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*Research Paper*

# Predicting the Tensile Strength of Compacted Multi-Component Mixtures of Pharmaceutical Powders

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***Purpose.*** Pharmaceutical tablets are generally produced by compacting a mixture of several ingredients, including active drugs and excipients. It is of practical importance if the properties of such tablets can be predicted on the basis of the ones for constituent components. The purpose of this work is to develop a theoretical model which can predict the tensile strength of compacted multi-component pharmaceutical mixtures.
***Methods.*** The model was derived on the basis of the Ryshkewitch-Duckworth equation that was originally proposed for porous materials. The required input parameters for the model are the relative density or solid fraction (ratio of the volume of solid materials to the total volume of the tablets) of the multi-component tablets and parameters associated with the constituent single-component powders, which are readily accessible. The tensile strength of tablets made of various powder blends at different relative density was also measured using diametrical compression.
***Results.*** It has been shown that the tensile strength of the multi-component powder compacts is primarily a function of the solid fraction. Excellent agreement between prediction and experimental data for tablets of binary, ternary and four-component blends of some widely used pharmaceutical excipients was obtained.
***Conclusion.*** It has been demonstrated that the proposed model can well predict the tensile strength of multi-component pharmaceutical tablets. Thus, the model will be a useful design tool for formulation engineers in the pharmaceutical industry.

**KEY WORDS:** compact-ability; multi-component blends; solid fraction; tablets; tensile strength.

## INTRODUCTION

Pharmaceutical tablets are the most popular dosage form for drug delivery. Tablets are generally manufactured by compacting a mixture of powder blends, including active drugs and excipients. The manufacturing processes consist of several distinct stages (1–3), including die filling, compaction and ejection. During die filling, the powder blends are deposited into a die using a shoe which runs across the die opening. Then the powder blends are compressed inside the die using a set of tooling, where the powder particles experience intensive deformation and the powder particles bond together through a number of mechanisms, including van der Waals forces, mechanical interlocking and the formation of solid bridges (4). Finally the compacted powder bed is ejected from the die so that a tablet is formed. The tablets comprise compacted porous materials, and they generally have a relative density (solid fraction) in the range of 0.7–0.9 (5).

Tablets have to be strong enough to sustain their integrity during the post-compaction processes, such as coating, packing and handling. In other words, the powder particles in the blends have to bond firmly together so that the tablet as a whole does not break. One of the important parameters which characterise whether the tablet is sufficiently strong is the tensile strength, which is the maximum tensile stress that can be tolerated in the tablet before it breaks. The typical method used to measure the tensile strength of a tablet is diametrical compression (6). In this test, a cylindrical tablet is compressed diametrically between two platens until it breaks/crushes. The crushing load is recorded and the tensile strength can be calculated from the crushing load together with the dimensions of the tablets as follows (6):

$$\sigma_t = \frac{2F}{\pi dt} \tag{1}$$

where $\sigma_t$ denotes the tensile strength, $F$ is the maximal diametrical crushing force, $d$ and $t$ are the diameter and thickness of the tablet, respectively.

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The tensile strength of tablets made of various powder blends can be measured using this approach. Many factors related to the powder blends influence the tensile strength of a tablet, such as the properties of constituent components, tablet porosity, particle shape and size, surface area and so on, which has hence attracted increasing interests, in particular, to explore the correlation between tensile strength and the properties of constituent components (7–13). Vromans *et al.* (7) explored the correlation between tensile strength and the surface area of the powder blends, which was determined by mercury porosimetry, for different types of crystalline lactose and found that the tablet strength is proportional to the surface area and that neither the presence of water in the α-lactose monohydrate nor the concentrations of α- and β-lactose in their mixtures have any influence on the tensile strength (4). De Boer *et al.* (8) also obtained a good linear relation between surface area and tensile strength of the tablets made of a series of sieved fractions of α-lactose monohydrate. In addition they found that the tablets made of smaller particles had a higher tensile strength at any given pressure. Similar trends were also observed for the tensile strength of various pharmaceutical materials with different size fractions (9–11). This is due to the fact that the powder blends with smaller particles have higher surface area than those with larger particles. Sebhatu and Alderborn (11) studied the tensile strength of amorphous and crystalline lactose and found that tablets made of amorphous lactose have higher tensile strength than those made of crystalline lactose. Wong and Pilpel (12) investigated the influence of particle shape of calcium carbonate on the tensile strength and found that a higher tensile strength is obtained for more irregular particles at a given solid fraction. Poquillon *et al.* (13) measured the tensile strength of compacts made from powders with irregular particles and with spherical particles and found that the compacts made of irregular particles gave higher strength than those made of spherical particles.

The effect of compression speed during the compaction process on the tensile strength of tablets has also been studied. Tye *et al.* (14) examined the effect of tableting speeds on tensile strength of four common pharmaceutical excipients (Microcrystalline cellulose-MCC, Pre-gelatinized starch, lactose monohydrate and dicalcium phosphate) and found that the relationship between tensile strength and solid fraction for all materials tested was essentially independent of tableting speed. Our recent study (15) on some widely used pharmaceutical excipients, including MCC, hydroxypropylmethyl cellulose (HPMC) and starch, also reached the same conclusion that the tensile strength of tablets was primarily dependent upon the solid fraction but was independent of the compression speed and the size of the tablets. This indicates that the relation between tensile strength and solid fraction is unique for a given material.

The influence of the properties of the compositions on the tensile strength of binary tablets has been widely investigated (14–20). Tye *et al.* (14) measured the tensile strength for tablets made of a placebo mixture (a mixture of MCC and lactose) at different compression speeds and showed that the tablet tensile strength is independent of compression speed but primarily depends upon the solid fraction. The tensile strength for a range of mixtures of MCC and HPMC and of MCC and starch was reported in (15), which clearly showed that tensile strength is primarily dependent of solid fraction. Surface area has been regarded one of the important factors which dominate the tensile strength, as stronger bonds can be formed for the powders with larger surface area during compaction. Hence, the dependence of tensile strength upon the surface area of binary tablets has also been widely investigated (16–20). The tensile strength of tablets made of binary mixtures of various types of lactoses were reported in (16–18) and it has been shown that that the tensile strength is proportional to the surface area for binary tablets. Similar patterns were also observed for binary mixtures of aspirin and metamizol, aspirin and caffeine (19), and of anhydrous lactose and sucrose (20).

Several theories have been developed attempting to model the tensile strength, in particular, for binary tablets. A theory for tensile strength of fine powder was developed by Cheng (21) and was modified by Chan *et al.* (22) to analyse the tensile strength of binary tablets. Concepts of reference state and a reduced tensile strength were introduced in the modified model. The model considered the effects of particle size and the composition of binary mixtures. However, this model is very difficult to use in practice, as some parameters in the model are not easily accessible, including the parameter describing intrinsic interaction between particles of different materials. Based upon percolation theory, Kuentz and Leuenberger (23) developed a model for tensile strength of binary tablets comprising well and poorly compactable substances. It was assumed that a tablet can only be produced with a solid fraction higher than a critical solid fraction ($D_c$), which is the threshold required to build a percolating system in the tablets. For tablets with a solid fraction $D$ ($\geq D_c$), the tensile strength $\sigma_t$ is given as

$$\sigma_t = c(D - D_c)^{2.7} \tag{2}$$

where $c$ is a proportional constant. For binary mixtures, the critical solid fraction $D_c$ was related to the critical solid fractions, $D_{c1}$ and $D_{c2}$, of single components as follows,

$$D_c = \xi_1 D_{c1} + (1 - \xi_1) D_{c2} \tag{3}$$

where $\xi_1$ is the weight fraction of the well compactable component. This model is primarily applicable if one dominant component in the mixture contributes to the overall strength of the tablets, while the other has nearly zero compact-ability and negligible contribution. Ramirez *et al.* (24) proposed a modified model for the cases in which both components can contribute to the tensile strength of binary tablets by introducing an initial strength parameter $\sigma_0$ into Eq. (2), i.e.,

$$\sigma_t = c(D - D_c)^{2.7} + \sigma_0 \tag{4}$$

By fitting the experimental data for the tensile strength of binary tablets at different solid fractions, the unknown parameters in the above models can be determined and then these models may be used to predict the tensile strength of binary tablets made of the same mixtures. However, it is impossible to use these models to predict the tensile strength of binary tablets based upon the knowledge of the properties of constituent components. In order to tackle this problem, we developed a simple predictive model for the tensile

strength of binary mixtures, based upon Ryskewitch-Duck worth equation for porous materials (15). Good agreement between the theoretical prediction and experimental data demonstrated that the proposed model could predict accurately the tensile strength of binary mixtures based upon the readily accessible properties of single component powders.

Although understanding the dependence of the tensile strength of binary tablets on the properties of single-component constituents is vital to fully understand how the constituent components contribute to the tensile strength of real tablets made of multi-components, it is still unclear whether there is a direct connection between binary tablets and multi-component tablets. Due to the complexity of the tableting process, little attention has been paid onto the tensile strength of multi-component tablets. In addition, it is of obvious interest to develop a model which can predict the tensile strength of multi-component tablets from the accessible information available for the individual constituents. In this study, for the first time, we aim to develop a predictive model for the tensile strength of multi-component tablets, based upon the extension of the model we developed for binary tablets (15). The proposed model will be validated with extensive experimental data for various mixtures at different concentrations.

## EXPERIMENTAL

We considered four pharmaceutical excipients widely used in the pharmaceutical industry: microcrystalline cellulose (MCC) (Avicel PH-102; FMC Corporation, Brussels, Belgium), Hydroxypropylmethyl cellulose (HPMC) (Methocel K100M), Pregelatinized starch (Starch 1500, Colorcon Ltd., Kent, UK), and lactose monohydrate (Pharmatose 50 M, DMV International). Among these, MCC Avicel PH-102 is one of the most used filler-binders in pharmaceutical products, HPMC is a Hydrophilic polymer excipient widely used as a diluent, and starch is widely used as a distintegrant, diluent and binder in pharmaceutical products. Lactose, in particular Pharmatose 50 M, is widely used as a dilute and also flow improvement agent in pharmaceutical tablet formulation. All the powders were used as received and their mean particle sizes are in the similar range of approximately 100–300 μm.

Binary, ternary (three-component) and four-component mixtures of these excipients were produced with different fractions. The typical powder systems considered in this study are presented in Table I. The powder mixtures of 100 g were mixed in a Turbula T2F Shaker Mixer (Basel, Switzerland) at 23 rpm for 30 min. The true density of the single-component powders and their mixtures were measured using a helium gas displacement pycnometer (Type AccuPyc 1330, Micromeritics®, Bedfordshire, UK).

For the tablets of single-component powders (i.e, Monolithic tablets of MCC, HPMC, starch and lactose), two batches of flat cylindrical tablets were manufactured using different approaches. The first batch was produced using a compaction simulator (ESH testing, Brierley Hill, West Midlands, UK). Batches of 200 mg of the powders were manually poured into a die of 8 mm in diameter and the powders were compressed and decompressed at 30 mm/s without holding between the compression and decompression stages, i.e., a V-shaped compaction profile was used. Tablets with different densities were produced by varying the total compaction duration, consequently minimal punch separation and the maximum compression force were also controlled. The second batch was produced using an Instron Universal Testing machine with a 30 KN load cell (Model 5567, Instron Ltd, Buckinghamshire, UK). Powders of 800 mg were filled into a 13 mm evacuable pellet die (Specac Ltd, Kent, UK) and were compressed and decompressed at 0.083 mm/s up to a specified compression force ranging from 3 to 18 kN. No lubricant was used in any of the tablet preparation. Since compact-ability (the variation of tensile strength of powder compact with the solid fraction) of the powders was found to be independent of the approaches employed (15), only the latter approach was employed to produce the tablets of powder mixtures.

The tablet weight was measured using an electronic balance (Type AG204, Mettler-Toledo Inc., Leicester, UK) and the diameter and the thickness were measured with digital callipers (Brown & Sharpe Ltd, Wiltshire, UK). From these measurements, the volume and density of the tablets

**Table I.** A List of Powder Systems Considered and Comparison of the Measured True Density with the Prediction of Eq. (10) for the Mixtures

| | Notation | Powder | Measured true density (g/cm$^3$) | Predicted true density (g/cm$^3$) |
|---|---|---|---|---|
| Single-component (pure) powders | MCC | MCC (Avicel PH-102) | 1.5897 ± 0.0028 | – |
| | HPMC | HPMC | 1.3160 ± 0.0003 | – |
| | Starch | Starch 1500 | 1.4934 ± 0.0014 | – |
| | Pharmatose | Pharmatose 50 M | 1.5388 ± 0.0006 | – |
| Binary mixtures | MixB1 | 50%MCC + 50%Starch (w/w) | 1.5425 ± 0.0014 | 1.5400 |
| | MixB2 | 20%MCC + 80%Starch (w/w) | 1.5215 ± 0.0014 | 1.5117 |
| | MixB3 | 80%MCC + 20%Starch (w/w) | 1.5643 ± 0.0013 | 1.5695 |
| Ternary mixtures | MixT1 | 40%MCC + 40%HPMC + 20%Pharmatose | 1.4425 ± 0.0004 | 1.4587 |
| | MixT2 | 20%MCC + 40%HPMC + 40%Pharmatose | 1.4439 ± 0.0003 | 1.4499 |
| | MixT3 | 40%MCC + 40%HPMC + 20%Starch | 1.4567 ± 0.0008 | 1.4503 |
| | MixT4 | 20%MCC + 40%HPMC + 40%Starch | 1.4482 ± 0.0016 | 1.4335 |
| Four-component mixtures | MixF1 | 40%MCC + 20%HPMC + 20%Starch + 20%Pharmatose | 1.4704 ± 0.0003 | 1.4982 |
| | MixF2 | 20%MCC + 20%HPMC + 20%Starch + 40%Pharmatose | 1.4713 ± 0.0002 | 1.4889 |

were determined. The solid fraction ($D$) was calculated by dividing the tablet density by the true density of the powders used. The tensile strength of the tablet was determined from diametrical compression tests, which were performed using an Instron Universal Testing machine with a 1 kN load cell in order to accurately measure the maximal diametrical crushing force ($F$). Together with the measured diameter and thickness of the tablets, the tensile strength ($\sigma_t$) is then calculated using Eq. (1).

## THE MODEL

### Ryshkewitch-Duckworth Equation

Ryshkewitch (25) investigated the tensile strength of porous sintered alumina and zirconia and showed that the tensile strength is related to the porosity. It was found that the logarithm of the tensile strength is inversely proportional to the porosity. A discussion of Ryshkewitch's paper by Duckworth (26) leads to the following equation for the correlation of tensile strength with the porosity:

$$\ln\left(\frac{\sigma_t}{\overline{\sigma}}\right) = -k\varepsilon \tag{5}$$

where $\varepsilon$ is the porosity of the compacts and $\varepsilon = 1-D$, $\overline{\sigma}$ is the tensile strength of the materials with zero porous (i.e., $\varepsilon = 0$ and $D = 1$), and $k$ is a constant representing the bonding capacity. A higher value of $k$ corresponds to stronger bonding of primary particles (27). It has been demonstrated that the Ryshkewitch-Duckworth equation given in Eq. (5) can well represent the variation of tensile strength with the porosity for a wide range of porous materials (14,15,27–30). Therefore the Ryshkewitch-Duckworth equation (Eq. 5) will be used as a starting point for developing a model for the tensile strength of multi-component tablets. It can also been seen from Eq. (5) that if the parameters $\overline{\sigma}$ and $k$ are known, the tensile strength of a powder compact can be estimated from its porosity (or, equivalently, the solid fraction).

### True Density for Multi-Component Mixtures

To determine the porosity or the solid fraction of a powder compact made of multi-component mixtures, its true density need to be known. The true density of $n$-components mixtures $\rho_m$ can be determined from the true densities of the constituent single-component powders $\rho_i$ ($i = 1,...,n$) according to the equilibrium of the volume of solids during the mixing, i.e.,

$$V_m = \sum_{i=1}^{n} V_i \tag{6}$$

where $V_m$ and $V_i$ are the total volume of solids particle in the mixture and in the constituent powder $i$, respectively, and can be given as

$$V_m = \frac{W_m}{\rho_m} \tag{7}$$

$$V_i = \frac{W_i}{\rho_i} \tag{8}$$

where $W_m$ and $W_i$ are the mass of powder mixture and the constituent powder $i$, respectively. Substituting Eqs. (7) and (8) into Eq. (6), we have

$$\frac{W_m}{\rho_m} = \sum_{i=1}^{n} \frac{W_i}{\rho_i} \tag{9}$$

Equation (9) can be rewritten as the

$$\frac{1}{\rho_m} = \sum_{i=1}^{n} \frac{W_i}{W_m \rho_i} = \sum_{i=1}^{n} \frac{\xi_i}{\rho_i} \tag{10}$$

where $\xi_i (= W_i/W_m)$ is the weight fractions of the constituent powder $i$ ($i = 1,...,n$). Eq. (10) is generally referred to as the rule of mixing.

A comparison of the measured true density (using pycnometer) and predicted true density for the mixtures considered in this study is also given in Table I. It is clear that the measured and predicted true densities are very close, which indicates that Eq. (10) can adequately predict the true density of multi-component mixtures.

### Tensile Strength for Multi-Component Mixtures

For compacted powder mixtures at zero porosity, the bonding capacity $k_m$ and tensile strength $\overline{\sigma}_m$ depends upon a number of factors, such as the corresponding properties of the constituent powders, the particle size, surface area, etc. Vromans *et al.* (31) investigated the tensile strength of a series of lactoses with various particle size, texture, water content, and the concentration ratio of α- to β-lactose and found that the bonding capacity was directly related to the surface area of the starting materials (uncompacted powder blends) and the tablet specific surface area is linearly proportional to the surface area of starting materials. Moon and Choi (32) found that the strength of powder compacts is directly proportional to the contact area between particles. It is hence reasonable to suggest that the surface area of the uncompacted powder blends is a dominant factor in determining the tensile strength at zero porosity and bonding capacity of the powder mixture.

Let us consider an idealistic multi-component mixtures system that consists of $n$ different powders with spherical particles of identical size (mono-sized spheres), as illustrated in Fig. 1a. The corresponding compacted powder blends at zero porosity is given in Fig. 1b. In Fig. 1 the different hatched spheres represent different constituent powders. For such a mixtures, the maximum force to break the compact along an arbitrary surface Ω can be written as

$$F_m = \overline{\sigma}_m S_m = \sum_{i=1}^{n}\sum_{j=1}^{n} \overline{\sigma}_{ij} S_{ij} \tag{11}$$

where $\overline{\sigma}_m$ and $S_m$ are the tensile strength and contact area along surface Ω of the compacted powder mixtures at zero porosity, $\overline{\sigma}_{ij}$ and $S_{ij}$ are the tensile strength and contact surface area between constituent powders $i$ and $j$ ($i = 1,...,n$, $j = 1,...,n$). Due to the complexity and diversity of pharma-

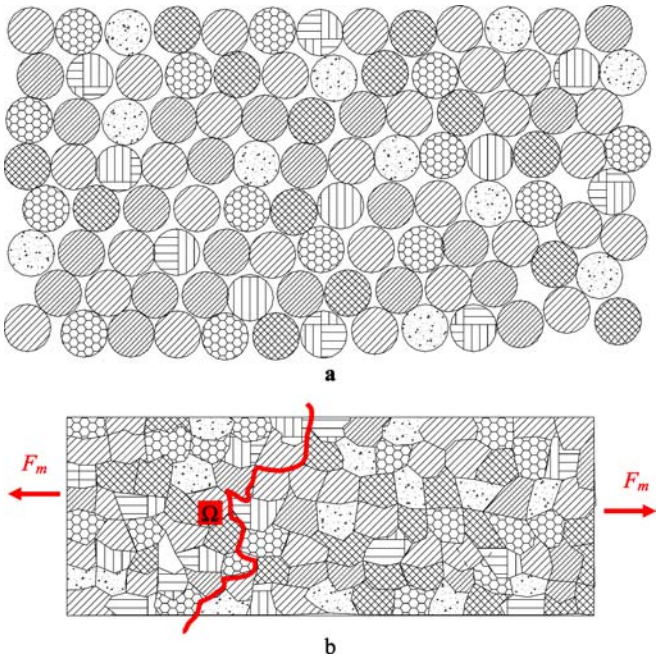



**Fig. 1.** Illustration of the powder blends at (a) loose compacted state and (b) compacted state with a porosity of zero.

ceutical powders, it is not a trivial task to rigorously determine the tensile strength between two different materials. As a first approximation, we assume that, compared to the tensile strength for single pure material, the tensile strength between two different materials is negligible, i.e.,

$$\overline{\sigma}_{ij} = 0 \quad \text{when } i \neq j \tag{12}$$

Equation (11) can hence be simplified as

$$\overline{\sigma}_m S_m = \sum_{i=1}^{n} \overline{\sigma}_i S_i \tag{13}$$

Since the tablet specific surface area is linearly proportional to the surface area of starting materials (31) and the number of bonding sites was proportional to the surface area (7), we can assume that for powders of spherical particles

$$S_m = \psi \frac{V_m}{d_m} \tag{14a}$$

$$S_i = \psi \frac{V_i}{d_i} \tag{14b}$$

where $d_m$ and $d_i$ are the diameters of corresponding powder particles. $\psi$ is the ratio of contact surface area to the total surface area. Substituting Eqs. (14a,b) into Eq. (13), we have

$$\overline{\sigma}_m \frac{V_m}{d_m} = \sum_{i=1}^{n} \overline{\sigma}_i \frac{V_i}{d_i} \tag{15}$$

for mono-sized powder mixtures, $d_m = d_i$. Eq. (15) can hence be rewritten as

$$\overline{\sigma}_m V_m = \sum_{i=1}^{n} \overline{\sigma}_i V_i \tag{16}$$

or

$$\overline{\sigma}_m = \sum_{i=1}^{n} \overline{\sigma}_i \frac{V_i}{V_m} = \sum_{i=1}^{n} \overline{\sigma}_i \zeta_i \tag{17}$$

where $\zeta_i$ is the volume fraction of the constituent powder $i$ and can also be expressed in terms of the weight fraction $\xi_i$ as

$$\zeta_i = \frac{V_i}{V_m} = \frac{\xi_i G_m / \rho_i}{G_m / \rho_m} = \frac{\xi_i \rho_m}{\rho_i} \quad (i = 1, \ldots, n) \tag{18}$$

where $G_m$ is the weight of the multi-component mixture.

It can be seen from Eq. (17) that the tensile strength of compacted powder mixtures, $\overline{\sigma}_m$, can be determined from the tensile strength of constituent components, $\overline{\sigma}_i$, weighted by their volume fractions, $\zeta_i$. Following the study of Vromans *et al.* (31) who pointed out that the binding capacity was directly related to the surface area of the starting materials, we assume that the bonding capacity $k_m$ of the powder mixtures at zero porosity can also be determined in a similar manner, i.e.,

$$k_m = \sum_{i=1}^{n} k_i \zeta_i \tag{19}$$

Using Eqs. (5), (17) and (19), the tensile strength of the multi-component mixtures can then be written as

$$\begin{aligned} \ln(\sigma_t) &= -k_m(1 - D) + \ln(\overline{\sigma}_m) \\ &= (D - 1)\sum_{i=1}^{n} k_i \zeta_i + \ln\left(\sum_{i=1}^{n} \overline{\sigma}_i \zeta_i\right) \end{aligned} \tag{20}$$

Using Eq. (10), Eq. (20) can also be expressed in terms of the bulk density $\rho$ and weight fraction $\xi_i$ as follows,

$$\ln(\sigma_t) = \left(\rho \sum_{i=1}^{n} \frac{\xi_i}{\rho_i} - 1\right) \sum_{i=1}^{n} k_i \zeta_i + \ln\left(\sum_{i=1}^{n} \overline{\sigma}_i \zeta_i\right) \tag{21}$$

It is clear that, for multi-component mixture at a given packing density $\rho$, its tensile strength can be determined from the information on the constituent powders. In other words, if knowing the properties of the constituent powders ($\rho_i, \overline{\sigma}, k_i, \xi_i$ *or* $\zeta_i$), the tensile strength of the powder mixtures can be determined using either Eq. (20) or Eq. (21).

## RESULTS AND DISCUSSION

In order to validate the model developed in previous section, a series of experiments were performed in which tensile strength of powder systems given in Table I were

measured. A comparison of the tensile strength between the model prediction and experimental results is presented in this section. In addition, experimental data in the literature published by other researchers are also used to validate the model.

### Tensile Strength for Single-Component Powders

Figure 2 shows the variation in tensile strength with solid fraction for the tablets made of various single-component powders considered. In this figure, we also superimposed the data obtained from literature (14) which are shown in open symbols, while the solid symbols show the results from the experiments described in Section 2. Some of these results were first reported in (15). It is interesting to note that, for MCC, our experimental data (15) were in excellent agreement with the ones produced by Tye *et al.* (14), event though different approaches and operator has been employed to produce the tablets. This indicates that the variation of tensile strength with the solid fraction (or porosity) of tablets is a unique index for characterising the compact-ability of powders. In addition, for a given solid fraction, MCC tablets had the highest tensile strength, and Pharmatose tablets had the lowest.

Furthermore, the logarithm of the tensile strength appears to be proportional to the solid fraction. A close examination of the data reveals that for all cases considered, correlation coefficients $r^2$ (by linear regression), which measure the strength of the linear relation between two variables, are all higher than 0.96, as given in Table II. This demonstrates that the relationship between the logarithm of the tensile strength and the solid fraction is linear. This is consistent with the analyses published in the literature (14,15,25–30). The experimental data can be well fitted by Ryshkewitch-Duckworth equation (i.e., Eq. 5) according to the principle of least squares. The fitted lines are also superimposed in Fig. 2 where solid lines are for the fitting of our experimental data and dashed lines are for the data of (14). The fitting gives the tensile strength at zero density $\overline{\sigma}$ and bonding capacity $k$ for the single-component powders considered. The corresponding values are presented in Table II. It is clear that MCC has the highest tensile strength at zero porosity, while Pharmatose has the lowest. However, Pharmatose has the highest bonding capacity while the bonding capacity for cellulose powders (MCC and HPMC) are similar and are the smallest ones. This implies that MCC can form strong tablets but increasing the solid fraction will not dramatically increase the tensile strength, on the contrary, tablets made of Pharmatose will have very low tensile strength but an increase in the solid fraction of the tablet will greatly increase the tensile strength. Therefore, $\overline{\sigma}$ and $k$ can indicate how well a powder can be compacted. These values given in Table II will be used to predict the

**Table II.** Tensile Strength at Zero Density $\overline{\sigma}$ and Bonding Capacity $k$ for the Single-Component Powders Considered

| Powder | $\overline{\sigma}$ (MPa) | $k$ | $r^2$ |
|---|---|---|---|
| MCC | 29.96 | 7.6 | 0.985 |
| HPMC | 13.46 | 8.8 | 0.990 |
| Starch | 12.18 | 12.0 | 0.985 |
| Pharmatose | 2.80 | 14.8 | 0.966 |
| MCC (14) | 24.53 | 6.9 | 0.985 |
| Lactose (14) | 13.50 | 12.7 | 0.982 |

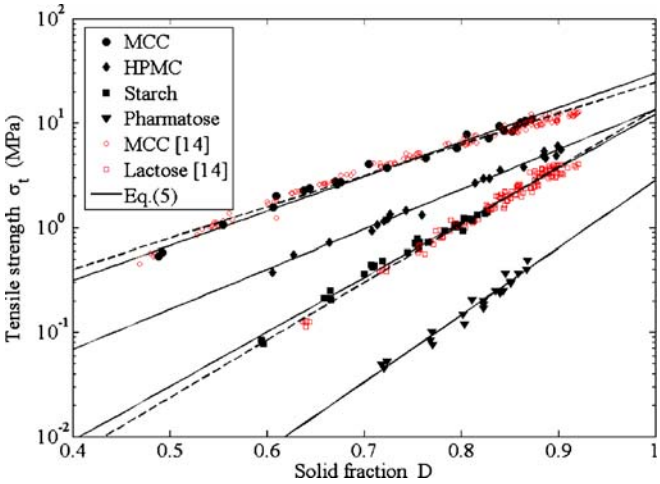



**Fig. 2.** The variation of tensile strength with solid fraction for single-component powders.

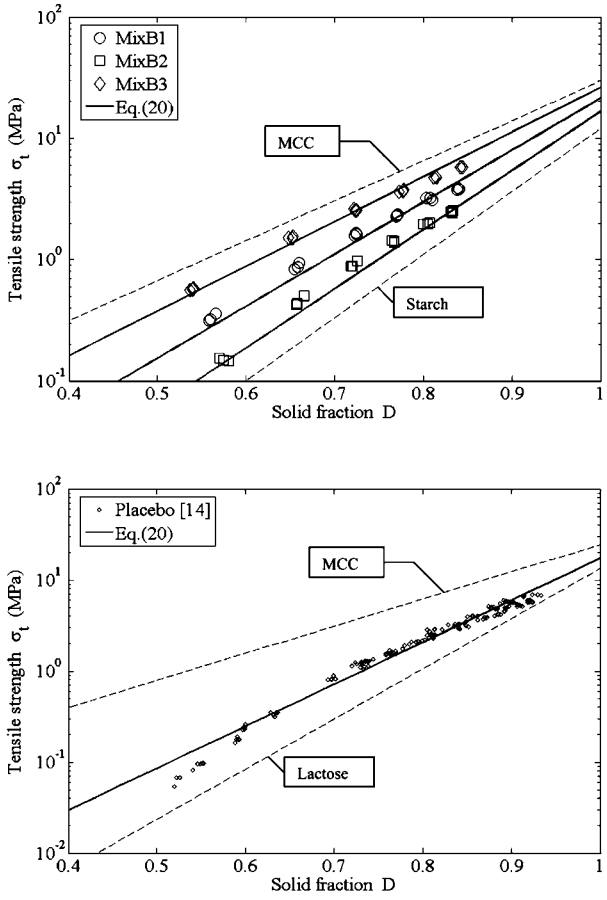
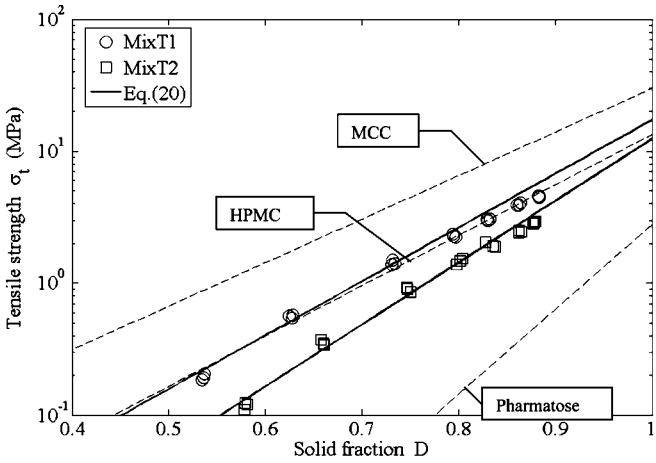



**Fig. 3.** The variation of tensile strength with solid fraction for various binary mixtures (a) Binary mixtures of MCC and starch (b) Placebo—a binary mixtures of MCC and lactose (data obtained by Tye et al (14)).

tensile strength for multi-component tablets in conjunction with Eq. (20).

### Tensile Strength for Multi-Component Mixtures

The variation of tensile strength with the solid fraction for binary, ternary and four component mixtures of various fractions of constituent powders are shown in Figs. 3, 4 and 5, respectively. In these figures, the symbols represent the experimental data and the solid lines are the predictions using Eq. (20). In addition, the fitted lines for relevant single-component powders, as given in Fig. 2, are also superimposed and shown in dashed lines. It is clear that experimental data almost lie on the lines given by Eq. (20) for various cases considered. In particular, the prediction of Eq. (20) agree very well with the experimental data published by Tye *et al.* (14), although Eq. (20) apparently overestimates the tensile strength when the solid fraction is less than 0.55. The overestimation in the low solid fraction range is believed to be an inherent consequence of Ryshkewitch-Duckworth equation, which appeared to overestimate the tensile strength for porous compacts with a solid fraction less than 0.55 (14,25).

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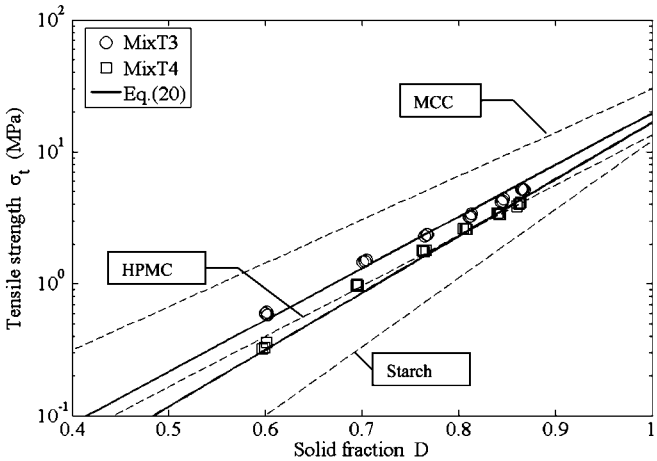


b

**Fig. 4.** The variation of tensile strength with solid fraction for various ternary mixtures (a) Ternary mixtures of MCC, HPMC and Pharmatose (b) Ternary mixtures of MCC, HPMC and Starch

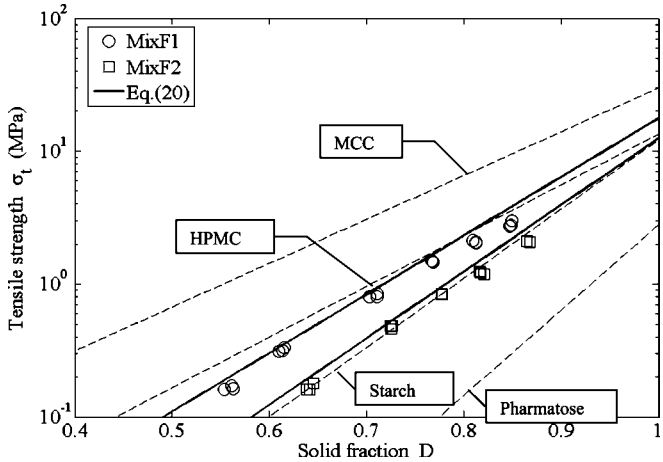


**Fig. 5.** The variation of tensile strength with solid fraction for four-component mixtures of MCC, HPMC, Starch and Pharmatose at different concentrations

Nevertheless, this is not practically important as argued by Tye *et al.* (14), because real pharmaceutical tablets will have a solid fraction in the range of 0.7–0.9 (5). As demonstrated in Figs. 3, 4 and 5, for tablets with a solid fraction in this range, Eq. (20) can well predict the variation of tensile strength with the solid fraction for the multi-component mixtures of various fractions of pharmaceutical excipients.

## CONCLUSION

The tensile strength of tablets made of various single-component of pharmaceutical excipients and of their binary, ternary, four-component mixtures at various concentrations were determined. It has been shown that the tensile strength of tablets of a particulate powder is primarily a function of the solid fraction or porosity. The logarithm of tensile strength is proportional to the solid fraction. A model has been developed on the basis of the Ryshkewitch-Duckworth equation. The validity of this model has been demonstrated with experimental data obtained both in our lab for various mixtures of widely used pharmaceutical powders and published in literature by other researchers. Most significantly, the proposed model can well predict the tensile strength of multi-component pharmaceutical mixtures merely from the readily accessible properties of the constituent single-component powders, which can be used as a design tool in pharmaceutical formulation engineering.

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