Powder Technology 270 (2015) 490–493

Contents lists available at ScienceDirect

Powder Technology

journal homepage: www.elsevier.com/locate/powtec

Compression prediction accuracy from small scale compaction studies to production presses

Kendal G. Pitt [a,*], Rachael J. Webber [a], Kirsty A. Hill [a], Dipankar Dey [b], Michael J. Gamlen [b]

[a] GSK Global Manufacturing and Supply, Priory St, Ware SG12 0DJ, UK
[b] Gamlen Tableting Ltd, Biocity Nottingham, Nottingham NG1 1GF, UK

ARTICLE INFO

Available online 18 October 2013

Keywords:
Tablet tensile strength
Scale-up
Tablet ejection
Tablet shape

ABSTRACT

Small scale compaction studies which utilise equipment representative of commercial scale tablet presses can be used to develop process understanding of pharmaceutical formulations using minimal quantities of material. In this study the scalability of compressibility (solid fraction vs. compaction pressure), tabletability (tensile strength vs. compaction pressure), compactibility (tensile strength vs. solid fraction) and ejection shear stress was examined over an eight-fold range in tablet size. Tablets of two representative commercially manufactured formulations were compressed and compared using a small scale compaction press and large scale industrial press. Different tablet sizes and shapes were produced from the two types of press. One formulation was manufactured by direction compression and the other by wet granulation. Generally, good agreement was found across the scales for all the measures assessed. In addition, the measurement of ejection shear stress data on the small scale was able to accurately predict tablet failure on commercial rotary presses.

1. Introduction

To develop process understanding of pharmaceutical formulations it is desirable to perform small scale compaction studies with minimal quantities of material. However, there are a number of known process differences between small and large scale tablet presses, including press speed and dwell time [1,2]. It is important that small scale studies utilise equipment that is representative of the large scale tablet presses used to manufacture commercial products. This enables data produced at different scales to be compared and for the performance of the formulation on large scale to be predicted from data collected at small scale.

Comparison of compression and ejection forces, tablet hardness and weight are only valid if the tablets have the same dimensions and shape. The tablets produced from small scale tablet presses are not necessarily the same size and shape as those produced at large scale. Measurement of the correct tablet properties allows tablets manufactured at different scales and using different equipment to be compared. The tablet dimensions are used to calculate the compaction pressure, tensile strength, solid fraction and ejection shear stress of the tablet which allows tablets of different sizes to be compared. The tensile strength, solid fraction and compaction pressures were rationalised in terms of compressibility (solid fraction vs. compaction pressure), tabletability (tensile strength vs. compaction pressure) and compactibility (tensile strength vs. solid fraction) [3].

The tensile strength for flat face tablets was calculated from Eq. (1) and for convex face tablets using Eq. (2) [4,5]. The tensile strength of caplet shape tablets was assessed using Eq. (3) [6].

$$\sigma_t = \frac{2P}{\pi D t} \tag{1}$$

$$\sigma_t = \frac{10P}{\pi D^2\left(2.84\frac{t}{D} - 0.126\frac{t}{W} + 3.15\frac{W}{D} + 0.01\right)} \tag{2}$$

$$\sigma_t = \frac{2}{3}\left(\frac{10P}{\pi D^2\left(2.84\frac{t}{D} - 0.126\frac{t}{W} + 3.15\frac{W}{D} + 0.01\right)}\right) \tag{3}$$

σ_t is the tensile strength, P is the fracture load, D is the length of the short axis or diameter of the tablet, t is the overall thickness and W is the wall height of the tablet.

Generally, a tensile strength greater than 1.7 MPa will usually suffice in ensuring that a tablet is mechanically strong enough to withstand commercial manufacture and subsequent distribution. Ideally, tensile strengths greater than 2 MPa should be targeted to ensure a satisfactory robust product. Tensile strengths as low as 1 MPa may suffice for small batches where the tablets are not subjected to large mechanical stresses [6].

The solid fraction, or relative density, of the tablets was another method of analysis used to compare tablets with different dimensions.

* Corresponding author.
E-mail address: kendal.5.pitt@gsk.com (K.G. Pitt).

0032-5910/$ – see front matter © 2013 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.powtec.2013.10.007

Table 1
Comparison of tablet compression conditions from bench top (GTP) and rotary press (Fette).

	DC1		WG1	
	GTP	Fette	GTP	Fette
Compaction force (kN)	1 to 5	6 to 30	1 to 5	6 to 30
Weight (mg)	100	800	80	350
Shape	6 mm diameter flat face, cylindrical tablets	Caplet shape tablets 17 mm by 7 mm	5 mm diameter flat face, cylindrical tablets	10 mm diameter round convex tablets

Solid fraction was calculated from the ratio of the tablet density and true density of the formulation. This indicates the ratio of air to solid in the tablet. Solid fractions in the range 0.85 ± 0.05 are optimal for tablet formulations [7,8].

The ejection force for a tablet is the force required to eject the tablet from a die after compaction. If the ejection force for a tablet is too high then capping and lamination will occur. The ejection force will be dependent on the compaction pressure applied to the tablet, typically the higher the compaction pressure, the higher the ejection force [9]. The effect of the ejection force depends on the size of the tablet; a larger tablet will be able to withstand a higher ejection force. Therefore, to compare across the scales, ejection shear stress was calculated by dividing the peak ejection force by the area of the tablet in contact with the die wall. The lower the ejection shear stress, the less likely that tablet defects will occur.

Generally an ejection shear stress of less than 3 MPa from a commercial tablet press will suffice in producing a tablet which does not cap or laminate. Ejection shear stresses up to 5 MPa may be acceptable where the tablets are not subjected to large mechanical stresses on subsequent processing such as film-coating. Ejection shear stresses above 5 MPa would be expected to cause failure [10,11].

2. Material and methods

2.1. Materials

A direct compression and a wet granulated formulation were examined in these studies.

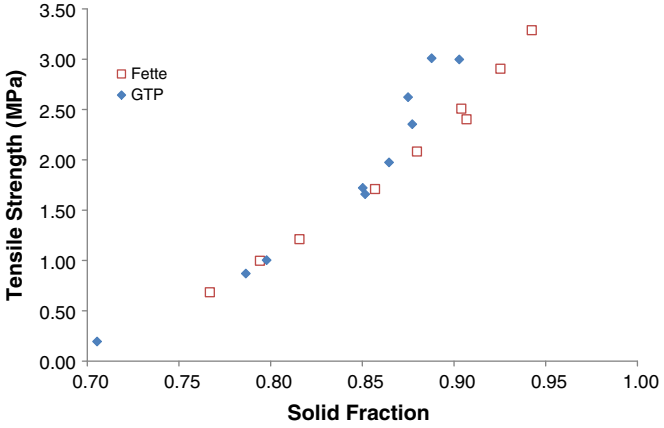

Fig. 2. Compactibility of DC1.

The direct compression formulation (DC1) was a blend of active pharmaceutical ingredient (API) with microcrystalline cellulose, sodium starch glycolate, silicon dioxide and magnesium stearate.

The wet granulated formulation (WG1) was composed of a granulation of API, mannitol and microcrystalline cellulose together with polyvinylpyrrolidone. The extra-granular excipients sodium starch glycolate, magnesium stearate and additional microcrystalline cellulose were blended with the granules.

2.2. Compression experiments

The compression experiments were performed using a Gamlen GTP-1 single punch bench top tablet press which has a uni-axial saw tooth displacement profile (Gamlen Tableting, United Kingdom). Compaction forces from 1 to 5 kN were used to compress 100 mg of the direct compression blend, DC1, and 80 mg of the granulated compression blend, WG1, to form either 5 or 6 mm diameter flat face cylindrical tablets. The same bench top tablet press was used to measure the diametral compression force i.e. the fracture strength of the tablets. Data was collected on the compression profile, ejection stress, weight and thickness of the tablets formed.

Fette rotary tablet presses (Fette, Germany) were used in commercial manufacture of these products. 800 mg caplet shaped tablets (for DC1) and 350 mg round convex tablets (for WG1) were produced. Compaction forces from 6 to 30 kN were used on the commercial presses and the fracture strength of the resulting tablets measured as before (Table 1).

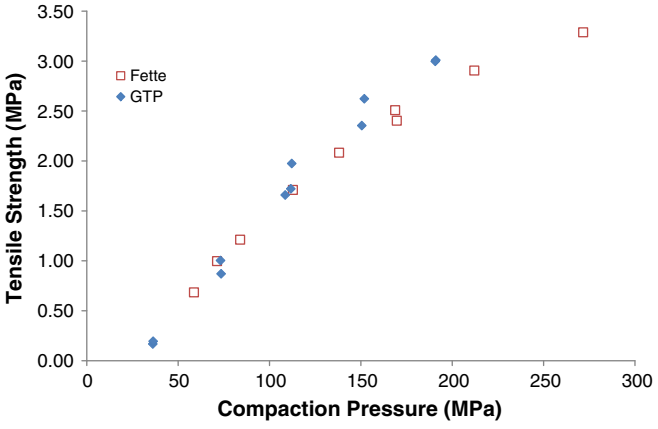

Fig. 1. Tabletability of DC1.

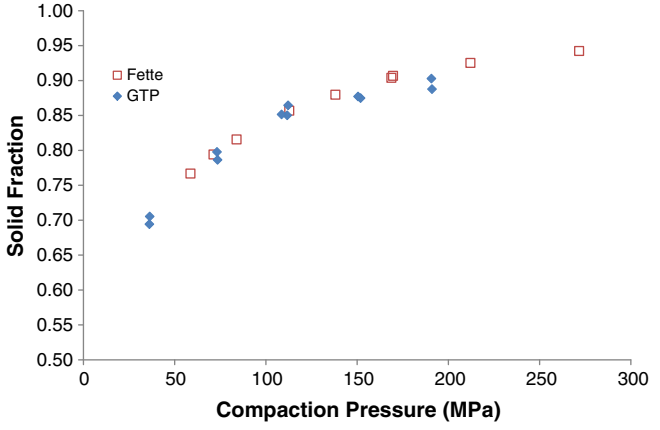

Fig. 3. Compressibility of DC1.