Characterization of the Properties of Powder Excipients Commonly Used in Pharmaceutical Compounding

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Introduction

Powder excipients are commonly used in pharmaceutical compounding for the extemporaneous preparation of capsules, a popular dosage form: flexible, tasteless, easily administered and easily filled extemporaneously (Sakr and Alanazi, 2013). Excipient selection is a crucial step in pre-formulation since the properties and behavior of the excipients affect not only the manufacturing process (e.g. compression and adhesion to surfaces) but also the final characteristics of the capsules (e.g. stability and bioavailability) (Ando and Radebaugh, 2005; O'Connor *et al.*, 2005). A comparative analysis of the properties and behavior of lactose and 3 commercial powder excipients was performed in order to predict the characteristics of the corresponding capsules.

Methodology

A Freeman FT4 Powder Rheometer (Freeman Technology Ltd) was the research instrument used for the analysis of the dynamic, bulk and sheer properties of the powder excipients since it provides sensitive, fast and repeatable measurements (Freeman, 2007). All tests were carried out using a 23.5 mm blade and a 25 mm vessel. Samples were tumbled prior to testing to achieve a homogeneous state of segregation. Aside from sample preparation, the majority of the tests were automated with no operator involvement and all tests were repeated twice. The powder excipients 1 and 2 correspond to Loxasperse and Loxoral, respectively (PCCA, 2013); 3 corresponds to an alternative commercial powder excipient; and 4 is lactose, a common capsule diluent in pharmaceutical compounding (Allen, 2000).

Dynamic properties: The dynamic properties of powder excipients - dynamic flow, aeration and consolidation - were determined by rotating a precision blade down a helical path through the powders.

Dynamic flow: The dynamic flow of each powder excipient was characterized by five tests: basic flowability energy (BFE, mJ), a measure of the energy required to displace a powder during non-gravitational, forced flow; specific energy (SE, mJ/g), a measure of the energy required for gravity induced flow; stability index (SI), a measure of the physical stability; flow rate index (FRI), a measure of the response to changing flow rates; and conditioned bulk density (CBD, g/mL), a fundamental physical property of powders.

Aeration: The aeration measures changes in the flow properties due to the introduction of air and predicts how the powder excipients will behave during the mixing process in capsule manufacturing. The presence or absence of air is deemed to be one of the most important factors that affect the dynamic properties of powders (Freeman, 2007). Both aerated energy (AE20) and aeration ratio (AR20=AE0/AE20) were determined at 20 mm/s air velocity.

Consolidation: This test measures the impact of tapping on the flow properties of the powder excipients and predicts potential problems during manufacturing or transportation of the corresponding capsules due to the consolidation of particles. The consolidation index (CI) was determined for the four powder excipients by tapping each vessel 50 times.

Bulk properties

Compressibility: This test measures the ability of the powder excipients to become compacted (when subjected to normal stress) and predicts the changes in volume during the manufacturing or transportation of the corresponding capsules. A high percentage of compressibility at 15kPa (CPS15) is indicative of a highly compressible powder excipient.

Permeability: This test measures the ease at which the powder excipients transmit or release air over a range of stress conditions and predicts the powder behavior during capsule filling. Permeability was tested by pressure drop across the powder bed with applied normal stress up to 15 kPa.

Shear properties

Sheer cell analysis: This test measures the sheer stress (τ) required to initiate flow in a pre-consolidated powder and is relevant for measuring the onset of flow (static to dynamic). The sheer stress was determined by applying increasing normal stress to the four powder excipients.

Wall friction: This test measures the ease at which the powder excipients flow in relation to the wall materials and predicts the adhesion to the surfaces of the mixing equipment and the capsule machine. This test was carried out using a 1.2 µm Ra 316 stainless steel coupon.

Powder excipients	1	2	3	4
BFE (mJ)	135	221	85.5	75.0
SI	0.9	1.0	0.9	0.9
FRI	1.5	1.3	1.9	1.8

Table 1.

Dynamic flow properties (BFE, SI and FRI) of the four powder excipients.

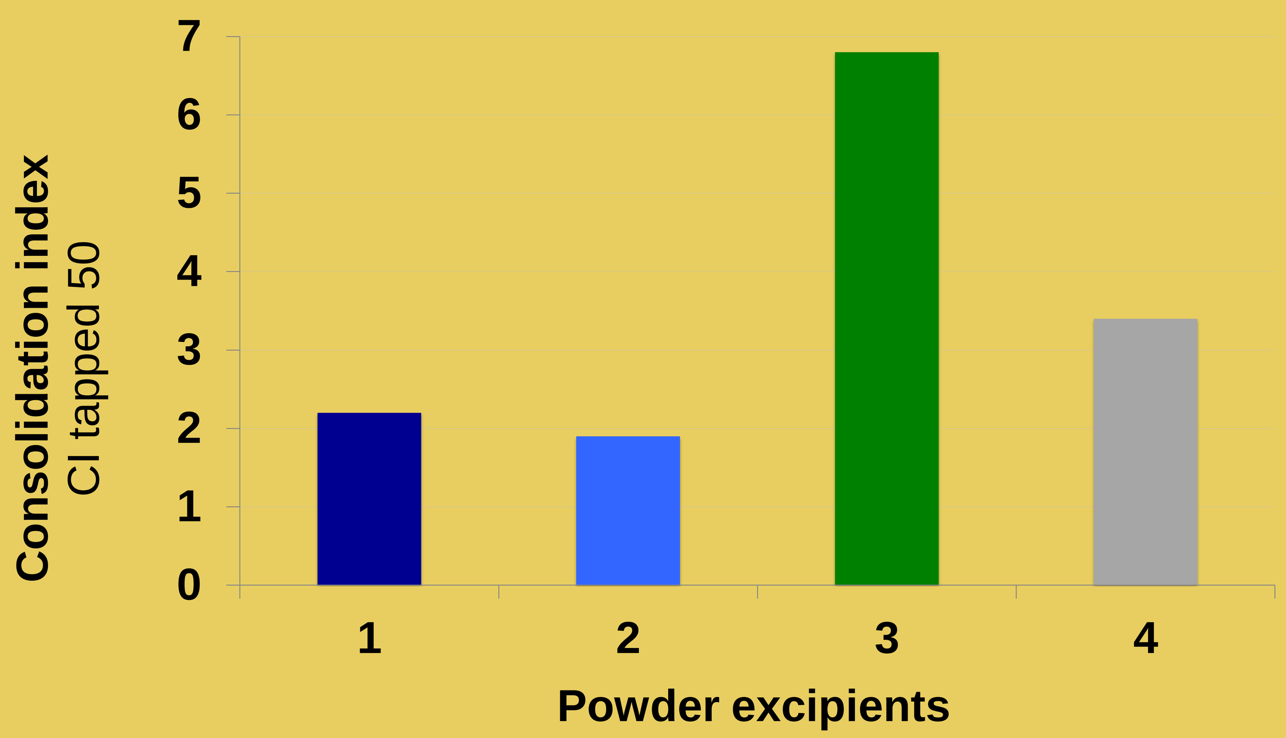

Figure 1.

Concentration index of the four powder excipients.

1. Allen, L. Featured excipient: capsule and tablet diluents. Int. J. Pharm. Compd. 4, 306-310 (2000).

2. Ando, H. and Radebaugh, G. Property-based drug design and preformulation, in Troy, D. (ed.) Remington The Science and Practice of Pharmacy. 21st edn. Baltimore and Philadelphia: Lippincott Williams & Wilkins, 720-744 (2005).

3. Freeman, R. Measuring the flow properties of consolidated, conditioned and aerated powders – a comparative study using a powder rheometer and a rotational shear cell. Powder Technol. 174, 25-33 (2007).

4. O'Connor, R.; Schwartz, J. and Felton, L. Powders, in Troy, D. (ed.) Remington The Science and Practice of Pharmacy. 21st edn. Baltimore and Philadelphia: Lippincott Williams & Wilkins, 702-719 (2005).

5. PCCA. Exclusives, Bases. Available at: http://www.pccarx.com/pcca-products/pcca-exclusives/bases (2013).

6. Sakr, A. and Alanazi, F. Oral solid dosage forms, in Felton, L. (ed.) Remington Essentials of Pharmaceutics. London: Pharmaceutical Press, 581-610 (2013).

Results and Discussion

Clear and repeatable differences were obtained for the properties and behavior of the four powder excipients, in particular the powders excipients 1 and 2, in comparison with lactose and the powder excipient 3.

Dynamic properties: Lactose and the powder excipient 3 exhibited similar resistance to flow in both constrained (BFE) and unconstrained environments (SE). All powder excipients showed a SI close to unity and hence are physically stable. Excipients 1 and 2 exhibited the lowest FRI and, therefore, are the least sensitive to varying blade tip speed (Table 1). The lowest CBD was found for Lactose (0.433 g/mL).

With regards to the aeration test, the powder excipient 2 exhibited the highest aerated energy (AE20=43.1) and, therefore, has a stronger inter particle bonding (higher absolute cohesion) in comparison to the other powder excipients tested.

The consolidation test indicated marked differences between all powders tested (Figure 1). The powder excipients 1 and 2 exhibited the lowest consolidation index (CITapped50=2.2 and 1.9, respectively), which indicates that these excipients are the ones least likely to be affected by consolidation during manufacturing and transportation of the corresponding capsules.

Bulk properties: Lactose exhibited the highest compressibility (CPS15=42.8%), which indicates that this excipient contains large amounts of entrained air, whereas the powder excipient 1 exhibited the lowest compressibility of all powders tested (CPS15=15.1%) and, therefore, has the most efficient particle packing.

The powder excipients 1 and 2 were the most permeable since these presented the lowest pressure drop values at 15 kPa (respectively, 1.4 and 2.3 mbar), in comparison to lactose and the powder excipient 3 (respectively, 4.7 and 5.0 mbar).

Shear properties: The lowest shear stress was generated by the powder excipient 1 ($\tau_{3.9}$=2.6 kPa and $\tau_{7.9}$=5.3 kPa) and, therefore, this is the least problematic powder excipient in the initiation of flow.

The lowest wall friction angles (WFA) were obtained for the powder excipients 1 and 2 (WFA1.2µm=23.7º and 21.6º, respectively), which indicates that these powder excipients are the least resistant to flow in relation to the wall materials of the mixing equipment and the capsule machine.

Conclusions

The properties and behavior of the four powder excipients analyzed are markedly different and, as a result, the corresponding capsules will exhibit different characteristics.

The powder excipients 1 and 2 are the least sensitive to varying blade tip speed and are the most permeable. These powder excipients are also the least resistant to flow in relation to the wall materials of the mixing equipment and the capsule machine, and are the least likely to be affected by consolidation during manufacturing and transportation of the corresponding capsules.

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