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Research Article

COMPACTIBILITY ASSESSMENT OF DIRECT COMPRESSION EXCIPIENTS: PROSOLV EASYTAB

JESÚS ANDRÉS RODRÍGUEZ VALADEZ, LEOPOLDO VILLAFUERTE ROBLES

Department of Pharmacy, National School of Biological Sciences, National Polytechnic Institute of Mexico, D. F., Mexico. Email: lvillaro@encb.ipn.mx, lvillarolvillaro@hotmail.com

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ABSTRACT

Objective: The aim of this work is to put side-by-side different methods to set up Prosolv EasyTab compactibility as a parameter to define the surrogate and the relative surrogate functionality of this ready-to-use direct compression excipient.

Methods: The evaluated parameters included the tablet crushing strength, D; tablet tensile strength, σ; specific crushing strength, SCS and compactibility coefficients, Cp.

Results: The defined parameters do not allow the identification of an all-purpose compactibility magnitude for Easytab. All parameters show a trend as the tablet weight changes although those using normalized values of tablet hardness display the smaller trend. Parameters considering the experimental values of the maximal compactibility have as disadvantage the requirement of equipment capabilities in a width span. Parameters considering the relative density have the disadvantage of calculating compactibility at a relative density of 1.0 that in some cases are not attainable due to compression problems. The compactibility parameters show an average of 26% lesser compactibility of Easytab compared to Helmcel 200.

Conclusion: All calculated parameters allow the reduction of compactibility to a numerical value that characterizes the surrogate functionality of materials as an absolute number and as a relative value referred to microcrystalline cellulose. Compactibility can be described through the potential to form a coherent compact, defined as D_{max}, σ_{max} or SCS_{max}, and the capability of a material to attain the maximal extent of interparticle bonds given by the slope of a linear relationship from a compactibility profile.

Keywords: Excipient functionality, Microcrystalline cellulose, Crushing strength, Specific crushing strength, Tensile strength, Compactibility coefficient.

INTRODUCTION

Tablet production is an essential operation for the pharmaceutical industry. Producing good quality tablets requires manipulation of variables such as compactibility to produce a formulation with high quality and high productivity. Most dosage forms require the addition of excipients to assist in the manufacture and delivery of the dosage form. In tablets, these include among others binders or agglutinants. Agglutinants are used in variable amounts to adjust the compactibility of formulations. The function of excipients goes progressively from inert to more specific and functional materials [1, 2].

The mechanical properties of tablets are determined by the properties of the raw materials and they distribution in the dosage form. These properties are achieved by controlling the attributes of raw materials and process intermediates within specified ranges, i.e., by operating within a material attribute design space[3].

A pharmaceutical tablet has been described in physical terms as a large cluster of particles, held together by bonds active between external particle surfaces. In this sense, the formation of a tablet is based on the properties of materials that make possible the formation of these bonds between particles[4].

The compaction properties of pharmaceutical powders are characterized by their compactibility. Compactibility is defined as the capability of a material to form coherent agglomerates or mechanically strong compacts after compression. However, for practical purposes it is important to know the compactibility of a powder bed, understood as the ability of a powdered material to be compressed into a compact of specified strength[5, 6].

One of the procedures to characterize and classify mechanical properties of pharmaceutical materials uses compact testing as a means to derive a series of indices of tableting performance. One of this method study the evolution of tablet tensile strength with increasing compaction pressure. Tensile strength has been observed to increase with an increasing compaction pressure up to a certain limit. Thereafter, with increasing compaction pressure, the tablet tensile strength leveled out. The overall compactibility profile tends to be sigmoid in shape[7, 8].

Compactibility profiles with sigmoid shape have been described with an equation based on the Weibull distribution (Eq.1) [9, 10]. Recently, this model has been used to describe the compactibility of celluloses as indicative of their functionality as tablet excipients[11].

$$\ln\left(-\ln\left(1-\frac{D}{Dmax}\right)\right) = n * lnPc + I \qquad \text{Eq. 1}$$

Where: D denotes the hardness of tablets or crushing strength, $Dmax$ the maximal tablet hardness attained, Pc the compaction pressure, n the slope of the curve, and I the intercept of the curve.

The compactibility of the studied materials has been defined using the regression parameters of eq. 1. The obtained compactibility curves describe the relationship between the hardness or crushing strength of the tablets and the compaction pressure used to obtain them.

The understanding and proper description of the properties of pharmaceutical materials is critical to effectively and rationally develop pharmaceutical dosage forms. The development scientist needs access to methods of analysis to comprehensively assess important functionality characteristics of drugs and excipients. Among them, the compactibility of materials, expressed as mechanical strength of a tablet, provides a measure of the bonding potential of the material concerned. This information can be used as a functionality parameter in the selection of excipients.

The role of excipients in drug product development involves some key elements. Among them: target the product profile, determine the characteristics of the final product that should remain within certain limits in order for Quality Assurance to approve the release of the product (Critical Quality Attributes - CQAs) and link raw material attributes and process parameters to CQAs and perform risk assessment. Linking raw material attributes to Critical Quality Attributes - CQAs is a valuable science-based process that can aid in identifying which material attributes and process parameters critically affect product [12].

The functional performance of tablet excipients can be assessed with the excipients as powders, as a dosage form of pure excipients and as a formulation of a given drug containing the excipients. The first two levels correspond to a surrogate functionality that belongs to a

preformulation phase. The knowledge of the surrogate functionality allow us to predict whether or not a particular excipient is likely to have the requisite functionality to produce a product that will meet finished product specifications in all respects. The third level corresponds to the explicit functionality of the excipients to develop an appropriate formulation of a drug and an effective manufacturing process to create a tablet [11].

The quantitative assessment of the functionality of excipients has the aim to control their lot-to-lot quality and consistency in the material manufacturing and to predict and compare the functionality of materials obtained from different trade name[13].

The excipients are included in a formulation because they own properties that in conjunction with a process allow the production of a dosage form with the required specifications. The desired properties of the excipients are known as functional performance or functionality[14, 15].

The paradigm of quality by design goes beyond identifying the excipient function and emphasizes performance through the identification, evaluation, and control of critical material attributes that assure consistent performance throughout the life cycle a product[16, 17].

The assessment of the excipients characteristics that determine their functionality allows the reduction of the powder properties to concrete numbers. In this sense, the assessment of compactibility through a quantitative performance test will allow a formulator to predict if a particular lot of the excipient fulfills the functionality requirements to manufacture a product with prearranged specifications. Moreover, excipients variability has to be considered when defining the excipients functionality. Therefore, we have to estimate and take in account this variability[18].

To reduce the number of additives in a formulation it has been developed a coprocessed excipient that acts as a binder, disintegrant, lubricant and a glidant, Prosolv Easytab. It is claimed that this new material gives a much higher tablet output, particularly in high-speed rotary presses. Even at high tableting speeds, the content uniformity of the coprocessed excipient was considered better than that of the physical mixture. The excipient is composed from a binder (microcrystalline cellulose), a glidant (colloidal silicon dioxide), a disintegrant (sodium starch glycolate) and a lubricant (sodium estearyl fumarate). Using a single excipient in tablet manufacture can enable an easy scale-up and saves quality control costs as only one starting material is tested rather than four individual excipients.The main recommended application is as a ready-to-use excipient composite[19, 20].

The aim of this work is to put side-by-side different methods to set up Prosolv EasyTab compactibility as a parameter to define the surrogate and the relative surrogate functionality of this ready-to-use direct compression excipient.

MATERIALS AND METHODS

Material

The materials used in this study were Prosolv Easytab SP, an excipient composite made of microcrystalline cellulose, colloidal silicon dioxide, sodium starch glycolate and sodium stearyl fumarate, obtained from Rettenmaier Mexicana S.A. de C.V. and microcrystalline cellulose type 102, Helmcel 200, obtained from Helm-México. The excipients were used as received.

Methods

Preparation of Tablets

Tablets weighing250 - 500 mg each were compacted into tablets in a hydraulic press equipped with a manometer, using 10.6 mm circular flat-faced punches at a series of different compaction pressures between 55 MPa and 525 MPa. Pressure was applied for 10 s.

Characterization of Tablets

Tablet crushing strength was measured in triplicate, registering the results as an average. For this purpose, it was used a hydraulic press with a pointer. The procedure was to place each tablet diametrically between two flat surfaces and to apply pressure until the tablet broke. The maximal pressure reached or the force used was taken as the tablet hardness. Tablets dimensions were determined with a Vernier caliper reading to hundredths of an inch.

RESULTS AND DISCUSSION

Methods to assess compactibility

Compactibility in the pharmaceutical literature is usually referred as tablet hardness. Hardness tests have been widely used in the pharmaceutical industry to examine solid dosage forms since the 1970's. The strength of tablets in common compression tests is often called hardness; however, mechanical strength is considered a more appropriate term. This term is associated with a failure mechanism, compressive, shear or tensional failure. Therefore, mechanical strength means tensile strength. The mechanical strength has been determined by pressing the tablet by some means diametrically between flat flattens, recording the force necessary to break the tablet [21-22]. The obtained data are expressed as compactibility curves or compactibility profiles. The obtained compactibility curves describe the relationship between the hardness or crushing strength of tablets and the compaction pressure used to obtain them.

Compactibility profiles of different pharmaceutical materials or different physical presentations of the same material has been defined by regression parameters of eq. 1[23-24]. Figure 1 shows the experimental data and the calculated compactibility curves for tablets of microcrystalline cellulose type 102 (Helmcel 200) weighing 300 mg and 500 mg. Microcrystalline cellulose type 102 (Helmcel 200) was taken as a reference excipient to experiment with the method to assess compactibility. As can be seen, the data can be described properly with the applied model.

It has been pointed out that there is no single value of the tensile strength of a compacted powder but a range of values[25]. A numerical value for compactibility can be obtained from every measure of tablet crushing strength along the compactibility profile. However, compactibility has been ascribed most often to the slope or regression parameters of compactibility profiles[26-27].

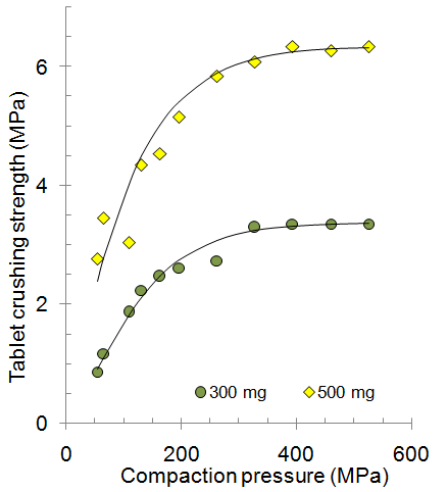

Fig. 1: Compactibility profiles of Helmcel 200 obtained with 10.6 mm circular flat faced tablets weighing 300 mg and 500 mg. Experimental points and calculated curves with equation 1.

In the current case, with tablets of different weight of the same material and using the model of eq. 1, the slopes of the curves (*n*) do not show a clear trend with increasing tablet weights on the contrary of the tablets maximal crushing strength (*Dmax*) attained at or near zero porosity. The slopes and the maximal tablet hardness of compactibility profiles displayed relationships against tablet weight described with equations 2 and 3:

$n = -0.00079060*\text{Tablet weight} + 1.497;\quad r^2 = 0.097$ Eq. 2

Dmax = 0.01366 * Tablet weight - 0.41000; r^2 = 0.94 Eq. 3

In a first approach, the maximal tablet crushing strength attained in a compactibility profile, can be expressed as the average of the last points of compactibility curves or as a by regression calculated value. This value provides a measure of the bonding potential of the material concerned and this information can be used as a functionality parameter to characterize excipients. It has to be described as an operational definition, in terms of the specific process or set of tests used to determine its presence and quantity. It means, using a particular procedure and a given tablet geometry and tablet weight. The compactibility described in this manner is sufficiently accessible, so that persons other than the definer may independently measure or test it at will. In the current case, tablets of weights from 300 mg to 500 mg display *Dmax* values in a range of 3.69-6.42 MPa.

Figure 2 depicts the calculated response surface curves for compactibility of Helmcel 200. The response surface curves were calculated from equations 2 and 3, obtained from five different compactibility profiles (Fig. 1) obtained with tablets of different weight.

The maximal tablet crushing strength (*Dmax*) displays a lineal trend toward increasing values as the tablet weight increases (eq. 3) while the slopes can be considered mostly as a constant value (1.18±0.20). This slope (*n*) is a characteristic of the material compaction behavior. It is indicative of the facility or capability of the powder to reduce its volume to reach the minimum porosity, under compaction. Otherwise, it displays the facility or capability of the powder to attain the maximal extent of interparticle bonds, under compaction.

In diametrical compression tests, cylindrical tablets are compressed diametrically until the tablets break/crush. The crushing load is recorded and the tensile strength can be calculated from the crushing load together with the dimensions of the tablets[27].

This procedure to characterize the compactibility of tablets is considered here as a second approach. In this case, compactibility is described with the tablet tensile strength (σ). This value is calculated as:

$$\sigma = 2P/(\pi * d * h) \quad \text{Eq. 4}$$

Where: *P* is the load required to diametrically fracturing the tablets, *d* is the compact diameter and *h* the tablet thickness[28].

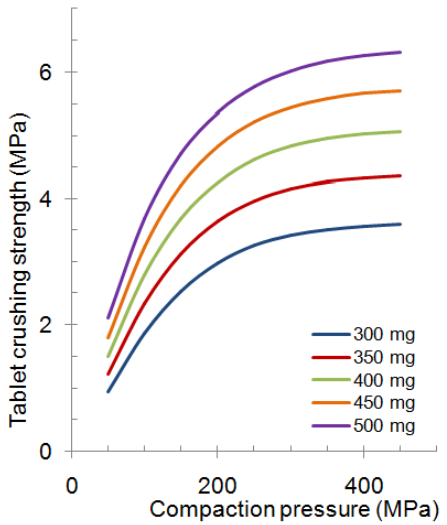

Fig. 2: Calculated response surface curves obtained from compactibility profiles of Helmcel 200. The tablets were 10.6 mm diameter, circular flat faced, with different weights.

The logarithm of tensile strength against the tablet relative density gives a linear relationship. The fitting gives the tensile strength at zero porosity or at a relative density of one, here designed as σ_{max}, and the slope (*k*) or bonding capacity for the powder considered (Figure 3). A higher value of (*k*) would correspond to stronger bonding of primary particles[27].

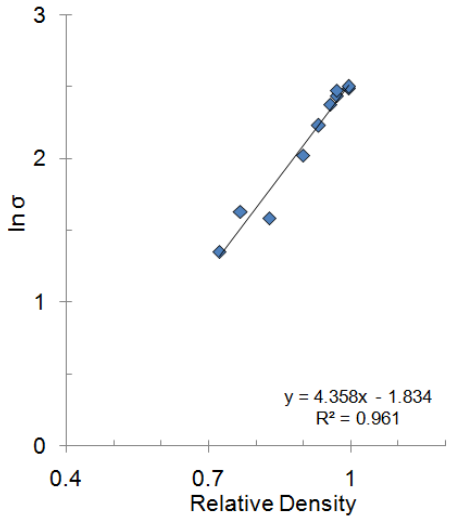

Fig. 3: Compactibility profile of Helmcel 200 relating the logarithm of tensile strength against the relative density of 500 mg tablets. σ_{max}=12.48 MPa/cm².

The results obtained for σ_{max} from regression parameters can be taken as a measure of compactibility or surrogate functionality of Helmcel 200 as agglutinant. These values against tablet weight display also a trend although not lineal and smaller. The compactibility of Helmcel 200, determined as the average σ_{max} or average tensile strength at or near zero porosity, was calculated as 12.50 MPa/cm², ranging from 12.0 MPa/cm² to 12.8 MPa/cm², with a slope (*k*) or bonding capacity of the powder of 5.23±1.42. The normalization of the tablet crushing strength with the geometrical parameters of the tablets allow the reduction of the span of the compactibility parameter, compared to that showed by *Dmax*, by varying the tablet weight.

From another point of view, the calculated tensile strength values for Helmcel 200 tablets display a sigmoid relationship against the compaction pressure used to obtain the tablets. The profile is similar to that showed for a simple compactibility profile (Fig. 1). In the same way as compactibility profiles, the *σ* profiles displayed a linear relationship when treated according to eq. 1. This occurs substituting the values of tablet hardness or crushing strength by the *σ* values. The σ_{max} values, calculated in this way for tablets weighing 300-500 mg, showed an average of 11.94±0.93 MPa/cm². As can be seen this value is similar to that obtained before (12.50±1.50 MPa/cm²) but using directly the compaction pressure, as independent variable, instead of calculating the relative density of the tablets.

In a third approach, it has been used a method for quantification of compactibility of pharmaceutical powders by a simple linear relationship between the diametrical compressive strength of tablets (*D*) and the applied compaction pressure (*Pc*). The mechanical strength of the tablets is defined as the crushing force normalized with the dimensions of the tablet (diameter and height) and termed the specific crushing strength, *SCS*.

$$SCS = D/(diameter*height) \quad \text{Eq. 5}$$

The proposed model estimates the slope of the regression line *Cp* as a dimensionless compactibility parameter, according to equation 6[29-31].

$$SCS=Cp*Pc+A \quad \text{Eq. 6}$$

The relationship between the normalized crushing strength or specific crushing strength and compaction pressure (eq. 6) showed a linear trend in all cases (Figure 4). However, this occurred only in the first part, almost the first 5 points of the current results of the *SCS* profile.

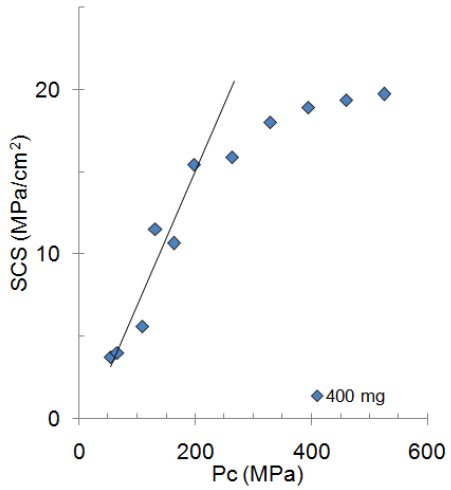

Fig. 4: Compactibility profile of 400 mg tablets of Helmcel 200, relating the specific crushing strength (*SCS*) against the compaction pressure. *Cp*=0.0816.

The obtained values for the slope of the linear regressions of Helmcel 200, defined as compactibility (*Cp*), showed a linear trend against the tablet weight (eq. 7). The compactibility coefficient decreasing as the tablet weight increased. Each one of these compactibility values (*Cp*) determined for each different tablet weight can be used as a functionality parameter, defined operationally for a given tablet weight. The *Cp* values calculated from the lineal regression vary from 0.0907 to 0.0537 for tablets weighing 250 mg to 500 mg. The average of experimental results of all studied tablets weights (250-500 mg) was $72.2*10^{-3}$. These values represent the binding potential of Helmcel 200 mixed with the compaction behavior or capability of the material to reduce its volume to attain a zero or near zero porosity. This value does not allow the discrimination between the binding potential and the compaction behavior.

$Cp=-0.0001478*Tablet\ Weight+0.12761$ $r^2 = 0.895$ Eq. 7

Given the inclusion of only few points in a linear relationship, the data of *SCS* and compaction pressure were treated according to eq. 1. All curves showed a linear trend with an average of determination coefficients of 0.933.

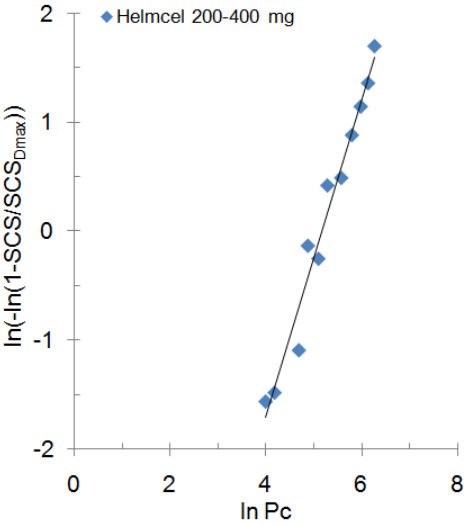

Fig. 5: Compactibility profile of 400 mg tablets of Helmcel 200. Data of specific crushing strength (*SCS*) and compaction pressure (*Pc*) treated according to equation 1.

In this way, the by regression calculated maximal specific crushing strength (SCS_{max}) or the specific crushing strength obtained at or near zero porosity can be used to define the compactibility of Helmcel 200 as 18.75±1.51 MPa/cm². The data display a small trend and the standard deviation seems to be only due to usual variability. The results obtained by regression are supported by the entire curve and provided a measure of the bonding potential of the material. The value of the slope obtained in this manner (Figure 5) complements the characterization of the compactibility of a material. This is considered as indicative of the compaction behavior or indicative of the capability of the powders to attain the maximal extent of interparticle bonds. It was defined as 1.274±0.159.

Concluding, compactibility as a functionality parameter of direct compression materials can be defined operationally for a given tablet weight trough all studied parameters: D_{max}, σ_{max}, *Cp* and SCS_{max}. The compactibility obtained through D_{max} and *Cp* displaying a clear trend as the tablet weight changes. However, compactibility obtained through σ_{max} and SCS_{max} decreases, eliminating practically this trend although keeping some variability. All studied relationships can be better described through the model based in the Weibull distribution. Moreover, parameters calculated considering the experimental values of the maximal compactibility have as disadvantage the requirement of equipment capabilities to determine this parameter in a width span. On the other hand, parameters calculated considering the relative density have the disadvantage of calculating compactibility at a relative density of 1.0 that in some cases are not attainable. These values of compactibility are theoretical because they cannot be obtained due to compression problems like lamination.

Compactibility of Prosolv Easytab

Experimental data and the calculated compactibility curves for tablets of Easytab are similar to that showed in Fig. 1. Data up to reach the maximal tablet hardness can be described properly with the proposed model (Eq. 1).

The slope and *Dmax* of Easytab compactibility profiles displayed relationships against tablet weight described with equations 8 and 9:

$Slope = -0.0015*Tablet\ weight + 1.9014$; $r^2 = 0.127$ Eq. 8

$Dmax = 0.0036*\ Tablet\ weight + 2.5776$; $r^2 = 0.8769$ Eq. 9

Eq. 7

In the same manner as Helmcel 200 tablets (Eq. 3), the maximal crushing strength (*Dmax*) of Easytab tablets displays a trend toward increasing values as the tablet weight increases (Eq. 9). The slopes of compactibility profiles of Easytab do not show a clear tendency. They can be considered mostly as a constant value with certain variability (1.35±0.39), in the same range than that of Helmcel 200 (1.18±0.20) although something higher. This meaning a faster increase of tablet hardness as compaction pressure increases by Easytab compared to Helmcel 200.

The calculated response surface curves for compactibility profiles of Easytab can be seen in figure 6. The data were calculated up to a compaction pressure of 197 MPa, considering this compaction pressure allows attain the maximal tablet crushing strength.

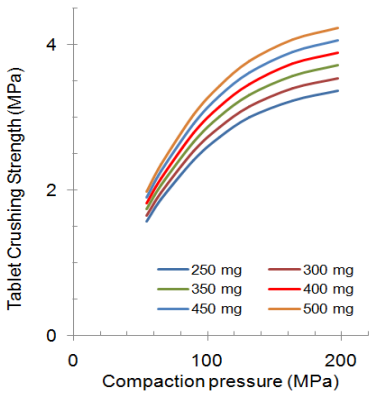

Fig.6: Calculated response surface curves obtained from compactibility profiles of Easytab. Tablets of 10.6 mm diameter, circular flat faced, with different weights.

Compared to Helmcel 200, the experimental compactibility of Easytab is lower and distributed in a narrower span. Tablets of Helmcel 200 weighing between 350 mg and 500 mg exhibit D_{max}values ranging from 4.72 MPa to 6.28 MPa while similar tablets of Easytab show D_{max} values ranging from to 3.62 MPa to 4.48 MPa. The average compactibility of Easytab is 4.07±0.36 while that of Helmcel 200 is 5.45±0.66. Figure 7 depicts the values of D_{max} that could be used as compactibility parameters to characterize the bonding potential of these excipients, in this case for tablets weighing 350-500 mg.

As can be seen, the slope is different for both excipients so that a relative value of compactibility of Easytab will be different as the tablet weight changes. Considering 500 mg tablets the relative compactibility of Easytab is 71% of that of Helmcel 200. However, if a tablet weight of 350 mg is considered, the relative compactibility of Easytab is 77%. The average relative compactibility of Easytab is 75% of that of Helmcel 200. The relative compactibility is useful when the reference is a well-known excipient like microcrystalline cellulose type 102 (Helmcel 200).

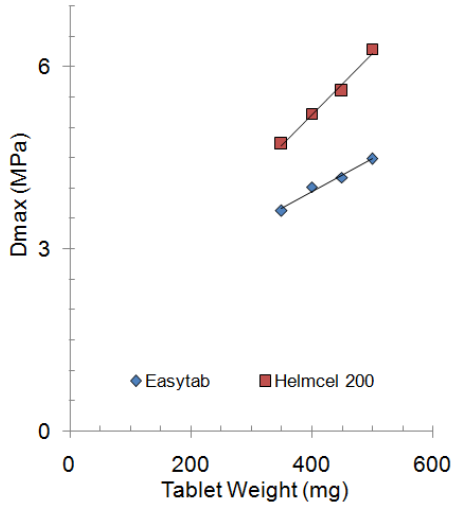

Fig.7: Effect of tablet weight on the maximal tablet crushing strength of tablets weighing 350-500 mg. Each value represents a possible operationally defined compactibility parameter for Helmcel 200 and Prosolv Easytab.

The application of the second approach to Easytab data produced a linear relationship of the logarithm of tensile strength against the relative density of the tablets. Regression parameters against tablet weight showed no specific trend. The compactibility of Easytab, determined as σ_{max} or the tablet tensile strength at or near zero porosity, was calculated as 15.56±8.39 MPa/cm^3, with a slope (k) or bonding capacity of the powder of 1.768±0.326. As can be seen the results display a quiet great variability in σ_{max} values while the slopes show similar variability as that of Helmcel 200 curves.

On the other hand, the calculated tensile strength values (σ) for Easytab tablets display a sigmoid relationship against the compaction pressure used to obtain the tablets. The σ profiles displayed a linear relationship when treated according to eq. 1. Figure 8 depicts the σ_{max} values obtained from the σ profiles of Easytab and Helmcel 200 tablets, expressed as a function of compaction pressure. In all cases, the tensile strength of Easytab is lower than that of Helmcel 200.

This approach allows the calculation of maximal values for σ (σ_{max}) in an average of 9.23±1.16 MPa/cm^2. This value exhibit a lower standard deviation and makes more trustworthy the comparison with Helmcel 200. The compactibility of Easytab is lesser than that calculated for Helmcel 200 tablets (11.94±0.93 MPa/cm^2). The slopes of σ profiles treated according to Eq. 1, for Easytab tablets, showed an average of 1.37±0.41. This value is in the same range than that for Helmcel 200 (1.29±0.19) although something higher. The average relative surrogate compactibility of Easytab is 77% of that of Helmcel 200.

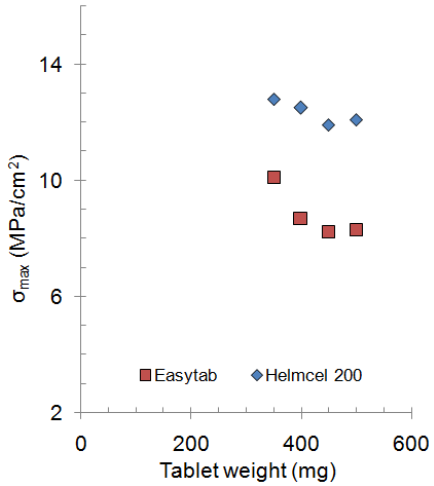

Fig. 8: Experimental maximal tablet tensile strength (σ_{max}) of Easytab and Helmcel 200 expressed as a function of tablet weight. Flat faced tablets with diameter of 10.6 mm.

According to the third approach, the normalized crushing strengths or specific crushing strength (*SCS*) of Easytab tablets against compaction pressures (*Pc*) displayed a linear trend on the first part of compactibility profiles. In this case, the experimental points used to calculate the regression were the first 6 points. In the same way as above mentioned, the slope of this relationship can be used to characterize the compactibility of different materials. Each one of these compactibility values (*Cp*), calculated for each tablet weight, can be used as a functionality parameter. The *Cp* values has to be defined operationally for a given tablet geometry and tablet weight.

The Easytab calculated compactibility values (*Cp*) exhibited a linear decrease as the tablet weight increased (eq. 10). These results are similar to those obtained for Helmcel 200 (Eq. 7).

$Cp = -0.000216*Tablet\ Weight + 0.1326$; $r^2 = 0.949$ Eq. 10

Figure 9 depicts the change of *Cp* as a function of the tablet weight, for Easytab and Helmcel 200. In all cases, the compactibility of Easytab is lower than that of Helmcel 200. However, the difference is greater as the tablet weight increases. The average of experimental results of all studied tablet weights (250-500 mg) was 51.6*10^{-3} for *Cp* of Easytab tablets while it was 72.2*10^{-3} for tablets made of Helmcel 200. The average surrogate relative compactibility of Easytab is 71% of that of Helmcel 200.

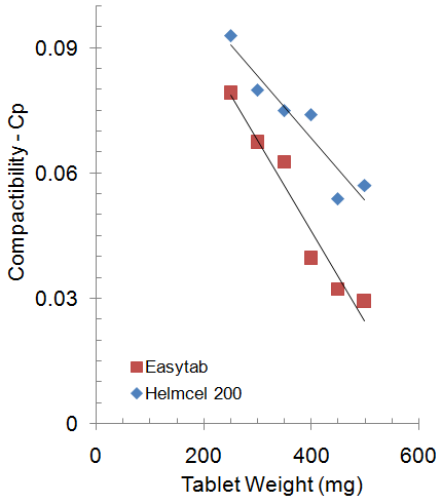

Fig.9: Compactibility (*Cp*) of Prosolv Easytab and Helmcel 200 described as a function of tablet weight. Calculated from 10.6 mm diameter, circular flat faced tablets.

Easytab data of *SCS* against compaction pressure were treated according to eq. 1. All curves showed a linear trend with an average of determination coefficients of 0.875. The by regression calculated maximal specific crushing strength (SCS_{max}) or the specific crushing strength obtained at or near zero porosity defines the average compactibility of Easytab (Figure 10) as 13.77±1.34MPa/cm^2. This parameter provides a measure of the bonding potential of this material. The value of the slope, considered as indicative of the compaction behavior or indicative of the capability of the powders to attain the maximal extent of interparticle bonds, was defined as 1.37±0.54.

The obtained compactibility of Easytab is smaller than that calculated for Helmcel 200 tablets (18.75±1.51 MPa/cm^2) while the slope is similar to that obtained for Helmcel 200 (1.274±0.159). The relative surrogate compactibility of Easytab is 73% of that of Helmcel 200.

Table 1 goes over the main points that can define the compactibility of the studied excipients. The main enlisted parameters exhibit greater values for Helmcel 200 than for Prosolv Easytab. This means greater compactibility for Helmcel 200. The D_{max} value shows about 25.3% lesser compactibility for Easytab while the SCS_{Dmax} value displays about 26.6%. The *Cp* value exhibits about 28.5% lesser compactibility for Easytab while the σ_{max} value displays an about 22.7%. Although all calculated parameters demonstrate a lower compactibility for Prosolv Easytab, the magnitude of the lesser compactibility is different for each parameter. Even so, it can be said that compactibility parameters are in the same range. These parameters indicating a 25.8% lesser compactibility of Easytab compared to Helmcel 200.

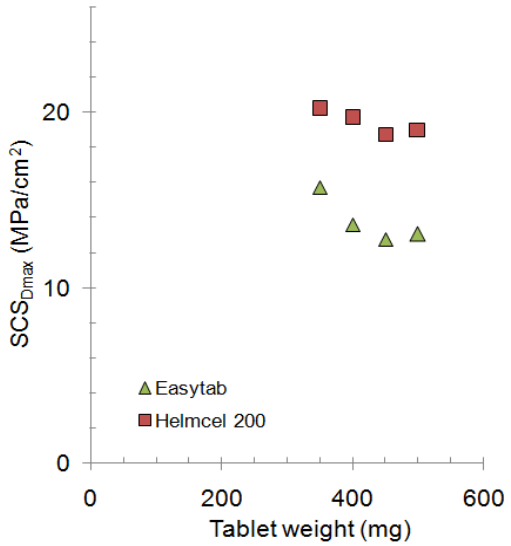

Fig.10: Normalized maximal tablet crushing strength values (SCS_{Dmax}) characterizing the compactibility of Helmcel 200 and Prosolv Easytab, as function of tablet weight.

Table 1: Different parameters useful to describe the compactibility of Prosolv Easytab and Helmcel 200 assessed with tablets of 10.6 mm diameter weighing 500 mg.

Compactibility Parameter	Prosolv Easytab	Helmcel 200	Easytab Relative Compactibility
SCS_{max}	13.77 ±1.34 (MPa/cm^2)	18.75 ±1.51 (MPa/cm^2)	73.4%
Cp	51.6*10^{-3} ±20.7*10^{-3}	72.2*10^{-3}±14.6*10^{-3}	71.5%
σ_{max}	9.23 ±1.16 (MPa/cm^2)	11.94 ±0.93 (MPa/cm^2)	77.3%
Intercept $_{average}$	-6.135	-6.363	
Slope $_{average}$	1.37	1.29	
Dmax	4.07 ±0.36 (MPa)	5.45 ±0.66 (MPa)	74.7%
Intercept $_{average}$	-4.2057	-5.137	
Slope $_{average}$	1.35	1.18	

The values including the ± standard deviation are the average of tablets with different weight.

Although every one of the above mentioned parameters can be used to characterize the compactibilty of the materials, those using experimental points covering up to the maximal mechanical strength or tablets covering relative densities up to 1.0 are more precise when calculated from a regression equation. Moreover, all sigmoid relationships of the above-mentioned parameters used to define the compactibility are better described with the mathematical model expressed in equation 1.

The advantage of models using the relative density is that the point representing the mechanical strength of the tablets is well defined. However, a disadvantage is that not always a relative density of one is attainable because of the technological materials properties. In this sense, it can be only a theoretical value. On the other hand, the relationships of the mechanical strength of the tablets against compaction pressure allow attain the experimental maximal mechanical strength of the tablets. Although it is a real value, it does not always correspond to a zero or minimal porosity of the tablets.

CONCLUSION

Although per definition, the functionality of an excipient is linked to the product where it will be used, from the point of view of the excipient the functionality is a technological property of the material that has to be defined independently of the formulation where it can be used. A material displays certain functionalities that can be suitable or not for a given formulation. The particular functional performance of an excipient is dependent not only of a given formulation but also of the type of process (unit operation) and type of dosage form where it is employed. An agglutinant or binder is still a binder if it is or is not suitable for a certain formulation.

No one of the different calculated compactibility parameters can be used as an all-purpose judgment of the compactibility of the materials. Some parameters show a clear trend as the tablet weight changes while some other display only a small trend, allowing the calculation of an average with a not too high standard deviation. Even so, all calculated parameters allow the reduction of the compactibility concept to a numerical value that can be used to characterize the functionality of the material. In this case, a numerical value representing the surrogate compactibility of Easytab.

Compactibility can be described through two concepts. The potential to form a coherent compact, defined as D_{max}, σ_{max} or SCS_{max}, and the "speed" or capability of a material to reduce its volume and to attain the maximal extent of interparticle bonds. The last one given by the slope of a linear relationship like that obtained from a compactibility profile, σ profile or *SCS* profile.

The use of microcrystalline cellulose type 102 as a reference allows the estimation of compactibility as a relative value. The relative surrogate compactibility of a material can be defined as a percentage or fraction of the surrogate compactibility of the known microcrystalline cellulose type 102.

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