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The Compaction Characteristics of Binary Mixture Powders

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Abstract. The compaction characteristics and tabletting properties of binary mixtures of five particle size fractions of gelatin, sodium chloride, maize starch and di-pac-sugar powders have been investigated at constant compaction speed. Pressure-density relationships, interpreted using the Heckel equation, show non-linear relationships among the constants determined from the equation and the proportion of the compenents of the mixture, for all particle sizes tested. Furtheremore, by employing the diametral compression test, the tensile strength of the compacts prepared from these mixtures showed also a non-linear relationship between the tensile strength and the mixture composition. In all cases, a minimum in the mean yield pressure is exhibited at certain mixture compositions ranging from 10 to 20% of the inferior (soft) mixture component. It is suggested that these effects are due to the dominant influence of the particular deformation and bonding mechanisms present at any given morphological mixture composition. These are largely influenced by the mixing conditions, particle size and shape distribution, as well as the mechanical properties of the mixture compenents and the kinematics of deformation involved in the process. However, the influence of the individual component is most pronounced at high concentrations. Generally, for all materials, it is found that the mean yield pressure increases and the tensile strength decreases as the particle sizes are increased.

Introduction

In the pharmaceutical industry, it is becoming increasingly important to characterise fully new tablet formulations at an earlier stage in their development and, ideally, not to alter significantly the formulation between the start of long term toxicity studies and sale. This, in turn, has accelerated development techniques to evaluate the physical and mechanical properties of the materials which will be used in the subsequent formulations, and this area of work has been known as "pre-formulation" [1].

The formulations used for pharmaceutical tablets have been comparatively simple (active material and excipient). Undoubtedly a few excipients are selected for a specific purpose (*e.g.* to aid tablet disintigration, to lubricate the die, etc.) but the "art" of formulation development and excipient selection is seldom based on scientific principles [2]. Pre-formulation studies should, therefore, be designed to identify the ideal formulation, and each excipient should be actively chosen to achieve this goal. The pre-formulation tests should cover the areas of stability, bioavailability and manufacturability, and the excipients should be chosen to optimise [3] performance of the formulation in these areas compatible with the acceptability of each material for subsequent registration worldwide.

The methods used to determine the optimum excipients vary from one manufacturer to another [3]. Most pharamaceutical companies have their own methods to predict possible stability and bioavailability problems at an early stage, but the prediction of manufacturability is still an "art". This is particularly so with respect to the actual compaction process at higher speeds and pressures [4]. Therefore, the need for development of better formulations to withstand the rapid changes in stresses and to design pre-formulation tests to assess them are essential and should be considered before embarking on a pre-formulation exerecise. A knowledge of the theories relating to the mechanics of compaction and a critical awareness of the techniques developed by previous workers is also required.

In recent years a number of techniques have been developed as pre-formulation tests by various workers. The most promising of these involve pressure-density relationships. For the compaction of pharmaceutical materials these relationships have been successfully interpreted using the approach of Heckel [5,6,7]. Although, Rue and Rees [8] and Es-Saheb [7] have expressed reservations in using Heckel plots to classify compaction behaviour, the approach is still useful in a study as the one under consideration here, where the speed of compaction used is low. Briefly, Heckel [5] relates the density of the compact to the applied pressure. He considers the compaction of powders to be analogous to a first order reaction, the pores being the reactant. Expressing the porosity in terms of the relative density (D) of the compact, {D=(current density)/(true zero porosity density)}, the Heckel equation can be derived:

$$\ln[1/(1-D)] = KP + A \tag{1}$$

where K and A are constants and P is the applied pressure. The value of the gradient, K, is a measure of the compaction characteristics and consolidation mechanisms of the material and it is used here to evaluate the compaction properties of the mixtures. The reciprocal of K is equal to the mean yield pressure.

Though, the compaction of simple mixtures of materials is a fairly common pharmaceutical operation, it has received little attention compared with compaction studies on single materials. A knowledge of the behaviour of simple mixtures of powders during compaction would be an advantage in formulation. Recently, several publications have appeared [9,10,11] for workers concerned with mixtures of direct compression materials which may have properties significantly better than the individual components. Fell and Newton [12], showed that the tensile strength of tablets prepared from mixtures of different forms of lactose could be predicted from a knowledge of the tensile strengths of tablets of the pure materials. Salem and Fell [11], working on mixtures of sodium chloride and lactose, found that the strength of the mixture compacts is not a simple function of the strength of the tablets of the individual components. Panaggio *et al.* [9], in compacting binary mixtures of dicalcium phosphate dihydrate and a modified pregelatinized starch found that the compaction properties of the mixtures were intermediate between those of the two pure components and varied linearly with their relative proportions. In the second category, the properties did not obey such a simple relationship and, in some cases, the properties of some mixtures were a lot greater than, or less than, either of the two pure components. However, a very important aspect of material properties which is common to most compacted materials is the effect of particle shape [13] and size [14,15] on tablet properties. Research on fractions of pure single materials has been done by many workers.

In this paper, a summary of an extensive research programme on the compaction characteristics and mechanics of binary mixtures of some non-metallic powders is presented. Our emphasis in the effect of particle size on the tabletting properties of these materials is also presented.

Materials, Experimental Equipment and Techniques

The test programme is carried out for four materials, namely, sodium chloride (B.D.H. Chemicals Ltd., U.K.), maize starch (Hopkin and Williams Ltd., U.K.), gelatin (MERCK, Darmstadt, Switzerland), all in their normal laboratory form; and ordinary sugar specially formulated for direct compression without granulation (I.C.I Imperial Chemical Industries Ltd., England, U.K.) and hence referred to in the text by the trade name of "di-pac-sugar".

All four materials are sieved, and five fractions of particle sizes of each powder are obtained. These are 54, 150, 250, 355 and 710 μm. Six sets of binary mixtures of di-pac-sugar and sodium chloride, gelatin and di-pac-sugar, maize starch and di-pac-sugar, gelatin and sodium chloride, maize starch and sodium chloride and gelatin and maize starch for all five particle size fractions of each material are prepared. Then four formulations (*i.e.* mixture composition) of each binary mixture, of the same particle size distribution, are prepared in the following weight ratios 20:80, 40:60, 60:40, and 80:20. In some cases, other extra ratios are prepared. Uniform blends of the materials are obtained by tumbling appropriate quantities, in a glass container for 16 min. This is based on some preliminary tests and analysis which showed that a suitable uniform mixes are produced.

The mixtures are compressed at constant speed of 5mm/min. on an Instron testing machine, using hard steel circular standard 10 mm flat faced punches and die sets (Ma-

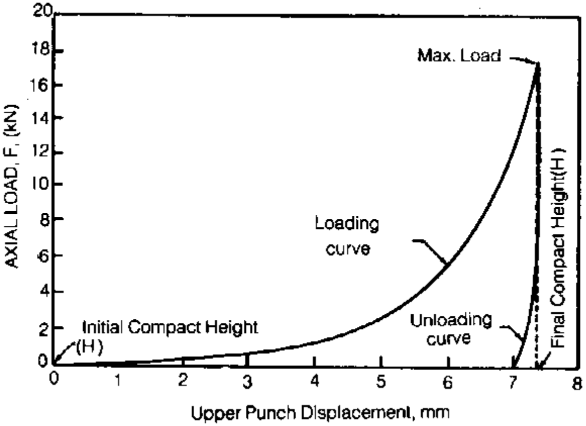


Fig. 1. A typical force-deformation characteristic curve for pure di-pac - sugar powder.

nesty Ltd., U.K.). The upper punch is used to apply the compaction pressure and, after compaction completion, to eject the compact. For each case, and for the same compaction conditions, the test is repeated, at least, five times to check for consistency. In all the tests load-displacement measurements are made. A typical force-deformation characteristic curve for 100% pure di-pac-sugar powder is shown in Fig. 1. To insure even relaxation conditions and free elastic recovery in a dry atmosphere, all tablets are stored, over silica gel, for 24 hours after preparation. Their thickness is then measured to within 0.01mm accuracy, and the tensile strengths determined by the diametral compression test [16] on an Instron testing machine at a constant speed of 2mm/min. For further details on equipment, materials, measuring methods and behaviour of other powders see ref. [7].

Experimental Results

The measurements in each test were processed for graphical presentation by employing the (LOTUS-123) computer programme package. The axial load is converted to axial pressure (P). Also from the punch displacement, knowing the true density of each material and the weight of each tablet, assuming a rigid die, the relative density (D) is calculated. Thus, it was possible to plot the Heckel equation for each test. Typical Heckel plots for the binary mixtures of di-pac-sugar and sodium chloride, for particle size distribution of 150μm, and the different mixture composi-

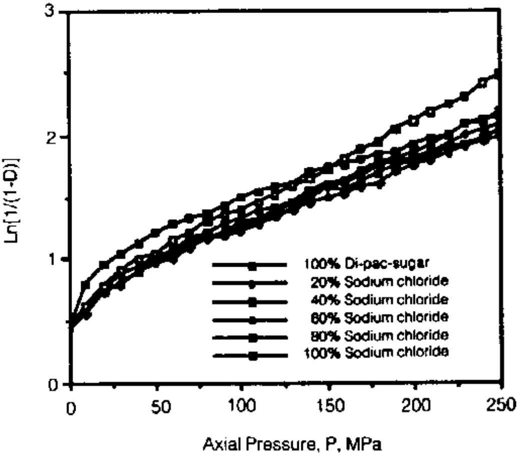


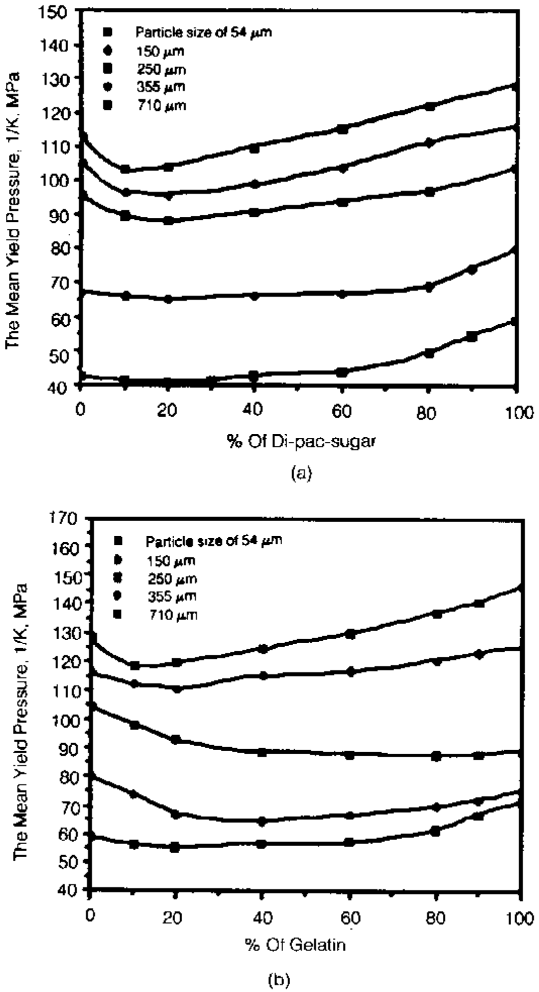
Fig. 2. Typical heckel plots for binary powder mixtures of di-pac - sugar and sodium chloride, of 150 μm particles size.

tions, are shown in Fig. 2. Each curve is obtained from a large number of experimental points and from more than one test. From the Heckel plots obtained, for all materials, the mean yield pressure (1/K) for all mixture compositions are calculated and shown in Figs 3,4 and 5. These are for the six binary mixtures and the five particle size fractions tested of di-pac-sugar and sodium chloride, di-pac-sugar and gelatin, maize starch and di-pac-sugar, gelatin and sodium chloride, maize starch and sodium chloride, and gelatin and maize starch respectively.

For each test the obtained compact tensile strength (s_t) is calculated using the following equation [16]:

$$s_t = (2F)/(\pi dT) \qquad (2)$$

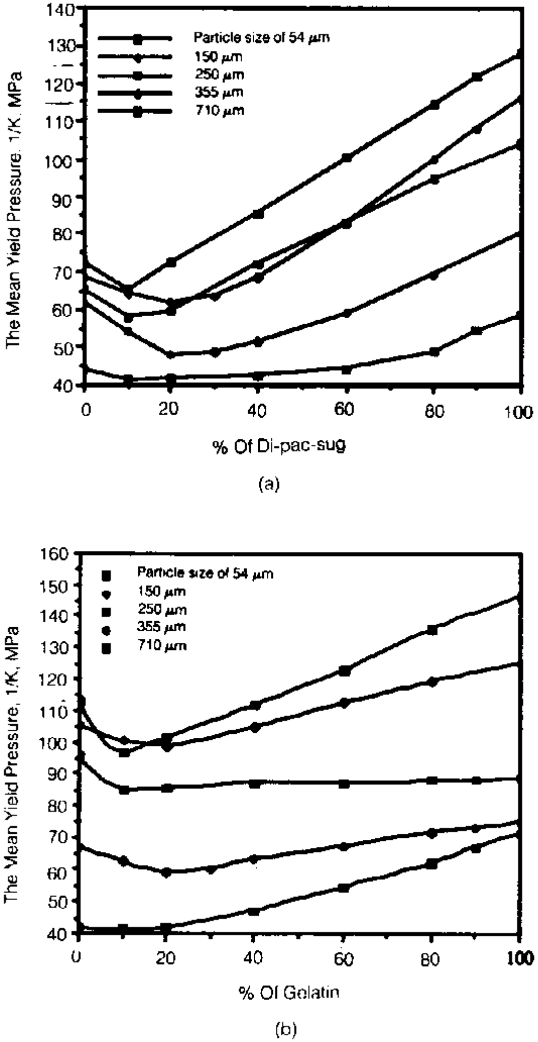
where, F is the breaking load obtained from the diametral compression test, and d and T are the compact diameter and thickness respectively. The tensile strength results evaluated for the final compacts for all mixtures are shown in Figs 6,7 and 8. The variation of the mean yield pressure (1/K) and the compact tensile strength for the pure four materials tested, with the average particle size are shown in Figs 9 and 10 respectively.



(a)

(b)

Fig. 3. The mean yield pressure variation with the mixture composition of (a) di-pac-sugar and sodium chloride and (b) di-pac-sugar and gelatin.



(a)

(b)

Fig. 4. The mean yield pressure variation with the mixture composition of (a) maize starch and di-pac-sugar and (b) gelatin and sodium chloride.

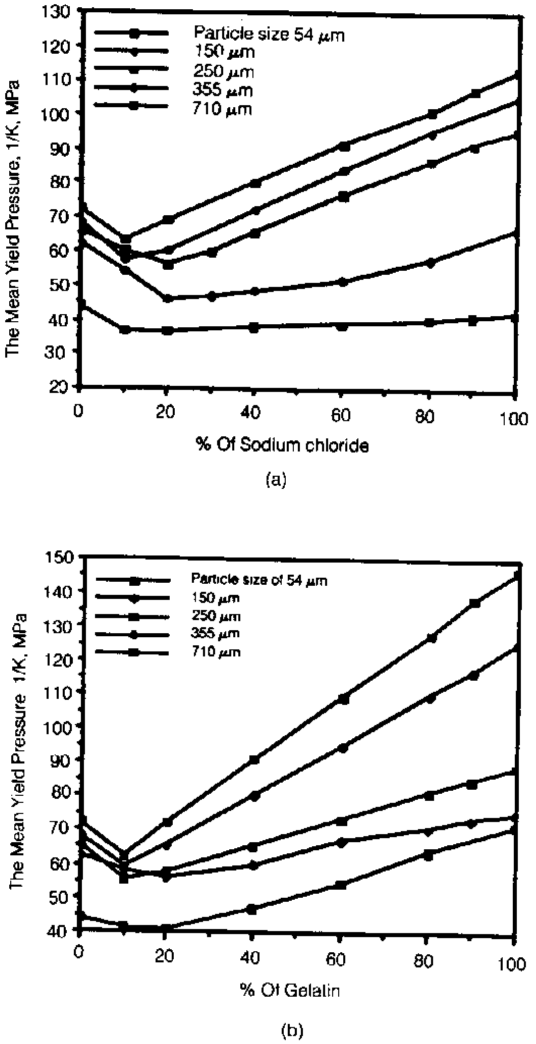
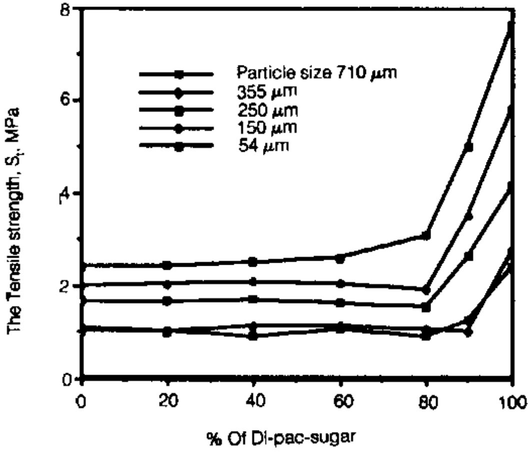
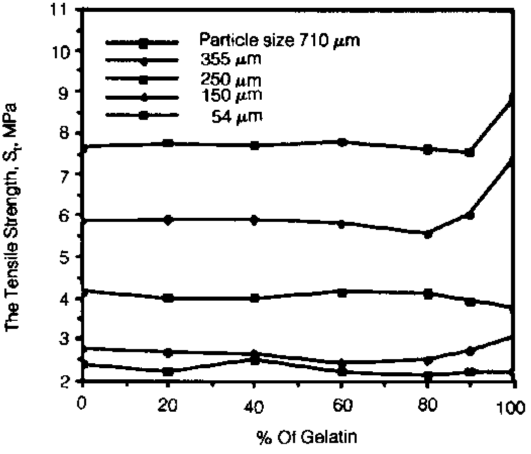


Fig. 5. The mean yield pressure variation with the mixture composition of (a) maize starch and sodium chloride and (b) maize starch and gelatin.



(a)



(b)

Fig. 6. The compact tensile strength variation with the mixture composition of (a) di-pac-sugar and sodium chloride and (b) di-pac-sugar and gelatin.

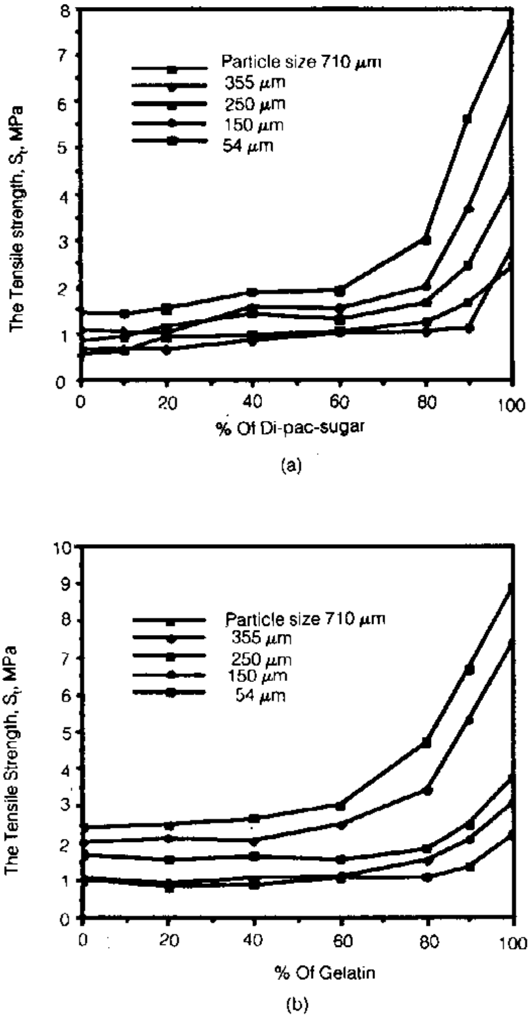


Fig. 7. The compact tensile strength variation with the mixture composition of (a) di-pac-sugar and maize starch and (b) gelatin and sodium chloride.

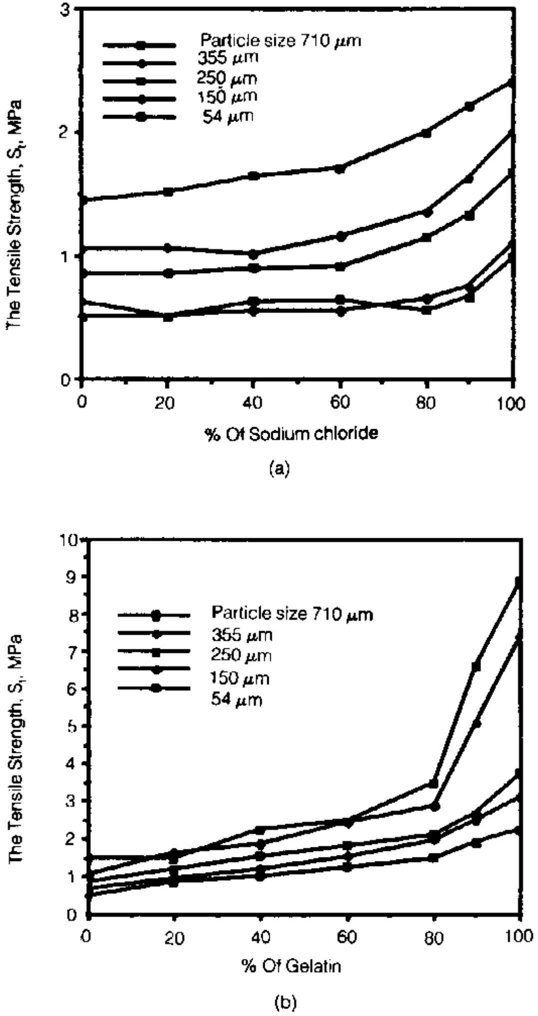


Fig. 8. **The compact tensile strength variation with the mixture composition of (a) sodium chloride and maize starch and (b) gelatin and maize starch.**

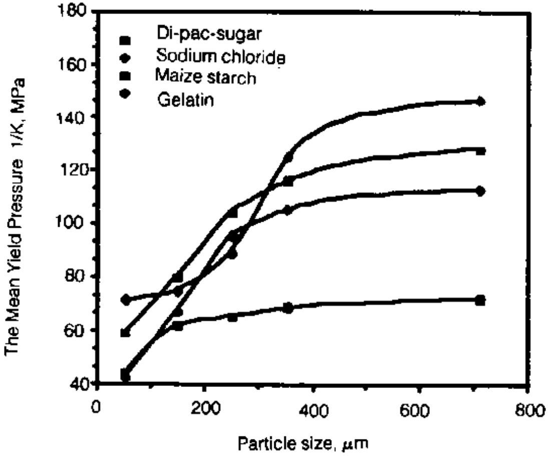


Fig. 9. The variation of the mean yield pressure with the particle size for the pure materials.

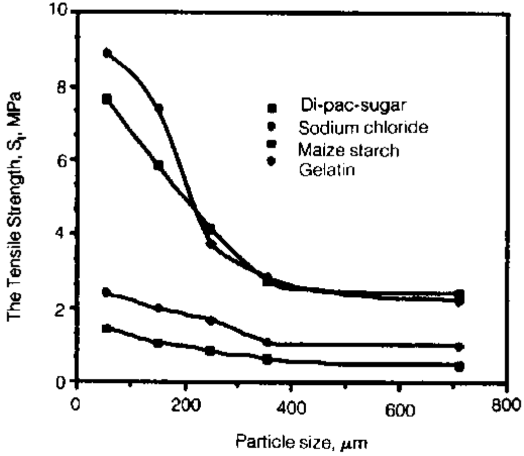


Fig. 10. The compact tensile strength variation with the particle size for the pure materials.

Discussion

For all materials tested, non-linearity is observed in the Heckel plots over the whole pressure and mixture composition ranges studied, as can be seen in Fig. 2. This indicates that all the materials examined do not deform exclusively by palstic deformation mechanisms, including the powders which are known to deform plastically such as gelatin and sodium chloride [15]. Deviation from linear behaviour at low pressures can be attributed to the powder rearranging itself by packing and generally behaving as loose powder and not a coherent mass. The transition from the curved region (first stage of compaction) to the relatively linear portion (the second stage of compaction) has been found to coincide with the minimum pressure required to form a coherent compact. Again, as the loading proceeds and the final stage of compaction starts, a second transition in the curve occurs and it becomes more nonlinear, tending to curl steeply upwards, and in some cases, intersection of some plots of various mixture composition is observed. It is noticed that the nonlinearity of the plots increases as the brittle material component in the mixture, such as maize starch, is increased. Also as the particle size distribution is increased the nonlinearity of the plots increases. This indicates that the fragmentation mechanism of deformation becomes increasingly dominant (*i.e.* brittle behaviour), hence higher values of 1/K and less values of the final compact tensile strength, which agrees with the findings of Hersey *et al.* [6], see Figs 3,4 and 5 also Figs 6,7 and 8. Meanwhile, the descending order of the materials tested regarding its plastic deformation and consolidation mechanisms is found to be; gelatin, di-pac-sugar, sodium chloride and maize starch, see Fig. 9. Their binary mixtures, also, follow the same order as displayed in Figs 3,4 and 5.

Although, Figs 3,4 and 5 showed that the relation between 1/K and the mixture composition is not simple, few of the large particle size fractions exhibited linear behaviour over the range 15% to 100% of mixture composition. Also a drop in the values of 1/K, at mixture composition of about 10-20%, is noticed for all materials. This drop becomes clearer as the two components of the mixture differ in their mechanical properties and, thus, their consolidation mechanisms. However, this drop is suggested to be due to the fact that the mixture is starting to act as a composite material made of soft matrix (ductile) and hard (brittle) material embedded in it. Consequently, the kinematics of deformation and the morphological mixture structure produced result in an overall consolidation mechanism with lower values of 1/K than any of the mixture constituent components. It should, of course, be borne in mind that this is also affected by many factors such as the mixing and friction conditions [17,18,19], the different mechanical properties of the materials involved, the speed of compaction, and the particle size and the shape distributions.

Again all materials tested showed nonlinear relationship between the tensile strength and the mixture composition, as shown in Figs 6,7 and 8. Also, it is interesting to note that, in most cases, the addition of either second component leads to a drop in the tensile strength of the tablets, giving rise to tablets with tensile strengths below those of either of the individual components alone. This is due to the fact that when a powder is added to another it "contaminates" its particle surfaces and, hence reduces the bonding (welding) among them. Also, it is clear from the tensile strength values of the individual materials that gelatin produces the strongest bonds (being the most ductile material), followed by di-pac-sugar, sodium chloride and finally maize starch, as shown in Fig. 10. Furthermore, it is shown that the harder (*i.e.* the more brittle) materials, such like maize starch, dominate the mixture system, and only when a high portion of the soft (ductile) material, such like sodium chloride or gelatin, is present tablets of a higher strength are produced. Changes in particle size, although altering the relative properties of fragmentation and plastic deformation mechanisms and therefore producing slightly differnet patterns of results, do not alter the overall behaviour.

It is generally accepted that the friction increases as the particle size in a powder mass decreases and the flow as well as the powder density decrease, together with the uniform blending and mixing of the powder [17,18]. While the final strength of granular materials increases with decreasing particle or grain size [11,12,19]. This is clearly shown in Fig. 10, where the final tensile strength of the compacts is found to increase as the particle size is decreasing, meanwhile, the mean yield pressure is increasing as shown in Fig. 9. Finally, the interaction between ductile (plastic) and brittle (fragmentation) behaviour in any binary mixture, affects the degree of particle crushing and bonding and hence the final compact strength.

Conclusions

From these cold compaction tests on a variety of binary mixtures of di-pac-sugar, sodium chloride, gelatin, and maize starch powders; it is possible to draw the following conclusions:

1) The Heckel plots constructed for all materials are non-linear. This indicates that all the materials examined do not deform exclusively by plastic deformation mechanisms.
2) Final properties of a mixture compact are not a simple addition of the properties of its individual components (this includes for example; the mean yield pressure and the tensile strength properties).
3) The tensile strength of the compacts decreases as the particles size increases.
4) The mean yield pressure of the material increases as the particle size increases.
5) The influence of the individual compenent of a mixture is mostly pronounced at higher concentrations.
6) Generally, the dominant properties are those due to the inferior component in the mixture. All the materials show this behaviour clearly at mixture compositions of 10% to 20% of the inferior mixture component.

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مميّزات اندماج المخاليط الثنائية للمساحيق

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قسم الهندسة الميكانيكية، كلية الهندسة، جامعة الملك سعود، ص.ب ٨٠٠،
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ملخص البحث. في هذا البحث تمت دراسة مميّزات الاندماج وخصائص صنع الأقراص من المخاليط الثنائية لخمسة أحجام من الحبيّبات لمساحيق: الجلاتين، ملح الطعام، نشا الذرة والسكر وذلك على سرعة اندماج ثابتة. وبمعالجة علاقات الضغط والكثافة لهذه المواد باستخدام معادلة هِكِل فقد تبينّ وجود علاقة لا خطيّة بين الثوابت المحسوبة من هذه المعادلة ونسب المركّبات للخليط لجميع أحجام الحبيّبات التي تم بحثها. وبناءً على استخدام اختبار (الضغط القطري) في تحديد قوى (إجهادات) الشد لجميع المضغوطات المحضّرة من هذه المخاليط فقد اتضح كذلك وجود علاقة لا خطيّة بين إجهادات الشد هذه ونسب مكوّنات المخلوط. وفي جميع الحالات فقد تبينّ وجود حد أدنى في قيم ضغط الإذعان المتوسط وذلك عند نسبة معيّنة لمركّبات المخلوط تتراوح بين ١٠-٢٠٪ من نسبة مركبة المخلوط الضعيفة (الطريّة). ويعتقد بأن السبب في ذلك يرجع إلى سيطرة أسلوب تشويه وربط معيّن متواجد في أي تكوين مورفولوجي للمخلوط والتي تتأكثر كثيرًا بظروف الخلط، وتوزيع حجم وشكل الحبيّبات بالإضافة إلى الخواص الميكانيكية لمركّبات الخليط وكذلك كينماتيكا (أو حركة) التشوه الداخلة في هذا الأسلوب. ولكن التأثير المنفرد للمركّبات كان أكثر وضوحًا وملحوظًا عند التركيزات العالية لها. وبشكل عام ولكل المواد فقد تبينّ أن ضغط الإذعان المتوسط قد ازداد بينما قوى الشد قد نقصت بازدياد حجم الحبيّبات.