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Precision of pharmaceutical powder flow measurement using ring shear tester: High variability is inherent to powders with low cohesion

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ABSTRACT

The purpose of this study is to assess the precision of pharmaceutical powder flow measurement using ring shear tester, and to understand whether certain types of powders are more error-prone than others. To answer these questions, we presented the nonlinear mathematical model which enables the calculation of flow function from raw experimental data from the ring shear tester. The variance of the flow function and its origin were evaluated through the first order Taylor expansion of the flow function model. These analyses indicated that the precision of flow function measurement can be compromised by powders with inherently low cohesion values. A marked increase in flow function variability is seen when the cohesion value of a powder is below 100 Pa (in measurements with pre-consolidation stress of 1 kPa). The variability in flow function measurement is attributed predominantly by cohesion, whereas friction angles have only minor contribution. The study also showed that the precision of flow function measurement cannot be improved by testing at higher pre-consolidation stresses. All the results were verified experimentally using six pharmaceutical powders exhibiting diverse flow behaviors. These results suggested that one must exercise caution when testing and analyzing powders with low cohesion values using ring shear tester. For such materials, an alternative testing method is recommended to corroborate the powder flow data from ring shear testing.

1. Introduction

Powder flowability is one of the most attended material attributes in development and manufacturing of pharmaceutical solid dosage forms [1,2]. A reliable manufacturing process requires a pharmaceutical powder to possess adequate flowability to enable its mobilization and transportation, such as the ability of powder to flow out of a hopper or into a die [3–5]. To understand and characterize pharmaceutical powder flow, multiple technologies have been adopted by the pharmaceutical industry over the years [6–8]. Among them, shear cell testers have gained popularity due to the sound theoretical basis and increasing level of automation allowing for ease of operation and data analysis.

Shear cell testers have long been established to determine flow properties of bulk solid [9–11]. By modeling bulk solid as a Coulomb material, Jenike showed that a shear cell tester in essence can simulate the measurement of unconfined yield stress in a uniaxial compression test [12,13]. The ring shear tester, which is a relatively recent modification of Jenike shear cell tester and operate on the same principle, is a common type of shear cell tester available in pharmaceutical development laboratories, thanks to its ability to generate greater strain and to reach steady-state flow with its circular structure [14].

In practice, the powder flow measurement using ring shear tester gives rise to a yield locus (and the corresponding parameters for the linearized yield function), and a pre-shear point at steady-state flow. From these raw data, Mohr semicircles were generated to evaluate major principal stress and unconfined yield stress. In most analysis, the flow function (ff_c), which is a ratio of major principal stress to unconfined yield stress resulting from the above analysis, is used as the primary index to rate flowability of bulk solids.

Despite the widespread use of ff_c as the main characteristic of pharmaceutical powder flow using ring shear tester, there has been little discussion on the general applicability of this method concerning the myriad of pharmaceutical powders exhibiting rather diverse flow behaviors [15]. It was recently reported that the powder flow properties, specifically the unconfined yield stress, determined from an annular shear tester have higher variability than the uniaxial compression tester [8]. It is also the authors' experience that certain types of pharmaceutical powders tended to exhibit broader ff_c standard deviations than others. Therefore, the purpose of the study is to present the mathematical description (i.e. nonlinear functions) leading to the determination of ff_c using ring shear tester, so that the origin of its variability can be fully analyzed and understood. Through the combination of mathematical simulations and experimental verification using various

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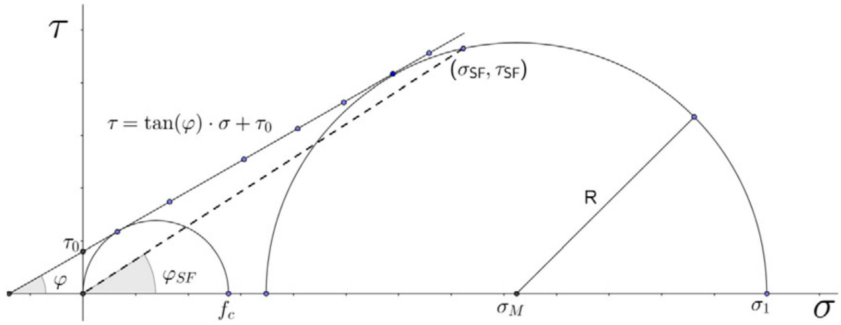

Fig. 1. Schematic representation of the linear yield locus and Mohr semicircles obtained from flow measurement using a ring shear tester.

pharmaceutical powders, we intend to identify powder flow properties most sensitive to the precision of ff_c determination, so that one may judge, *a priori*, whether ring shear testing is the most appropriate method for powder flow measurement.

2. Theoretical preliminary

2.1. Calculation of flow function

In shear cell testing, the flow function (ff_c) of a pharmaceutical powder is typically calculated by assuming the ideal Coulomb material, following the linear yield function:

$$\tau = (\tan\varphi)\cdot\sigma + \tau_0 \tag{1}$$

where τ and σ are shear stress and normal stress upon yielding, respectively. φ and τ_0 are friction angle and cohesion, representing the slope ($\tan\varphi$) and y-intercept of the linear yield locus, respectively.

The yield locus could potentially show significant curvature toward the lower end of the normal stress, and can be modeled by other equations [16]. In this work, we limit our calculations on Coulomb type, linear yield function, which is a close approximation and the basis for the vast majority of analysis used in ring shear tester measurements.

Experimentally, the flow function is obtained by measuring two sets of data points: 1) a pre-shear point, which is a pair of normal and shear stress (σ_{SF},τ_{SF}) leading to steady-state flow under a pre-selected normal stress σ_{SF}, and 2) a collection of (σ,τ) pairs at incipient flow, measured on the same powder repeatedly pre-consolidated at σ_{SF}. The yield locus is then calculated by fitting the (σ,τ) data to a linear line, with its endpoint defined as the point of tangency on the large Mohr semicircle passing through the pre-shear point (σ_{SF},τ_{SF}), showing in Fig. 1.

The unconfined yield stress, f_c, is defined as the far end of the Mohr semicircle running through the origin and tangent to the linear yield locus. f_c can be obtained by geometric calculations as the following (Fig. 1):

$$f_c = \frac{2\tau_0\cos\varphi}{1-\sin\varphi} \tag{2}$$

The major principal stress at steady-state flow, σ_1, is located at the far end of the large Mohr semicircle which runs through the pre-shear point (σ_{SF},τ_{SF}), and is tangent to the linear yield locus at a point to the left of (σ_{SF},τ_{SF}). As shown in Fig. 1, the radius of the large Mohr semicircle, R, is:

$$R = \sqrt{(\sigma_{SF}-\sigma_M)^2 + (\sigma_{SF}\cdot\tan\varphi_{SF})^2} \tag{3}$$

where σ_M is the center of the large Mohr semicircle along the σ_1 axis; and φ_{SF} is the angle of internal friction at steady-state flow, which is the angle between the σ-axis and the line connecting the origin and the pre-shear point (Fig. 1). Because the large Mohr semicircle is tangent to the linear yield locus, basic geometry shows that:

$$\sin\varphi = R\Big/\left(\sigma_M + \frac{\tau_0}{\tan\varphi}\right) \tag{4}$$

Combining Eqs. (3) and (4) gives rise to σ_M as:

$$\sigma_M = \tan^2\varphi\cdot\sigma_{SF} + \tan\varphi\cdot\tau_0 + \sigma_{SF} - \frac{\sqrt{(\tan\varphi\cdot\sigma_{SF}+\tau_0+\sigma_{SF}\cdot\tan\varphi_{SF})\,(\tan\varphi\cdot\sigma_{SF}+\tau_0-\sigma_{SF}\cdot\tan\varphi_{SF})}}{\cos\varphi}. \tag{5}$$

The major principal stress at steady-state flow, σ_1, can therefore be determined as:

$$\sigma_1 = \sigma_M + R = \sigma_M + \sqrt{(\sigma_{SF}-\sigma_M)^2 + (\sigma_{SF}\cdot\tan\varphi_{SF})^2} \tag{6}$$

The flow function, defined below, can then be obtained using Eqs (2), (5) and (6), through the experimentally determined linear yield locus ($\tan\varphi$ and τ_0), and pre-shear point (σ_{SF},τ_{SF}).

$$ff_c = \sigma_1/f_c \tag{7}$$

2.2. Calculation of variance of flow function

The variance of the flow function originates from the parameters intrinsic to the ring shear cell measurements, i.e. $\tan\varphi$ and τ_0 through linear regression of (σ,τ) pairs at incipient flow, and pre-shear point (σ_{SF},τ_{SF}). As shown in the preceding section, the flow function is a nonlinear mathematical function of φ, τ_0, σ_{SF} and φ_{SF}. Therefore, to simplify

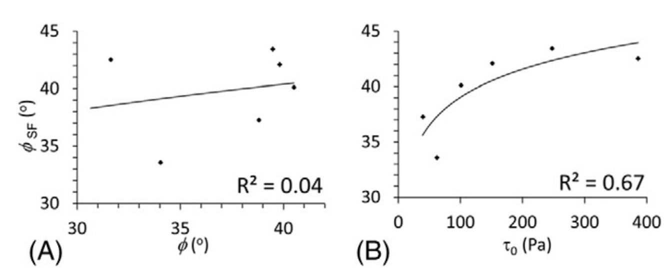

Fig. 2. Correlation between φ and φ_{SF} (A) and between τ_0 and φ_{SF} (B) from the ring shear tester measurements on 6 pharmaceutical powders with different flowability.