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Equation relating to the Higuchi R-ratio of lubrication

Hatem Fessi [1], J.-P. Marty, [1], F. Puisieux [1] and J.T. Carstensen [2]

[1] *Faculté de Pharmacie, Université de Paris-Sud, Laboratoire Galénique, Châtenay-Malabry 92290 (France) and*
[2] *School of Pharmacy, University of Wisconsin, Madison, WI 53706 (U.S.A.)*

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Summary

The Higuchi R-ratio of lubrication relates the ratio of upper punch force (F) or pressure (P) to that sensed by the lower punch (F′ or P′) to the state of lubrication of the mass being compressed. The ratio R = F′/F or P′/P is denoted the lubrication index. It is shown in the article to follow that F′ is linear with F, but that the intersect is not zero. The logical approach, in cases where this holds, is therefore to measure the lower punch pressure (P_1' and P_2') for two upper punch pressures (P_1 and P_2) and calculate the values of a and b in the relation $P' = a \cdot P + b$. The index is then $R' = (P' - b)/P$.

Introduction

In tablet compression a force F or a pressure P is applied to an upper punch (or to both punches). A force F′ or a pressure P′ is sensed by the lower punch. The ratio:

$$F'/F = P'/P = R \quad (1)$$

is the coefficient of lubrication introduced in the 1950's and 1960's (Nelson et al., 1955; Shotton and Ganderton, 1960; Lewis and Train, 1965). It depends on a multitude of factors such as size and shape of particles (Shotton and Ganderton, 1960; Lewis and Shotton, 1965; Hersey et al., 1967; Rees and Shotton, 1969) and interparticle contact (Merle, 1977). In recent years (Marshall, 1977; Guyot et al., 1977), there has been a tendency to replace the ratio R with other ratios, primarily from a point of view of sensitivity.

The relation in Eqn. 1 is semiempirical. The argument is forwarded that a part of the pressure (P − P′) is "lost" to the die wall and other "walls" (surfaces of particles) and the smaller this is the better the state of lubrication.

It is the aim of this article to test Eqn. 1 and evaluate whether it is correct or not. If correct, the refinements may be in order, but if not correct, then it should be replaced by an applicable expression.

Materials and Methods

Tablets were made containing 20% dihenhydramine hydrochloride. They contained one of the polymers listed in Table 1, in a concentration of 50% unless otherwise stated in the table. They

Correspondence: M.F. Puisieux, Faculté de Pharmacie, Université de Paris-Sud, Laboratoire Galénique, Châtenay-Malabry 92290, France.

TABLE 1
LEAST-SQUARES PARAMETER VALUES OF LINES ACCORDING TO EQN. 2

Formula	Correlation coefficient	a *	b	95% confidence limits on b (mean)
PVC	0.9999	0.91	−10.9	7.2
PVC + Excipients	0.9997	0.83	2.0	12.8
PVA	0.996	0.80	−10.8	44
PVA + Excipients	0.9996	0.84	−23.4	20
PVA/PVC	0.997	0.86	−32	28
PVA/PVC (50%) **	0.9994	0.86	−16	13
PVA/PVC (60%) **	0.998	0.92	−17	33
PVA/PVC (70%) **	0.999	0.84	5.4	17
PVA/PVC, 50% + lubricants **	0.999	0.90	−16	28
PVA/PVC, 50% + lubricants (+CH_2Cl_2) †	0.999	1.00	−33	(n = 3) ***
PVA/PVC, 60% + lubricants (+CH_2Cl_2) †	0.999	0.98	−2	19
PVA/PVC, 70% + lubricants (+CH_2Cl_2) †	0.993	0.95	−2	20

* 95% confidence limits on a are all about 0.01.
** Only the formulae marked "lubricants" contain talc and magnesium stearate.
*** Three points only. Insufficient for proper interval calculation.
† Only formulae marked with "†" have been granulated with methylene chloride; all others have been granulated with isopropanol.

contained 1.5% polyvinylpyrrolidone and a q.s. quantity of tricalcium phosphate. Three data sets were done with 3% lubricant (1% magnesium stearate, 2% talc). The polymers referred to are polyvinyl acetate (PVA) [1], polyvinyl chloride (PVC) [2], and a copolymer (PVA/PVC) [3]. Their particles sizes are respectively: 40–60 mesh (250–400 μm, as determined microscopically), < 5 μm (as determined microscopically, and as received from the supplier), and 100–200 mesh (80–125 μm, as determined microscopically).

The powders were mixed and granulated with 50% v/w of isopropanol or methylene chloride (as noted in Table 1). They were dried for 20 min at 60°C in a small fluid bed drier [4]. They were passed through an oscillating granulator equipped with a 1 mm screen. The material was then screened and the fraction of size 0.2–0.8 mm was used for compression. The compression took place on an instrumented single punch tablet machine [5] (Touré, 1979) operating at a speed so that the cycle lasted 1/60 s. 12 mm, flat-faced punches were used and 0.5 g of powder was compressed. Compressions were carried out at accurately recorded upper punch pressures of approximately 100–600 MPa (about the same pressure range used by Hölzer and Sjögren, 1977, 1978) and the upper (P) and lower (P′) punch pressures were measured.

[1] Rhodopas H, Rhone-Poullenc, France.
[2] Pevikon, 637P, Seppic, Paris, France.
[3] 50PVA/85PVC, Solvic, Solvay, France.
[4] Glatt, Basel, Switzerland.
[5] Single punch machine, Frogerais type AO, Societe Edmond Frogerais, Vitry-sur-Seine, France.

Results and Discussion

The Higuchi equation may be written as:

$$P' = a \cdot P \qquad (2)$$

It is noted that it does not contain a term relating to tablet thickness. Hölzer and Sjögren (1977) suggested that deviations of data from Eqn. 2 might be expressed by:

$$P - P' = a_1 + b_1 P' \quad \text{or} \quad P' = (1 - b_1)P + a_1 \qquad (3)$$

regardless of tablet dimensions and (Hölzer and Sjögren, 1978) later suggested a relation of the type:

$$\ln P = a_2 - b_2' \cdot x + \ln P' \quad (4)$$

where x is the ratio h/D of thickness (h) to diameter (D) of the punch. For one given diameter of punch, this becomes:

$$\ln P = a_2 - b_2 \cdot h + \ln P' \quad (5)$$

where $b_2 = b_2'/D$. Since P and P′ are close in value, the approximation $\ln(1 - c) = -c$, where c is small, will transform Eqn. 5 into:

$$P' = (1 + a_2 + b_2 \cdot h)P \quad (6)$$

If h is a function of P (constant tablet weight), then a plot according to Eqn. 6 should not be linear, i.e. should not follow Eqn. 3; and if weight compensation were made in a study, so that h were always the same, then there should be no non-zero intercept, i.e. the Higuchi equation (Eqn. 2) should apply. But the slope would be in excess of unity.

A different functionality has been attempted here, and all the data show that Eqn. 7 below is rather well adhered to, correlation coefficients, as shown in Table 2, being very close to unit:

$$P' = a_3 + b_3 \cdot P + c_3 \cdot y \quad (7)$$

y is here the distance between upper punch and lower punch at deepest penetration (measured via displacement measurements). It is related to, but not identical to the thickness of the tablet after ejection, and y, essentially, should be a more relevant parameter than h. The least-squares fit values are shown in Table 2.

One difference between the set-up used by Hölzer and Sjögren (1977, 1978) and the one reported here is that of punch speed, which in this study is considerably faster. The fact that Hölzer and Sjögren found no thickness effect in one study (1977) and for other systems (1978) found such an effect is quite plausible. The thickness effect is generally less drastic than to be expected, and if all the data in the study reported here are presented according to the general equation:

$$P' = a \cdot P + b \quad (8)$$

then plots as shown in Fig. 1 result. Least-squares fit values for the parameters a and b are shown in Table 1. It is noted that in many cases the inter-

TABLE 2
LEAST-SQUARES PARAMETER VALUES OF LINES ACCORDING TO EQN. 7

Formula	Correlation coefficient	a_3	b_3	c_3
PVC	0.999	−67	−0.90	−6.66
PVC + Excipients	0.999	−20.3	−0.83	−3.86
PVA	0.99	149.6	−0.95	−70.1
PVA + Excipients	0.998	−164.7	−0.79	30.9
PVA/PVC	0.999	123.15	−0.89	−26.9
PVA/PVC (50%) **	0.999	−38.7	−0.85	3.57
PVA/PVC (60%) **	0.999	−90	−0.93	9.29
PVA/PVC (70%) **	0.998	−228.14	−0.82	26.9
PVA/PVC, 50% + lubricants **	0.999	198.3	−0.96	−46
PVA/PVC, 50% + lubricants (+CH_2Cl_2) †	0.999	−137.2	−0.98	21.5
PVA/PVC, 60% + lubricants (+CH_2Cl_2) †	0.999	−81.7	−0.99	9.6
PVA/PVC, 70% + lubricants (+Ch_2Cl_2) †	0.999	−499.3	−0.87	57.7

** Only the formulae marked "lubricants" contain talc and magnesium stearate.
*** Three points only. Insufficient for proper interval calculation.
† Only formulae marked with "†" have been granulated with methylene chloride; all others have been granulated with isopropanol.

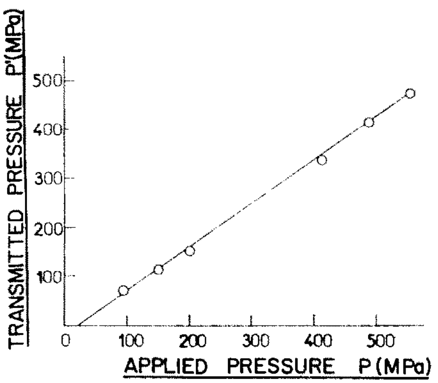

Fig. 1. Force transmitted to lower punch (P'(MPa)) as a function of force applied to upper punch (P(MPa)). Formulation is PVA/PVC (50%) + Excipients.

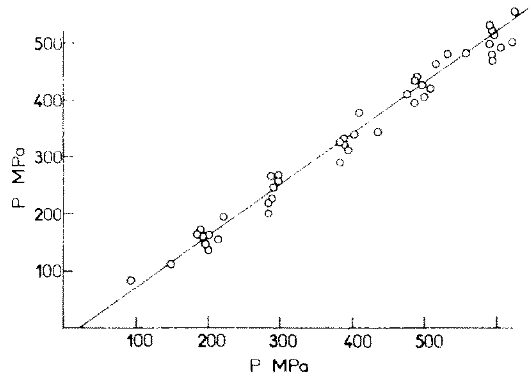

Fig. 2. P' as a function of P. Composite graph for all the non-lubricated formulae (the top 8 formulae of Table 1).

cepts vary significantly ($P = 0.95$) from zero. It is also noted that the slopes for the unlubricated systems are all fairly much alike, varying from 0.84 to 0.92. This is not surprising and it is probably particular to the systems tested, since the polymers might well behave in a very similar fashion under compression. The slopes are not claimed to be general, but only alike for the systems tested here. This proximity of values allows graphical presentation of all the data on one graph. This has been done in Fig. 2, and it is seen that the linearity with non-zero intercept is present. Furthermore, the intercepts are negative. It is seen, hence, that even though there is some dependence on thickness parameter, omitting this parameter is not serious, and that Eqn. 8 is a good approximation in general.

The question arises why the intercepts should be negative and a plausible explanation is that a certain amount of pressure is necessary to accomplish rearrangement of particles at the initial phase of compression. This amount of pressure would be $-a/b$ (> 0). Beyond this point, the Higuchi relation (Higuchi, 1954) applies so that rationally $R = a$, i.e.

$$R = (P' - b)/P \tag{9}$$

The three lubricated formulae all have larger slopes (close to unity). This is in accordance with the concept that the better the lubrication the better the force transmission (Higuchi, 1954). It is also to be noted (Table 1) that in this case the intercepts cannot be shown to differ from zero, and if they indeed are not different from zero, then this would imply that particle rearrangement is more rapid with lubrication, a notion which is quite logical.

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