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Relation between structural characteristics of talc and its properties as an antisticking agent in the production of tablets

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Abstract

Antisticking power varies according to the talc considered. Besides its chemical properties, it is necessary to assess its physical properties related to functionality. It is difficult to define the physical properties of talc implicated in its antisticking power. In this work, different talcs were characterised and their performance in reducing sticking in tablet manufacturing was evaluated. The following parameters were studied: apparent density, morphogranulometry, roughness, and the specific surface through the adsorption–desorption of argon. Next, the relationship between the characteristics of talcs and their antisticking power was considered. Talc before and after delamination—which is a way to obtain talcs with different physical characteristics—was compared. Antisticking power appeared to be dependent on the basal dimensions of talc, and on the ratio value of the external specific surface measured by diffractometry to the total specific surface by the BET method. Models to express the effect of textural factors of talc particles on antisticking power were defined.

Keywords: Talcs; Antisticking power; Physical properties; Functionality assay

1. Introduction

In a previous work, the antisticking power of different types of talc, some of which are derived from the same initial talc but have undergone the physical process of delamination and/or granulometric classification, was studied (Flament et al., 2002). It was noticed that antisticking power in relation to Avicel PH 102 tablets was variable. The performance of these materials is closely related to their physico–chemical properties and to their structural characteristics.

This work included the study of characteristics such as apparent density, morphogranulometry, roughness and the specific surface through the adsorption–desorption of argon.

Also, the relationship between the characteristics of talcs and their antisticking power was considered to determine the talc structure factors that best explain variations in the antisticking power of tablets.

2. Materials and methods

2.1. Materials

The materials chosen were the same as those used in a previous work:

- Avicel PH 102 was used as a reference for evaluating antisticking power; and
- talc of pharmaceutical quality (talc 1) from which different samples were obtained by delamination and/or granulometric classification. For this purpose, a dynamic air classifier, Hosokawa-Alpine 50 ATP, was used.

Three products were obtained after classification (Baudet et al., 1998):

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- product X.1 collected from the filter;
- product X.2 collected from the cyclone; and
- product X.3 collected from the turbine;

with X=1 in the case of a direct classification of talc and X=2 when talc 1 was classified after delamination.

Fig. 1 shows the different types of talc 1 obtained after these procedures. Two other talcs were also tested:

- talc 1b, of the same nature as talc 1, not delaminated, used to study interbatch variations; and
- talc X, provided by another supplier, with different structural characteristics.

2.2. Methods

2.2.1. Determination of apparent density of different talcs

After 10 taps, the apparent density (MV_{10}) was calculated using the method described in the European Pharmacopoeia (2002).

2.2.2. Morphogranulometric analysis

This was carried out by laser diffractometry with a Malvern Mastersizer S size analyzer based on the Fraunhofer model. Particle size distribution of very fine talcs was determined using the theory of Mie. The index of refraction was 1.56 and that of adsorption was 0.0555. Measurements were made on diluted aqueous suspensions of known concentrations (0.06–0.23 g/l according to talc granulometry) with laminar flow through the fine cell (0.5 mm) under analysis. This type of flow favours the selective orientation of lamellar particles, which present their basal surfaces perpendicularly to the laser beam.

Under these conditions, measurements make it possible to determine (Baudet et al., 1993):

- the projected area distribution of particles according to their basal dimensions so as to calculate the mean basal surface diameter (dmL) and the projected area diameter ($d99L$) corresponding to 99% of cumulative undersize); and
- the distribution spreading index (IEL): an indication of the extent of the projected area distribution of talc particles in relation to the basal dimension given by the equation: $(d90L - d10L)/2d50L$ where (dxL) is the basal dimension corresponding to X% of the cumulated projected area.
- The projected surface area of the lamellar particle population.

The mean thickness h of lamellar particles, which is given by the ratio of their specific volume to their specific projected area. The mean shape factor or the mean geometric aspect ratio (AR) is defined by the relation: $AR = dmL/h$. The mean specific geometric surface area SSAL, corresponds to the external surface area developed by a smooth, non-porous disc, which has average dimensions dmL and h. It is given by the relation:

$$SSAL = (2dmL + 4h)/(\rho dmLh)$$

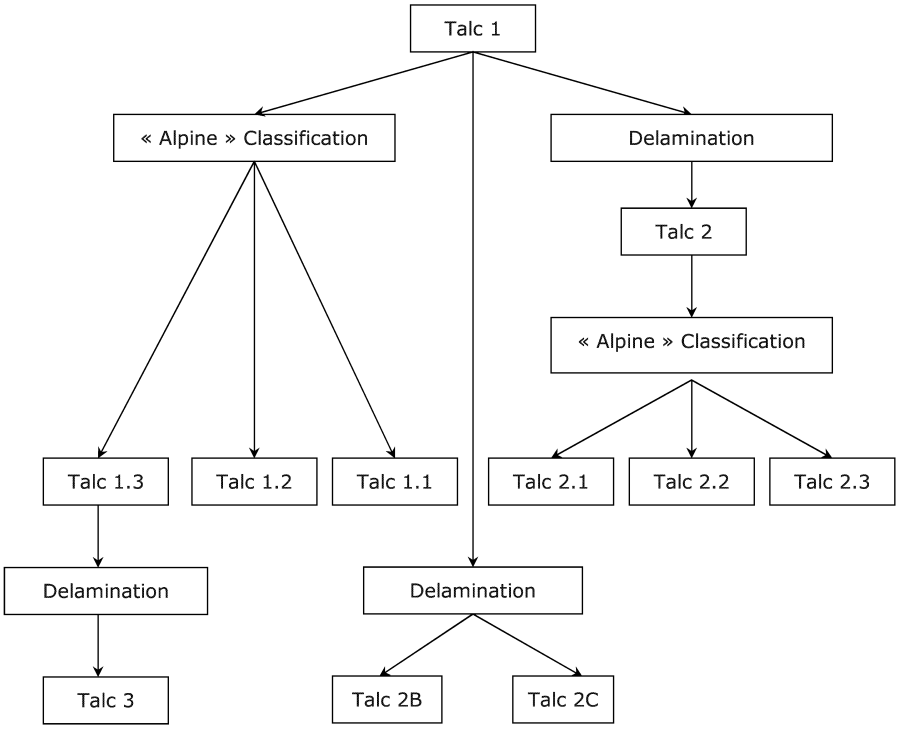

Fig. 1. Diagram of the treatment of talc.

The granulometric distribution in volume of Avicel 102 particles, which are considered to be spherical, was determined using laser diffractometry under dry conditions and based on the Fraunhofer model.

2.2.3. Roughness of basal surfaces of talcs

The diffused reflection in the field of vision was used to evaluate the influence of delamination over brightness. There is a correlation between brightness and roughness of talc particles. The spectra were obtained with a Lambda 9 spectrophotometer from Perkin-Elmer. The device was equipped with an integration sphere whose surface was completely coated with barium sulfate. The roughness of the particle surface was assessed from the measurement of specular reflection R_s. R_s is defined by the relation $R_s = R_t - R_d$ where R_t is the total reflection and R_d is the diffused reflection of the surface.

The roughness of the particle surface and the specular reflection are related as follows:

$$R_s = R_o \exp - \left[\frac{4\pi\sigma^2}{\lambda} \right]$$

with R_o = specular reflection of an ideally plane surface, σ = surface roughness, and λ = wavelength.

2.2.4. Specific surface area determined by adsorption–desorption of argon

The specific surface area was calculated from the adsorption and desorption of argon at 77 K using a sorptiometer of discontinuous volumetry (Carlo Erba Sorptomatic 1900). For each product, the specific surface area was defined using, on the one hand the classic BET method (Rouquerol et al., 1999), which gives the SSA BET value, and on the other hand, the method of *t*.plot (De Boer et al., 1966; Rouquerol et al., 1999).

According to the latter method, the specific surface area was determined by the gradient of two linear portions of the diagrams indicating the specific volume of the adsorbed argon (the volume corresponding to each gram of material) relating to the statistical thickness t of the adsorbed argon in a monomolecular or multiple layer form.

The thickness t at different relative pressures was determined using De Boer reference isotherms on non-porous metallic oxide powders.

The first linear part, which has low t values and relative pressure represents the coverover of the free space on the particle surface and the inner area of mesopores (the size of each mesopore is larger than 2 nm) by molecules of argon. Where ordinates of a clearly identifiable origin were missing, the surface of micropores and areas of very high adsorption energy were not taken into consideration.

The total surface area comparable to SSA − BET was calculated from the gradient of this first linear part.

The second linear part, with high t values (>1.6 nm) and of relative pressure (>0.97–0.98), follows capillary condensation in mesopores (from a width of 2 to 40 nm approx.) during adsorption and accounts for multilayer adsorption on the partition walls of the macropores (width larger than 40–120 nm, according to the average dimensions of lamellar particles).

The second linear part represents adsorption over the remaining surface after the mesopores and small macropores have been filled. The surface calculated from the gradient of the second linear part is considered to be the estimated specific external surface area of particles, comparable to SSAL, while the surfaces of mesopores are considered to be the internal surface originating from the inner sides of intra-particle pores.

2.2.5. Evaluation of antisticking power of talc in relation to Avicel PH 102

In a previous work, a functionality assay was defined on a simple punch press to evaluate the antisticking power of talcs (Flament et al., 2002). The assays were performed on a Frogerais OA single punch press where the feed shoe was set up to measure the force required to detach the tablet from the lower punch surface.

The transducer was calibrated so that 1 mV squared with 10^{-1} N. The measurement precision was 1%. The assays were realized with blends of Avicel PH 102 and 1% talc.

3. Results

Measurements of the apparent densities are presented in Table 1. For the same talc (1 or 2), the comparison of samples after granulometric classification indicates that the apparent density decreases with the size of particles. On the other hand, the apparent density of a granulometric fraction before and after delamination (1.1 and 2.1; 1.2 and 2.2; 1.3 and 2.3) varies only slightly. Delamination seems to have little influence on apparent density. However, in this preliminary study of the data presented in Table 1, it should be noted that each of the separate fractions of talc, whether delaminated or not, presents different granularity

Table 1
Apparent densities of talcs

Talc	MV_{10} (g/l)
X	568.2
1b	480.8
1	463
1.1	128.9
1.2	208.3
1.3	757.6
2	266
2.1	116.8
2.2	183.6
2.3	595.2
2b	235.9
2c	277.8
3	367.7

Table 2
Results of the morphogranulometric tests of talcs determined with laser size analyzer

Talc	*d*99*L* (μm)	*dmL* (μm)	IEL	*h* (μm)	A.R.	SR (%) Talc projected area /Avicel area
X	59.97	9.95	2.24	1.10	9.05	3.90
1b	67.13	11.77	2.27	0.62	18.92	6.89
1	69.55	12.16	2.31	0.56	21.64	7.63
1.1	9.49–8.5[a]	2.13–1.32[a]	1.33–3.52[a]	0.11	19.02–11.79[a]	
1.2	18.07	4.52	1.22	0.26	17.52	16.61
1.3	66.04	13.33	1.83	1.70	7.84	2.52
2	53.22	10.45	1.67	0.29	35.91	14.73
2.1	10.76–9.93[a]	2.23–1.54[a]	1.58–3.26[a]	0.12	18.74–12.94[a]	
2.2	17.81	4.84	1.23	0.23	20.68	18.32
2.3	56.15	15.15	1.11	0.78	19.42	5.49
2b	54.27	10.40	1.68	0.29	35.86	14.78
2c	59.21	10.70	1.67	0.30	36.27	14.53
3	57.02	12.30	1.50	0.50	24.60	8.57

[a] Mie theory.

and different factors of morphology. Consequently, variations in apparent density reflect variations in these two parameters, even between two separate fractions in the same initial talc.

Talc 1b behaves similarly to talc 1. Talcs 2b and 2c are comparable to talc 2.

Morphogranulometric analysis is presented in Tables 2 and 3.

For talc 2 compared to talc 1, modifications in morphology caused by delamination lead to a notable decrease in mean thickness *h* of lamellae and to an increase in mean shape factor AR and the external specific surface calculated from the dimensions determined through laser diffraction.

The moderate relative diminutions of *d*99*L* and *dmL*, compared with a considerable reduction in *h*, show that the comminution of lamellae in directions parallel to basal forces (delamination) is more active than the comminution in normal directions (breakage of lamellae).

The apparent densities of talc powders increase when the mean basal dimension increases and when the mean shape factor of particles decreases.

Estimation of the external surface SSAL (laser diffractometry) was compared to those of external SSA deducted from *t*.plots. The results shown in Table 3 indicate an acceptable compatibility considering the implied differences in the definition of external surfaces in the two methods. The results for total SSA obtained by the two methods, BET and *t*.plot, are quite similar. They clearly show the remarkable increase in the surface area of the delaminated products. A comparison of internal/total surface ratios shows an increase after delamination. This is mainly due to the creation of new internal surfaces after the incomplete delamination of particles as is shown in

Table 3
Specific surface area of the different talcs determined according to different methods

Talc	External SSAL (m^2/g) (diffractometry)	BET total SSA (m^2/g)	*t*.plot total SSA (m^2/g)	*t*.plot external SSA (m^2/g)	*t*.plot internal SSA (m^2/g)	Int. SSA/ total SSA (*t*.plot) (%)	SSA ratio: SSAL/ SSA BET
X	0.81	3.69					0.219
1b	1.29	3.64					0.355
1	1.41	3.14	3.1	1.4	1.7	54.8	0.450
1.1	7.18–7.60[a]	20.94	19.3	8.1	11.2	58	0.343–0.363
1.2	3.14	10.37	9.6	3.7	5.9	61.5	0.303
1.3	0.54	3.56	3.4	0.5	2.9	85.3	0.151
2	2.64	11.94	11.2	2.9	8.3	74.1	0.221
2.1	6.76–7.06[a]	32.60	30.8	ND	ND	77.9–77.1°	0.208–0.216
2.2	3.41	17.95	17.0	3.6	13.4	78.8	0.190
2.3	1.03	5.11	4.9	0.7	4.2	85.7	0.201
2b	2.65	9.94					0.266
2c	2.60	8.99					0.289
3	1.57	5.85					0.269

ND, non-determinable; °, (total SSA − SSAL)/total SSA ratio.
[a] Mie theory.

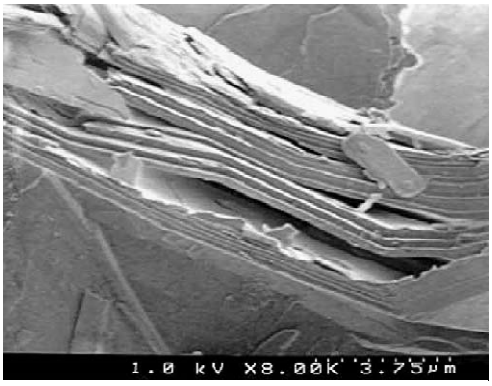

Photo 1. Microscopic porosity of a delaminated particle.

Photo 1, taken with a scanning electron microscope: incomplete interlamellar detachment creates intra-particle pores whose walls constitute the internal surfaces.

The results concerning brightness are presented in Fig. 2. The results clearly indicate that delamination improves particle brightness by a factor of 4. This increased brightness, signifying a decrease in roughness, is mainly attributed to the new external basal surfaces, which are less rough and have a low level of contamination by colouring impurities generated during mechanical treatment. The decrease in roughness of basal surfaces should contribute to increased detaching force in the case of delaminated talcs (Pietsch, 1991).

The results of measurements of tablet detaching force compared to the functioning time of the tablet machine are summarised in Table 4. Talcs 1.1 and 2.1 were tested at a concentration of 0.5% to differenciate them because there is no sign of sticking when used at a concentration of 1%.

Looking at the data, three groups of talcs are noteworthy:

- The first group consisted of talcs 1.1 and 2.1 for which there is no sticking when they are used at a concentration of 1%. Their *d*99*L* and *dmL* values are the smallest: about 10 and 2 μm, respectively.
- A second group made up of talcs 1.2 and 2.2 for which detaching values are lower than those obtained with other talcs. Their *d*99*L* and *dmL* are close to 18 and 4.5 μm, respectively.
- The third group made up of the other talcs. They present more pronounced sticking that cannot be distinguished. The *d*99*L* and *dmL* values are higher: around 60 and 12 μm, respectively.

The detaching force of tablets appears to be dependent on:

- the maximum basal dimension (*d*99*L*) of talc lamellae and on the SSAL/SSA BET ratio at the beginning (between 0.5 and 3 min) of press function. Within this period, the talcs which present the coarsest and the densest particles (slightly mesoporous) are those that induce the greatest detaching force;
- the mean basal dimension (*dmL*) of lamellae for functioning periods of 3 min and more. The required detaching force increases with *dmL*. This mean dimension indirectly justifies the scope and distribution type of lamellar particle basal dimension.

The Van der Waals molecular dispersion forces between the punch metallic surface and the particles of Avicel PH 102, between the metallic surface and talc particles proportionally to the surface concentration of talc particles on the punch–tablet interface area, are implicated in the mechanism of tablet adhesion, along with other surface phenomena like electrostatic forces or roughness. The Van der Waals interactions among Avicel PH 102 particles, among the talc and Avicel PH 102 particles, among talc particles themselves, can also be implicated as some

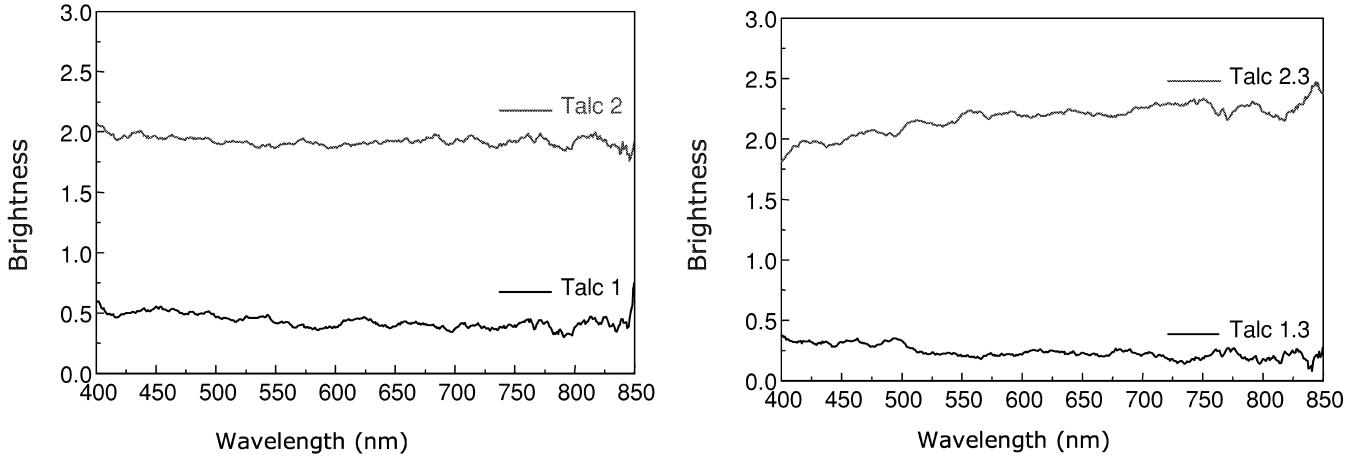

Fig. 2. Spectra of diffused reflexion obtained on samples of talc 1 and delaminated talc 2, on the 1.3 and 2.3 fractions isolated from talc 1 and delaminated talc 2.

Table 4
Detaching values (N) of tablets containing Avicel PH 102 associated with different samples of talc at different functioning times of the tablet press

(% Talc) sample	Detaching value					Ratio (0.5:5)
	After 0.5 min	After 1 min	After 3 min	After 4.5 min	After 5 min	
Avicel PH 102 (1%)	59.00	73.47	114.1	114.1	131.75	
X	61.00	73.00	77.30	77.60	77.20	1.266
1b	82.89	96.98	106.58	109.82	110.90	1.338
1	97.27	103.20	103.46	104.22	104.47	1.074
1.2	52.27	48.38	44.86	49.86	46.98	0.899
1.3	72.84	85.10	89.54	91.06	99.83	1.370
2	64.88	66.68	76.54	77.70	70.88	1.092
2.2	34.30	29.07	29.18	27.30	19.68	0.574
2.3	71.60	71.60	135.80	134.90	138.80	1.939
2b	67.16	71.46	60.42	65.04	66.58	0.991
2c	68.42	68.04	70.08	74.22	75.59	1.150
3	51.09	66.88	76.52	78.22	77.48	1.517
(0.5%)						
1.1	58.25	65.16	72.18	88.60	90.66	1.556
2.1	88.56	83.42	81.70	83.76	86.40	0.976

Avicel and talc particles can be more strongly attached to the metallic surface than other particles.

The expression of potential interaction energy Φ between one block of material where the three dimensions are considered to be infinite, and a disc, which has diameter D and thickness e, and whose basal face is at a distance d from one of the block bases, is developed using the general method presented by Hiemenz (1986):

$$\Phi = -\frac{AD^2}{48}\left[\frac{1}{d^2} - \frac{1}{(d+e)^2}\right] \quad (1)$$

where A is the Hamaker constant related to the medium and materials considered.

This expression indicates that the attraction energy between the punch and the talc particles is proportional to the square of the basal dimension of the particle, which is considered as a disc of diameter D and thickness e. Based on the actual values of d (1–10 nm) and on the average values of talc particle thickness (110–1700 nm), the term in brackets in Eq. (1) varies slightly according to e. Eq. (1) may explain the detaching tablet force that is dependent on the square of the basal dimensions of lamellar particles of talc without any significant influence of thickness.

Particles of Avicel PH 102 microcrystalline cellulose made up of easily distorted material, approach the punch (reduced d) during the final stage of compression. Avicel particles are coarser than talc particles; their distribution in volume corresponds to $D99$, 320.9 μm; $D90$, 222.5 μm; $D10$, 29.5 μm, with mean D, 116.5 μm. Based on these facts, the interaction between one Avicel particle deformed by compression and one talc particle, which has a small basal dimension compared to the average dimension of an Avicel particle can also be easily evaluated using Eq. (1). The attraction forces between talc and the punch, or Avicel PH 102, are dependent on the square of the basal dimension of particles but not on their mean thickness within the field of mean thickness variation measured.

In the experiment carried out with talc at 1%, only the parameters of talc were implicated in the observed variations of the detaching force while the parameters associated with Avicel PH 102 remained constant. The detaching force corresponds to the shearing force at the punch–tablet interface, and, by a friction factor, is proportional to the adhesion force represented by Φ/d for each particle.

At the beginning of press functioning, Eq. (1) indicates that the adhesion force, Φ/d, between talc and punch surface would be maximum for lamellae, which present the largest basal dimensions. This could lead to irreversible sticking of some of them on the metallic surface of the punch if the corresponding interaction energy exceeds the attraction energy among these particles and the particles adjacent to Avicel PH 102 or talc. This process can evolve during the press functioning period until a very thin layer (film) of talc particles (and Avicel PH 102 particles) is created on the surface of the punch. The interactions at the punch–tablet interface level are modified: from metal–Avicel and metal–talc attractions, they turn into talc–talc, Avicel–talc and Avicel–Avicel attractions. This could account for the temporary evolution in the detaching force during the first 3 min of the press function. In terms of force, variation is dependent on the nature of the materials, which are more or less in contact (which affects the value of the Hamaker constant) and on the dimensions of talc and Avicel particles in the punch–tablet interface. In the second phase, which comes after the creation of partial or total film on the punch surface, the talc–talc or Avicel–talc attractions are better represented by the mean basal dimension dmL of lamellar particles than by the maximum dimension $d99L$, which is likely to intervene during the creation of film, especially if segregation of coarse talc particles takes place during the filling of die.

The variable SSA ratio is indicative of the mesoporosity and the roughness of talc particles. These two factors become more important as the value of the ratio becomes lower.

The latter has a positive effect on detaching force during the first 0.5–3 min, for two talcs with the same $d99L$ value, so the required detaching force is inferior for talcs with the most mesoporous particles. This effect is attributable to decreased molecular interaction, which results after the reduction in the number of atoms per unit of apparent volume of particles. This has a role in diminishing the Hamaker constant and the adhesion force.

4. Conclusion

For mixtures of Avicel–1% talc, the force necessary to detach tablets from the punch surface seems to be:

- variable according to the functioning time of the tablet machine. The greatest variations are observed between 0.5 and 3 min, especially with the coarsest talcs. Beyond 3 min sticking is almost stabilised;
- variable according to the maximum basal dimension $d99L$ of talc particles and of the ratio (SSA ratio) value of the external specific surface measured by diffractometry (SSAL) to the total specific surface by the BET method, between 0.5 and 3 min of press functioning. The SSA ratio principally reflects the mesoporosity of talc particles. It becomes lower as the porosity increases;
- variable according to the mean basal dimension dml of talc particles beyond 3 min functioning; and
- independent of the mean thickness h, of the mean shape factor $AR = dmL/h$ and independent of the distribution spreading index of the basal dimensions of talc particles.

The attraction force model of Van der Waals between a disc and a block of infinite extension, applied to lamellar particles of talc and on the punch surface, takes into account the dependence of force on the square of the basal dimension and its independence of particle thickness.

The effect of the variable SSA ratio, at the beginning of press functioning, shows the influence of mesoporosity on the value of the Hamaker constant. The low value of this ratio, indicating high mesoporosity or low mean density of atoms per volume unit of particles, implies a decrease in the Hamaker constant and, consequently, diminished attraction force.

The evolution in the detaching force in function of time, between 0 and 5 min, could be explained by greater attraction force between the punch and some of the particles, the coarsest and densest. This leads to irreversible adhesion of particles by creating a very thin film and by modifying the punch–tablet interface. The ratio of the projected surface of talc particles to the external surface of Avicel PH 102, without being an important factor in variations of detaching force, could indicate a non-homogeneous distribution of talc particles, especially of those lamellae which are coarsest. The ratio of the surface of talc particles to the surface of Avicel particles, in the punch–tablet interface, could represent a supplementary variable making it possible to improve the explanation rate of observed variances on the values of sticking.

From a practical point of view, the results indicate that the best reductions in sticking will be obtained when using the finest talcs where particle porosity is highest. These characteristics favour the selection of microcrystalline talcs for this application.

The mean basal dimension and the $d99L$ of talc particles, measured by laser diffractometry, could be used to give a satisfactory explanation for the antisticking power. This is a classically used method.

The value of AR does not affect sticking directly, within the context of experimentation carried out with 1% talc. However, it presents an important parameter in relation to the external specific surface created by talc particles. If the basal dimensions are small enough to diminish the adhesion forces, then the dose of talc needed to suppress sticking will be as low as the mean shape factor is high.

References

Baudet, G., Bizi, M., Rona, J.P., 1993. Estimation of the average aspect ratio of lamellae-shaped particles by laser diffractometry. Particulate Sci. Technol. 11, 73–96.

Baudet, G., Blazy, P., Chahdi, A., Pineau, J.L., 1998. Efficacité de la classification ultra-fine en voie sèche par un sélecteur dynamique. Mines et Carrières, Les Technique I, septembre 1998, pp. 4–19.

De Boer, J.H. et al., 1966. The t-curve of multimolecular adsorption. J. Colloid Interf. Sci. 21, 405–414.

European Pharmacopoeia, 2002. 2.9.15 volume apparent, pp. 223–224.

Flament, M.P., Leterme, P., Bizi, M., Baudet, G., Gayot, A., 2002. Study of talcs as antisticking agents in the production of tablets. Eur. J. Pharm. Sci. 17, 239–245.

Hiemenz, P.C., 1986. Principles of Colloid and Surface Chemistry, 2nd Edition. Marcel Dekker Inc, New York.

Pietsch, W., 1991. Size Enlargement by Agglomeration. John Wiley and Sons, New York.

Rouquerol, F. et al., 1999. In: Adsorption by Powders and Porous Solids. Academic Press, New York, pp. 165–190.