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A physical analysis of the phenomenon of tablet disintegration

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Summary

A physical analysis is presented of the phenomenon of disintegration of compressed tablets, using an equation which expresses the normalized disintegration force, F/F_∞, as a function of time. The theory utilizes two parameters, an expansion rate constant, k, and an exponent, n, which vary depending on the composition of the tablets tested. The values of these parameters indicate if the disintegration phenomenon is controlled by the interfacial detachment of particles from the surface of the tablet or by the local diffusion of particles once they have been detached. The new theory is verified with experimental data of tablet disintegration for a number of tablets containing disintegrants of varying water swelling properties.

Introduction

In recent years, investigation of the process of compressed tablet disintegration has become very important because of its influence on the bioavailability of drugs administered by conventional oral dosage forms. For example, often the disintegration process becomes a limiting factor of the drug dissolution, especially for drugs with low solubility in water or in biological fluids.

Over the years, the phenomenon of tablet disintegration has been studied by a number of research groups. Various mechanisms have been proposed, including the swelling of disintegrant particles (Bolhuis et al., 1982; Caramella et al., 1984; Shangraw et al., 1980), capillary pressure effects (Kanig and Rudnic, 1984), particle–particle interactions (Ringard and Guyot-Hermann, 1981), air dilation (Matsumaru, 1959), and wicking (Kanig and Rudnic, 1984).

Researchers in our laboratory have performed in recent years a series of experimental studies to determine the main mechanisms involved. In fact, we have developed a novel experimental technique for the measurement of the disintegration force developed during this phenomenon (Caramella et al., 1984; 1986 a and b; Colombo et al., 1980; 1984).

From a mathematical point of view, several approaches have been taken to describe the disintegration process, including a description of the tablet dissolution in terms of its weight as a function of time (Carstensen et al., 1980).

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Another mathematical approach was developed by us (Colombo et al., 1984; Caramella et al., 1986a) to analyze the force of disintegration as a function of time. The well-known Weibull distribution curve, given by Eqn. 1, was used to express these experimental data.

$$\log[-\ln(1 - F/F_\infty)] = b \log(t - t_0) - \log a \quad (1)$$

According to this equation, F/F_∞ is the normalized force of disintegration, where F_∞ is the maximum determined disintegration force, and t is the time. The terms a and b are parameters characteristic of the experiment, and the parameter t_0 takes into consideration the induction period that is sometimes observed in these experiments.

Although the previous mathematical analysis provided a very important phenomenological explanation of the experimental data of this phenomenon, a more physicochemical interpretation was necessary. Recently, we have developed such a novel physicochemical approach to analyze the tablet disintegration phenomenon.

Physical analysis

Development of the theoretical model

To describe the physical situation discussed before, we offer a new model based on a step-wise development of the disintegration phenomenon. This model is best presented in Fig. 1. Here the disintegration of particles is assumed to occur only in layers parallel to the surface of largest area of the tablet.

It is proposed that the phenomenon of disintegration is the opposite of a phenomenon of nucleation and growth of particles (Avrami, 1939, 1940; Peppas and Hansen, 1982). Two main processes can be differentiated during disintegration that can be considered as rate-limiting steps. The first one is the detachment of particle layers from the solvent/tablet interface, which will be henceforth called an *interface-controlled mechanism*. The second process is the diffusion of particle layers away from the interface which will be called a *diffusion-controlled mechanism*.

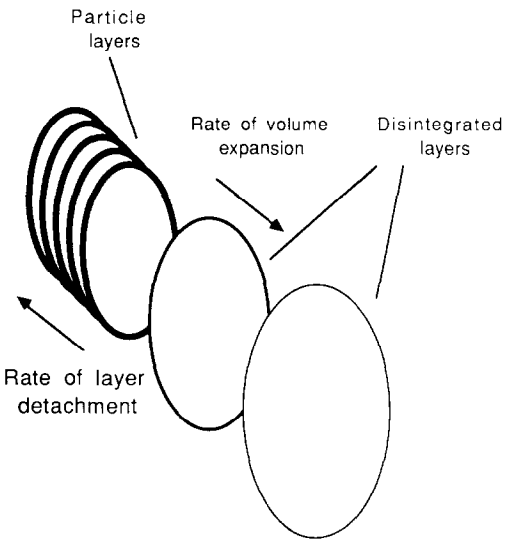

Fig. 1. Physical model of tablet disintegration indicating the progressive tablet expansion along with the associated layer detachment. This schematic depicts only the situation of disintegration force development. Therefore, solvent enters the tablet from the facial side only.

During a disintegration process, the controlling step may be either the ease of detachment of particles from the tablet (which will be related to wettability or a certain cohesive energy of the system) or their ability to diffuse outward. In both situations, a disintegration force may be measured because of the resulting volume expansion of the tablet. Indeed, if the expanding surface were prevented from moving, it would exert a force, F, which could be related to the expanding core.

Let now the term $\dot{N}$ (in s^{-1}) be the detachment rate of successive particle layers from the tablet due to bond separation as a result of water penetration. In addition, the term $\dot{v}$ (in $cm^3\ s^{-1}$) indicates the expansion rate of these particle layers, which in many cases may be related to the swelling of particles themselves. Then, the fraction of the total volume of the tablet that has been disintegrated by time t is $X(t)$.

The number of particle layers, dn, detached from the tablet per unit time must decrease as the process continues. Thus, the number of layers separated between time τ and $\tau + d\tau$ is

$$dn = \dot{N}(\tau)[1 - X(\tau)]\, d\tau \quad (2)$$

For a given tablet its expansion of the volume after time t must be

$$v(t, \tau) = \int_{\tau}^{t} \dot{v}\, dt \tag{3}$$

Thus, the volume fraction that has disintegrated is

$$X(t) = \frac{1}{V_0}\int_0^t v(t, \tau)\, dn$$

$$= \frac{1}{V_0}\int_0^t \dot{N}(\tau)[1 - X(\tau)]\, v(t, \tau)\, d\tau \tag{4}$$

where V_0 is the initial volume of the tablet. This is the basic equation of disintegration. Thus, Eqns. (3) and (4) indicate that the detachment and expansion rates of particle layers, $\dot{N}$ and $\dot{v}$, respectively, are coupled.

Since the normalized force of disintegration corresponds to the disintegrated fractional volume we may also write:

$$\frac{F}{F_\infty} = X(t) = \frac{1}{V_0}\int_0^t \dot{N}(\tau)\left[1 - \frac{F}{F_\infty}\right] v(t, \tau)\, d\tau \tag{5}$$

It remains to write the functionality of $\dot{N}$ and $\dot{v}$ in time and to solve for F/F_∞.

In fact, in situations similar to this one Avrami (1939, 1940) has expressed the fractional volume change as

$$X(t) = 1 - \exp\left[-\frac{1}{V_0}\int_0^t \dot{N}(\tau) v(t, \tau)\, d\tau\right] \tag{6}$$

We can now calculate the form of $v(t, \tau)$ for the disc geometry described here. Indeed, if the controlling mechanism were diffusional, then the detached particles would diffuse a distance d

$$d = \sqrt{Dt} \tag{7}$$

where D is the particle diffusion coefficient in the solvent.

If a disc of initial height, h, has partially disintegrated in the axial direction to a new height $(h - d)$, the volume change is readily calculated as

$$v(t, \tau) = \pi R^2 d = \pi R^2 D^{1/2}(t - \tau)^{1/2} \tag{8}$$

If the limiting process were interfacial, then the rate of expansion of particle layers would be constant, since particles are always present at the surface, and surface sites are emptied at a constant frequency. Thus:

$$d' = k't \tag{9}$$

where k' is a frequency term.

Therefore, when a height, d', of a disc has disintegrated by the interface-controlled mechanism, the volume change may be written as

$$v(t, \tau) = \pi R^2 d' = \pi R^2 k'(t - \tau) \tag{10}$$

Consequently, by comparing Eqns. (8) and (10) we see that the volume change, $\tau(t, \tau)$, due to the disintegration can be always described by an expression of the form of Eqn. (11) where the only changing parameter is the exponent p. Thus, exponent p is uniquely specified by the rate-controlling mechanism, where C_1 is a constant.

$$v(t, \tau) = C_1(t - \tau)^p \tag{11}$$

Inserting Eqn. (11) into Eqn. (6) and integrating we obtain

$$\frac{F}{F_\infty} = X(t) = 1 - \exp\left[-\frac{C_1}{V_0}\int_t^0 \dot{N}(\tau)(t - \tau)^p\, d\tau\right] \tag{12}$$

The limiting cases for $\dot{N}(\tau)$ are those of instantaneous and purely homogeneous layer detachment. In the former case, the term $\dot{N}(\tau)$ is represented by a δ function (a sudden change of the rate, followed by zero) and Eqn. (12) becomes

$$\frac{F}{F_\infty} = 1 - \exp\left[-k(t - \tau)^p \Big|_t^0\right] = 1 - \exp(-kt^p) \tag{13}$$

For the latter case, $\dot{N}(\tau)$ is constant with time. Thus,

$$\frac{F}{F_\infty} = 1 - \exp\left[-k(t-\tau)^{p+1}\Big|_{t}^{0}\right]$$

$$= 1 - \exp(-kt^{p+1}) \qquad (14)$$

Thus, the final general form of the equation is

$$\frac{F}{F_\infty} = 1 - \exp(-kt^{n}) \qquad (15)$$

In conclusion, the exponent n is indicative of the rate-controlling mechanism of disintegration, either interfacial or diffusional.

Analysis of disintegration force isotherms

The previous analysis has shown that it is reasonable to expect that the normalized disintegration force, F/F_∞, be a function of time according to Eqn. 15. The meaning of the exponent n was discussed before (Colombo et al., 1988).

When experimental data are available, one may plot the term $\ln\{-\ln[1-F/F_\infty]\}$ versus $\ln\ t$ according to Eqn. 16.

$$\ln\left\{-\ln\left[1-\frac{F}{F_\infty}\right]\right\} = \ln\ k + n\ \ln\ t \qquad (16)$$

Thus, both values k and n can be calculated from the intercept and the slope of the associated logarithmic graphs.

The constant k is an expansion rate constant which can also be determined from the half-life, θ (time when $F/F_\infty = 0.5$) and from the average value of n, as follows:

$$k = \ln 2/\theta^{n} \qquad (17)$$

A comparison of Eqns. 1 and 16 indicates that the Weibull distribution equation and the Avrami equation have the same mathematical form. Effectively, the term a of the Weibull equation is equivalent to the expansion rate constant, k, and the term b is equivalent to the exponent n. However, the advantage of the new Avrami-type analysis is that the parameters k and n are assigned to specific physical phenomena.

Expansion rate during disintegration

The magnitude of the expansion rate constant, k, can provide additional information about the disintegration of a tablet. To analyze the expansion behavior, the extension of the Turnbull-Fisher nucleation theory (1949) was used, whereby the term k was expressed as:

$$k = k_0 \exp\left[-\frac{\Delta E_1}{RT_d}\right] \cdot \exp\left[-\frac{\Delta E_2}{RT_d}\right] \qquad (18)$$

Here k_0 is a constant independent of temperature, ΔE_1 is the activation energy for diffusion of the disintegrated particles in the solvent, ΔE_2 is the activation energy of interfacial detachment of the particles during disintegration, and T_d is the disintegration temperature.

The activation energy ΔE_1 can be expressed by the Williams–Landel–Ferry (WLF) equation (Ferry, 1984) as:

$$\Delta E_1 = \frac{17{,}300T_d}{51.6 + T_d - T_g} \qquad (19)$$

where T_g is the glass transition temperature of the material of the tablets.

It must be noted that T_g is in principle the temperature at which a material changes from glassy to rubbery. Although such a value can be easily determined for a polymeric material (using for example differential scanning calorimetry), T_g can be defined equally well for small molecular weight compounds which can be typical excipients in pharmaceutical tablets.

The interfacial activation energy, ΔE_2 can be expressed in terms of parameters characteristic of the tablet dimensions and the thermodynamics of disintegration (Avrami, 1939; 1940)

$$\Delta E_2 = \frac{4l\sigma_s\sigma_e}{\Delta H_m} \cdot \frac{T_g}{T_g - T_d} \qquad (20)$$

Here l is the thickness of a single (monoparticulate) surface layer of the material of the disin-

tegrating tablet, and σ_s and σ_e are the surface free energies of the side and end planes of the tablet, respectively.

From Eqns. 18 to 20 upon further algebraic manipulations we obtain

$$\ln k = \ln k_0 - \frac{17{,}300}{R(51.6 + T_d - T_g)} - \frac{C_2 \cdot T_g}{(T_d - T_g) \cdot T_d} \quad (21)$$

where C_2 is a constant defined directly from Eqn. 20 as

$$C_2 = \frac{4l\sigma_s\sigma_e}{\Delta H_m} \quad (22)$$

Therefore, one may plot the term ln k versus $T_g/T_d(T_d - T_g)$ to obtain a straight line and calculate the slope parameters which define energetic and kinetic characteristics of the disintegration process.

Materials and Methods

To test the validity of the previous model, a number of tablets were prepared and their disintegration force was measured as a function of time. Tablets were made by mixing a disintegrant with a model substance.

Disintegrants used were sodium starch glycolate (Primojel, Deimos, Milan, Italy), cross-linked poly(*N*-vinyl pyrrolidone) or crospovidone (Polyplasdone XL, GAF, Milan, Italy), crosslinked sodium carboxymethylcellulose (Acdisol and Nymcel ZSB10, Eigenman and Veronelli, Milan, Italy), microcrystalline cellulose (Avicel PH101, Gianni, Milan, Italy), poly(vinyl alcohol) (Elvanol 70–30, du Pont de Nemours, Wilmington, DE), and poly(potassium methacrylate-co-divinyl benzene) copolymer (Amberlite IRP 88, Rohm and Haas Co., Philadelphia, PA).

The model substances used were acetylsalicylic acid (ASA, Bayer, Milan, Italy), α-lactose monohydrate and β-lactose (+100 mesh, DMV, Veghel, the Netherlands), and calcium diphosphate (Emcompress, Mendell, Carmel, NY).

The model substance (always 500 mg per tablet) was mixed with various quantities of disintegrant in a mixer (Turbula, model T2G, Bachhofen, Basle, Switzerland) and compressed at 20 °C and 50% RH with a mean force of 25 ± 0.5 kN using a reciprocating tablet press (Kilian Co., Cologne, F.R.G.) employing flat punches of 11.28 mm diameter. One series of tablets was prepared with varying compression forces between 9.8 to 34.3 kN.

Measurement of the disintegration force was done in water at 7, 20, 30, 37 and 40 °C, using the apparatus and method described by Colombo et al. (1980). A number of experiments was also run with dissolution media at temperatures ranging from 7 to 40 °C, and having viscosity between 1×10^{-3} and 230×10^{-3} Pa · s, which was obtained with different concentrations of sodium carboxymethylcellulose.

The disintegration time of tablets was measured in the same media and conditions of the disintegration force determinations using the USP XXI apparatus without discs.

Results and Discussion

General observations

The development of the disintegrating force was followed as a function of time for all the tablets tested in this contribution. Fig. 2 indicates the increase of this force in two different types of tablets. In both cases, the force has been normalized with respect to the maximum force attained.

Curve 1, which refers to the disintegration of a tablet made of $CaHPO_4 \cdot 2H_2O$ and 1 wt% Polyplasdone XL, indicates a continuous increase of the force with a fast disintegration rate. However, the disintegration curve for a tablet made of $CaHPO_4 \cdot 2H_2O$ and 20 wt% Polyplasdone XL (curve 2) indicates that more time is needed for the force development.

The results of Fig. 2 for all the prepared tablets were analyzed using Eqn. 15 or its logarithmic form as described by Eqn. 16. Often during the analysis, we found that the fitting could be better

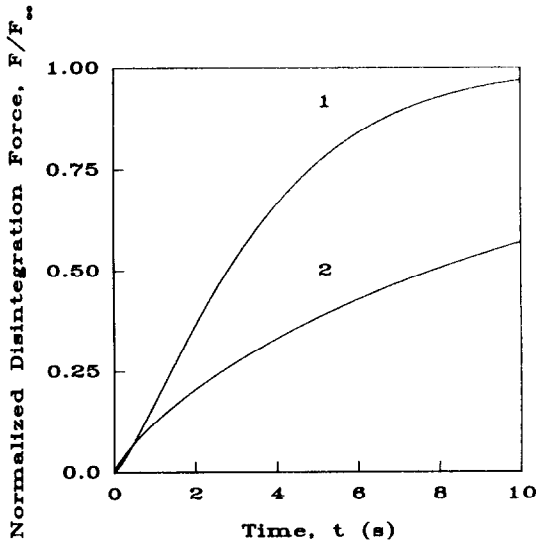

Fig. 2. Normalized disintegration force vs time for two tablets disintegrating in water at 20 °C. Tablet 1 (Curve 1) was made of $CaHPO_4 \cdot 2H_2O$ with 1 wt% Polyplasdone XL. Tablet 2 (Curve 1) was made of $CaHPO_4 \cdot 2H_2O$ with 20 wt% Polyplasdone XL.

done using a delay time t_0 as indicated by Eqn. 23.

$$\ln\left[-\ln\left(1-\frac{F_t}{F_\infty}\right)\right] = \ln k + n \ln(t - t_0) \qquad (23)$$

In this analysis, a weighing function was applied to the fitting procedure according to the technique of Langenbucher (1976) in order to take into consideration the fact that the number of data points taken at the early portion of the disintegration curve was smaller than the number of points at the late portion of the same curve.

When particles of a disintegrant are compressed together with particles of a model substance to form a tablet, the former (usually being smaller and fewer) are found under compressive stresses exerted by the latter particles. When this tablet is placed in the aqueous environment of the disintegration force experiment, water (or aqueous solution) enters the pores of the tablet by a combination of several processes, such as porous diffusion and capillarity. Thus, a phenomenon of disintegrant swelling is observed, since the disintegrant particles are always hydrophilic polymers. This swelling process leads to the application of a certain pressure on the particles of the model substance. In this section, we will describe the physical dependence of various structural and other parameters of components of the system on the values k and n of Eqn. 15. Consequently, this analysis will allow an evaluation of the mechanisms of tablet disintegration.

Effect of the model substance properties

The disintegration curves of tablets prepared with 4 model substances were compared in order to show the influence of the substance's hydrophilicity on the parameters k and n of Eqn. 15 and, thus, on the mechanism of disintegration of these tablets. The substances used were the hydrophobic ASA, the insoluble but hydrophilic $CaHPO_4 \cdot 2H_2O$, the soluble α-lactose and the very hydrophilic β-lactose. With the non-swellable and non-hydrophilic ASA, the exponent n of Eqn. 15 is greater than 1 (Table 1) and the expansion constant k is the highest. The values of n indicates that the delamination of particle layers of the tablet is controlled by an interfacial mechanism.

TABLE 1

Values of the maximum force developed, disintegration time, and disintegration constants of Eqn. 15 for tablets prepared from various model substances with 4 wt% Polyplasdone XL as a disintegrant

Model substance	Max. disint. force, F_∞ (N)	Exp. rate constant, k	Exponent, n	Half-life, θ (s)	Disintegration time (s)
ASA	15.5	0.305	1.72	1.7	8.0
$CaHPO_4 \cdot 2H_2O$	43.1	0.216	1.08	2.9	4.7
α-Lactose	30.3	0.097	1.23	4.9	8.6
β-Lactose	16.9	0.080	0.79	15.3	41.0

In practical terms, disintegration phenomena in tablets containing a non-hydrophilic model substance and a disintegrant are controlled by the swelling pressure on the model substance particles. However, as the hydrophilicity of the model substance increases (for example, in our case according to the sequence $CaHPO_4 \cdot 2H_2O < \alpha$-lactose $< \beta$-lactose), interfacial separation of layers is not as critical or as prominent. Due to the hydrophilic interactions between particles, diffusion becomes the prevailing mechanism of disintegration and the values of the exponent n become smaller. The higher the model substance hydrophilicity, the lower the k values are, since diffusion slows down the tablet expansion process.

Table 1 also presents values of the half-life, θ, of the disintegration force experiment as calculated by Eqn. 17. This parameter gives a first indication of the velocity of disintegration, although it should be always associated to the relative values of k and n. In a comprehensive analysis of the disintegration process, the values of n and k must be considered together, in relation to their influence on tablet disintegration time. Such consideration arises from the observation that the units of k are related to the exponent n. Therefore, a correlation may be derived between n, k and F_∞ for the results presented in Table 1.

Finally, this table presents some data of the disintegration time of these tablets. There is no direct correlation between any single parameter determined from or calculated through the force disintegration experiments and the disintegration time. This is not surprising since the experiment by which the time of disintegration is measured is a three-dimensional swelling experiment whereas the force disintegration experiment relates to a one-dimensional swelling case.

However, a further analysis of the various values indicates that there may be a trend in these data. For example, it is reasonable to expect that a tablet containing β-lactose as a model substance will exhibit a very long disintegration time since: (i) it disintegrates by a slow diffusional mechanism (low k value and $n < 1$); (ii) it does not exhibit a large disintegration force; and (iii) it has a rather long half-life. Indeed, this is the case presented in Table 1 for this tablet. Similarly, one would expect that a tablet containing $CaHPO_4 \cdot 2H_2O$ would show a very short disintegration time (as it does), because it expands very fast (high k) by an interfacial mechanism ($n = 1.08$) and exhibits a rather high maximum disintegration force and a short half-life. However, a complete analysis of the three-dimensional experimental case which leads to the determination of the disintegration time is beyond the scope of the present work and will be discussed in a future contribution.

Influence of properties and quantity of disintegrant

Comparison of the disintegration characteristics and parameters calculated for a number of tablets containing ASA with various disintegrant is shown in Table 2. Among the various disintegrants, tablets containing Avicel PH 101, the disintegrant with the lowest hydrophilicity, exhibit an interface-controlled mechanism with a surprisingly high value of $n = 2.32$. On the other side,

TABLE 2

Values of the maximum force developed, disintegration time and disintegration constants of Eqn. 15, for tablets prepared using acetylsalicylic acid as a model substance and 4 wt % of various disintegrants

Disintegrant	Max. disint. force, F_∞ (N)	Exp. rate constant, k	Exponent, n	Half-life, θ (s)	Disintegration time (s)
Primojel	33.1	0.051	1.44	6.1	18
Acdisol	56.1	0.054	1.32	6.9	10
Polyplasdone XL	29.7	0.160	1.36	2.9	10
Amberlite IRP 88	68.6	0.213	0.94	3.5	9
Avicel PH 101	18.7	0.0004	2.32	24.9	535
Nymcel ZSB 10	42.5	0.090	0.85	11.0	30
Elvanol	29.7	0.022	1.27	15.1	134

tablets with Nymcel ZBS 10 which is the most soluble disintegrant seem to have a diffusion-controlled mechanism (with $n = 0.85$). All other disintegrants present a behavior intermediate between that of the previously mentioned excipients. The highest expansion rate constant k is observed with Amberlite IRP 88 that is capable to develop the highest disintegrating force.

The disintegrating properties of the mixtures are better expressed by the values of the half-life time, θ, which of course couples the two parameters k and n. The values calculated show that the fastest disintegration phenomena are exhibited by tablets containing Polyplasdone XL and Amberlite IRP 88.

An interesting trend is observed again between the disintegrant characteristics and the disintegration time. Indeed, Avicel PH 101 which disintegrates by a purely interfacial determination process and has one of the small expansion constants determined in this work, has a very long disintegration time. Clearly, Avicel PH 101 is not hydrophilic enough to counter-balance the hydrophobicity of the model substance acetylsalicylic acid. An exactly opposite conclusion can be drawn from results of disintegration of Amberlite-containing tablets.

By increasing the disintegrant amount in tablets containing the same model substance, the value of n decreases. This indicates a change of the disintegration mechanism from interfacial to diffusional, except for the disintegration of the more soluble β-lactose (Table 3). The expansion rate constant k, on the contrary, does not change in a continuous manner by increasing the concentration of disintegrant in the tablet. For amounts of disintegrant larger than usual the tablet becomes very hydrophilic and the diffusion of particles away from the disintegrating tablet surface becomes the controlling mechanism, possibly due to the associated major increase of hydrogen bonding. The kinetic constant, k, shows almost constant values, whereas the values of half-life, θ, tend to increase (except for the β-lactose tablets)

TABLE 3

Values of maximum force developed and the disintegration constants of Eqn. 15 for tablets containing various model substances and increasing amounts of Polyplasdone XL as a disintegrant

Model substance	Polyplasdone content (wt%)	Max. disint. force, F_∞ (N)	Exp. rate constant, k	Exponent, n	Half-life, θ (s)
ASA	1	7.6	0.237	1.55	1.9
	5	15.5	0.305	1.72	1.6
	10	38.7	0.215	1.18	2.7
	20	47.9	0.302	0.74	3.1
	40	62.6	0.210	0.62	6.8
$CaHPO_4 \cdot 2H_2O$	1	15.9	0.188	1.27	2.8
	5	43.1	0.216	1.08	2.9
	10	62.9	0.162	1.00	4.2
	20	82.7	0.126	0.87	7.1
	40	102.0	0.119	0.66	14.4
α-Lactose	1	10.9	0.082	1.40	4.6
	5	30.3	0.097	1.23	4.9
	10	45.0	0.108	1.07	5.7
	20	62.0	0.131	0.81	7.8
	40	61.6	0.119	0.72	11.5
β-Lactose	1	3.8	0.112	0.72	12.5
	5	16.9	0.080	0.73	15.3
	10	26.8	0.089	0.73	16.6
	20	34.1	0.090	0.77	14.1
	40	34.4	0.139	0.64	12.3

after an initial decrease (probably around the optimal disintegrant concentration).

Effect of solvent

The solvent temperature has a small effect on the values of the exponent, n, which remain relatively unchanged as the temperature increases from 7 to 40 °C (see Table 4). However, a much larger effect of the temperature on the expansion rate constant, k, is observed. As Eqn. 18 indicates, for relatively constant values of the activation energy, the expansion constant increases as the solvent temperature increases.

The viscosity of the solvent plays an important role in the kinetics of the disintegration phenomenon (Table 5). The increase of the viscosity from 1×10^{-3} Pa · s to 230×10^{-3} leads to a dramatic change in the value of the expansion rate constant k that drops by two orders of magnitude. The values of the exponent n tend to increase as the viscosity of the solvent increases, but always indicate the prevailing diffusional mechanism. The expansion rate of the detached layers is dramatically affected by viscosity, as shown by the k values. The high solvent viscosity leads to more difficult swelling of disintegrant particles and therefore lowers the "pressure" on the model substance particles, as it is clearly indicated by the values of the maximum force developed that decreases by increasing viscosity.

These changes in force maximum and expansion rate of the tablet are in strict agreement with the values of disintegration time, that increase due to increasing viscosity.

TABLE 4

Values of the maximum force developed and disintegration constants of Eqn. 15 for tablets containing $CaHPO_4 \cdot 2H_2O$ and 4 wt % Acdisol, tested for disintegration at various solvent temperatures

Disintegrant temperature (°C)	Max. disint. force, F_∞ (N)	Exp. rate constant, k	Exponent, n	Half-life, θ (s)
7	51.9	0.104	0.56	29.0
20	51.9	0.114	0.68	14.3
30	43.1	0.115	0.66	15.2
37	42.0	0.133	0.64	13.4
40	43.1	0.169	0.59	10.9

Influence of tablets parameters

For tablets prepared from the hydrophobic model substance ASA and Nymcel® as a disintegrant, and compressed with forces of 9.8, 17.6 25.5, and 34.3 kN, the values of the exponent n tend to increase slightly as the force increases (Table 6). Since the increasing compression force leads to a closer contact between the non-hydrophilic model substance and the disintegrant, the interfacial mechanism is promoted by the compression force. Otherwise, as the compression force increases, the value of the expansion rate constant k decreases, evidently because of the reduction of tablet porosity.

The influence of compression force is more pronounced on the kinetics of the phenomenon, if one considers that the value of F_∞ remains almost constant, or in some cases tends to increase slightly. The reduction of the expansion rate, k, is

TABLE 5

Values of maximum force developed, disintegration time and the disintegration constants of Eqn. 15 for tablets containing $CaHPO_4 \cdot 2H_2O$ as a model substance and 4 wt % Acdisol as disintegrant, tested in solutions of changing viscosity

Solvent viscosity $\times 10^3$ (Pa · s)	Max disint. Force, F_∞ (N)	Exp. rate constant, k	Exponent, n	Half-life, θ (s)	Disintegration time (s)
1	51.9	0.104	0.59	25	18
5	42.0	0.066	0.56	67	38
65	36.3	0.009	0.78	262	181
230	25.4	0.004	0.79	682	663

TABLE 6

Values maximum force developed, disintegration time and parameters of Eqn. 15 for tablets containing ASA as a model substance and 4 wt % Nymcel as a disintegrant, and prepared with different compression forces

Compression force (kN)	Max disint. force, F_∞ (N)	Exp. rate constant, k	Exponent, n	Half-life, θ (s)	Disintegration time (s)
9.8	31.4	0.153	0.82	9.8	17
17.6	38.2	0.146	0.72	8.6	30
25.5	42.1	0.090	0.85	10.9	30
34.3	45.0	0.067	0.90	13.6	46

related to the clear increase of disintegration time with the increase of compression force.

Conclusions

The work presented here includes a physicochemical model which describes tablet disintegration in terms of the coupling of diffusional and interfacial mechanisms of particle detachment. It was shown that the expansion rate constant, k, and the disintegration exponent, n, are two parameters that can describe the specific disintegration situation. They are affected by the structure and hydrophilicity of the disintegrant and the model substance, and by other parameters characteristic of the tablet system and the surrounding medium.

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