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Quantitative evaluation of tablet sticking by surface roughness measurement

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Summary

Effect of lubricant and manufacturing conditions on sticking were investigated by measuring quantitatively surface roughness (R_{rms}) of the tablet in two formulations. The R_{rms} values increased in proportion to the number of tablets produced (N). At a low concentration of lubricant, there was a good linear relationship between logarithm of R_{rms}/N and magnesium stearate percent. The slopes of the straight line, ks, were about 60 and 3 for the respective two formulations. The k value would become a parameter for the effectiveness of lubricant added against sticking. Because the R_{rms}/N deviated widely in Formulation I with high concentrations of lubricant, it is suggested that there are critical percents of magnesium stearate for sticking.

Introduction

One of the difficulties met in manufacturing tablets is surface damage caused by compressing. This is known as "sticking" which is a serious problem in large scale production. Therefore, pharmaceutical formulators have long sought a simple method of predicting sticking. Only a few studies have been undertaken on the quantitative measurement of sticking because of the lack of evaluation methods. Naito et al. (1969, 1971, 1977) have reported a method for determining the slipping force of tablet surface and passive pressure of lower punch involved during compression, and discussed tableting troubles such as capping and sticking. More recently, Schmidt et al. (1983) have developed a simple method to measure the force of removing the tablet from the punch-surface by using a new transducer. These studies, however, have dealt with the force between tablet and punch-surface, whereas sticking is the scratching of the tablet surface. Therefore, the measurement of surface roughness of tablet would be one of the most direct and suitable methods to evaluate this phenomenon.

The purpose of this paper was to quantitatively evaluate sticking on the basis of tablet surface roughness. Attention was focused upon the lubricant added, compression pressures, and mixing times, dependent on the surface roughness of the tablet.

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Materials and Methods

Materials

The materials used were as follows: Lactose 100 mesh (De Melkindustrie, Veghel, The Netherlands) and magnesium stearate (Taihei Chemical Co., Japan) were worked through a 500 μm sieve to break any large agglomerates present. Avicel PH101 (Asahikasei Co., Japan) was used without any treatment. Formulation I and the properties of the granules are shown in Table 1. Formulation II consisted of an active ingredient under investigation in our laboratories and its excipients.

Methods

All materials, in 1 kg batches, were mixed with magnesium stearate in varying proportions in the range 0–1.0 w/w%. The mixing was carried out in a 5 litre stainless steel can for an appropriate time with a Drum mixer (Nishida Doko Co., Japan) or in a polyethylene bag manually for 5 min and then tableted. An instrumented single punch tableting machine N-20 Type (Okada Seiko Co., Japan), incorporating a 10 mm diameter, 15 mm radius of curvature punch, and die set, was used. Prior to each compression, the die wall and punches were cleaned with water and ethanol and then dried to equalize experimental conditions. The tablet production rate was 15 tablets per minute and the tablets were formed by filling the die with 400 mg of the required powder. Each tablet was numbered in order of tableting. The maximum number of tablets was 2000.

Surface roughness measurement

Measurement of surface roughness was carried out with a surface analyzer (Surfcom 700B Tokyo Seimitsu Co., Japan). The tablet, with the upper surface up was attached to the stage, and a skid-filled pin was placed at the edge of the tablet and scanning was performed through the center of the tablet. The specifications used in the experimental studies were as follows: sensitivity 1000 and 50 μm full scale; scan speed 0.3 mm/s; cut-off value 0.8 mm; scan length 7 mm. These procedures were analogous to the method of Rowe (1978). The output voltage corresponding to the surface profile measured by Surfcom was fed into a spectrum analyzer (DATA 6000 Analogic Co., U.S.A.). The signal was divided into about 1000 points every 20 ms, and the $R_{rms} = \sqrt{1/L \times \int f(x)^2 dx}$ was calculated, where L is analytical length. In all cases investigated, unexpected high and/or low peaks, as shown in Fig. 1, were observed both at the beginning and the end of the profile and these were thought to be due to an insufficient cut-off because of the sharp fall at the circumference of the tablet. Therefore, these peaks should be eliminated from the analytical length, which is representative of surface roughness. The analytical length L was arbitrarily assigned by the operator on the basis of the profile. The R_{rms} values are larger than the corresponding R_a (arithmetic mean roughness) one by a factor of 1.1. The mean R_{rms} values were calculated from measurements of 5 or 10 tablets.

TABLE 1

Formulation and properties of granules for Formulation I

Lactose	$70 - X$%
Avicel PH101	30%
Magnesium stearate (St-Mg)	X%
	100%

$d_{50\%} = 120$ μm
Density = 1.55 g/cm^3

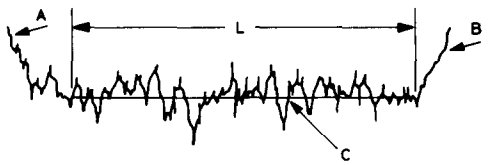

Fig. 1. Typical surface profile. L, analytical length; C, center line; A, B, unusually high peaks because of insufficient cut-off.

Results and Discussion

The typical effect of tableting quantity on the surface roughness (R_{rms}) is shown in Fig. 2. It was found that as the number of tablets increased, the R_{rms} increased in proportion to the tableting quantity (N). The slope of this line (R_{rms}/N) shows the average increase in surface roughness.

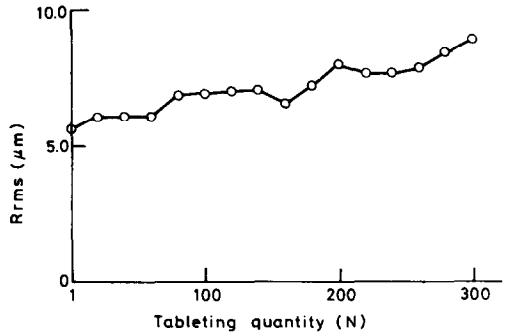

Fig. 2. R_{rms} as a function of tableting quantity for Formulation I.

That is, the R_{rms}/N would become a parameter of sticking tendency. The value of the R_{rms}/N calculated from the regression line of R_{rms} vs N at different concentrations of magnesium stearate, mixing time, and compression pressure for Formulation I are summarized in Table 2. Correlation coefficients are also shown to calibrate the linearity

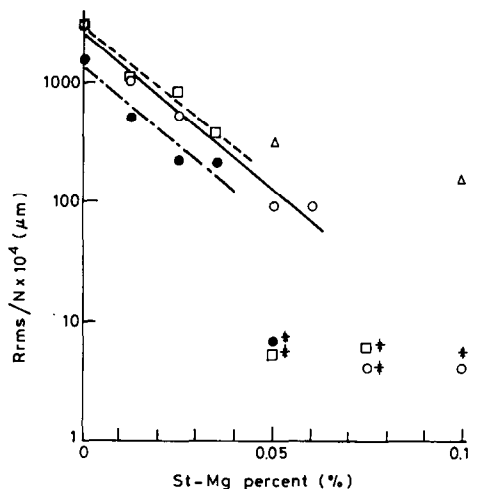

Fig. 3. Effect of magnesium stearate percent on average surface roughness (R_{rms}/N) for Formulation I. * = 2000 tablets. Compression pressure/mixing time: ○———○, 0.4 ton/10 min; □———□, 0.4 ton/30 min; ●———●, 0.8 ton/10 min. △———△, 0.4 ton/5 min manually; ▲———▲, 0.8 ton/5 min manually.

TABLE 2

Effect of magnesium stearate percent, mixing time, and compression pressure on average surface roughness (R_{rms}/N) for Formulation I

Expt. no.	St-Mg percent (%)	Mixing time (min)	Compression pressure (ton)	R_{rms}/N (μm)	Correlation coefficient
1	0	10	0.4	3240×10^{-4}	0.923067
2	0	10	0.8	1540×10^{-4}	0.820517
3	0.0125	10	0.4	1030×10^{-4}	0.961808
4	0.0125	10	0.8	507×10^{-4}	0.904820
5	0.025	10	0.4	529×10^{-4}	0.992775
6	0.025	10	0.8	237×10^{-4}	0.940942
7	0.035	10	0.8	227×10^{-4}	0.969023
8	0.050	10	0.4	92.6×10^{-4}	0.941315
9 *	0.050	10	0.8	7.42×10^{-4}	0.944941
10	0.060	10	0.4	93.5×10^{-4}	0.958407
11 *	0.075	10	0.4	4.04×10^{-4}	0.971538
12 *	0.100	10	0.4	4.20×10^{-4}	0.712394
13	0.0125	30	0.4	1055×10^{-4}	0.924567
14	0.025	30	0.4	864×10^{-4}	0.958512
15	0.035	30	0.4	390×10^{-4}	0.976113
16 *	0.050	30	0.4	5.32×10^{-4}	0.980748
17 *	0.075	30	0.4	6.34×10^{-4}	0.883110
18	0.050	manual **	0.4	320×10^{-4}	0.983684
19	0.050	manual **	0.8	282×10^{-4}	0.926840
20	0.100	manual **	0.4	155×10^{-4}	0.982866
21	0.100	manual **	0.8	134×10^{-4}	0.954045

* More than 2000 tablets.

** Mixed in a polyethylene bag manually for 5 min.

ties of slopes. Almost all the correlation coefficients investigated were more than 0.9, showing the R_{rms} increased linearly with increasing quantity of tablets. In other words, sticking proceeded in proportion to tableting. In some cases, tableting quantity was 2000 and noted by the asterisk, and this was the maximum amount of tablets produced. In other cases, the tablets produced were fewer, depending on the degree of surface roughness.

When the data in Table 2 were plotted with logarithm of the R_{rms}/N as ordinate and magnesium stearate percent as abscissa, Fig. 3 was obtained. As a whole, an increase in magnesium stearate causes a decrease in R_{rms}/N, whereas no significant differences in R_{rms}/N were seen between mixing times of 10 and 30 min. Large R_{rms}/N values, however, were observed for the manual mixing in the polyethylene bag. As a result, it was confirmed that the manual mixing could not prevent sticking. The R_{rms}/N values of a high compression pressure of 0.8 ton were smaller than those of the lower one, 0.4 ton, in all experimental conditions. "These findings are consistent with the general common sense in this field. That is, the longer the mixing time and the higher the compression pressure, the greater the lubricity and the less the surface roughness. This general correlation has widely been accepted in most product development laboratories."

As is evident from Fig. 3, there was a good linear correlation between the logarithm of R_{rms}/N and magnesium stearate percent over the range 0–0.06%. The slopes of 3 lines were almost the same, indicating that the increase of magnesium stearate percent affects R_{rms}/N to a similar extent. This relation can be expressed $\ln(R_{rms}/N) = -kx + \alpha$ where x is magnesium stearate percent, α is intercept, and k is slope. The values of k, as shown in Table 3, are about 60, respectively, under different mixing times and compression pressures. Interestingly, above 0.05% or 0.075%, the R_{rms}/N deviated widely from the straight line. This tendency was found in three conditions: mixing times and compression pressures of 10 min and 0.4 ton, 10 min and 0.8 ton, 30 min and 0.4 ton, respectively, and indicates that 0.05 and 0.075 are the critical percents of magnesium stearate for sticking. A similar phenomenon was also seen between the angle of repose and magnesium stearate percent (Hegde, 1985).

TABLE 3

Relationship between mixing time, compression pressure, and k for Formulation I

Mixing time (min)	Compression pressure (ton)	k	Correlation coefficient
10	0.4	60.6	0.985672
10	0.8	56.2	0.953624
30	0.4	55.6	0.967549

On the basis of the above considerations, the sticking tendency of Formulation II, containing an active ingredient, was studied. The results of R_{rms}/N, and compression pressure are summarized in Table 4. With regard to 0.4 ton pressure, higher than 0.9 correlation coefficients were obtained in most of the experiments. Contrastingly, for 0.8 ton pressure, correlation coefficients were about 0.7, showing that R_{rms} did not vary in proportion to the quantity of tablets produced. The curve R_{rms} vs tableting quantity, in the case of 0.8 ton, showed that at the beginning of tableting, the R_{rms} was exponentially increased, and thereafter constant. The reason for this behavior is not understood. The profile of R_{rms} vs tableting

TABLE 4

Effect of magnesium stearate percent, mixing time, and compression pressure on average surface roughness (R_{rms}/N) for Formulation II

Expt. no.	St-Mg percent (%)	Mixing time (min)	Compression pressure) (ton)	R_{rms}/N (μm)	Correlation coefficient
1	0	10	0.4	968×10^{-4}	0.933676
2	0	10	0.8	147×10^{-4}	0.743261
3	0.025	10	0.4	648×10^{-4}	0.990439
4	0.050	10	0.4	730×10^{-4}	0.949903
5	0.050	10	0.8	119×10^{-4}	0.740555
6	0.10	10	0.4	422×10^{-4}	0.993620
7	0.10	10	0.8	101×10^{-4}	0.844401
8	0.30	10	0.4	232×10^{-4}	0.969189
9	0.30	10	0.8	53.0×10^{-4}	0.735359
10	1.0	10	0.4	43.7×10^{-4}	0.805130

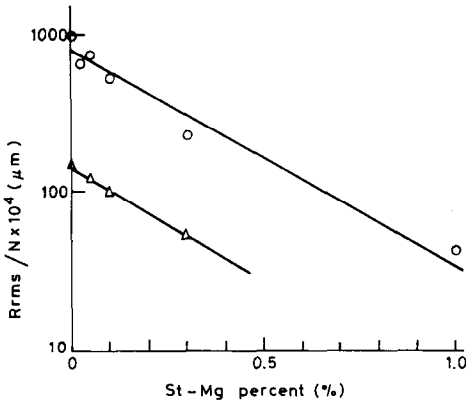

Fig. 4. Effect of magnesium stearate percent on average surface roughness (Rrms/N) for Formulation II. ○———○, 0.4 ton; △———△, 0.8 ton.

quantity may reflect the characteristic aspects of a formulation for sticking; work is in progress to clarify this point. The plot of logarithm of R_{rms}/N against magnesium stearate percent also resulted in a straight line (Fig. 4). The critical percents of magnesium stearate, which were observed in Fig. 3, were not found for Formulation II under the conditions investigated.

The effectiveness parameter for sticking, k, calculated from the regression line of logarithm of R_{rms}/N vs magnesium stearate percent are shown in Table 5. The values of k were 2.90 and 3.34 for 0.4 ton and 0.8 ton, respectively. The values of k in Formulation II were less than those in Formulation I by a factor of 20, confirming that the magnesium stearate in the former had less effect in terms of sticking than in the latter. Thus k would become a parameter for the effectiveness of lubricant added against sticking.

TABLE 5

Relationship between compression pressure and k for Formulation II

Mixing time (min)	Compression pressure (ton)	k	Correlation coefficient
10	0.4	2.90	0.980379
10	0.8	3.34	0.998875

In addition, upper punch, lower punch and ejection forces, which are closely correlated with lubrication of granules (Lewis et al., 1965a and b; Matsuda et al., 1976; Holzer et al., 1977), were also investigated along with tableting quantity. However, no significant relationship between these forces and sticking was observed.

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