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Compaction characteristics of binary mixtures

W.E. Jetzer *

School of Pharmacy, University of Basel, CH-4051 Basel (Switzerland)

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Summary

Tableting characteristics of binary mixtures of materials which exhibit similar and dissimilar compaction behaviour were examined. Compacts were produced over a range of pressures and characterized in terms of indentation hardness and radial tensile strength. A comparison of these mechanical properties is indicative of bonding and capping tendency. The evaluated compression parameters permit an interpretation of tableting performance of a substance in a quantitative way. Furthermore they allow an estimation and prediction of the behaviour of a mixture from the behaviour of pure materials. The influence of the individual component is most pronounced at high concentrations up to a critical ratio where an inversion of the measured parameters occurs. Interactions are mainly to be expected with mixtures of components of dissimilar compaction mechanisms.

Introduction

The mechanical properties of compressed tablets can be characterized by measuring indentation hardness and tensile strength. These indicate how a powder responds to pressure during the process of tablet fabrication. Each test specifically quantifies the resistance to deformation and fracture of a compact, respectively. In a previous report a unifying description in terms of compaction performance parameter ($\gamma_P - \gamma_T$), (CPP) and bonding index [1] (BI) σ_{Tm}/P_m was made (Jetzer, 1986). They permit an interpretation or prediction of the variety of tableting properties in a more quantitative way.

The magnitude of indentation hardness, P, and tensile strength, σ_T, varies with the relative density, ρ_r, of the compact. Leuenberger et al. (1981) proposed a mathematical equation to describe this variation: $P = P_m\ [1 - \exp(-\gamma \cdot \sigma_c \cdot \rho_r)]$. In a combined description for hardness and tensile strength the following expression can be obtained (Jetzer et al., 1986):

$$\frac{\sigma_T}{P} = \frac{\sigma_{T_m}}{P_m}\left(1 - \frac{1 - \exp[(\gamma_P - \gamma_T)\sigma_c \cdot \rho_r]}{1 - \exp(\gamma_p \cdot \sigma_c \cdot \rho_r)}\right) \qquad (1)$$

P_m is the magnitude of P when relative density, ρ_r, approaches unity, i.e. when porosity is zero. In analogy, σ_{T_m} is the maximum magnitude of σ_T, but in this case ρ_r can assume values $\leqslant 1$. γ_P and γ_T, respectively, are proportionality constants.

* *Present address for correspondence*: Kantonsspital Bruderholz, Pharmaceutical Department, CH 4101 Bruderholz BL, Switzerland.

[1] The bonding index is one of three indices proposed by Hiestand and Smith (1984).

They may specify the rate at which compact hardness and strength, respectively, build up with an increase in the applied compression stress, σ_c. γ may reflect compressibility.

This paper in particular reports the results of a study of the compaction performance parameter $(\gamma_P - \gamma_T) = \Delta\gamma_{PT}$ and the bonding index σ_{T_m}/P_m for binary mixtures. The main aim of this study was to establish a convenient basis for interpreting tableting performance of materials and for classifying them.

Materials and Methods

Materials

The following binary mixtures were prepared, using materials of Pharmacopoeial grade.

(A) Aspirin FC (aspirin fine crystals 150/350, Bayer, F.R.G.) and Emcompress (dicalcium phosphate dihydrate, Ed. Mendell, U.S.A.).

(B) Aspirin 150 (aspirin powder 150, Bayer, F.R.G.) and Metamizol (natrium novaminsulfonicum, Siegfried, Switzerland).

(C) Aspirin FC and Caffeine (caffeine anhydr. free-flowing, fine granulate, Boehringer, F.R.G.).

The choice of materials and mixtures was based on differences and possible interactions in their compaction mechanism. For example, caffeine was previously found to exhibit capping tendency. Dicalcium phosphate dihydrate is highly brittle and furthermore it has a negative influence on the stability of aspirin.

Methods

The powder mixtures were prepared by weight as follows:
(a) disagglomeration of starting materials by sieving;
(b) mixing in a tumbler mixer (Turbula T 2A, W.A. Bachofen, Basle, Switzerland) at 25 rpm for 5 min;
(c) disagglomeration of mixture by sieving;
(d) remixing as before.

The materials and their binary mixtures were compressed without excipients on an Instron Universal Testing Instrument (Modell TT-DM, Instron, High Wycombe, U.K.). Before each tablet was compressed, the surface of the press tools was slightly coated with magnesium stearate applied with a cotton plug. The weighed amount of powder (400 mg) was manually filled into the die and tablets (round, flat-faced, diameter 11 mm) were compressed at loads between 50 and 310 MPa (lower punch pressure). The tablets were stored at room temperature, 45 ± 10% RH for at least 48 h before being tested. The mechanical properties of the tablets were measured as indentation hardness and radial tensile strength. Experimental procedures and evaluation of the compression parameters have been described in detail in previous papers (Jetzer et al., 1983a; Jetzer and Leuenberger, 1984).

All compacts were visually examined before measurement of the mechanical properties, those showing laminar cracks being rejected. The mean values for 6 tablets are given.

Results and Discussion

The results and estimated values of compression parameters P_m, σ_{T_m}, γ_P and γ_T of the individual components and binary mixtures are given in Table 1. They were computed by the mathematical equation proposed by Leuenberger et al. (1981), using non-linear regression analysis [2]. In an earlier report, compactibility and compressibility of a number of binary mixtures, consisting of substances of similar and dissimilar compaction behaviour, were determined (Jetzer et al., 1983b). The same materials were also used in this study.

Figs. 1–6 show the relationship between the mentioned compression parameters and composition of the mixtures.

Compactibility parameter P_m and σ_{T_m} (Figs. 1 and 2)

As expected, compactibility parameter P_m, plotted against the ratio of components in the mixture, did not give a straight line. Deviation

[2] Non-linear regression analysis program No. 09835-15040 Hewlett-Packard; and NLIN Procedure by SAS Institute, Cary, NC 27511 (thanks are extended to Dr. E.N. Hiestand for kindly providing this facility).

TABLE 1

COMPACTION PARAMETERS OF THE STUDIED BINARY MIXTURES

Substance 1	Substance 2	P_m [MPa]	γ_P 10^2 [MPa^{-1}]	σ_{T_m} [MPa]	γ_T 10^2 [MPa^{-1}]	Bonding index σ_{Tm}/P_m	Compaction performance parameter $\Delta_{\gamma PT} = (\gamma_P - \gamma_T)$ 10^2 [MPa^{-1}]
Aspirin FC (weight %)	Emcompress (weight %)						
0	100	752.6	0.17	14.12	0.11	0.019	0.06
20	80	313.4	0.36	10.84	0.12	0.035	0.24
40	60	176.6	0.68	6.39	0.23	0.036	0.45
60	40	129.8	0.89	5.14	0.31	0.040	0.58
80	20	124.1	1.11	3.84	0.50	0.031	0.61
100	0	87.2	1.34	2.96	0.70	0.034	0.64
Aspirin 150 (weight %)	Metamizol (weight %)						
0	100	90.8	0.79	2.38	0.37	0.026	0.42
20	80	104.9	0.87	2.61	0.46	0.025	0.41
40	60	103.2	0.94	2.46	0.51	0.024	0.43
60	40	98.8	1.03	2.70	0.56	0.027	0.47
80	20	95.6	1.11	2.87	0.62	0.030	0.49
100	0	91.4	1.23	3.13	0.70	0.034	0.53
Aspirin FC (weight %)	Caffeine (weight %)						
0	100	288.1	0.58	2.26	2.19	0.008	−1.61
10	90	261.8	0.63	2.41	1.72	0.009	−1.09
20	80	241.0	0.67	2.43	1.73	0.010	−1.06
30	70	209.9	0.74	2.92	1.16	0.014	−0.42
40	60	178.3	0.85	2.89	1.18	0.016	−0.33
50	50	161.7	0.91	2.78	1.21	0.017	−0.30
60	40	138.0	0.96	3.03	0.86	0.022	0.10
70	30	115.4	1.06	2.87	0.87	0.025	0.19
80	20	105.2	1.18	2.96	0.74	0.028	0.44
90	10	90.6	1.32	2.94	0.73	0.032	0.59
100	0	87.2	1.34	2.96	0.70	0.034	0.64

from linearity does not exhibit a uniform trend either and depends on the characteristics of and interactions between the components of the mixture. It is evident that a material non-specific treatment of the subject is not yet possible. The P_m values can be satisfactorily linked using a fitting curve obtained by simultaneous evaluation applying a model for mixtures (Jetzer et al., 1983b). However, some inaccuracies were observed with materials having highly dissimilar deformation properties.

The tensile strength, σ_{T_m}, development for mixtures shows a different trend from the observed characteristics for indentation hardness measurements (see Fig. 2). Generally, the mixtures exhibit a two-straight line dependency, indicating a more drastic change in this mechanical property at a critical composition ratio.

In the case of aspirin–emcompress mixtures, the addition of aspirin to the highly brittle emcompress leads to a sharp drop in strength, as similarly observed with hardness.

This behaviour seems to be typical of materials which compact by totally different mechanisms

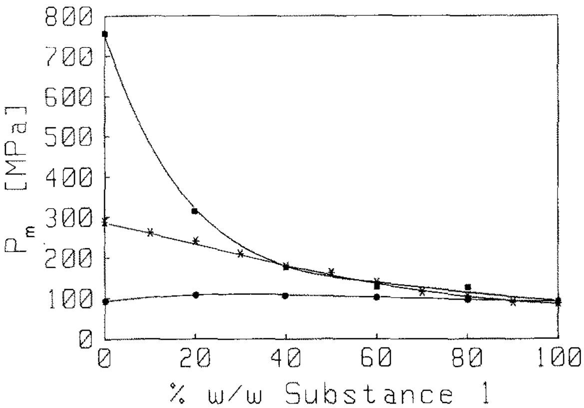

Fig. 1. Relation between indentation hardness compactibility parameter P_m and composition ratio (% w substance 1/%w substance 2). ■, mixture Aspirin FC–emcompress; ●, mixture Aspirin 150–metamizol; ★, mixture Aspirin FC–caffeine.

and was also observed with sodium chloride–lactose mixtures (Sheikh-Salem and Fell, 1981).

In contrast, a trend of increasing magnitude of the σ_{T_m} parameters, compared to the P_m parameters, is found with aspirin–caffeine mixtures. The caffeine investigated was reported to exhibit a high degree of capping tendency (Jetzer and Leuenberger, 1984). Here, increasing amounts of aspirin improve bonding and reduce fracture tendency resulting in higher tensile strength values of the compacts. The determined indentation hardness values P_m, by contrast, are not sensitive enough to detect capping problems. Possibly, more information could be obtained by measuring the depth of the identation field instead of the diameter.

The examined aspirin 150–metamizol binary mixtures exhibit the most similar, almost linear, relation between σ_{T_m} and P_m against composition ratio, the two materials having similar plastic deformation properties.

Compressibility parameter γ_P and γ_T (Figs. 3 and 4)

The individually estimated compressibility parameters, γ_P and γ_T respectively, plotted against the ratio of components in the mixtures, exhibit a dissimilar development for indentation hardness and tensile strength measurement, too. For γ_P values the linear relationship obtained suggests a simple additive property. In earlier studies, however, a departure of γ_P from linearity was found in mixtures with microcrystalline cellulose–lactose and potassium bromide–potassium chloride (Jetzer et al., 1983b). The observed departure from linearity increases with a rise in the proportion of microcrystalline cellulose — a viscoelastic deformable component. For the KBr–KCl system, crystal defects are the determining factor in the behaviour of these highly plastic, ionic crystals. Rohera et al. (1985) investigated

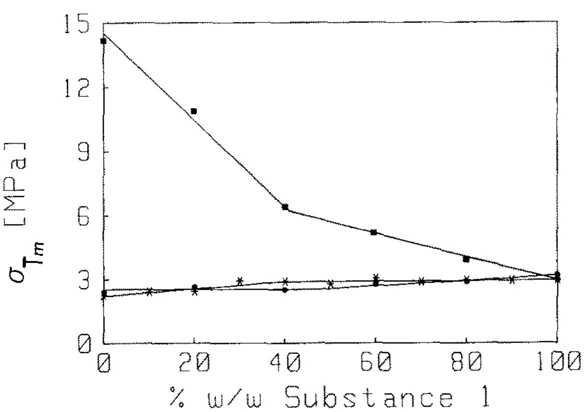

Fig. 2. Relation between tensile strength compactibility parameter σ_{Tm} and composition ratio (%w substance 1/%w substance 2). ■, mixture Aspirin FC–emcompress; ●, mixture Aspirin 150–metamizol; ★, mixture Aspirin FC–caffeine.

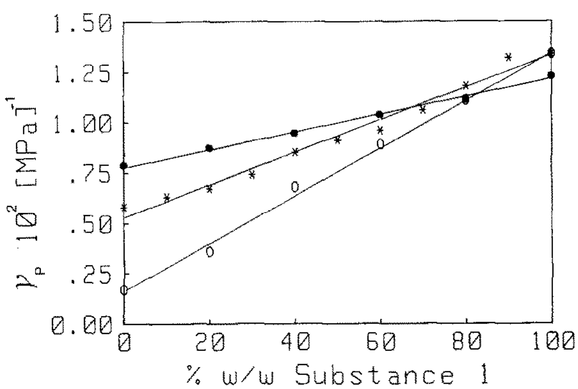

Fig. 3. Relation between indentation hardness compressibility parameter γ_P and composition ratio (%w substance 1/%w substance 2). ●, mixture Aspirin 150–metamizol; ★, mixture Aspirin FC–caffeine; O, mixture Aspirin FC–emcompress.

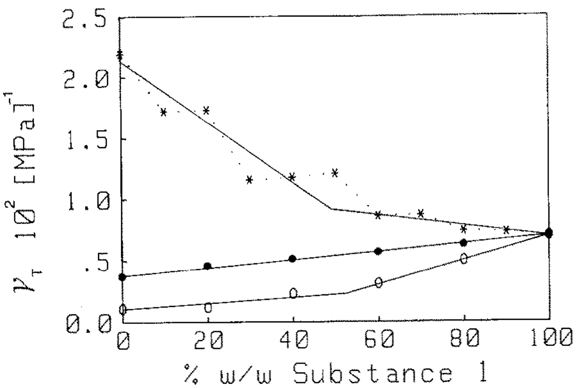

Fig. 4. Relation between tensile strength compressibility parameter γ_T and composition ratio (%w substance 1/%w substance 2). ●, mixture Aspirin 150–metamizol; ★, mixture Aspirin FC–caffeine; O, mixture Aspirin FC–emcompress.

binary systems consisting of extremely dissimilar compaction behaviour, i.e. brittle and plastic, and they observed a trend of two straight lines indicating a process of phase inversion.

For tensile strength measurements (see Fig. 4) a linear γ_T relationship is observed only in the case of aspirin–metamizol mixtures, these two materials having a similar compaction behaviour. The different compaction properties of aspirin and emcompress become further evident when plotting γ_T values of their mixtures against the ratio of components. The trend of two straight lines intersecting each other at a point indicates a change in compression behaviour in which one component dominates the other up to a critical mixture ratio. This point of view is also in agreement with the conclusions of Führer and Schmidt (1981) and Sheikh-Salem and Fell (1981).

The addition of increasing amounts of aspirin, reducing the fracture tendency of caffeine, changes the development of tensile strength which is reflected by dramatic changes in the γ_T values of the mixtures. Apart from the jumps in the single values, the relationship of γ_T vs mixture composition shows a two-straight line trend, too.

The foregoing results suggest that the mechanical properties of compacts, due to the various properties and interactions of the mixed materials, do not exhibit a uniform trend that could be treated material unspecifically. In particular, it is difficult to detect capping problems only by means of indentation hardness measurements. Indentation hardness and tensile strength measurements quantify two competing mechanical responses—deformation and fracture. It is therefore more useful to combine such parameters in a unifying description by means of bonding index (BI) and compaction performance parameter (CPP). The BI and CPP values are given in Table 1 and are graphically represented in Figs. 5 and 6.

Bonding index (BI) (Fig. 5)

Comparing index values, it is obvious that in the three mixtures studied, the addition of aspirin tends to improve bonding. A drastic effect is seen when aspirin is added to emcompress. The tendency of a two-straight line relationship is also observed with the BI. One component of the mixture dominates the other up to a critical composition ratio. It is interesting to note that for the mixture aspirin–metamizol, the critical composition ratio occurs within the limit of experimental error, approximately at a w/w composition ratio 1 : 1, these two materials having a similar plastic deformation behaviour.

By contrast, the other two mixtures of materials with dissimilar compaction mechanisms exhibit an inversion point of the BI values at a w/w composition ratio of approximately 3 : 7. However, further investigation is necessary to elucidate this

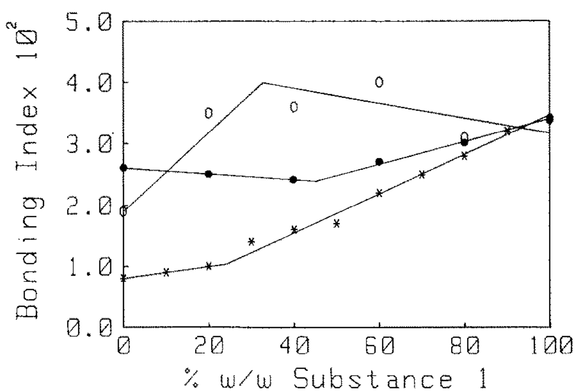

Fig. 5. Relation between bonding index (BI = σ_{Tm}/P_m) and composition ratio (%w substance 1/%w substance 2). ●, mixture Aspirin 150–metamizol; ★, mixture Aspirin FC–caffeine; O, mixture Aspirin FC–emcompress.

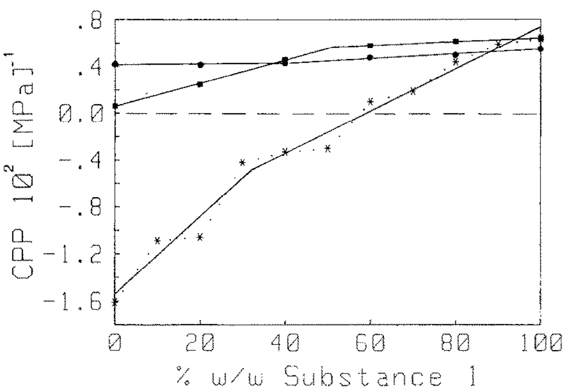

Fig. 6. Relation between compaction performance parameter (CPP = $\gamma_P - \gamma_T$) and composition ratio (%w substance 1/%w substance 2). ●, mixture Aspirin 150–metamizol; ■, mixture Aspirin FC–emcompress; ★, mixture Aspirin FC–caffeine.

behaviour. An open question is how other physical properties (i.e. particle size, specific surface area, etc.) of the materials influence the critical ratio at which one component dominates the other?

Compaction performance parameter [3] *($\Delta\gamma_{PT}$) (Fig. 6)*

On examination of Fig. 6 for the aspirin–caffeine mixtures the compaction performance parameter assumes negative values that, with increasing amounts of aspirin, gradually become positive. As observed in earlier studies (Jetzer and Leuenberger, 1984; Jetzer et al., 1985), the caffeine compacts investigated exhibit a high capping tendency. The low bonding index and a negative compaction performance parameter indicate this. Addition of plastic deformable aspirin produces a gradual increase in tablet strength. In fact the BI value for aspirin (0.034) and the magnitude of the CP parameter (+0.064), reported in Table 1, are about 4 times higher than the values for caffeine. It is evident that in this case aspirin acts also as a binder, gradually improving bonding.

For the other two mixtures investigated, the CP parameter exhibits a positive range of values, indicating that significant fracture problems do not occur. The development of the ($\Delta\gamma_{PT}$) values, as a function of the mixture ratio, essentially reflects here the change in deformation behaviour of the tableting powders as manifested by measurement of the mechanical properties of the compact. The highly dissimilar compaction mechanism of aspirin and emcompress causes the influence of the individual components to be most pronounced at high concentrations until inversion of the properties occurs. As expected, the values observed with the aspirin–metamizol mixture change almost linearly as a function of the ratio of the two components, having similar deformation properties.

Conclusions

The ultimate objective of all studies of tableting powders obviously is to use the known properties of pure materials in order to predict the compaction behaviour of material mixtures. Very little is known about interactions between particles of dissimilar materials that cause mixtures to produce tablets with different properties than those produced from the pure substances. Because of the variety and complexity of tableting properties that may arise, a theory enabling prediction of the occurrence, magnitude or direction of these interactions does not exist at the present.

The foregoing results show that the compaction characteristics of mixtures are principally directed by the behaviour of the individual materials. Interactions are mainly to be expected with mixtures of components of dissimilar compaction mechanisms. Here, the influence of the individual component is most pronounced at high concentrations up to a critical composition ratio where an inversion of the measured parameters occurs. The more readily deformable substance predominantly undergoes plastic deformation whereas the other component of the blend changes little in shape and becomes encapsulated until enough particles are available. The values and development of compression parameters as a function of the composition ratio indicate this. Similar results were observed by Führer and Schmidt (1981), Humbert-

[3] Obviously, instead of using the parameter $\Delta\gamma_{PT}$, it is also possible to formulate a dimensionless compaction performance index as the ratio γ_P/γ_T which gives the same information.

Droz et al. (1983) and Rohera et al. (1985).

The addition of increasing amounts of aspirin to the examined caffeine gradually improves bonding and reduces capping tendency of pure caffeine. In practice, capping problems can be avoided by using binders which are of plastic nature. Even small amounts of aspirin show a drastic improvement in bonding. Capping tendency seems to be a transitional process that gradually increases until visible fracture occurs. The compression parameters obtained by testing mechanical properties of compacts permit an interpretation of the tableting performance of substances and mixtures in a more quantitative way. For this purpose a combined description in terms of hardness and strength is advantageous. Finally, the index and parameters should allow the formulator to estimate the behaviour of a mixture from the behaviour of pure materials. This is a simplification. Obviously, more than one parameter is necessary to describe the variety and complexity of the tableting behaviour.

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