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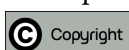
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Study of talcs as antisticking agents in the production of tablets

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Abstract

Talc is defined as a crystalline structure characteristic of lamellar structures. Antisticking power varies according to the talc considered. Besides chemical properties, it is necessary to assess physical properties related to functionality. It is difficult to define the physical properties of talc implicated in its antisticking power. In this work, we characterized different talcs and then evaluated their performances in reducing sticking in tablet manufacturing. We compared talcs before and after delamination which is a way to obtain talcs with different physical characteristics. Granulometric analysis was carried out by laser diffractometry using a method which made it possible to assess the mean thickness of the lamellar particles. We defined a functionality assay on a single punch press to assess the antisticking power of talcs. The different talcs tested possess a very variable antisticking power towards Avicel PH 102. They present different basal dimensions and particle thickness. The force necessary to detach tablets from the punch surface varies according to the functioning time of the tablet machine, the percentage of talc and the basal dimension of talc.

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Keywords: Talcs; Antisticking power; Functionality test; Physical properties; Delamination

1. Introduction

The European Pharmacopoeia monography defines talc only by its chemical characteristics: “it is a selected and pulverized native hydrous magnesium silicate with a chemical structure $[\text{Mg}_3\text{Si}_4\text{O}_{10}(\text{OH})_2]$ (European Pharmacopoeia, 2002). It sometimes contains variable quantities of associated minerals including predominantly chlorites (hydrous magnesium and aluminium silicates), magnesite (magnesium carbonate), calcite (calcium carbonate) and dolomite (calcium and magnesium carbonate)”. Talc is defined as a crystalline structure characteristic of lamellar structures.

Besides its chemical properties, it is necessary to assess physical properties related to functionality. It has been shown that according to the preparation method used, the antisticking power of talc could vary. It is difficult to define very precisely the physical properties linked to its

antisticking power. Delamination is a way to obtain talcs with different physical characteristics.

Delamination is a mechanical treatment, in a wet process, that consists of reducing the initial layers of talc lamellae by tangential shearing. Forces are applied parallel to the basal faces of lamellae minimizing perpendicular fractures on these.

This treatment produces new basal surfaces associated with:

- the creation of defects like microfractures, particularly on the lateral surfaces of the lamellae
- incomplete interlamellar detachment, constituting intraparticle porosity
- the liberation of fine lamellar particles that were initially stuck on the basal surfaces.

The generation of new basal surfaces that are less rough generally improves the brightness of particles.

The appearance of new surfaces could influence the antisticking power of talc, which is why delaminated and nondelaminated talcs were compared.

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Fig. 1. Observation of talc 1 using SEM.

Different talcs were characterised and then their performances in reducing sticking in tablet manufacturing evaluated.

2. Material and methods

2.1. Materials

A talc of pharmaceutical quality was used for delamination (Talc 1, BRGM, Orléans, France). Talc 1 particles were examined with a scanning electron microscope (SEM) Hitachi 54200 fitted with a field emission gun. Fig.

1 shows the presence of small lamellae and of a great number of small irregularities on the basal surfaces because of the combination of disordered microcrystals which implies nonnegligible surface roughness and solid–solid interface porosity.

Talc 1 was delaminated in water using a Netzsch-LME1 stirring microball mill with a horizontal agitator and continuous feeding.

Talc, delaminated or not, was submitted to granulometric classification. Classification was carried out by dry sieving using a Hosokawa-Alpine 50 ATP air dynamic selector and occurs principally in a rotor with radial plates. A second classification was performed in a cyclone (Baudet et al., 1998): under the influence of the aerodynamic carrying force, fine particles went through the rotor whereas coarser particles were rejected outside the rotor by gravity and centrifugal force to be then drained off at the base selector. For each assay, three products were obtained:

- a product X-1 collected from the filter
- a product X-2 collected from the cyclone
- a product X-3 collected from the turbine

with X=1 in the case of direct classification of talc 1, X=2 when talc 1 was classified after delamination (Fig. 2).

Talc 3 made it possible to study the influence of delaminating after granulometric classification. Talcs 2B

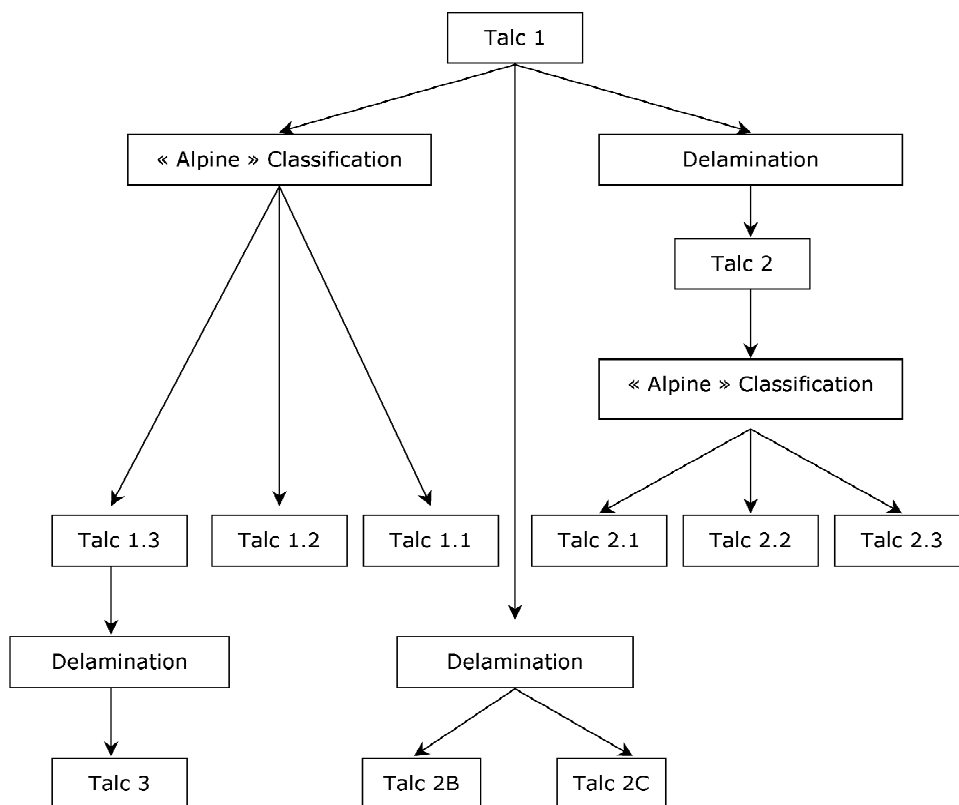


Fig. 2. Diagram of the treatment of talc.

and 2C obtained by talc 1 delamination enabled us to assess intrabatch variation in comparison to talc 2 whereas interbatch variation was assessed by comparing dimensions and the antisticking power of batches 1 and 1B.

2.2. Method

2.2.1. Granulometric analysis

This was carried out by laser diffractometry with a Malvern Mastersizer X laser size analyser, using the Fraunhofer theory (Agrawal et al., 1991; Bott and Hart, 1991; ISO 13320-1, 1999). For talcs below 5 μm , sizes were also determined using the Mie theory with the following optical parameters: refractive index of 1.56 and absorption index of 0.055. Measurements were made on very diluted aqueous suspensions (0.06–0.23 g/l according to talc granulometry) with a laminar flow through the fine cell under analysis. This type of flow favours selective orientation of the lamellar particles that present their basal surfaces perpendicularly to the laser beam. Comparisons of electronic microscopy associated with image analysis and of laser diffractometry on talc particles with dimensions between 1 and 40 μm showed that the distribution of the projected area of particles concords with basal surface distribution (Baudet, 2000).

Measurements by laser diffractometry using previously described conditions made it possible to determine:

- the projected area distribution of particles with
 - dmL = mean basal surface diameter
 - 99 L = projected area diameter corresponding to 99% of cumulative undersize.
- the mean thickness according to the method presented by Baudet et al. (1993). The mean thickness h of the lamellar particles is given by the ratio of their specific volume to their specific projected area. The mean shape factor or mean geometric aspect ratio (AR) is defined as $\text{AR} = \text{dmL}/h$.

2.2.2. Measurement of antisticking power

To assess talc capacity to eliminate the sticking power, we defined a functionality assay on a single punch press. The assays were performed on a Frogerais OA single punch press with an instrumented feed shoe (Fig. 3) (Bleuse et al., 1983).

On a single punch press, tablet ejection takes place when the lower punch rises to bring the tablet to the top of the die, followed by a forward movement of the feed shoe. By equipping this feed shoe with a hardened steel strip fitted with strain gauges connected to an electronic device, it is possible to measure the force necessary to detach the tablet from the lower punch surface. We carried out a transducer calibration with a standard spring balance so that 1 mV squared with 10^{-1} N.

Measurement precision is 1%.

The model used to assess the antisticking power of talc

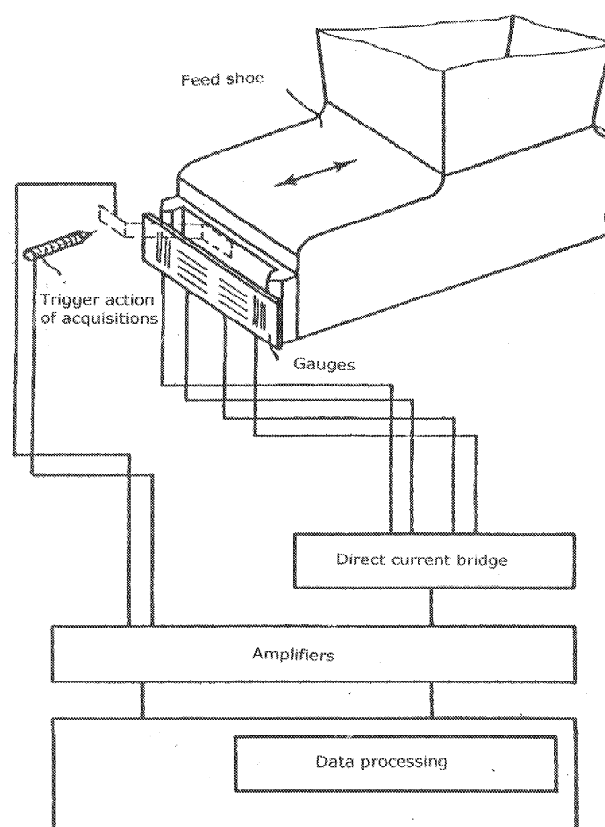


Fig. 3. Structure of the measurement line.

is a microcrystalline cellulose—Avicel PH 102. It was chosen because previous studies in our laboratory had shown that Avicel PH 102 alone was compressible and the tablets obtained adhered firmly to the lower punch and were vigorously ejected by the feed shoe of the tablet machine (Delacourte-Thibaut et al., 1984). Moreover, it does not feature a die wall friction phenomenon that could obstruct the assessment of sticking on the lower punch.

The operating conditions are the following:

- blending of Avicel PH 102+1% or 3% talc for 5 min with a Turbula blender at 54 rpm
- flat punches of 11.28 mm diameter
- constant volumetric filling of the die: 1 cm^3
- press speed of one tablet per second
- upper punch displacement adjusted to give tablets with a hardness of 180 N with 1% talc and 160 N with 3% talc.
- For a given percentage of talc, we worked in the same conditions of adjustment of the tablet machine. To obtain tablets with the same crushing strength, we did not have to modify the compression force whatever the tested talc.
- Hardness is measured on 10 tablets with a Schleuniger tablet tester (IMA France, Rueil Malmaison, France).

All the experiments are realised in the same operating

Table 1
Granulometric results of the different samples of talc determined with laser size analyzer

Sample	d _{mL} (μm)	d _{99 L} (μm)	<i>h</i> (μm)	A.R.
Talc 1	12.16	69.55	0.56	21.64
Talc 1.1	2.13–1.32 ^a	9.49–8.50 ^a	0.11	19.02–11.79 ^a
Talc 1.2	4.52	18.07	0.26	17.52
Talc 1.3	13.33	66.04	1.70	7.84
Talc 1B	11.77	67.13	0.62	18.92
Talc 2	10.45	53.22	0.29	35.91
Talc 2.1	2.23–1.54 ^a	10.76–9.93 ^a	0.12	18.74–12.94 ^a
Talc 2.2	4.84	17.81	0.23	20.68
Talc 2.3	15.15	56.15	0.78	19.42
Talc 2B	10.40	54.27	0.29	35.86
Talc 2C	10.70	59.21	0.30	36.27
Talc 3	12.30	57.02	0.50	24.60

^a Mie theory.

conditions with the same batch of Avicel and the same quantity of blend.

The detaching force of the tablet can be read as soon as sticking occurs and then 1, 3, 4.5 and 5 min after the start of the single punch press. The values are the average of

five measurements which are made under standardised conditions of temperature and relative humidity, that is to say 20 °C and 20%.

3. Results and discussion

The absence of contamination (iron and/or carbon likely to come from the milling equipment used) after delamination was verified. Total carbon and total iron contents do not vary after delamination. The equipment used does not affect the quality of delaminated products.

The results of size analysis with laser size analyser are presented in Table 1 and Fig. 4.

The modifications in the mean morphology of particles caused by delamination led to an appreciable decrease in the mean thickness, *h*, of lamellae and to an increase in the mean geometric aspect ratio (AR) of talc 2 when compared to the initial talc 1. The moderate relative decreases in the d_{99 L} and the d_{mL} of delaminated samples, compared to the considerable reduction in *h*, show that the comminution of lamellae in directions parallel to the basal faces (delami-

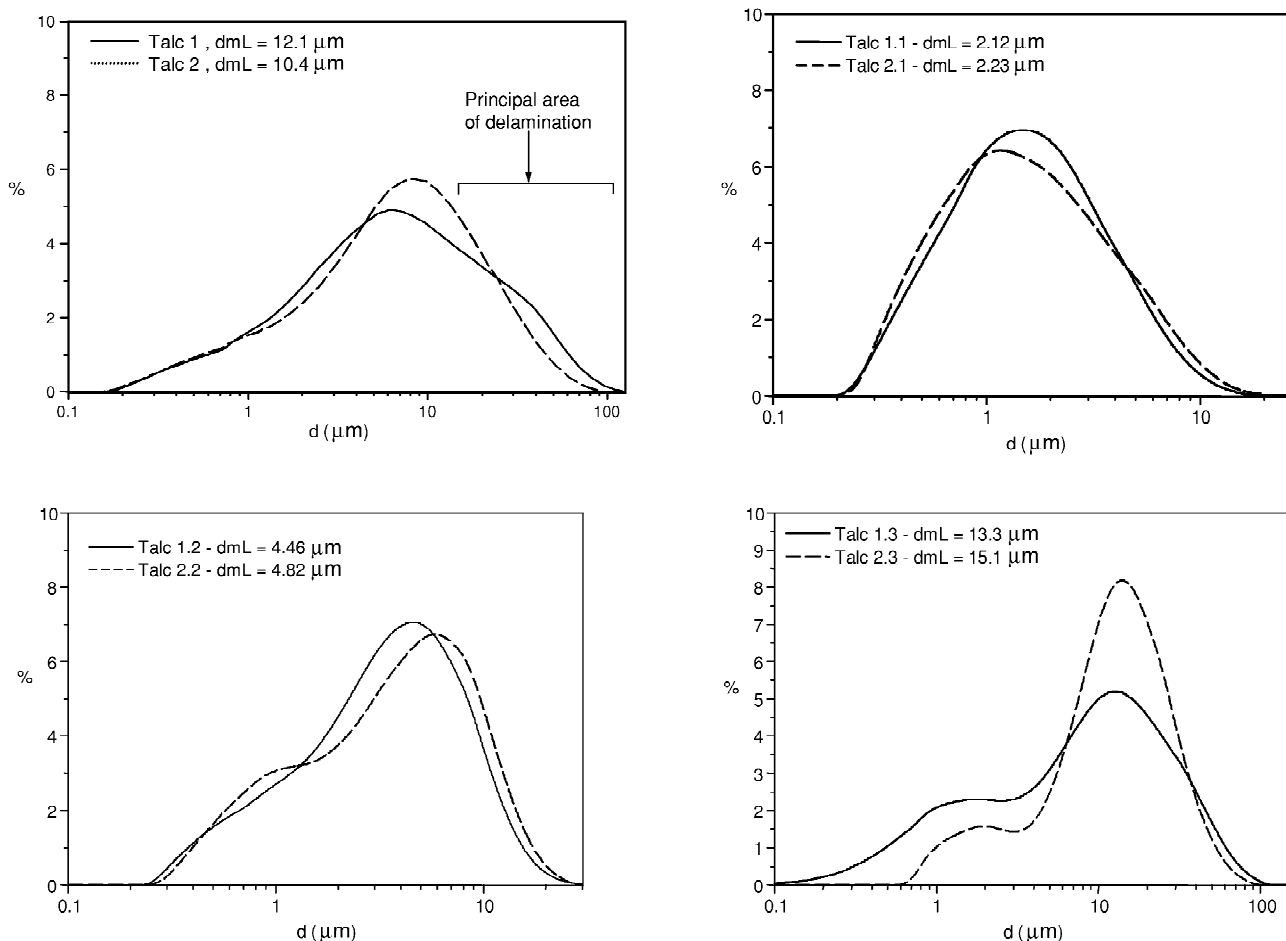


Fig. 4. Granulometric distribution of talc before and after delamination (talc 1 and 2, respectively), and aftergranulometric classification.

Table 2

Unsticking force of tablets containing Avicel PH 102 associated with different samples of talc, at different functioning times of the tablet press

Sample	Unsticking force (N) after 0.5 min	Unsticking force (N) after 1 min	Unsticking force (N) after 3 min	Unsticking force (N) after 4.5 min	Unsticking force (N) after 5 min
Avicel PH 102 alone	59.00 (± 0.75)	73.47 (± 4.0)	114.1 (± 2.5)	114.1 (± 2.8)	131.75 (± 1.8)
+1% talc					
1	97.27 (± 3.16)	103.20 (± 3.2)	103.46 (± 1.24)	104.22 (± 3.4)	104.47 (± 3.1)
1.2	52.27 (± 2.2)	48.38 (± 1.35)	44.86 (± 1.06)	49.86 (± 2.4)	46.98 (± 1.64)
1.3	72.84 (± 2.54)	85.10 (± 3.18)	89.54 (± 2.0)	91.06 (± 1.04)	99.83 (± 1.60)
1b	82.89 (± 2.8)	96.98 (± 2.55)	106.58 (± 3.0)	109.82 (± 2.13)	110.90 (± 2.05)
2	64.88 (± 2.1)	66.68 (± 1.6)	76.54 (± 2.45)	77.70 (± 3.5)	70.88 (± 2.64)
2.2	34.30 (± 1.36)	29.07 (± 1.31)	29.18 (± 0.54)	27.30 (± 1.2)	19.68 (± 0.65)
2.3	71.60 (± 3.1)	71.60 (± 3.1)	135.80 (± 5.0)	134.90 (± 2.75)	138.80 (± 5.11)
2b	67.16 (± 2.43)	71.46 (± 2.02)	60.42 (± 2.97)	65.04 (± 2.61)	66.58 (± 2.45)
2c	68.42 (± 3.9)	68.04 (± 0.68)	70.08 (± 0.45)	74.22 (± 0.23)	75.59 (± 0.31)
3	51.09 (± 2.18)	66.88 (± 3.5)	76.52 (± 1.32)	78.22 (± 2.21)	77.48 (± 1.93)
+ 0.5% talc:					
1.1	58.25 (± 2.1)	65.16 (± 1.6)	72.18 (± 1.45)	88.60 (± 1.72)	90.66 (± 0.98)
2.1	88.56 (± 4.15)	83.42 (± 1.8)	81.70 (± 2.7)	83.76 (± 4.0)	86.40 (± 3.2)

nation) is more active than that in the normal directions (breakage of lamellae).

Comparisons of granulometric distribution (Fig. 4) and of the mean thickness (Table 2) of talc fractions before and after delamination clearly indicate that comminution in the two principal directions of particles (basal dimensions and thickness) is notably more active on lamellae with basal dimensions higher than 10 μm (fractions X.3). For the other fractions, only the thickness decreases.

The time-related evolution of the detaching force of

tablets containing Avicel PH 102 alone and associated with different samples of talc is presented in Table 2 and Fig. 5.

The addition of talcs 1.1 and 2.1 at a concentration of 1% completely eliminates the sticking of Avicel PH 102 tablets that is to say there is no detaching force measured. To differentiate these two fractions they were tested at a concentration of 0.5%.

Sticking appears after the single punch press has functioned for about 30 s, whatever the blend considered. Tablets of Avicel PH 102 alone strongly adhere to the

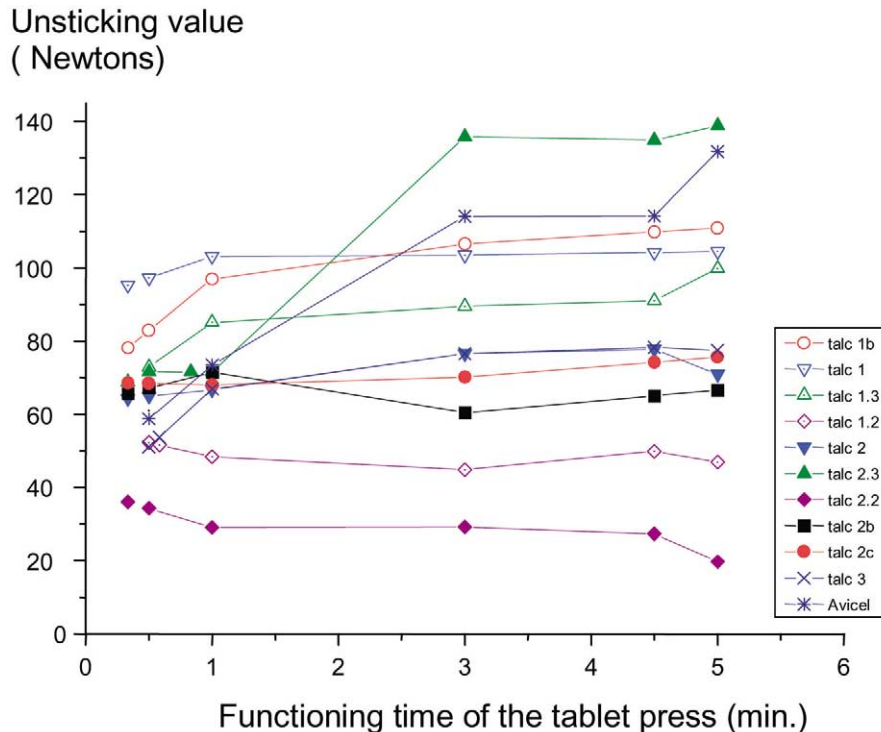


Fig. 5. Evolution in the sticking of tablets of Avicel PH 102 alone and associated with 1% of different talcs.

lower punch; the force necessary to eject the tablet is about 60 N at the beginning of sticking and gradually increases with time to reach about 132 N after 5 min.

When talc 2.3 is associated with Avicel PH 102, the detaching force follows the same progression but the values obtained are higher than those of Avicel PH 102 alone. An increase in talc percentage to 3% slightly decreases sticking; dmL is therefore the highest (15.15 μm) for this talc.

Blends of Avicel PH 102 associated with talcs 1, 1b and 1–3 behave similarly to the above: the detaching force increases especially in the first minute and is higher than that of Avicel PH 102 alone. Then the detaching force stabilises and remains close to that obtained with Avicel PH 102 alone. These talcs also present the highest dmL (12.16, 11.77 and 13.33 μm).

If the percentage of these talcs is increased to 3%, the detaching force is reduced by half but remains high (Table 3).

Another group of talcs made up of talcs 2, 2b, 2c and 3 is noteworthy. With these talcs, the detaching force of tablets is comparable to that obtained with Avicel PH 102 alone in the first minute and it only slightly evolves (from 60–65 to 70–75 N) whereas that of Avicel PH 102 alone is doubled after 5 min. The dmL values of these talcs are close to those of the previous talcs but their thickness is inferior. When these talcs are used at a concentration of 3%, sticking is suppressed (Table 3).

For the two blends containing talcs 1.2 and 2.2, the general tendency in the evolution of detaching force is a weak or moderate decrease in relation to the functioning time of the tablet press. Levels of the signal are notably lower than those obtained with other talcs used at a concentration of 3% and totally eliminate sticking (Table 3). These two talcs have dmL values of 4.5 and 4.8 μm .

With the two talcs 1.1 and 2.1 whose dml is about 2 μm , there is no sign of sticking when they are used at a concentration of 1%. To differentiate them, they were used at a concentration of 0.5%. In this case, talc 2.1 behaved like talcs 2, 2b, 2c, 3 that is to say it has a detaching force

which varies slightly with time. With talc 1.1, the detaching force regularly evolved to reach values close to those obtained with talc 2.1.

The results of talcs 1 and 1b are similar and indicate there is no interbatch variability. The comparison of the results of talcs 2, 2b, 2c demonstrates there is no intrabatch variability.

The efficacy of talc against sticking in these blends with Avicel PH 102 seems to be related to the mean basal surface diameter of particles. The influence of the mean thickness h is difficult to determine as other characteristics may intervene in the antisticking power of talc. It would seem that delamination is not an essential element as to the effectiveness of talc as an antisticking agent.

On the other hand, classification in different granulometric classes seems to be favourable.

4. Conclusion

The different talcs tested possess considerable variations in antisticking power towards Avicel PH 102. Some talcs fail to carry out their function entirely and even increase the adherence of Avicel PH 102 tablets to the lower punch of the tablet machine.

For blends Avicel PH 102–1% talc, the force necessary to detach tablets from the punch surface seems to vary according to the functioning time of the tablet machine. The greatest variations are observed between 0.5 and 3 min, in particular with the coarser talcs. Beyond 3 min, sticking is almost stabilised.

The suitability of talc for use can be assessed by a functionality assay. This requires an instrumented single punch press and feed shoe. However, it presents the drawback of being performed in the compression conditions of a single punch press, at a given speed and, like all functionality assays, poses the problem of upscaling. That is why it is necessary to confirm specifically through statistical methods, the possible relation(s), between anti-

Table 3
Unsticking forces of tablets containing Avicel PH 102 associated with 3% of different samples of talc, at different functioning times of the tablet press

Sample	Unsticking force (N) after 0.5 min	Unsticking force (N) after 1 min	Unsticking force (N) after 3 min	Unsticking force (N) after 4.5 min	Unsticking force (N) after 5 min
1	–	42.64 (± 0.91)	44.63 (± 1.44)	46.26 (± 1.1)	44.58 (± 0.5)
1.2	–	–	No sticking	–	–
1.3	–	49.7 (± 1.31)	49.22 (± 0.95)	49.3 (± 0.64)	48.9 (± 1.24)
1b	–	50.46 (± 1.8)	54.54 (± 2.7)	52.44 (± 2.81)	45.68 (± 2.07)
2	–	–	No sticking	–	–
2.2	–	–	No sticking	–	–
2.3	76.8 (± 1.2)	121.2 (± 2.0)	117.5 (± 2.25)	111.5 (± 0.21)	111.5 (± 0.24)
2b	–	–	No sticking	–	–
2c	–	–	No sticking	–	–
3	–	–	No sticking	–	–

Data expressed as mean \pm S.D.

sticking power and the basal dimension and thickness of particles.

In the same way, it is necessary to study other characteristics of talc like roughness to fully explain variations between talcs.

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