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The compressibility and compactibility of powder systems

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Summary

This paper investigates the problem of compressibility and compactibility of powder systems. The term 'compressibility' is defined as the ability of a powder to decrease in volume under pressure, and the term 'compactibility' is defined as the ability of the powdered material to be compressed into a tablet of specified strength (i.e. radial tensile strength or deformation hardness). A novel approach leads to the following equation, which describes the deformation hardness P of the compact as a function of the applied pressure σ_c and the relative density ρ_r:

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

The parameter P_{max} is equal to the theoretically maximal possible deformation hardness at $\sigma_c\rho_r \to \infty$. P_{max} describes the *compactibility* and the parameter γ, termed the *compression susceptibility*, describes indirectly the compressibility. The equation is valid for pure substances as well as for binary mixtures An attempt is made to develop 'additivity rules' for the parameters P_{max} and γ in case of binary mixtures. For the general case it is necessary to introduce an interaction term, which can be explained qualitatively.

Introduction

The compressibility of a powder system

Measurements made on eccentric presses and rotary tabletting machines are capable of providing quantitative information on materials to be used for tablet

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manufacture. The general principle is to derive quantitative data specific to the material by interpreting the curves relating *pressure* to *volume reduction*, or *pressure* to *residual porosity* (Kawakita and Lüdde, 1971; Heckel, 1961; Hersey, 1973). Rather than basing their interpretation on the pressure–volume curve, some authors have measured the energy absorption of tabletting materials (Führer, 1977; Parmentier, 1978; Dürr, 1976).

The aim in all cases is to derive from the compression behaviour of a particulate solid a prediction of its ability to form tablets. More than 15 different mathematical descriptions of the compression process have been compiled in the literature (Kawakita, 1971). They quantify the compressibility of the powder system, i.e. the *volume reduction under pressure* (Kawakita and Lüdde, 1971).

The compactibility of a tabletting material

Compressibility, the ability of a powder to decrease in volume under pressure, is only an indirect measure of its ability to form tablets. What is important in practice is that compression produces a compact of adequate *strength*. The ability to form tablets, or compactibility, may therefore be defined as the ability of the powdered material to be compressed into a tablet of specified strength (radial tensile strength and hardness).

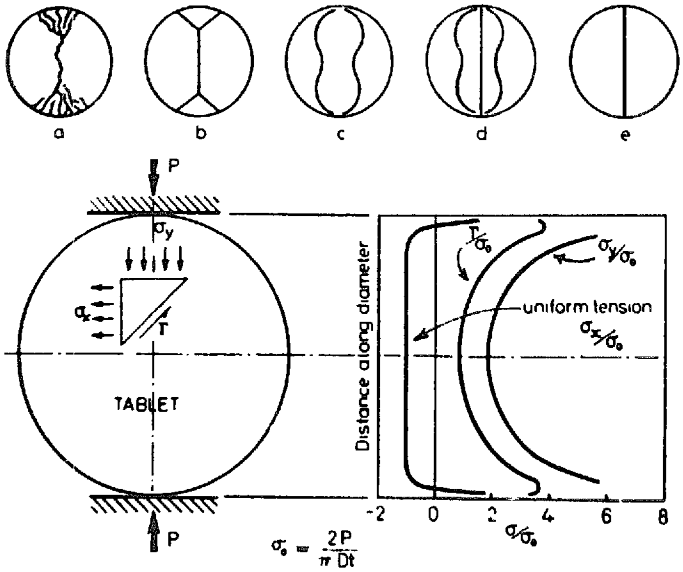

Fig. 1. Failure of tablets subjected to diametral compression.(a) Compression failure locally at the loading points. (b) Failure under local shear at and near the loading points. (c) Failure along maximum shear loci when point loading applied. (d) 'Triple-cleft' fracture due to transfer of load to each half-disc after breakage along the vertical diameter. (e) Ideal tensile failure. The lower part of the figure illustrates the stress conditions in a tablet which are present when ideal tensile failure occurs. The tensile stress (σ_x) on the vertical diameter is constant at $2P/\pi Dt$ over most of the graph. The compressive stress on the same diameter is σ_y. If ideal point loading was obtained this would tend to infinity. The shear stress is τ. The tablet material must be eight times stronger in compression and six times stronger in shear than it is in tension if the ideal tensile failure is to be obtained (Newton et al., 1971).

Crushing strength (radial tensile strength) and hardness

In pharmaceutical practice only the diametral crushing strength (involving tensile failure) of tablets is normally measured. In the ideal case (Newton et al., 1971), which is observed almost solely in relatively brittle materials, the crushing strength can be calculated by the following formula:

$$\sigma_B = \frac{2K}{\Pi D t} \tag{1}$$

where σ_B = radial tensile strength, D = tablet diameter, t = tablet height, K = force applied to fracture (tensile failure).

As shown in Fig. 2, instead of ideal fracture (ideal tensile failure) complicated fracture patterns may occur with some materials, so that the above equation is not applicable. The *hardness* of a material is defined as the resistance which it presents to a penetrating object (Römpp, 1969). In metallurgy, e.g., this property is measured by means of the Brinell hardness test. In the static Brinell hardness test a hard steel sphere is pressed against the surface of the material for a specified time. The steel sphere produces an indentation of greater or lesser diameter in the material, depending upon its *plasticity*. From the dimensions (see Fig. 3) of the indentation

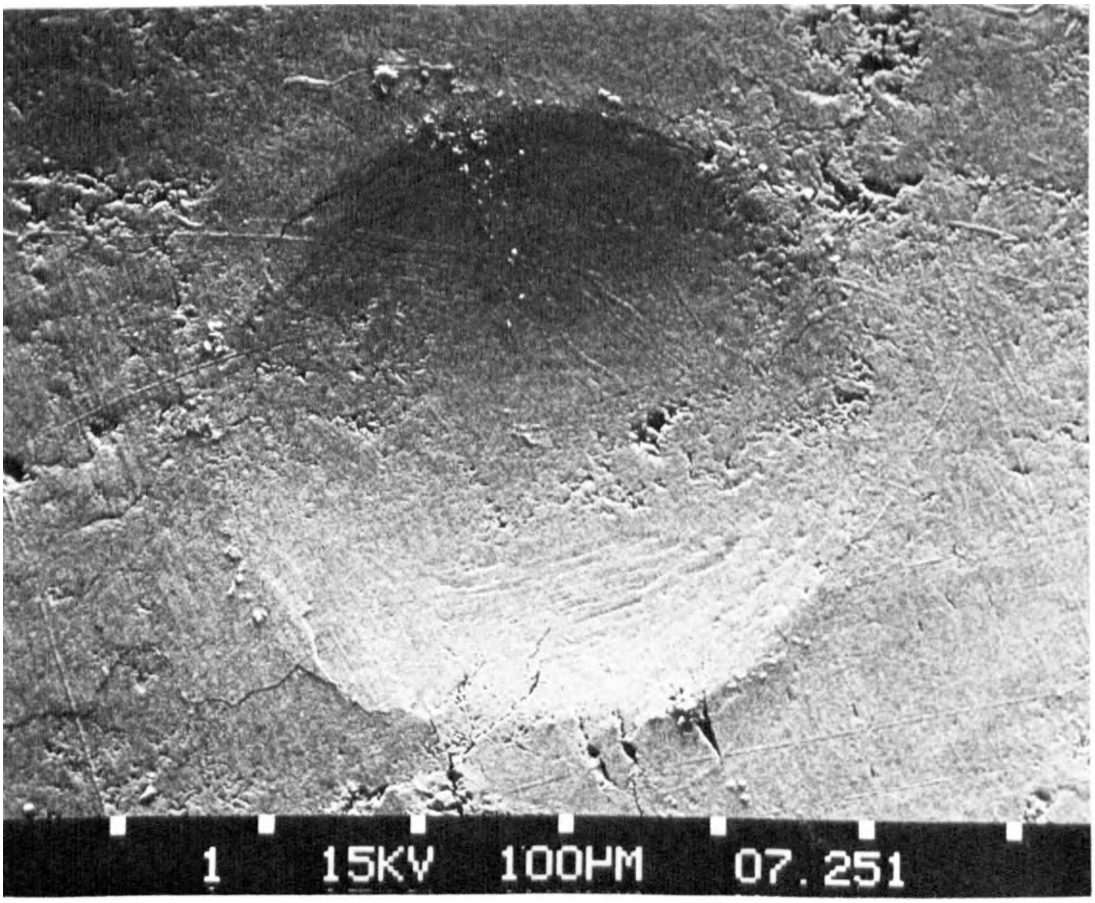

Fig. 2. Indentation produced by the Brinell hardness test sphere (Leuenberger, 1980).

and the magnitude of the force applied a hardness number is obtained for the material.

$$P = \frac{2K}{\Pi D\left(D - \sqrt{D^2 - d^2}\right)} \tag{2}$$

where d = diameter of the indentation, D = diameter of the test sphere, K = force applied to the material with the test sphere.

Since the hardness, defined as above, is a measure of the plasticity of the material, the hardness number is in general the preferred variable for characterizing compactibility. The Vickers or Tabor hardness numbers (Römpp, 1969; Hiestand et al., 1971) and in certain cases the radial tensile strength may equally well be used instead of the Brinell hardness.

Compression equations which take account of tablet strength

The literature contains very few mathematical descriptions of compression which include a prediction of the strength of the compact.

T. Higuchi et al. (1954) found a linear relationship between the Strong Cobb Hardness and the logarithm of the maximum compressional force K_c

$$H = a \cdot \ln K_c + b \tag{3}$$

Deviations from Eqn. 3 occurred only at high compressional forces. H = tablet hardness (Strong Cobb hardness tester), K_c = maximum compression force, and a, b = constants.

Ryshekewitch (1953) found that the following equation held for ceramic materials:

$$F = F_0\, e^{-c \cdot \varepsilon} \tag{4}$$

where F = tablet strength, F_0 = tablet strength at porosity $\varepsilon = 0$, c = constant, ε = porosity.

Shotton and Ganderton (1961) investigated the relation between the crushing force F for a tablet and the particle size L, employing the following equations:

$$F = K/\sqrt{L} \tag{5}$$

$$F = F_1 + K/\sqrt{L} \tag{6}$$

where F = crushing force (N), F_1, K = constants specific to the material, L = mean particle size.

An approach to quantify simultaneously the compactibility and compressibility of a powder system

Theory

Leuenberger (1980) assumed that the cross-sectional area A of a cylindrical tablet contains a number N_+ of bonding contact points and a number N_- of non-bonding contact points, thus the relatively simple Eqn. 14 can be derived along the following lines (Eqns. 7–14):

$$A = N_0 a = (N_+ + N_-)a \tag{7}$$

$$N_0 = N_+ + N_-$$

where A = cross-sectional area, a = unit area per bonding point, N_+ = number of bonding points, N_- = number of non-bonding points.

It is also postulated that the resistance to deformation, P (hardness), is proportional to the number of bonding points N_+:

$$P = \lambda N_+ = \lambda(N_0 - N_-) \tag{8}$$

where λ = proportionality factor.

If it is further assumed that the relative decrease in the number of non-bonding points dN_-/N_- changes in proportion to the externally applied compression force σ_c and the change in relative density $d\rho_r$, the following simple differential equation is obtained:

$$\frac{dN_-}{N_-} = -\gamma\sigma_c \, d\rho_r \tag{9}$$

where γ = proportionality factor.

Incorporating the limiting condition that when $\rho_r = 0$ there are only non-bonding points ($N_- = N_0$), and integrating, we have:

$$N_- = N_0 \, e^{-\gamma\sigma_c\rho_r} \tag{10}$$

The expression obtained for the deformation resistance P is then:

$$P = \lambda N_0(1 - e^{-\gamma\sigma_c\rho_r}) \tag{11}$$

while for $\sigma_c \rightarrow \infty$ a maximum deformation resistance P_{max} is attained

$$P_{max} = \lambda N_0 \tag{12}$$

The final expression obtained for the deformation resistance P is then

$$P = P_{max}(1 - e^{-\gamma\sigma_c\rho_r}) \tag{13}$$

The physical interpretation of P_{max} and γ

P_{max} may be used to quantify compactibility and the variable γ to quantify compressibility. However, the quantity γ is more accurately termed compression susceptibility, since it only indirectly defines the volume reduction (compressibility). Since the equation for deformation resistance takes into account the relative density ρ_r, or the porosity ε (since $\rho_r = 1 - \varepsilon$) of the tablet, further investigations will be necessary in order to show whether the value of the compression susceptibility γ is independent of batch variation — i.e. whether it is truly a characteristic of the material. Jointly with Hiestand, efforts are underway to further elucidate the physical significance of γ (Hiestand, 1980). As a consequence of experimental evidence and for physical reasons it is necessary to introduce for certain materials an initial compression stress σ_0, corresponding to the force necessary to produce a tablet with deformation resistance $P \sim 0$:

$$P = P_{max}\left(1 - e^{-\gamma(\sigma_c \rho_r - \sigma_0 \rho_0)}\right) \tag{14}$$

Compressibility and compactibility of binary mixtures

Additivity of compression variables? If it is assumed that Eqn. 13 holds for the mixtures as for the pure substances, it may be shown that the following equations are applicable if P_{max} and γ behave additively (see appendix):

$$P_{mixture} = P_{M_{max}}\left(1 - e^{-\gamma_M \sigma_c \rho_r}\right) \tag{15}$$

Condition for additivity of $P_{M_{max}}$:

$$P_{M_{max}} = P^{x}_{max_1}\, P^{(1-x)}_{max_2} \tag{16}$$

where x = proportion of substance 1, $P_{M_{max}}$ = maximum deformation resistance of the mixture, $\gamma_M = \gamma$ mixture, i.e. the *logarithmic* mean is calculated.

In examining the additivity of compression susceptibility it is sufficient to use the *arithmetic* mean:

$$\gamma_M = x\gamma_1 + (1 - x)\,\gamma_2 \tag{17}$$

where x = proportion of substance 1, $\gamma_M = \gamma$ mixture.

Interactions between the components. If it is postulated that Eqn. 14 holds for mixtures as it does for pure substances, the following generally applicable equation is obtained when interactions are taken into account:

$$P = P^{x}_{max_1}\, P^{1-x}_{max_2}\, P^{x(1-x)}_{WW}\left(1 - e^{-[x\gamma_1 + (1-x)\gamma_2 + \gamma_{WW} x(1-x)][\sigma_c \rho_r - \sigma_0 \rho_0]}\right) \tag{18}$$

where x = proportion of component 1 (% w/w), P_{max_1} = maximum deformation resistance for component 1, P_{max_2} = maximum deformation resistance for component 2, P_{WW} = interaction term, γ_1 = compression susceptibility for component 1, γ_2 =

compression susceptibility for component 2, γ_{WW} = interaction term.

As mentioned in the previous section, for brittle materials the corresponding radial tensile strength values σ_B may be used instead of the deformation resistance P:

$$\sigma_B = \sigma^{x}_{B_{max1}} \sigma^{1-x}_{B_{max2}} \sigma_{B_{WW}} \left(1 - e^{-[x\gamma'_1 + (1-x)\gamma'_2 + x(1-x)\gamma'_{WW}][\sigma_c\rho_r - \sigma_0\rho_0]}\right) \tag{19}$$

Materials and methods

Compacts of aspirin (lot 3494X, 4489C), ibuprofen (lot A, lot B), lactose (4095C, MK1), Methenamin, NaCl, phenacetin, sucrose (519 A6, 694DN; K1) and sitosterin were made at Upjohn (Hiestand, 1979) with a hydraulic press (Model 341-20, Loomis Engineering and Manufacturing, Caldwell, New York). Values for the deformation resistance P were measured by Hiestand (1979) with the pendulum apparatus described in detail by Hiestand et al. (1971).

Lactose Sheffield water-free (lot 7860275), lactose 200 mesh DMV (lot 7903144) and sucrose (lot 7801102) were used to prepare tablets with the Instron Model TT-DM (Instron, High Wycomte, Buchs, England). Before compression the die was lubricated with magnesium stearate. The powders (pure substance, binary mixtures of lactose and sucrose) did not contain a lubricant.

Measurements on these fairly brittle materials such as sucrose and lactose have further shown that radial tensile strength values σ_B may be used for characterization of tablet strength. The tablets show almost ideal fracture in the diametral compression test and a smaller scatter than the deformation resistance values P, obtained with a semistatic Brinell hardness test, developed by Leuenberger (1980).

For the evaluation of the data Eqns. 13 and 14 were used for pure substances and binary mixtures. In addition to that the binary mixtures were evaluated according to Eqn. 19. The parameters of the equation were obtained from non-linear regression calculations.

Results and discussion

Results of single and binary mixtures

The validity of the proposed equations has been checked for a number of different substances (Leuenberger et al., 1980; Leuenberger, 1980) and good agreement between theory and practice was found (Fig. 3, Fig. 4 and Table 1). Fig. 5 shows the experimental and theoretically predicted radial tensile strength values for binary mixtures of *lactose (anhydrous Sheffield)* and sucrose. Within the limits of experimental error, the radial tensile strength σ_B and the compression susceptibility γ' of the mixtures investigated behave additively.

Evaluation of the radial tensile strength data for mixtures of sucrose and *lactose DMV 200 mesh* showed that the proposed Eqn. 19 including interaction terms accounted for the experimental data to a close approximation (Fig. 6, Table 2). The

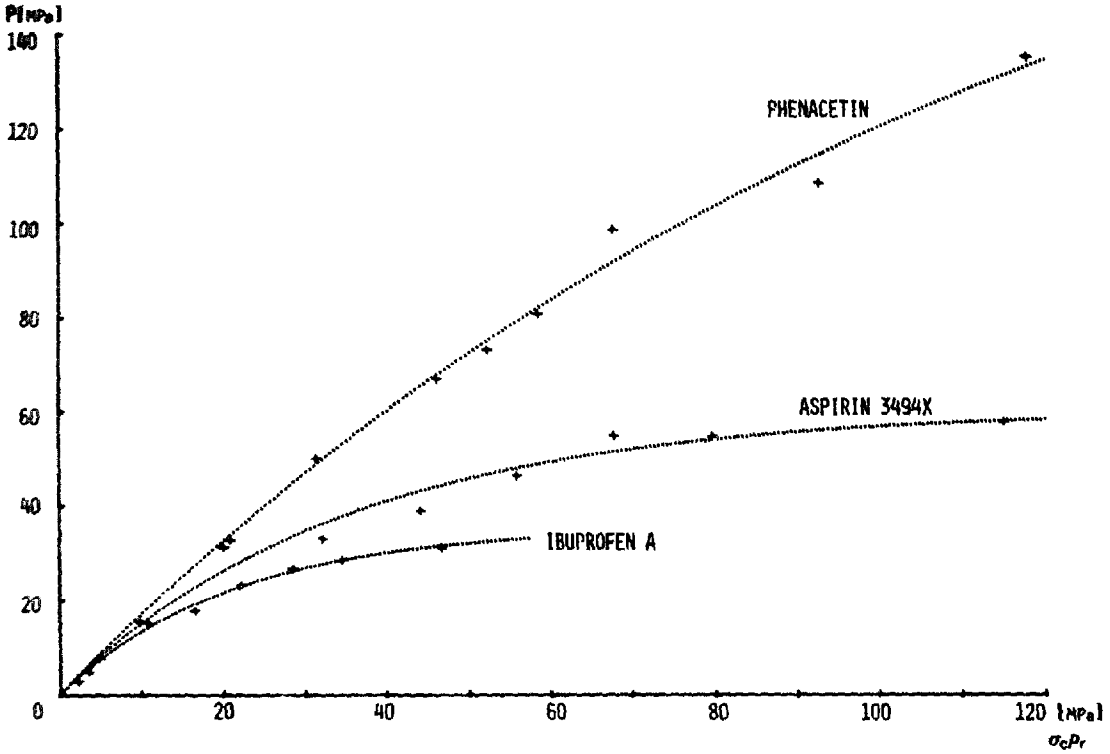

Fig. 3. Comparison of calculated values for deformation resistance P with measured values.

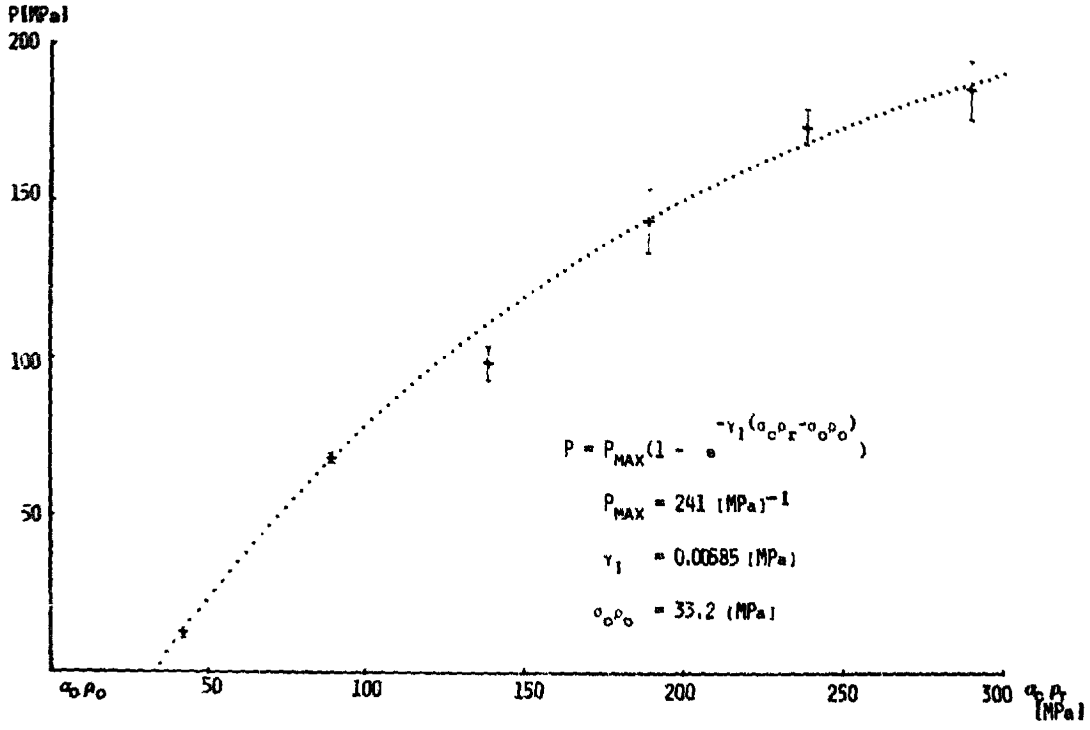

Fig. 4. Introduction of an initial stress σ_0, corresponding to the force necessary to produce a tablet with deformation resistance P~0 (sucrose-lactose DMV 200 mesh 1:3 w/w).

TABLE 1

VALUES OF THE MAXIMAL DEFORMATION HARDNESS P_{max} AND OF THE COMPRESSION SUSCEPTIBILITY γ FOR DIFFERENT SUBSTANCES AND BATCHES

These values were obtained from non-linear regression calculations, which yield the following minimum sum of the squares QS_{min} for each experimental series:

$$QS_{min} = \sum_{i=1}^{n} \left[P_i(\sigma_c\rho_r) - \hat{P}_i(\sigma_c\rho_r)\right]^2$$

where $P_i(\sigma_c\rho_r)$ = experimental deformation hardness, $\hat{P}_i(\sigma_c\rho_r)$ = calculated deformation hardness. The subsequently calculated square root qs of the mean of variance per experimental deformation hardness P_i show reasonable values.

Substance	P_{max} (MPa)	γ $(\frac{10^{-3}}{MPa})$	QS_{min} $(MPa)^2$	$qs = \sqrt{\frac{QS_{min}}{n}}$ (MPa)
Aspirin 3494X	60.1	28.4	73.3	3.03
Aspirin 4489C	54.8	22.7	7.4	1.11
Ibuprofen A	35.4	46.8	5.2	0.76
Ibuprofen B	162	22.8	37.1	2.49
Lactose 4095C	515	4.65	26.3	2.29
Lactose MK1	251	8.42	47.3	2.81
Methenamin	232	13.7	61.2	3.19
Sodium chloride	653	5.39	120.3	4.48
Phenacetin	213	8.19	93.1	3.41
Sucrose 519A6	1046	2.10	96.9	4.40
Sucrose 694DN	1723	1.12	79.9	3.65
Sucrose K1	1224	1.42	191.9	6.20
Sitosterin	198	18.7	226.0	6.72

factorial interaction term σ_{BWW} differs from unity by about one power of 10, and the interaction term γ'_{WW} departs to only a minor extent from the arithmetic mean (according to Eqn. 17) of the separate compression susceptibilities (Fig. 7). The compression susceptibility interaction term γ'_{WW} may therefore, to a first approximation, be neglected.

Interpretation of interactions

Bonding forces between the individual particles contribute significantly to the strength of the tablet. In a binary mixture, containing particles of both components, A and B, interactions may occur as follows: (a) A bonds preferentially with A and B bonds preferentially with B; (b) the affinity of A for A is the same as the affinity of A for B; and/or (c) A bonds preferentially with B.

The three possibilities are shown diagrammatically in Fig. 8. In case (b) no interaction occurs. The two other cases show a positive or negative deviation from linearity, which according to Eqn. 18 is at a maximum for a 1:1 mixture. Further

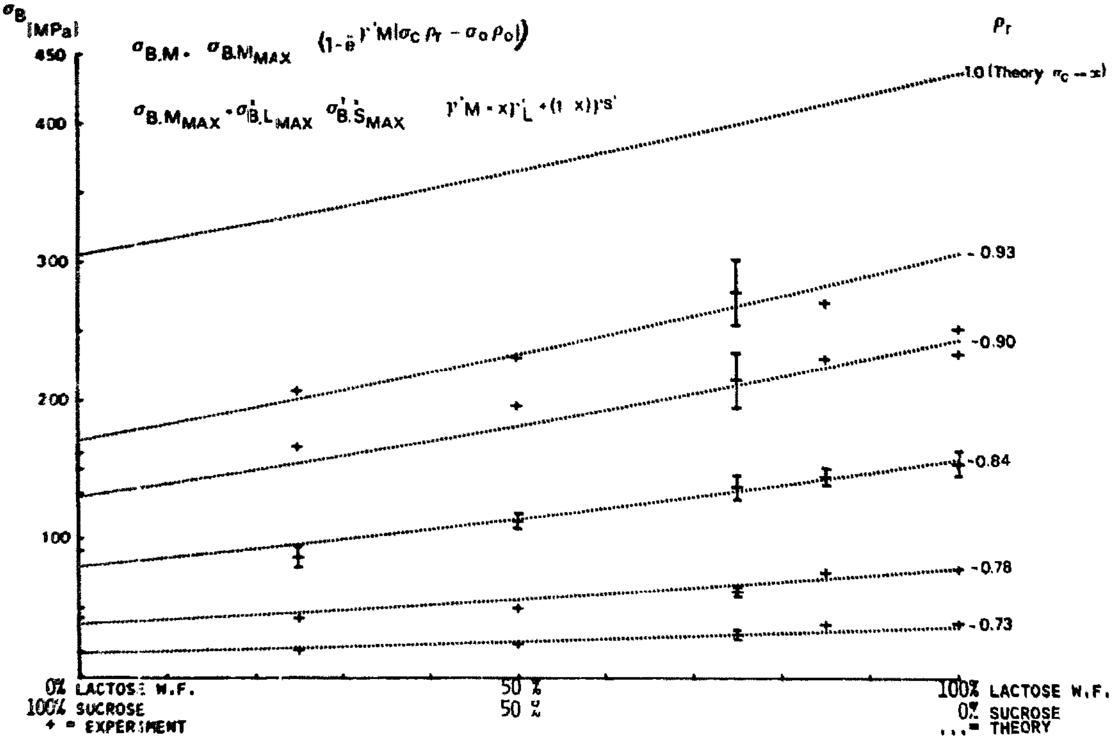

Fig. 5. Tensile strength values σ_B for the model mixture (x = lactose W.F., 1 − x = sucrose).

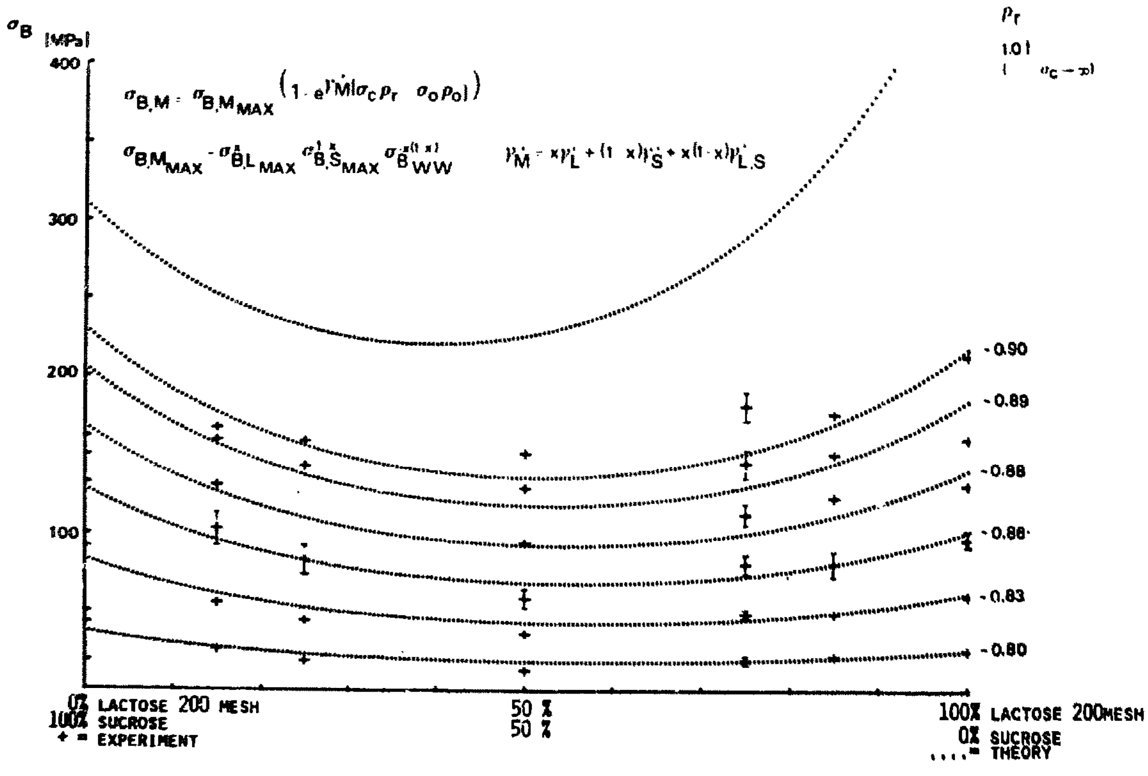

Fig. 6. Tensile strength values for the model mixture (x = lactose 200 mesh, 1 − x = sucrose).

TABLE 2

EVALUATION OF THE RADIAL TENSILE STRENGTH σ_B FOR MIXTURES OF LACTOSE (x) AND SUCROSE (1−x) INCLUDING INTERACTION TERMS $\sigma_{B_{ww}}$ AND γ'_{LS} ACCORDING TO EQN. 19

x	1−x	σ_{B_M} (MPa)	$x\gamma'_L+(1-x)\gamma'_S+x(1-x)\gamma'_{LS}$ 10^{-3} (MPa)$^{-1}$
0	1.0	311	4.43
0.15	0.85	252	3.97
0.25	0.75	231	3.68
0.5	0.5	225	3.01
0.75	0.25	289	2.43
0.85	0.15	345	2.22
1.0	0.0	488	1.93

$\sigma_0\rho_0 = 14.3$ (MPa)
$\sigma_{B_{ww}} = 0.112$
$\gamma'_{LS} = -0.676\cdot10^{-3}$ (MPa)$^{-1}$
$\sigma_{B_{ww}}$ = interaction term (dimensionless)
γ'_{LS} = interaction term (the subscripts L, S correspond to lactose resp. sucrose)
where σ_0 = initial compression stress; ρ_0 = relative density.

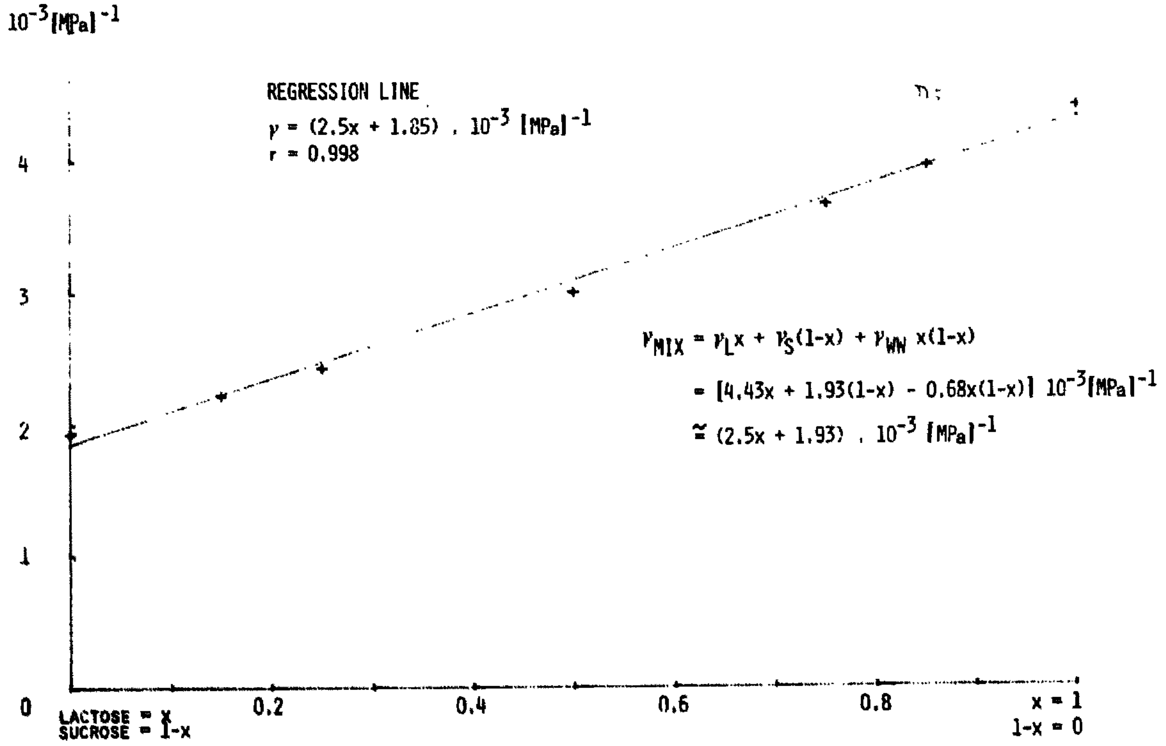

Fig. 7. Compression susceptibility γ of lactose–sucrose mixtures.

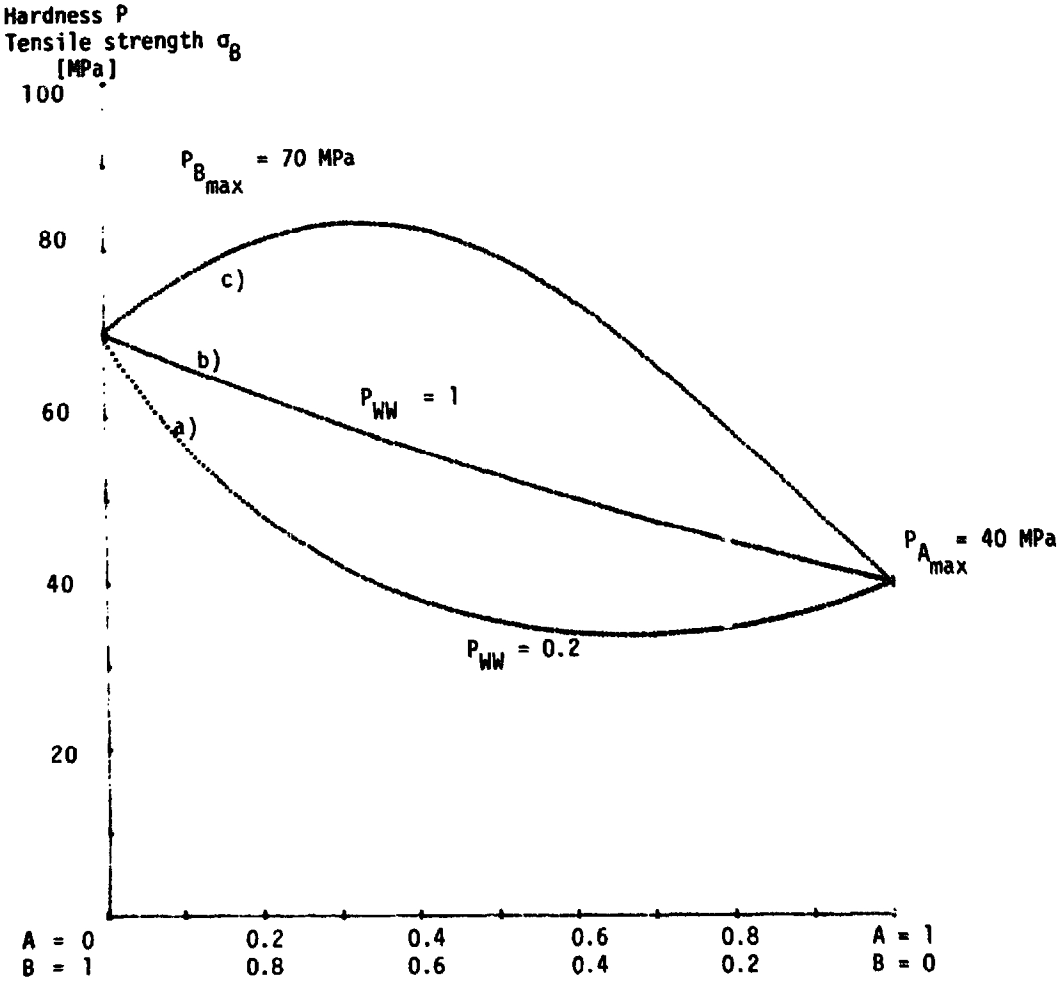

Fig. 8. Curves predicted by applying the mixture Eqn. 18 to pairs of substances showing (logarithmically) negative (a) and positive (c) interactions, and showing no interaction (b).

investigations will be required to show whether the maximum deviation always occurs for 1 : 1 mixtures. In particular we need to know how such a 1 : 1 mixture should be specified — whether by weight percentage, molar percentage, percentage surface area or other units. It may well be found in practice that the maximum departure from linearity occurs at weight proportions other than those of a 1 : 1 mixture.

As shown in Fig. 9, the relative position of the overall extreme value (maximum or minimum) is also dependent on the difference between the magnitudes $P_{B_{max}}$ $P_{A_{max}}$ for the separate components.

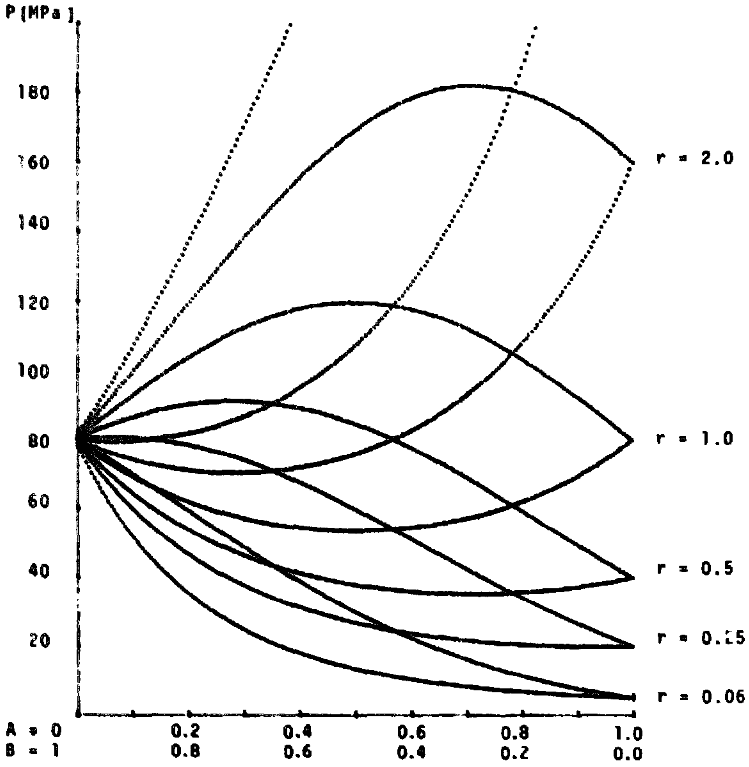

Fig. 9. Dependence of the overall extreme value on the ratio $r = P_{B_{max}}/P_{A_{max}}$ where $P_{A_{max}} = 80$ MPa and the interaction term $P_{WW} = 0.2$ or 5 (corresponding to a concave or a convex curvature).

Appendix

Conditions for the additivity of the parameters P_{max} and γ

$P_1 = P_{max_1}(1 - e^{-\gamma_1 \sigma_c \rho_r})$ single substance 1

$P_2 = P_{max_2}(1 - e^{-\gamma_2 \sigma_c \rho_r})$ single substance 2

$P_M = P_{max_M}(1 - e^{-\gamma_M \sigma_c \rho_r})$ mixture substance 1/2

$$\frac{dP_1}{d\sigma_c \rho_r} = P_{max_1} e^{-\gamma_1 \sigma_c \rho_r} \cdot \gamma_1$$

$$\frac{dP_2}{d\sigma_c \rho_r} = P_{max_2} e^{-\gamma_2 \sigma_c \rho_r} \cdot \gamma_2$$

geometric mean $x = 0.5$; $(1 - x) = 0.5$

$$\frac{dP_1^{0.5}\, dP_2^{0.5}}{d\sigma_c \rho_r} = P_{max_1}^{0.5}\, P_{max_2}^{0.5}\, e^{-(0.5\gamma_1 + 0.5\gamma_2)\sigma_c \rho_r} \cdot \gamma_1^{0.5}\, \gamma_2^{0.5}$$

Integration:

$$P_M = \frac{P_{max_1} P_{max_2} \gamma_1^{0.5} \gamma_2^{0.5}}{0.5\gamma_1 + 0.5\gamma_2} \left(1 - e^{-(0.5\gamma_1 + 0.5\gamma_2)\sigma_c \rho_r}\right)$$

Generalization:

$$P_M = \frac{P_{max_1}^{x} P_{max_2}^{1-x} \gamma_1^{x} \gamma_2^{1-x}}{x\gamma_1 + (1-x)\gamma_2} \left(1 - e^{-(x\gamma_1 + (1-x)\gamma_2)\sigma_c \rho_r}\right)$$

Approximation:

$$P_M \approx P_{max_1}^{x} P_{max_2}^{1-x} \left(1 - e^{-(x\gamma_1 + (1-x)\gamma_2)\sigma_c \rho_r}\right)$$

As a consequence, the following additivity rules may be applied and checked:

$$P_{max}\ (\text{mixture } 1/2) = P_{max_1}^{x} P_{max_2}^{1-x}$$

$$\gamma\ (\text{mixture } 1/2) = x\gamma_1 + (1-x)\gamma_2$$

In case of interactions it is necessary to introduce the parameters P_{WW} and γ_{WW}

$$P_{max}\ (\text{mixture } 1/2) = P_{max_1}^{x} P_{max_2}^{1-x} P_{WW}^{x(1-x)}$$

$$\gamma\ (\text{mixture } 1/2) = x\gamma_1 + (1-x)\gamma_2 + \gamma_{WW} x(1-x)$$

where x = percentage of substance 1, $1 - x$ = percentage of substance 2.

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