, cannot be obtained by helium pycnometry. An alternative method suitable for water-containing solids is the Sun method, where true density is determined by non-linear fitting of tablet density vs. pressure data over a wide range of compaction pressure [12]. An advantage of this method is that the compacts could be subsequently characterized to allow an assessment of tablet mechanical properties as a function of porosity [10,13].

In order for the Sun. method to yield accurate true density values, tablet density must be accurately determined. Tablet density is usually determined by dividing tablet weight with tablet volume, which can be calculated from dimensions of a regularly shaped tablet. Determination of tablet dimension using a digital caliper is straightforward. However, complexity could arise, particularly for highly plastic materials, when flashing or crowning phenomenon occurs [14–15]. In this phenomenon, the material has sufficient plasticity for moving toward the narrow gap between punch and die-wall at high pressures to form an edge. Without being properly removed, tablet flashing will cause an overestimation of tablet thickness of flat faced tablets and, consequently, larger tablet volume and lower tablet density. One common practice is to use the edge of the caliper outside jaws to remove the flashed edges. Although helpful,

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it is possible that flashing cannot be completely removed by this method, especially for strong flashing formed when compression is carried out at a high pressure. If flashing is not completely eliminated, errors in tablet density due to tablet flashing lead to erroneous true density values from the Sun method. Errors in true density values propagate to cause errors in porosity calculations and any subsequent analyses involving tablet porosity.

In this work, we have developed an efficient method to eliminate the tablet flashing problem simply by polishing tablets with a fine sand paper. This method has been validated using several plastically deforming soft materials that are susceptible to flashing. We have also shown the surprisingly severe negative impact by the tablet flashing, if not removed, on assessment of material deformability.

2. Materials and methods

2.1. Materials

Plastic theophylline anhydrate (TH) (BASF, Ludwigshafen, Germany), potassium bromide (KBr) (Fisher Scientific, Pittsburgh, PA), Sodium iodide (NaI), and Hydroxypropyl cellulose (HPC) (Sigma Aldrich, St Louis, MO) were used to study the flashing phenomenon. Microcrystalline cellulose (MCC) (Avicel PH102, FMC Biopolymer (Philadelphia, PA) and magnesium stearate (Mallinckrodt, St Louis, MO) were employed to prepare binary mixtures with HPC.

2.2. Methods

2.2.1. Blending and tableting of powders

Mixtures between HPC and MCC with 25% increments were prepared. HPC and MCC, after passing through a sieve (mesh #60, cut-off size ~250 μm, United States sieve standards), were mixed following a geometric dilution procedure. Magnesium stearate (0.25% *w*/w) was added to 10.0 g of this blend and mixed in a 50 mL bottle mounted on a blender (Turbula, Glen Mills, Clifton, NJ) for 2.5 min. All powders were conditioned at 33% RH (saturated $MgCl_2$ solution) at ambient temperature for at least 48 h prior to compaction on a compaction simulator (Presster™; Metropolitan Computing Corporation, NJ) simulating a Korsch XL100 press (10 stations) at a dwell time of 25 ms, corresponding to 49,300 tablets per hour.

The plastic materials, NaI, KBr, and TH, were compacted (with external lubrication) on a universal material testing machine (model 1485; Zwick/Roell, Ulm, Germany) under compaction pressures ranging from 25 MPa to 350 MPa using an 8 mm flat faced punch-die set at a speed of 5 mm/s. Tablets were made in duplicate for treating with digital caliper (6-in. stainless steel; General Tools and Instrument, Secaucus, NJ) or sand paper (superfine grade - P400, 3M Inc., Saint Paul, MN), respectively. For all tablets, thickness and diameter were measured immediately after ejection and treatment with sand paper or caliper.

2.2.2. Method for removing tablet flashing

A simple method to minimize tablet flashing of plastically deforming materials is scrapping the tablet edge with the sharp edge of the caliper jaws. To do that, a tablet was placed between the two outside jaws of a caliper. While being pressed tightly against the tablet surfaces, the jaws were rocked back and forth to allow the right-angled edges to remove flashing. An alternative approach is polishing tablet surface with a sand paper. In this work, a tablet was gently pressed against a flat fine sand paper and gently rubbed in a circular fashion. A sudden increase in resistance signaled the end of the polishing process, at which point the whole tablet surface was in contact with the sand paper.

2.2.3. Determination of true density of individual excipients and binary mixtures

True density of pure and mixture powders was obtained by the Sun. method, which involves fitting tablet density vs. pressure data to Eq. (1) [12],

$$P = \frac{1}{C}\left[(1-\varepsilon_c) - \frac{\rho}{\rho_t} - \varepsilon_c \ln\left(\frac{1-\frac{\rho}{\rho_t}}{\varepsilon_c}\right)\right] \tag{1}$$

where ρ, ρ_t and P denote tablet density, true density, and compaction pressure, respectively. C and ε_c are constants related to yield strength and critical porosity for tablet formation, respectively.

A nonlinear fitting of the P-ρ data for a batch of 12–15 tablets reveals the three constants in Eq. (1), i.e., ρ_t, C, and ε_c, which are characteristics of a specific powder. The tablet porosity (ε), was obtained according to Eq. (2):

$$\varepsilon = 1 - \frac{\rho}{\rho_t} \tag{2}$$

2.2.4. Determination of true density by helium pycnometry

True density of pure materials, such as NaI, KBr and TH, was measured by helium pycnometry. Samples were dried in an oven at 60 °C for 4 h before true density measurements. An accurately weighed sample (1–2 g) was placed into the sample cell of a helium pycnometer (Quantachrome Instruments, Ultrapycnometer 1000e, Byonton Beach, FL) and the measurements were repeated for a maximum of 100 times. The experiment was terminated when the coefficient of variation of five consecutive measurements was below 0.005% and the mean of the last five measurements was reported as the true density of the sample.

2.2.5. Assessment of deformation behaviors of powders

Heckel analysis was performed to assess deformation behaviors of both pure powders and mixtures [1,16]. Heckel equation (Eq. (3)) describes the relationship between porosity (ε) and compaction pressure (P).

$$-\ln \varepsilon = k \cdot P + A \tag{3}$$

The parameter *k* is the slope of the linear region of the Heckel plot. The mean yield pressure (P_y), which is related to material plasticity, was obtained from Eq. (4):

$$P_y = \frac{1}{k} \tag{4}$$

Deformation characteristics were also assessed using the Kuentz - Leuenberger (KL) equation (Eq. (5)) [3]:

$$P = \frac{1}{C}\left[\varepsilon - \varepsilon_c - \varepsilon_c \ln\left(\frac{\varepsilon}{\varepsilon_c}\right)\right] \tag{5}$$

A nonlinear fitting of P-ε data yields two parameters, powder compressibility (C) and critical porosity (ε_c), which are the same as the corresponding parameters in Eq. (1). The parameter, 1/C, similar to P_y from Heckel analysis can be used to assess powder plasticity. The parameter ε_c corresponds to maximum porosity at which the powder just starts to exhibit mechanical rigidity. An inherent advantage of the KL analysis is that all data points are used for regression instead of using only a portion of data (linear region) in Heckel analysis.

2.2.6. Height profiling of flashing

The height profile of tablet flashing was characterized using profilometry. Briefly, as prepared tablets or tablets after treatment