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Research Article

Percolation Theory and Compactibility of Binary Powder Systems

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Defined size fractions of polyethyleneglycol powder (MW = 10,000) were mixed with defined size fractions of α-lactose monohydrate in order to study the effect of compaction as a function of the weight ratios of the two excipients. For a precise control of the compression cycle, tablets were compressed on a Universal Testing Machine (Zwick 1478). Tablet tensile strength σ_T was quantified as a function of compressional stress σ_c and relative density ρ_r using a two-parameter model with $\sigma_{T_{max}}$ = maximal tensile strength at zero porosity and γ = compressibility. The results have been analyzed on the basis of the percolation theory. As soon as the component with the lower mechanical stability is percolating the powder system, tablet hardness is controlled entirely by this component. The percolation threshold is a function of the geometrical arrangement of the particles in the compressed powder system. The expected two percolation thresholds can be distinguished as a function of the composition weight ratios if the particle size distributions of the two components differ enough.

KEY WORDS: percolation theory; compactibility; binary powder systems; polyethyleneglycol; α-lactose monohydrate.

INTRODUCTION

Percolation Theory

Different types of percolation can be distinguished: random-site, random-bond, random-site–bond, correlate chain, etc. Generally, percolation theory deals with the number and properties of clusters (1). A percolation system is considered to consist of sites in an infinitely large real or virtual lattice. Applying the principles of random-site percolation to a particulate system, a cluster may be considered as a single particle or a group of similar particles which occupy bordering sites in the particulate system. In the case of bond percolation, a group of particles is considered to belong to the same cluster only when bonds are formed between neighboring particles (see Figs. 1a and b).

In random-bond percolation, the bond probability and bond strength between different components can play an important role. The bond probability p can assume values between 0 and 1. When $p = 1$, all possible bonds are formed and the tablet strength is at its maximum, i.e., a tablet should show maximal strength at zero porosity when all bonds are formed. In order to form a stable compact it is necessary that the bonds percolate to form an "infinite" cluster within the ensemble of powder particles filled in a die and put under compressional stress.

Site percolation is an important model of a binary mixture consisting of two different materials. In the three-dimensional case, two percolation thresholds, p_c, can be defined: a lower threshold, p_{c1}, where one of the components just begins to percolate, and a second upper percolation threshold, p_{c2}, where the other component ceases to have an infinite cluster. Between the two thresholds the two components form two interpenetrating percolating networks. Below their percolation thresholds, the clusters of the components are finite and isolated. Thus, in site percolation of a binary powder mixture, p_c corresponds to a critical concentration ratio of the two components. From emulsion systems these concentrations are well known where oil-in-water or water-in-oil emulsions can be prepared exclusively.

Table I shows critical volume-to-volume ratios for well-defined geometrical packaging of monosized spherical particles. The critical volume-to-volume ratios depend on the type of percolation and the type of lattice. In the case of real powder systems the geometrical packaging is a function of the particle size, the particle size distributions and the shape of the particles.

As different types of packaging of monosized spherical particles show different porosities, a powder system which has the porosity ϵ can be represented in an idealized manner as an ensemble of monosized spheres having the hypothetical mean diameter x and a mean coordination number k corresponding to hypothetical (idealized) geometrical packaging. Table II shows the coordination number of isometric spherical particles for different packaging structures. Using

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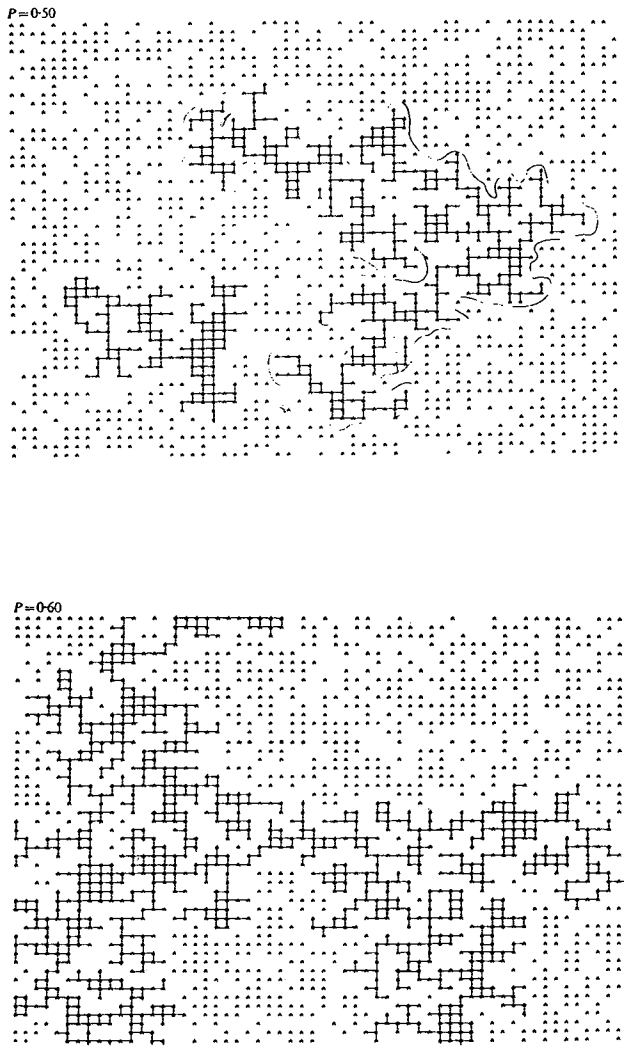

Fig. 1. (a) Example for percolation on a 60 × 60 square lattice for $p = 0.50$. Occupied sites are shown as *; empty sites are ignored, and two clusters are marked by bonds (1). (b) Example for percolation on a 60 × 60 square lattice for $p = 0.60$. The "infinite cluster" is marked by bonds (1).

the simplified model of powder systems mentioned, the following equation was developed (2):

$$k = \pi/\epsilon \tag{1}$$

for porosities in the range

$$0.25 < \epsilon < 0.5$$

This equation is a rough estimate and does not hold for compacts, where ϵ usually is less than 0.25.

Table I. Selected Percolation Thresholds for Three-Dimensional Lattices [1]

Lattice type	Site	Bond
Diamond	0.428	0.388
Simple cubic	0.3117	0.2492
Body-centered cubic	0.245	0.1785
Face-centered cubic	0.198	0.119

Table II. Coordination Numbers of Isometric Spherical Particles for Different Packaging Structures

Lattice type	Coordination number	Porosity
Diamond	4	0.66
Simple cubic	6	0.48
Body-centered cubic	8	0.32
Face-centered cubic	12	0.26

At a percolation threshold some property of a system may change abruptly or may suddenly become evident. Such an effect starts to occur close to p_c and is usually called a critical phenomenon. As an example, the electrical conductivity of a tablet consisting of copper powder mixed with Al_2O_3 powder may be cited. The tablet conducts electricity only if the copper particles form an "infinite" cluster within the tablet, spanning the tablet in all three dimensions.

Mathematical Models to Describe the Compaction Process

It is possible to find more than 15 different mathematical models in the literature (3–8). Some authors analyzed the equations critically. Notably, Burger *et al.* (6), using different equations, were unable to quantify the compaction process and came to the conclusion that it is not possible to derive general rules for the compaction properties of drugs.

As it is more important in pharmaceutical sciences to get a compact of defined strength rather than of defined volume reduction, we used the following equation (8–10):

$$P = P_{max} [1 - \exp(-\gamma \sigma_c \rho_r)] \tag{2}$$

with

P = deformation hardness (Brinell hardness);
P_{max} = maximum deformation hardness at porosity ϵ = 0 or relative density $\rho_r = (1 - \epsilon) = \rightarrow 1$, i.e., compressional stress $\sigma_c \rightarrow \infty$;
σ_c = compressional stress;
γ = compressibility (susceptibility to volume reduction)

The exact derivation of Eq. (2) was published earlier (9,10). It is possible to use the same equation to describe the radial tensile strength σ_T (8,11).

$$\sigma_T = \sigma_{T_{max}} [1 - \exp(-\gamma_T \sigma_c \rho_r)] \tag{3}$$

γ_T = compressibility (susceptibility to compressional stress)

The two compressibilities γ and γ_T need not necessarily be identical (7). It is possible to use Eqs. (2) and (3) for pure substances as well as for powder mixtures (8,9). In addition, the concept of binding and nonbinding sites in the tablet, which was used for the derivation of the equation (10,11), is able to quantify interactions between the components of a binary powder mixture.

Besides our own effort (8,12–17), only a few papers study the compression properties of binary powder systems. Fell and Newton (18) investigated the tensile strength of compacts of the binary powder mixture α-lactose anhydrate/β-lactose. The tensile strength increased linearly with increasing amounts of α-lactose. Sheik-Salem and Fell

(19) investigated the compression characteristics of the mixture lactose with NaCl. York (20) studied the binary mixtures between α-lactose monohydrate and different fatty acids. To characterize the compression characteristics, he used the Heckel equation (21) and the equation of Cooper and Eaton (22). Both equations describe the volume reduction under compressional stress. According to York (20) the Heckel equation showed (21) that with increasing amounts of fatty acid, the binary powder mixture becomes more plastic. Schmidt (23) investigated the effect of different qualities of sorbit as filler and binder in a binary mixture with ascorbic acid. He did not find an effect of the particle size of ascorbic acid.

MATERIALS AND METHODS

The excipient lactose (α-lactose monohydrate, 80 mesh, Lot No. 123'878/02 DMV Veghel, NL), representing a brittle and hard substance, was chosen, as it is one of the most commonly used substances in tabletting (23–27). Polyethyleneglycol (PEG 10,000, Lot No. 605331, DAB 8 powder, Hoechst AG, Werk Gendorf, D-8269 Burgkirchen) is plastic and soft and is used as a vehicle for solid solutions and as a binding and lubrication agent in chewable and effervescent tablets, respectively (16,28). The mechanical properties of PEG vary according to the molecular weight (28).

Batches of both substances containing coarse powder material were selected, in order to be able to achieve defined sieve fractions. The following sieve fractions were used: 125–180 μm (PEG 10,000, lactose), 90–125 μm (lactose), and 250–355 μm (lactose).

In Table III, the physical characteristics of the substances are compiled.

Tablets (round, flat-faced; diameter, 11 mm; tablet weight, 400 ± 1 mg) were prepared and tensile strength was tested using the Zwick 1478 universal testing machine (29). The moisture content of the starting material was kept constant by storage at 21 ± 2°C and at 45 ± 5% relative humidity of air over a K_2CO_3 solution. At each compression level (1.25, 2.5, 7.5, 10.0, 12.5, 15.0, 22.5, 25.0, 30.0, 35.0 kN) twelve tablets were made.

Tensile strength, tablet diameter, and thickness of the tablets were determined 24hr after preparation of the tablets with a precision of 0.01 mm. The relative density was calculated as the ratio of apparent to true density. The apparent density was determined from the geometrical dimensions. The true density was measured using a Beckman 930 pycnometer (Beckman Inc., Fullerton, California). To calculate porosities ϵ the relation $\epsilon = 1 - \rho_r$ was used.

The tensile strength was determined on the basis of Eq. (4).

$$\sigma_T = 2F/\pi D t \tag{4}$$

σ_T = tensile strength,
F = force at failure (≥2 N),
D = tablet diameter, and
t = thickness of tablet.

For the determination of mean values for the tensile strength five or six tablets were tested at a compression rate of 0.5 mm/min.

The values for the parameters $\sigma_{T_{max}}$ and γ_T were calculated according the Eq. (3) using the nonlinear regression program HP 09835-15044 of the Hewlett Packard desk calculator HP 9835. This program calculates simultaneously $\sigma_{T_{max}}$ and γ_T, confidence intervals and minimum sum of squares QS according to Eq. (5).

$$QS = \sum_{i=1}^{n} (Y_i - \hat{Y}_i)^2, \tag{5}$$

Y_i = experimental value (σ_T), and
$\hat{Y}_i$ = calculated value according to Eq. (3).

RESULTS

Tensile Strength σ_T and $\sigma_{T_{max}}$ of the Mixtures Lactose/PEG 10,000

In Fig. 2 the tensile strength of compacts consisting of PEG 10,000 (pure), lactose (pure), and the mixtures (weight-to-weight ratios PEG 10,000/lactose) 80/20, 60/40, 40/60, 20/80, 10/90, and 5/95 are plotted as a function of $\sigma_c\rho_r$ according to Eq. (3) for the sieve fractions 125–180 μm PEG 10,000 and 125–180 μm lactose. Similar results have been found for the mixtures with other ratios of sieve fractions. In Fig. 3 the results for $\sigma_{T_{max}}$ [compare Eq. (3)] are compiled for all ratios of sieve fractions studied as a function of the weight fraction PEG 10,000.

It is evident that with increasing amounts of PEG 10,000 the tensile strength of the tablets decreases in a nonlinear way up to 20 and 40%, respectively, of PEG 10,000. At higher percentages of PEG 10,000 a slight linear increase in $\sigma_{T_{max}}$ can be observed. The parameter $\sigma_{T_{max}}$ can be interpreted as a compactibility parameter, as this tensile strength cannot be exceeded even using infinite compressional stress σ_c, i.e., porosity $\epsilon = 0$.

Table III. Physical Properties of the Substances

Substance	Sieve fraction (μm)	True density (g/ml)	Bulk density (g/ml)	Tapped density (g/ml)	Sieve analysis data, RRS-B (μm)			Moisture content (%, w/w)
					n	d'	O'_k	
Lactose		1.54	0.77	0.89	3.10	250	319	0.4
Lactose	90–125	1.54	0.74	0.89				0.4
Lactose	125–180	1.54	0.77	0.86				0.4
Lactose	250–355	1.64	0.74	0.81				0.4
PEG 10,000		1.24	0.59	0.75	2.44	175	510	0.3

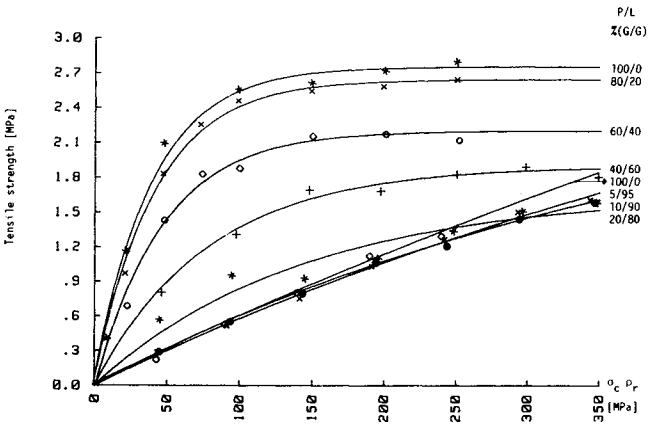

Fig. 2. Tensile strength of compacts for different ratios (w/w), P/L, i.e., polyethyleneglycol (PEG 10,000)/lactose, as a function of $\sigma_c \rho_r$ according to Eq. (3).

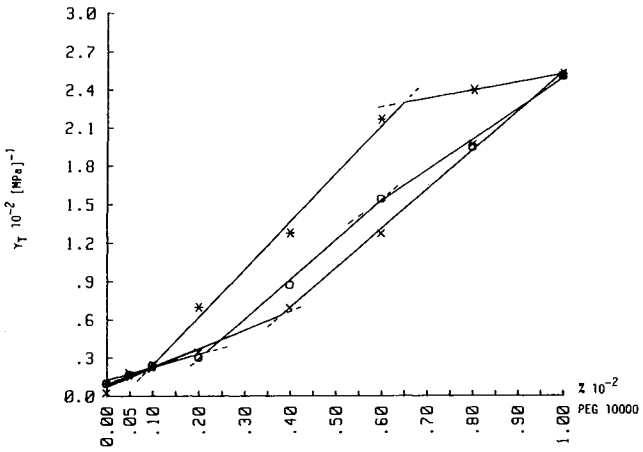

Fig. 4. Compressibility parameter γ_T of Eq. (3) as a function of PEG 10,000 weight concentration of PEG/lactose compacts for the following sieve fractions (PEG/lactose): (X) 125–180/90–125 μm; (○) 125–180/125–180 μm; (*) 125–180/250–355 μm.

Compressibility γ_T

In Fig. 4 the compressibility parameter γ_T of Eq. (3) is plotted as a function of PEG 10,000 weight percentage for the different mixtures compacted. Because of the high plasticity of PEG 10,000, γ_T has a value as high as $2.4 \cdot 10^{-2}$ $[MPa]^{-1}$, whereas the compressibility parameter γ_T of lactose is one magnitude smaller, γ_T (lactose) $= 0.13 \cdot 10^{-2}$ $[MPa]^{-1}$. In the case of the coarse sieve fraction lactose, the influence of PEG 10,000 on the value of γ_T becomes marked at 20% (w/w) of PEG. The value of γ_T increases approximately linearly up to about 60% (w/w) of PEG 10,000. The value γ_T does not seem to change much between 60 and 100% of PEG 10,000. It can be assumed that in this range the lactose particles do not contribute to the consolidation process, i.e., are completely surrounded by the soft and plastic PEG 10,000.

DISCUSSION

Tensile Strength

The maximum strength $\sigma_{T_{max}}$ of the compact consisting of different weight ratios of the brittle and soft component can be interpreted on the basis of the percolation theory. The probability of each component to form an infinite cluster spanning the whole tablet in all three directions is proportional to its volume ratio. It is reasonable that the mechanical properties of the compact are determined by the softer component (30). This statement is true as soon as the softer component forms an infinite cluster, i.e., percolates at the percolation threshold. The percolation threshold is a function of the packing structure, i.e., the particle size and size distribution of the components. In case of the more coarse sieve fraction of the brittle lactose with the smaller specific surface, a lesser amount of the softer PEG 10,000 is needed to form an infinite cluster than in the case of the finer sieve fraction of lactose. Thus, percolation thresholds are found at 20% w/w ratio PEG 10,000 for the coarse lactose (250–355 μm) and at 40% w/w ratio for the fine lactose (90–125 μm) using the minimum of σ_T as the criterion for percolation (see Fig. 4). It is interesting to note that it is generally assumed that polyethyleneglycol is effective as a lubricant for a granular tabletting mixture only at percentages of ca. 20% (w/w) and more. At higher weight percentages of 10,000 PEG, the system consists of two simultaneously percolating structures. At a certain weight percentage of PEG 10,000 the lactose particles no longer exist as infinite clusters but occur as finite clusters. This second percolation threshold could not be detected from the $\sigma_{T_{max}}$ values as a function of the percentage of lactose on PEG in the mixture.

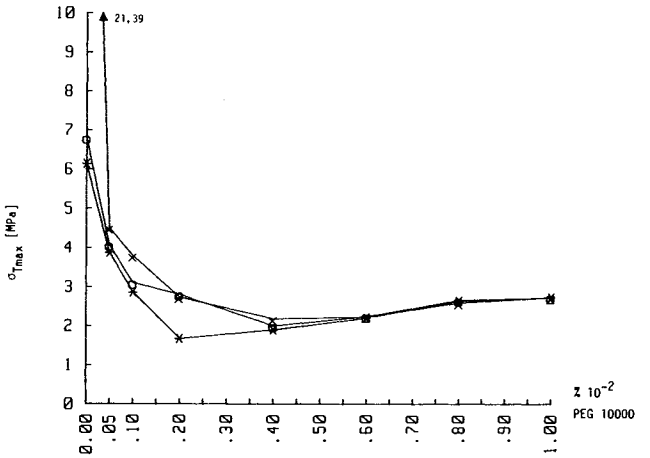

Fig. 3. Compactibility parameter $\sigma_{T_{max}}$ according to Eq. (3) as a function of PEG 10,000 weight concentration on PEG/lactose compacts. For the symbols, see the legend to Fig. 4.

An "ideal solid dispersion" of lactose particles will be achieved only when the amount of lactose particles is far below the percolation threshold of lactose. At such low concentrations, the lactose particles do not interact with each other.

Compressibility Parameter γ_T

In view of the percolation theory the coarse sieve fraction of lactose (250–355 μm) mixed with PEG 10,000 (125–180 μm sieve fraction) shows a typical behavior.

In the range between ca. 20% (w/w) PEG 10,000 and

60% (w/w) PEG 10,000, both components form an "infinite" cluster simultaneously, i.e., both percolation thresholds p_{c1} (20%, w/w, PEG 10,000) and p_{c2} (60%, w/w, PEG 10,000, i.e., 40%, w/w, lactose) can be distinguished. In the case of the fine sieve fraction of lactose, only one percolation threshold seems to become effective at 40% PEG 10,000, when PEG 10,000 starts to percolate. It may be argued that the upper (second) percolation threshold is not visible because of the limited size of the tablet, i.e., the effect of friction at the die wall by the fine lactose particles on the compaction process (boundary effect) is more pronounced than by the coarse particles. In the case of more or less equally sized sieve fractions of lactose and PEG 10,000, the situation is similar, i.e., only a lower percolation threshold is perceptible. This is just what percolation theory predicts between p_{c1} and p_{c2}, whereby the p_c's depend on the lattice type (see Table I).

CONCLUSIONS

The results of the compaction behavior of binary powder systems can be satisfactorily explained with the help of the percolation theory. As the percolation thresholds are a function of the geometrical arrangement of the particles, which differ in their properties with different excipient and active substances, percolation theory can also be applied in other areas of pharmaceutical technology. Thus, this concept (1) provides new insights to dosage form design.

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