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Research paper

A new theoretical approach to tablet strength of a binary mixture consisting of a well and a poorly compactable substance

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Abstract

The objective of this study was to analyse the tensile strength of a well and a poorly compactable substance in a tablet mixture. Recent developments in the theory of percolation were taken into account and two power laws are proposed, one for the tensile strength as a function of the relative density of the mixture, and the other for the relationship between the strength and compaction pressure. Both equations are assumed to be valid in a comparatively low pressure range. A universal testing instrument Zwick UPM 1478 was used for the manufacture and testing of the compacts. Mixtures of Avicel PH101 and paracetamol at different ratios were chosen as model systems. The experimental results showed that the proposed model equations fitted the experimental data reasonably well for all mixture ratios. It was observed that the critical solid fraction of the mixture, i.e. the strength percolation threshold, increased with rising amounts of the drug. We investigated the strength threshold not only in terms of the solid fraction, but also in terms of the mass fraction (excipient percolation threshold). It is assumed that a tablet can only be produced with a certain minimal amount of the well compactable substance that is needed to build a percolating cluster in the tablet. An interpretation is therefore provided for the dilution capacity of a direct tableting excipient with a poorly compactable drug. The dilution capacity was experimentally determined according to the method of Minchom and Armstrong (Br. Pharm. Conf. (1987) 69 pp.). Our experimental estimate of 79.9% drug is in perfect agreement with our proposed theoretical calculation of 79.7%. These estimates are, however, much higher than the one reported in a recent study (Y. Habib, L. Augsburger, G. Reier, Th. Wheatley, R. Shangraw, Dilution potential: a new perspective, Pharm. Dev. Tech. 1 (2) (1996) 205–212) where the dilution capacity of the same mixture was investigated. This discrepancy can be explained based on the different pressure ranges and extrapolation techniques that were used. As a conclusion, concepts of the percolation theory can successfully be applied to the kind of mixture studied in this paper. It is conceivable that the theoretical tools presented can also be applied to mixtures of more than two substances if they consist of a single well compactable excipient and several poorly compactable components. Such mixtures are relevant for the development of direct compressible tableting formulations.

Keywords: Binary mixture; Dilution capacity; Fracture exponent; Percolation theory; Tensile strength

1. Introduction

The mechanics of tablets is very complex. A lot of scientific effort has been devoted to the analysis of the compaction of single component tablets. However, it can be claimed that the physics of compression is not yet properly understood. It is therefore not surprising that most studies on mixtures deal with simple binary systems rather than more realistic multicomponent mixtures. In most studies, a mechanical property like the tensile strength is plotted against the mass fraction of the components. Complex non-linear relationships were reported by several authors [1–3] and it seems difficult to postulate clear trends. The investigation of a given mechanical property as a function of the mass fraction of a substance is surely meaningful from a practical point of view but has the drawback that the relative density is not constant. It is therefore a valid option to extrapolate the given mechanical parameter to zero porosity and then to analyse its behaviour for the different mass fractions. The Leuenberger theory of bonding points in the tablet was proposed for the measured strength of binary mixtures [4,5]. It was assumed that every component contributes to the tablet strength individually. Hence, the tensile strength $\sigma_{t(AB)}$ of a mixture of the two components A and B results in

$$\sigma_{t(AB)} = \sigma_{tmax(AB)}\left(1 - e^{\gamma_{(AB)}\rho_{(AB)}\sigma}\right) \quad (1)$$

where $\sigma_{tmax(AB)}$ is the maximal tensile strength of the mixture at zero porosity ($\rho_{(AB)} = 1$), and $\gamma_{(AB)}$ is a constant of the mixture that describes the degree of volume reduction under the applied pressure, σ, i.e. $\gamma_{(AB)}$ represents a system specific parameter, the compressibility. It is a challenging goal to

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deduce the mixture parameters from the behaviour of the single substances. Thus, *additivity* rules were proposed for the compressibility of the components A and B, Eq. (2). Also, the maximal strength in the mixture was predicted from the zero porosity strength of the individual substances in Eq. (3) where $X_{(A)}$ stands for the mass fraction of component A:

$$\gamma_{(AB)} = X_{(A)}\gamma_{(A)} + (1 - X_{(A)})\gamma_{(B)} \quad (2)$$

$$\sigma_{t\max(AB)} = \sigma_{t\max(A)}^{X_{(A)}}\sigma_{t\max(B)}^{1-X_{(A)}} \quad (3)$$

The above equations can also be formulated with an additional parameter taking into account interactions between the components and a link to the theory of the solid solubility parameters was reported [6]. However, despite the usefulness of these classical concepts, some often observed experimental phenomena remained unexplained. Mixture properties can show abrupt changes at defined component mass ratios. Such critical concentrations were interpreted using percolation theory [7,8].

2. Theory

2.1. Recent developments in the theory of percolation

The classic percolation model assumes a lattice where the sites are either occupied with the probability p or remain empty with the counter probability $1 - p$ [9]. At a defined probability p_c, i.e. the percolation threshold, a cluster is formed that spans the entire lattice. From this threshold p_c on, this percolating cluster dominates the overall properties of the lattice. Any macroscopic cluster property Φ obeys in the vicinity of the percolation threshold, p_c a power law according to the expression

$$\Phi \propto (p - p_c)^q \quad (4)$$

The exponent q remains the same for different lattice types which means that q holds universally.

Percolation is a theory for disordered systems and its possible application to binary mixtures can be instructively shown with the electrical conduction of a binary composition [10]. It can be imagined that the occupied sites in a lattice represent the component A that is a good conductor whereas the empty lattice sites represent the component B that is an insulator. Below the percolation threshold, the conductor A has a low concentration and forms isolated clusters in the non-conducting matrix of substance B. Accordingly, the lattice exhibits no macroscopic conductivity. This behaviour changes tremendously above the defined concentration p_c where the conductor builds a coherent cluster spanning the whole lattice. The function of the conductivity, Σ follows a power law behaviour in analogy to Eq. (4) with an exponent $\mu \cong 2$ (in three dimensions). This characteristic exponent also plays an important role in diffusion processes and was used to describe the release kinetics of a water soluble substance in an inert matrix [11]. From a theoretical point of view, it is interesting to study the mixture of a conductor with a superconductor. It was shown that the conductivity obeys a power law with a new critical exponent $s \cong 0.87$ that is different from μ [12]. The most general case in which a mixture of two finite conductors is considered, produces a rather complex formula for the conductivity [10]. The percolation transition is less pronounced than in the special cases treated before and the change of macroscopic conductivity decreases if the two types of finite conductors A and B are similar. The example of the conductivity is illustrative as it shows how the property of the components can create different types of physical problems. For our considerations, mechanical properties are of interest but unfortunately, they are less extensively studied on a theoretical level than conductivity.

To formulate a mechanical model of percolation, elements like springs or beams are introduced into a virtual lattice. In case of the Young's modulus, a lattice can be imagined in which elastic springs represent the occupied sites. First, it was assumed that the elastic behaviour is similar to that of the conductivity until it was theoretically shown that the occurrence of bond-bending forces, i.e. torque's lead to a significantly higher elastic exponent τ than the exponent μ [13,14]. Thinking again of a binary mixture, it would be of interest to study the more general case of a lattice where two types of springs with different force constants are considered. There are reports in the literature dealing with the so called *superelastic* problem [15,16], where a two-component system of a rigid and a soft material is treated. From experimental measurements of the Young's modulus of gel–alumina and gel–zirconia mixtures, Benguigui and Ron [17] proposed a superelastic exponent of $s' \cong 0.67$.

To study mechanical strength in a percolation model, brittle beams can be imagined in a lattice, or also springs that undergo brittle fracture if their elastic limit is exceeded. Guyon et al. proposed a theoretical value for the strength or fracture exponent that is $T_f \cong 2.7$ [18]. There exists, however, a lack of knowledge on the general case where two different microscopic strengths coexist in the mixture. Thus, it is apparent that percolation models of mechanical properties constitute a field in physics of ongoing development. Accordingly, the application to pharmaceutical compacts is a rather new field. The modified Young's modulus was analysed in uniaxially compressed tablets of different types of microcrystalline cellulose (MCC). The experimental value $\tau = 4.0 \pm 0.1$ [19] was reasonably close to its theoretical prediction. Also, the tensile strength of MCC tablets was tested in a diametrical compression test yielding an experimental value for the strength exponent $T_f = 3.2 \pm 0.1$ [20], slightly higher than theoretically predicted. Note that in both studies a single component was examined or in other words, a binary mixture of the solid fraction and pores was considered. It is the main scope

of this paper to extend these investigations to a real binary mixture.

2.2. Mixtures of a good and a poorly compactable substance

In line with these theoretical considerations, it seems that a classification of tablet mixtures is meaningful. One can not expect to model all types of mixtures with a single critical exponent for a given tablet property. In case of the tensile strength, this means that a mixture should have characteristics for which the use of the already known fracture exponent, T_f is acceptable. Thus, a binary mixture of a well and a poorly compactable substance is of special interest for this study. In such a mixture, the component A is assumed to create adequate strength whereas substance B exhibits practically no bonding strength. The latter substance is therefore treated like the porosity, in the sense that only the matrix of substance A is relevant for the tensile strength.

This paper treats the model mixture of MCC, i.e. Avicel PH101 and paracetamol where the MCC holds for the well compactable excipient and the drug is well known for its poor compactibility. The dependence of the tensile strength on the mixture solid fraction as well as on the compaction pressure is investigated.

Besides the percolation threshold of the relative density of the mixture there exists also a threshold of the mass fraction. This aspect stresses a topic of current investigations in the pharmaceutical literature. A direct tableting excipient has the ability to incorporate a certain amount of a poorly compactable drug. For this maximal amount of drug, the term *dilution capacity* was proposed by Wells and Langridge [21]. Later, Minchom and Armstrong [22] proposed a method to determine this value. The dilution capacity is understood as a critical value of the mass fraction above which the compactibility of the tableting mixture vanishes. The problem of finding the dilution capacity seems to be related to the problem of elucidating a percolation threshold of the excipient. This view is promising regarding the possibility of a new interpretation and theoretical description of the dilution capacity.

3. Materials and methods

Tablets (round, flat, 11 mm diameter, 400 ± 1 mg weight) for the subsequent determination of the tensile strength using the Zwick® UPM 1478 Universal Testing Instrument (Zwick® GmbH, Ulm, Germany) were prepared. As a model mixture, Avicel® PH101(FMC) batch No.6918 and paracetamol Ph.Eur. II krist. (Siegried®, Zofingen, Switzerland) were used.

The true density was determined with a Beckman Air Comparison Pycnometer® Model 930 (Table 1). The mixtures were prepared by a 7-min blending using a tumbler mixer (Turbula T2A, W.A. Bachofen AG, Basel, Switzerland) at 25 rev./min. For each powder system, four tablets were compressed at different pressure levels ranging from 5.26 to 52.61 MPa at a relative air humidity of 45 ± 10%. The compression speed was 10 mm/min and the die wall was lubricated with magnesium stearate before every compression cycle. Forty-eight hours after manufacture, the radial tensile strength of the compacts was tested. The pre-force was 0.3 N and the testing speed was 25 mm/min. The radial tensile strength was calculated according to Newton et al. [23]:

Table 1
Density characterisation of the components

	True density (g/cm^3)	Relative bulk density	Relative tapped density
Avicel PH101	1.57	0.205	0.260
Paracetamol	1.27	0.397	0.509

$$\sigma_t = \frac{2F}{\pi \cdot D \cdot h} \tag{5}$$

where F is the maximal force recorded, D the tablet diameter and h its thickness. Only compacts, showing an ideal fracture were taken into account for the subsequent statistical evaluation.

The determination of the dilution capacity was performed according to the method described by Armstrong and Minchom [22]. Note that in this paper, the normalized area under a tensile strength- pressure curve is called *area ratio* and not *work potential* as in the original work.

All statistical evaluations were conducted with the program SYSTAT® for Windows Version 7.0 (SPSS Inc., Evanston, IL).

4. Results and discussion

4.1. Tensile strength in relation to the solid fraction of the mixture

Taking into account the recent finding that the tensile strength of MCC tablets scales with the fracture exponent T_f [20], it is reasonable to propose a similar behaviour for a tablet consisting of Avicel PH101 and paracetamol. This assumption is based on the fact that the dominating solid fraction of Avicel PH101, $\rho_{(A)}$ is proportional to the mixture solid fraction, $\rho_{(AB)}$ and so Eq. (6) is proposed:

$$\sigma_{t(AB)} = k_1\left(\rho_{(AB)} - \rho_{c(AB)}\right)^{T_f} \tag{6}$$

If the tensile strength is set to the inverse power of the exponent T_f, (*inverse exponent plot*) a straight line is obtained with the slope a and intercept b:

$$\sigma_{t(AB)}^{1/T_f} = k_1^{1/T_f}\left(\rho_{(AB)} - \rho_{c(AB)}\right) = a\rho_{(AB)} + b \tag{7}$$

The tensile strength obtained from the diametrical compression test fulfilled indeed the above stated linearity in the inverse exponent plots (Table 2; Fig. 1). This linear relationship was in principle shown by all mixtures. Yet, the r^2

Table 2
Linear regression according to Eq. (7)

Amount Avicel PH101 (%)	a	b	$\rho_{c(AB)} = -b/a$	r^2
100	3.410	−0.866	0.245	0.999
90	3.045	−0.868	0.285	0.997
80	2.913	−0.914	0.314	0.997
70	2.832	−0.978	0.345	0.996
60	2.769	−1.045	0.377	0.994
50	2.664	−1.113	0.418	0.989
40	2.499	−1.182	0.473	0.987
30	2.338	−1.230	0.526	0.975

values decreased with increasing amounts of drug. This can to some extent be explained by the fact that the regression coefficient depends on the slope that also decreases with higher amounts of paracetamol (Table 2). But apart from this, it is still conceivable that the high dilution of Avicel PH101 affects the exponent. The range of validity in Eq. (7)

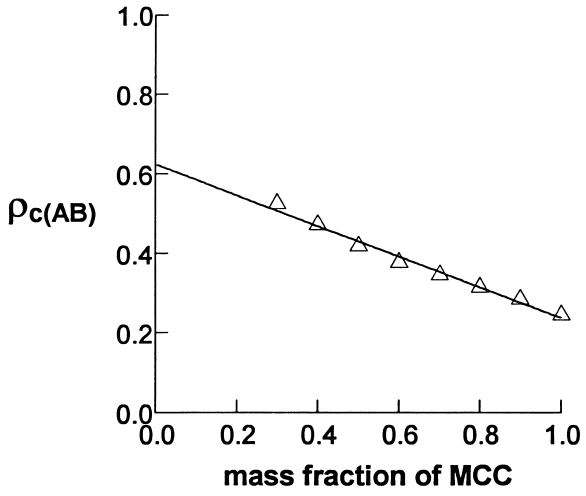

Fig. 2. The determined values of the critical mixture solid fraction $\rho_{c(AB)}$ as a function of the mass fraction of Avicel PH101. The line shows the calculated model according to Eq. (8).

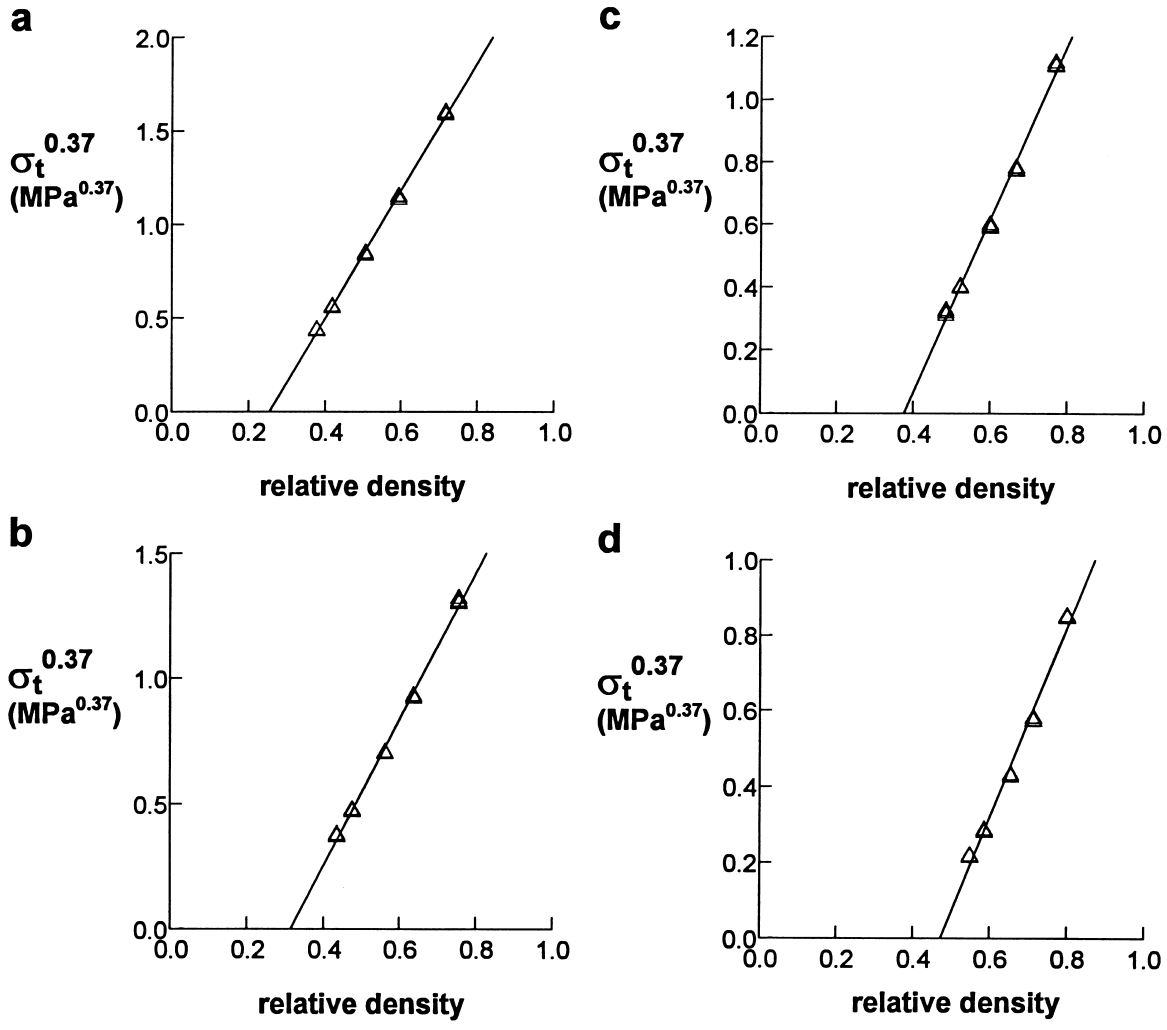

Fig. 1. Tensile strength $\sigma_t^{0.37}$ ($MPa^{0.37}$) versus the relative density for the different mass fractions of Avicel PH101 (%) in mixture with paracetamol: (a) 100%; (b) 80%; (c) 60%; (d) 40%. The solid line represents the model according to Eq. (7).

for example may be influenced by the mass fraction of the drug.

The strength percolation threshold was shown to increase with decreasing MCC mass fraction (Fig. 2). This observation is expected from the fact that the strength producing part in the mixture solid fraction, i.e. the excipient, is diminished with higher amounts of drug. The critical values of the solid fraction of the mixture, $\rho_{c(AB)}$ were found to follow Eq. (8):

$$\rho_{c(AB)} = X_{(A)}\rho_{c(A)} + (1 - X_{(A)})\rho_{c(B)} \quad (8)$$

The fitted parameters were $\rho_{c(A)} = 0.237$ and $\rho_{c(B)} = 0.624$ ($r^2 = 0.985$). The first value is close to our estimate of the percolation threshold from the single component Avicel PH101 (Table 2). The corresponding value for component B, $\rho_{c(B)}$ is more difficult to interpret since even above this value, paracetamol percolates the tablet but produces no significant compact strength.

4.2. A new strength–pressure function in the low pressure range

A mathematical function combining the compression pressure and the resulting strength is of general interest. The pressure is an independent variable whereas the relative density is a response parameter of the given material. To formulate a strength–pressure function, a valid pressure–relative density relationship is needed. There exist many model equations in literature. In this study, the recently published modified Heckel equation was chosen [24]:

$$\sigma = \frac{1}{k_2}\left[\rho_c - \rho - (1 - \rho_c)\ln\left(\frac{1-\rho}{1-\rho_c}\right)\right] \quad (9)$$

The critical solid fraction, ρ_c marks the onset of mechanical resistance to the applied compaction pressure. A Taylor expansion of the form Eq. (10) can be performed with the modified Heckel equation:

$$\sigma(\rho) = \sum_{n=0}^{2} \frac{1}{n!}\,\sigma^{(n)}(\rho_c)(\rho - \rho_c)^n \quad (10)$$

The resulting Eq. (11) is a priori only accurate in the vicinity of the percolation threshold, ρ_c:

$$\sigma \cong \frac{1}{2k_2}\,\frac{(\rho - \rho_c)^2}{1 - \rho_c} \quad (11)$$

This result can in principle also be applied to a mixture. Accordingly, the solid fraction of the mixture replaces the relative density in Eq. (11) and as an approximation, the critical values in Eqs. (6 and 11) are assumed to be equivalent. The combination of these equations leads to an elimination of the relative density and Eq. (12) is obtained:

$$\sigma_t = k_3\sigma^{T_f/2} \quad (12)$$

This power law describes a tensile strength that increases slightly steeper with the compaction pressure than would be expected from a linear relationship ($T_f/2 \cong 1.35$). This unlimited growth of the tensile strength holds only at low pressures. It is well known, that at higher pressures, an increasing pressure does not always result in tablets with greater strength. After a maximum of surface bonding area is achieved, a further increase of compaction pressure leads to an enlargement of the hydrostatic pressure that does not increase bonding in the tablet. The effects of a levelled off compact strength during the consolidation process is theoretically shown by Eq. (1). Yet, for the low pressure range dealt with in this study, the validity of Eq. (12) applies and can be checked experimentally.

Adequate non-linear regressions were obtained with a deduced T_f that was found reasonably close to the theoretical prediction of 2.7 (Table 3; Fig. 3). Slightly increasing exponent values were observed for the mixtures with a high amount of paracetamol. It is again possible that this effect may account for the dilution of the excipient by the high amounts of paracetamol. It should be noted that there exist several possible sources for a deviation from the experimental and theoretical estimate of a critical exponent [20].

Table 3 shows that the proportionality constant k_3 decreases with increasing drug amounts in the mixture. This change of the constant appears to be non-linear. Unfortunately, percolation theory provides no theoretical arguments for proportionality constants like k_1 or k_3. Yet, it can be stated that both constants need to include the maximal tensile strength as a factor. Since this maximal strength is an indicator for the ability to form compacts, the decrease of k_3 can be interpreted as a loss of compactibility with rising amounts of drug.

4.3. The dilution capacity interpreted as a percolation phenomenon

The area under the curve (AUC) in a tensile strength–compaction pressure diagram was proposed as a measure of compactibility by Minchom and Armstrong [22]. It can be qualitatively inferred from Fig. 4 that this area decreases with increasing amounts of the poorly compressible drug. In the method of Minchom and Armstrong, the curves were fitted with a quadratic equation and numerically integrated. The individual AUC values were normalized by the AUC

Table 3
Non-linear regression according to Eq. (12)

Amount Avicel PH101 (%)	T_f	k_3	r^2
100	2.76	0.015	0.999
90	2.65	0.015	0.999
80	2.76	0.009	0.999
70	2.71	0.008	0.999
60	2.82	0.005	1.000
50	2.95	0.003	1.000
40	3.05	0.002	1.000
30	3.24	0.001	0.995

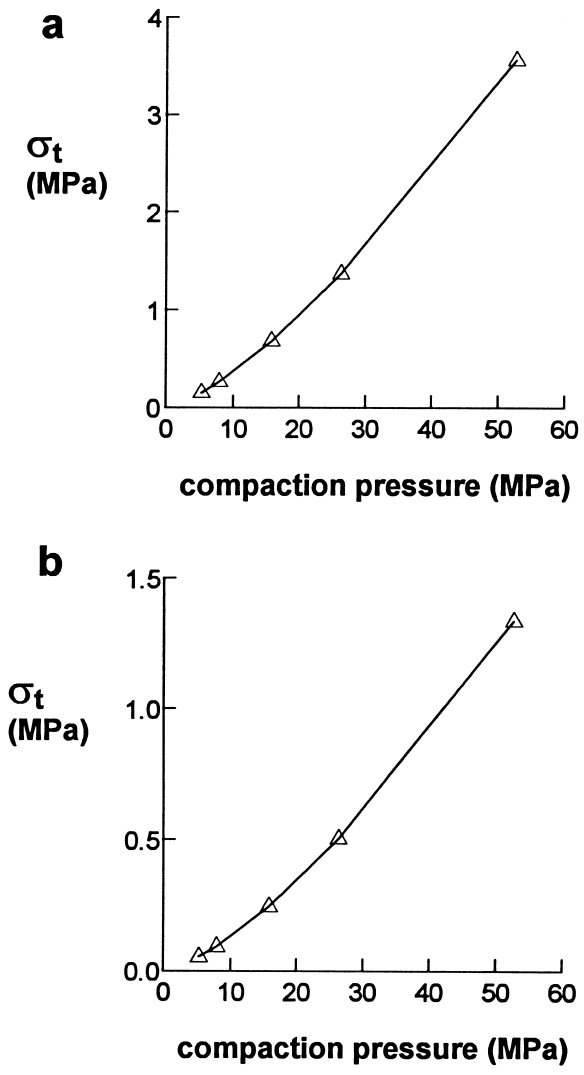

Fig. 3. Tensile strength, σ_t (MPa) as a function of the compression pressure, σ (MPa) for (a) 100% Avicel PH101; and (b) 60% Avicel PH101. The solid line shows the model according to Eq. (12).

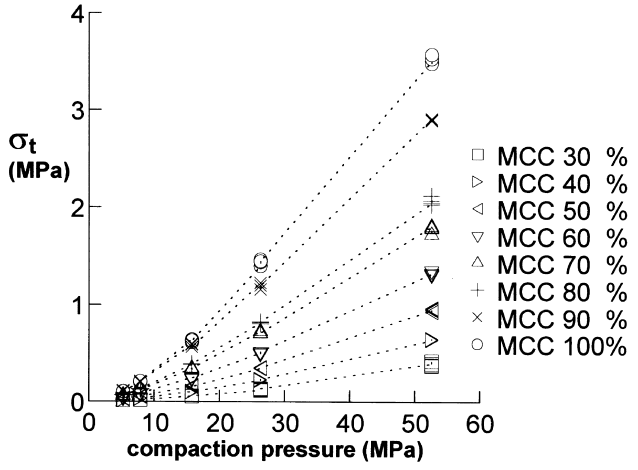

Fig. 4. Tensile strength, σ_t (MPa) versus the compaction pressure (MPa) in case of the different mass fractions of Avicel PH101.

for the excipient without the drug. These area ratios were linearly extrapolated to zero compactibility to find the dilution capacity. A recent study applied this method to the mixture studied in this paper [25]. A dilution capacity of 65% was found by extrapolation which amounts to a MCC mass fraction of 0.35. In should however be kept in mind that in this work, tablets were obtained over the entire pressure range even with a drug load of 70%. Even though these tablets were comparatively fragile, a manufacture and testing were possible. A critical MCC mass fraction of 35% is therefore obviously overestimated. Our study, compared to the mentioned reference [25], investigated different ranges in terms of the mass fractions and in terms of the compaction pressures. In view of these ranges, one would have to consider the extrapolation in reference [25] as conducted from afar. Such an extrapolation is especially problematic as it is not theoretically based. Thus, it is interesting to see that in this study, no linearity was observed for the area ratios along the mass fractions of MCC (Fig. 5). We approached the critical value of the mass fraction by a linear regression of the lowest four values. A zero compatibility (area ratio) was found at $X_{c(A)} = 0.201$ ($r^2 = 0.984$) corresponding to the dilution capacity of 79.9% drug.

Considering the nature of the dilution potential, the interpretation as a percolation phenomenon seems promising. At very low mass fractions, the well compactable component is not able to form a percolating cluster that ensures minimal strength in the tablet. The mechanical properties of such a compact are expected to be similar to those applying to the situation where only component *B* is present, that means the compact strength is practically zero. Yet, the question whether component *A* percolates or not is of course, also depending on the state of consolidation, i.e. it is pressure dependent. We define the dilution capacity as follows: the dilution capacity corresponds to a critical mass fraction of

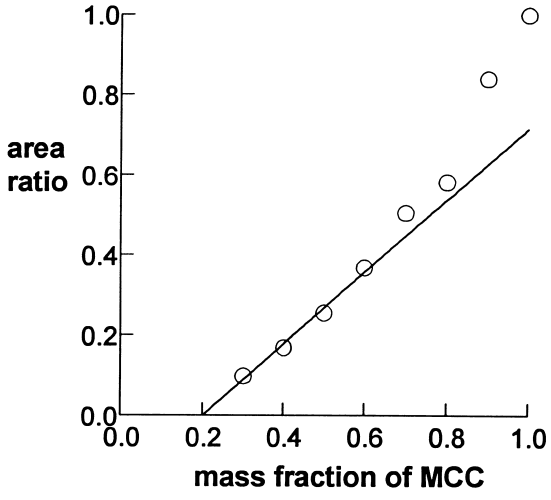

Fig. 5. Area ratios calculated according to Minchom and Armstrong [22] versus the mass fraction of Avicel PH101. The solid line shows the linear regression of the four lowest values.

the well compactable substance in which percolation is only attained at zero porosity.

4.4. A theoretical calculation of the dilution capacity

Eqs. (12 and 13) are expected to hold for multicomponent mixtures of i substances:

$$\sum X_i = 1 \tag{13}$$

$$\sum X_i \rho_i = \rho_{\text{mix}} \tag{14}$$

In case of a binary mixture with the components A and B at zero porosity ($\rho_{(AB)} = 1$), we have:

$$X_{(A)}\rho_{(A)} + \left(1 - X_{(A)}\right)\rho_{(B)} = 1. \tag{15}$$

From the definition of the relative density as a ratio of the apparent and the true density, Eq. (16) is obtained:

$$\frac{\rho_{(A)}}{\rho_{(B)}} = \frac{m_{(A)}}{m_{(B)}} \frac{\rho_{t(B)}}{\rho_{t(A)}} \tag{16}$$

Since the mass fraction of the excipient is given by $X_{(A)} = m_{(A)}/(m_{(A)} + m_{(B)})$, it is easy to show that:

$$\frac{m_{(A)}}{m_{(B)}} = \frac{X_{(A)}}{1 - X_{(A)}} \tag{17}$$

the combination with Eq. (16) leads to:

$$\rho_{(B)} = \rho_{(A)} \frac{1 - X_{(A)}}{X_{(A)}} \frac{\rho_{t(A)}}{\rho_{t(B)}} \tag{18}$$

Thus, $\rho_{(B)}$ in Eq. (15) can be replaced by the above expression and Eq. (19) is obtained:

$$X_{(A)}\rho_{(A)} + \frac{\left(1 - X_{(A)}\right)^2}{X_{(A)}} \rho_{(A)} \frac{\rho_{t(A)}}{\rho_{t(B)}} = 1 \tag{19}$$

At the strength percolation threshold of component A, $\rho_{c(A)}$, the mass fraction takes a defined critical value, $X_{c(A)}$ at zero porosity. Taking these critical concentrations into account, and multiplying by $X_{c(A)}$ yields:

$$X_{c(A)}^2\rho_{c(A)} + \left(1 - 2X_{c(A)} + X_{c(A)}^2\right) \times \rho_{c(A)} \frac{\rho_{t(A)}}{\rho_{t(B)}} - X_{c(A)} = 0 \tag{20}$$

The analytical solution of this quadratic equation takes the form:

$$X_{c(A)1/2} = -\frac{\varphi}{2} \pm \sqrt{\left(\frac{\varphi}{2}\right)^2 - \phi} \tag{21}$$

with:

$$\varphi \equiv \frac{-2\rho_{c(A)}\rho_{t(A)} - \rho_{t(B)}}{\rho_{c(A)}\left(\rho_{t(A)} + \rho_{t(B)}\right)}, \qquad \phi \equiv \frac{\rho_{t(A)}}{\rho_{t(A)} + \rho_{t(B)}} \tag{22}$$

For the value $\rho_{c(A)}$, the percolation threshold for 100% Avicel was used (Table 2). The true densities are listed in Table 1. As a result Eqs. (21 and 22) yield numerically one possible solution $X_{c(A)} \cong 0.203$. This calculation gives a dilution capacity of 79.7% that is in perfect agreement with our extrapolated estimate.

In the praxis of an industrial pharmacist, it is possible that only the knowledge of the dilution capacity is needed. However, Eq. (22) requests a value for the mechanical percolation threshold of the excipient alone. In this case, the determination of this threshold may be rather tedious. For a rough estimate of the percolation threshold of the tensile strength, the relative bulk density can be proposed [20]. In the present study the strength threshold was found in the interval of the relative bulk and tapped density. The evaluation of Eqs. (21) and (22) results in $X_{c(A)}{}' = 0.178$ if the relative bulk density is taken for the threshold value and $X_{c(A)}{}'' = 0.212$ in case of using the relative tapped density. To be on the safe side with an estimate of the dilution capacity, the calculation involving the relative tapped density seems advisable.

5. Conclusions

The mechanics of tablet mixtures display a vast complexity. This paper focussed therefore on a special mixture type involving a well compactable excipient and a poorly compactable drug. It was shown that a previously reported power law for the strength in the monosystem with MCC can also be applied to the tablets of mixtures with paracetamol, a poorly compactable drug. The critical values of the mixture solid fraction increase with increasing amounts of the drug. Because only the relative density of the microcrystalline cellulose is mechanically relevant. The percolation threshold of the pure component Avicel PH101 defines a minimal solid fraction required to obtain strength in compacts. This minimal value has to be included in the solid fraction of the mixtures to manufacture adequate tablets. Thus, a lower amount of Avicel PH101 in the mixture produces a higher percolation threshold.

Another conclusion of this study is that the slight upwards curvature of tablet strength as a function of the pressure can be explained with a power law of percolation theory. Yet, the model presented is only valid in a low pressure range since tablet strength is well known to level off at higher pressures.

From a practical point of view, the dilution capacity is certainly an important characteristic of a direct tableting excipient. It is potentially also of relevance in compositions with more than one poorly compactable drugs. In this respect, it has to be kept in mind that only the minimal solid fraction of the well compactable substance is needed to create a compact of adequate strength. The theoretical calculation of the dilution capacity will be useful for the formulation of direct compressible mixtures. For a practical application it is advantageous that the percolation threshold of the tensile strength is expected to be close to the interval defined by the relative bulk and tapped density. A scientist working in the development of direct compressible formu-

lations can therefore approximate the critical mass fraction only using these experimentally easily accessible densities.

Additional experimental studies are needed to confirm our findings. The applicability of the proposed theoretical concepts in an extended range of the compaction pressure remains to be seen.

List of symbols

a	slope of the inverse exponent plot
b	intercept of the inverse exponent plot
A	component A of the binary mixture that is here Avicel PH101
B	component B of the binary mixture that is here paracetamol
D	diameter of the tablet
F	maximal force from the diametrical compression test
h	thickness of the tablet
k_i	proportionality constants that are numbered consecutively
$m_{(A)}$, $m_{(B)}$	tablet mass of substance A and B
p, p_c	occupational probability in a lattice with its percolation threshold
q	arbitrary critical exponent in the fundamental power law of percolation theory
s	conductivity exponent in a mixture of a finite conductor and a superconductor
s'	critical elasticity exponent in a mixture of a rigid and soft material (*superelasticity exponent*)
T_f	critical fracture exponent (critical exponent of strength)
X_i	mass fraction of an arbitrary component i
$X_{(A)}$, $X_{c(A)}$	mass fraction of component A and its threshold value
$X_{(B)}$, $X_{c(B)}$	mass fraction of component B and its threshold value
$\gamma_{(A)}$, $\gamma_{(B)}$	constants of the individual components A and B that describe the ability of the given substance to reduce volume under applied pressure (compressibility)
$\gamma_{(AB)}$	compressibility constant of a binary mixture
φ	term of the analytical solution of the quadratic Eq. (20), where the definition is given in Eq. (22)
ϕ	term for the analytical solution of Eq. (20) that is defined in Eq. (22).
Φ	arbitrary macroscopic cluster property of a lattice in percolation theory
μ	critical exponent of conductivity (conductor-isolator mixture)
ρ, ρ_c	relative density (solid fraction) with its critical threshold value
$\rho_{(A)}$, $\rho_{c(A)}$	relative density and critical threshold value (strength percolation threshold) of substance A
$\rho_{(B)}$, $\rho_{c(B)}$	relative density and critical threshold value (strength percolation threshold) of substance B
$\rho_{(AB)}$, $\rho_{c(AB)}$	relative density and critical threshold value of the binary mixture
σ	compaction pressure
$\sigma_{t(A)}$, $\sigma_{tmax(A)}$	tensile strength and maximal tensile strength at zero porosity of substance A
$\sigma_{t(B)}$, $\sigma_{tmax(B)}$	tensile strength and maximal tensile strength at zero porosity of substance B
$\sigma_{t(AB)}$, $\sigma_{tmax(AB)}$	tensile strength and maximal tensile strength at zero porosity of the binary mixture
Σ	macroscopic conductivity
τ	critical exponent of the elastic modulus

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