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Die wall pressure measurement for evaluation of compaction property of pharmaceutical materials

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Abstract

The aim of this study was to evaluate the compaction property of several pharmaceutical materials by measuring the die wall pressure. The profile of die wall force during tabletting process was measured with the compaction process analyzer (TabAll). Several compaction parameters such as maximum die wall pressure (MDP), residual die wall pressure (RDP) and pressure transmission ratio (PTR) from upper punch to lower punch were calculated. The ejection pressure (EP) of tablet compacted was also measured as a parameter for sticking property of the compacts. The profile of die wall force observed was classified to the typical two types, a small type and a large one. Partly pre-gelatinized starch (PCS), cornstarch and low substituted hydroxypropylcellulose (L-HPC) were the small type, while crystalline lactose, ascorbic acid and potassium chloride were the large type. The die wall force of crystalline lactose remarkably increased at the ejection of tablet and then capping was observed. RDP value of PCS, cornstarch, L-HPC was smaller than that of crystalline lactose, ascorbic acid, potassium chloride. As the higher pressure transmission ratio from upper punch to lower punch means a good compressing property of the powder, we proposed that RDP/MDP is a useful parameter for evaluating the compaction property of powders. Although potassium chloride which is strongly plastic deformable powder showed the highest RDP value among the powders tested, the RDP/MDP value was lower than that of crystalline lactose or ascorbic acid and the tensile strength of resultant tablet of potassium chloride was much higher than these powders.
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Keywords: Residual die wall pressure; Compaction parameter; Capping; Plastic deformation

1. Introduction

There are various types of dosage form such as tablet, granule and capsule in oral dosage form. Above all, tablet is the most useful dosage form for its simplicity and portability to take from patient's point of view. In addition, tablet is also a desirable dosage form for its cost performance and productivity in point of manufacturing process (Swarbick and Boyan, 2002). It is well known that the quality of tablets is influenced by the following two factors. One is tabletting condition such as compaction pressure (Nyström et al., 1993), compaction speed (Roberts and Rowe, 1985) and continuous process (Chulia et al., 1994). Another is compaction property of pharmaceutical materials such as elastic, plastic deformation and fragmentation (Eriksson and Alderborn, 1995; Adolfsson et al., 1999).

The compaction property of powders has been evaluated with various parameters such as yield pressure

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measured by Heckel analysis (Humbert-Droz et al., 1983), stress relaxation (Van der voort maarschalk et al., 1997) and elastic recovery (Picker, 2001). It is possible to estimate an inconvenient property in tabletting such as capping by using these parameters, because elasticity of compacted powder is one of the main factors for capping. The measurement of die wall pressure may be also an useful method to evaluate the compaction property of powders because residual die wall pressure (RDP) reflects plastic property of compacted powder in die (Carless et al., 1974). Some papers have reported that the residual die wall pressure is one of the main factors for capping like elastic recovery during decompression (Carless et al., 1974) as well as the stress concentration due to die wall pressure at decompression (Hiestand et al., 1977) and the entrapped air in tablet during compaction process (Tanino et al., 1995). Sugimori reported that capping occurs when tablet is cracked by residual die wall pressure at the final stage of the decompression process (Sugimori and Mori, 1989; Sugimori et al., 1989). However, this study was carried out on static conditions and there are few papers reporting the relationship between capping and residual die wall pressure measured on dynamic conditions.

In the present paper, we evaluated compaction property of various pharmaceutical powders under dynamic compressing conditions by using a single punch machine equipped with several force analysis parts. Based on the change in the die wall pressure during compression, their compacting properties were characterized.

2. Materials and methods

2.1. Materials

Partly pregeratinized starch (PCS, Asahi Chemical Co., Japan), cornstarch (Nihonshokuhinkako Co., Japan), low substituted hydroxypropylcellulose (LH-21, Shinetsu Chemical Co., Japan), crystalline lactose (Pharmatose200M, DMV, Netherlands) were used as model powder for compaction. Ascorbic acid (Takeda Chemical Industries Co., Japan) having sticking property and potassium chloride (Yamazen Pharmaceutical Co., Japan) showing strong plastic deformation were also used. Particle size of the materials is shown in Table 1.

Table 1
Particle size of various types of excipients and drugs

Sample	Particle size (μm)		
	D_{16}	D_{50}	D_{84}
PCS	22.3 ± 1.7	53.4 ± 0.5	95.4 ± 6.7
Cornstarch	9.8 ± 0.3	15.0 ± 0.7	21.4 ± 1.5
L-HPC	17.2 ± 0.1	40.5 ± 1.3	95.4 ± 6.7
Crystalline lactose	8.8 ± 0.3	25.6 ± 1.7	59.7 ± 11.6
Ascorbic acid	9.1 ± 0.6	25.5 ± 1.3	87.5 ± 4.7
Potassium chloride	404.6 ± 67.8	619.8 ± 74.8	826.7 ± 40.7

The data are the average values of four runs.

2.2. Tabletting

Sample powder of 200 mg was compressed in tabletting process analyzer (TabAll; Okadaseiko Co., Japan) with flat faced punches with diameter of 8 mm. For compressing potassium chloride, 300 mg of powder was used to obtain the similar thickness of resultant tablet. The applied compression pressure was 100 MPa otherwise stated. The compression speed was set up at 10 tablets per minute (10 spm) in all samples. Tensile strength of tablet was measured by a particle hardness tester (GRANO; Okadaseiko Co., Japan). The average value was taken with four runs. Porosity of tablet was calculated with dimension of tablet and true density of powder measured by air comparison pycnometer (Model 930; Beckman-Toshiba, Ltd., Japan).

2.3. Calculation of compaction parameters

Various forces measured using TabAll is schematically shown in Fig. 1. The force profiles and punch displacements were recorded by use of software (DAATSU II; Okadaseiko Co., Japan). Maximum die wall pressure (MDP) and residual die wall pressure (RDP) were calculated by dividing each force by the area of tablet contacted with the die wall at each process. Pressure transmission ratio (PTR) was calculated by dividing the lower punch pressure by the upper punch pressure when the upper pressure reached the maximum value. Residual die wall pressure is defined as described in the following results and discussions. In measuring ejection pressure (EP) of tablet, the maximum value was directly observed on control unit of TabAll. The mean of four determinations was taken as the average value.

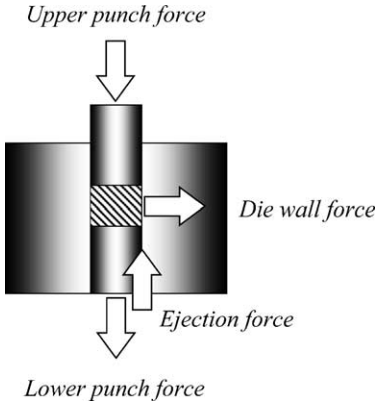

Fig. 1. Scheme of various forces measured by TabAll.

3. Results and discussions

3.1. Profile of die wall force

The profiles of force applied to the die wall as well as upper and lower punches during tabletting process were measured for potassium chloride, PCS, cornstarch, L-HPC, crystalline lactose and ascorbic acid. The profiles and punch displacements in tabletting potassium chloride are shown in Fig. 2 as a typical example. The profiles and punch displacements are corresponded to each tabletting process: compression, decompression, and ejection. The die wall force reached a maximum value just after the upper and lower punch showed maximum values, and showed a constant residual value after upper punch and lower punch forces became zero. The residual die wall force was observed till the ejection process started. When the ejection process started, the die wall force was increased to record a peak in the force profile.

Based on the typical profile of die wall force, the residual die wall force was calculated by taking the average of values in the constant region shown in Fig. 2. When the upper punch force reached zero, the difference of displacement between upper and lower punch was measured to calculate the area of tablet contacted with the die wall. The calculated residual die wall force was converted to the die wall pressure by dividing it by this area.

The die wall force profiles measured for various types of pharmaceutical materials are shown in Fig. 3. The residual die wall force of PCS is the smallest among the four sample powders. It has been reported that the pre-gelatinized starch (PCS) has a large relaxation behavior during decompression process (van Veen et al., 2000). In general, the large relaxation

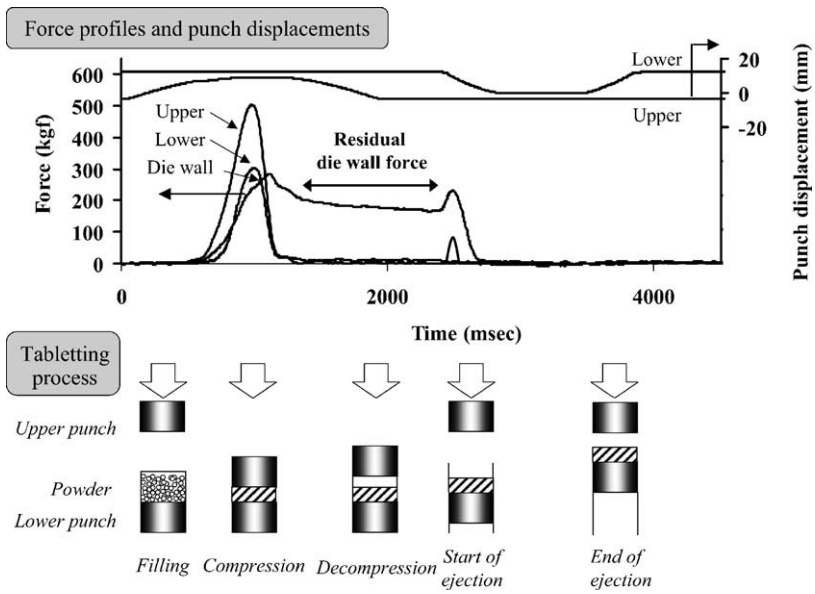

Fig. 2. Force profiles and punch displacements during tabletting process.

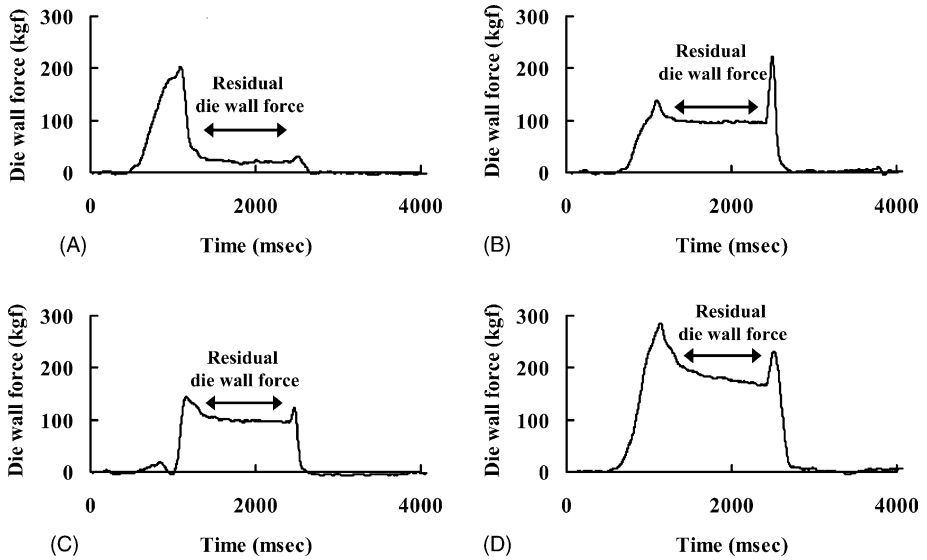

Fig. 3. Profiles of die wall force of various types of excipients and drugs during tabletting process: (A) PCS; (B) crystalline lactose; (C) ascorbic acid; (D) potassium chloride.

behavior is closely related to the elastic property of powders. Cornstarch and L-HPC having a good elastic property showed almost the same die wall force profile as that of PCS (not shown in Fig. 3). Potassium chloride which has extensively plastic property (Eriksson and Alderborn, 1995; Adolfsson et al., 1999) showed a large residual die wall force. The value was the largest in all materials tested. These results confirmed that the residual die wall force clearly related to the degree of plastic or elastic deformation of powders.

Crystalline lactose and ascorbic acid showed the medium values of the residual die wall force. It was also characteristic that crystalline lactose having considerable fragmentation property (Eriksson and Alderborn, 1995; Adolfsson et al., 1999) showed a remarkably large peak at ejection process and capping occurred. The value was higher than the peak at maximum die wall force in compressing process. This high die wall force at ejection process is a sign of adhesive property of the powders to the die. In fact, adhesion of powder on the die wall was observed after the ejection process. The strong friction property of crystalline lactose may be responsible for the adhesion to die wall. As the strong friction is one of the factors of capping of tablet, the reduction of this die wall force at ejection process should be effective in improving the tabletting process. Ascorbic acid has sticking and capping tendency (Kawaguchi et al., 2000) also showed adhesion of powder on the die wall after ejection of tablet. However, the high die wall force at ejection process was not observed. This may be explained by lower adhesive property of ascorbic acid than crystalline lactose.

3.2. Compaction parameters of various pharmaceutical powders

Table 2 shows the compaction parameters of various materials. The maximum die wall pressure is the value observed in the compressing process. This value may indicate the pressure transmission because the powder bed was compressed with the same pressure by the upper punch. As the pressure transmission is usually evaluated by comparing the pressures of upper and lower punches, this value was also listed in the table. Ejection pressure was measured with the lower punch pressure.

RDP values for PCS, cornstarch and L-HPC are almost the same and small. These powders showed the smaller EP. The smaller EP values may be correlated with their good compacting property. This result confirmed that RDP value is useful to evaluate the compactibility of powders. The RDP and EP values measured for crystalline lactose, ascorbic acid and potassium chloride were much higher.

Table 2
Compaction parameters of various types of excipients and drugs

Sample	RDP (MPa)	MDP (MPa)	RDP/MDP (%)	PTR (%)	EP (MPa)
PCS	3.9 ± 0.4	26.4 ± 2.2	14.9 ± 0.9	66.7 ± 3.7	0.1 ± 0.0
Cornstarch	3.2 ± 0.6	17.8 ± 1.3	18.3 ± 4.5	58.2 ± 3.3	0.2 ± 0.1
L-HPC	3.4 ± 0.4	21.2 ± 1.2	16.0 ± 2.8	67.1 ± 3.3	0.3 ± 0.2
Crystalline lactose	11.7 ± 1.0	18.7 ± 0.9	62.8 ± 8.2	57.0 ± 1.0	8.9 ± 1.1
Ascorbic acid	16.6 ± 1.6	24.9 ± 1.0	66.4 ± 5.5	57.6 ± 0.4	12.4 ± 1.3
Potassium chloride	21.8 ± 1.6	37.0 ± 2.3	59.1 ± 7.7	65.6 ± 3.5	5.7 ± 0.6

The data are the average values of four runs. RDP, residual die wall pressure; MDP, maximum die wall pressure; PTR, pressure transmission ratio; EP, ejection pressure of tablet.

Maximum die wall pressure measured in die wall profile during compression is also a useful parameter. It may represent the pressure transmission from upper punch to die wall. We examined the suitability of a parameter RDP/MDP as well as RDP value itself. As the lower RDP and the higher MDP values are preferable in tabletting, the tabletting property may be more precisely evaluated by use of this parameter. The compaction property of ascorbic acid is poor compared to the others. Actually, EP of ascorbic acid was the highest among the sample powders tested and a serious sticking tendency was observed. RDP/MDP value for ascorbic acid was the highest, which reflected the poor compactablity. The potassium chloride showed the highest RDP in all powders tested. This highest RDP may be caused by strong plastic deformation property. The elastic deformable property could be detected by the high MDP value. Resultantly, RDP/MDP value for potassium chloride was lower than that of ascorbic acid.

3.3. Effect of compaction pressure on the profiles of die wall force and compaction parameters

Fig. 4 shows the profiles of die wall force of PCS, ascorbic acid and potassium chloride at various compression pressures. Table 3 shows the compaction parameters of these powders at each compression

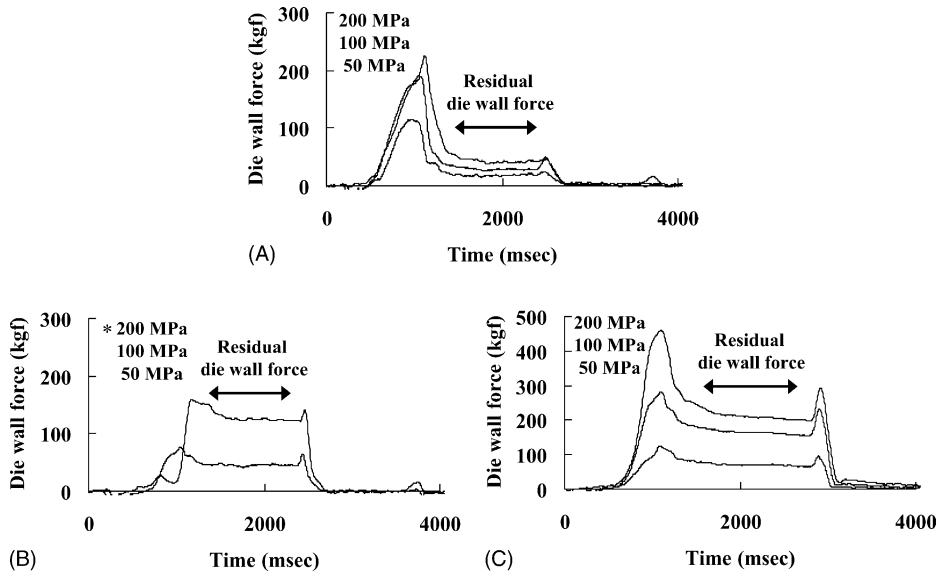

Fig. 4. Effect of compression pressure on the profiles of die wall force of PCS, ascorbic acid and potassium chloride during tabletting process: * tabletting was impossible because of higher ejection pressure at 200 MPa. (A) PCS; (B) ascorbic acid; (C) potassium chloride.

Table 3
Effect of compression pressure on the compaction parameters of PCS, ascorbic acid and potassium chloride

Sample	Compression pressure (MPa)	RDP (MPa)	MDP (MPa)	RDP/MDP (%)	PTR (%)	EP (MPa)
PCS	50	1.5 ± 0.3	13.0 ± 1.0	11.7 ± 1.8	63.0 ± 5.0	0.1 ± 0.0
	100	3.9 ± 0.4	26.4 ± 2.2	14.9 ± 0.9	66.7 ± 3.7	0.1 ± 0.0
	200	5.8 ± 0.4	41.3 ± 0.8	14.0 ± 1.3	63.1 ± 1.0	0.2 ± 0.2
Ascorbic acid	50	5.9 ± 0.3	10.8 ± 0.8	55.3 ± 5.6	37.3 ± 5.8	0.2 ± 0.1
	100	16.6 ± 1.6	24.9 ± 1.0	66.4 ± 5.5	57.6 ± 5.8	12.4 ± 1.3
	200[a]	–	–	–	–	–
Potassium chloride	50	8.8 ± 0.0	15.6 ± 0.6	56.3 ± 2.1	58.7 ± 1.3	2.8 ± 0.0
	100	21.8 ± 1.6	37.0 ± 2.3	59.1 ± 7.7	65.6 ± 3.5	5.7 ± 0.6
	200	25.3 ± 0.9	64.4 ± 3.9	39.4 ± 1.6	75.2 ± 0.5	13.6 ± 0.3

The data are the average values of four runs. RDP, residual die wall pressure; MDP, maximum die wall pressure; PTR, pressure transmission ratio; EP, ejection pressure of tablet.
[a] Tabletting was impossible because of higher ejection pressure.

pressure. Fig. 5 summarizes the data shown in Table 3. RDP increased with increasing the compression pressure in all materials, while RDP/MDP is almost constant regardless of compression pressure. This also implies the usefulness of RDP/MDP as a parameter for compaction.

In case of potassium chloride, RDP/MDP at 200 MPa is a little bit smaller than that at 50 or 100 MPa. A possible explanation for the decreased RDP/MDP value with increasing compression pressure is the appeared elasticity of powder. Although potassium chloride is strongly plastic material, the elastic recovery may occur in decompressing at high pressure. RDP may be reduced by this elastic property. PTR of PCS is almost constant regardless of compression pressure, while that of ascorbic acid and potassium chloride increases with increasing compression pressure. The constant PTR

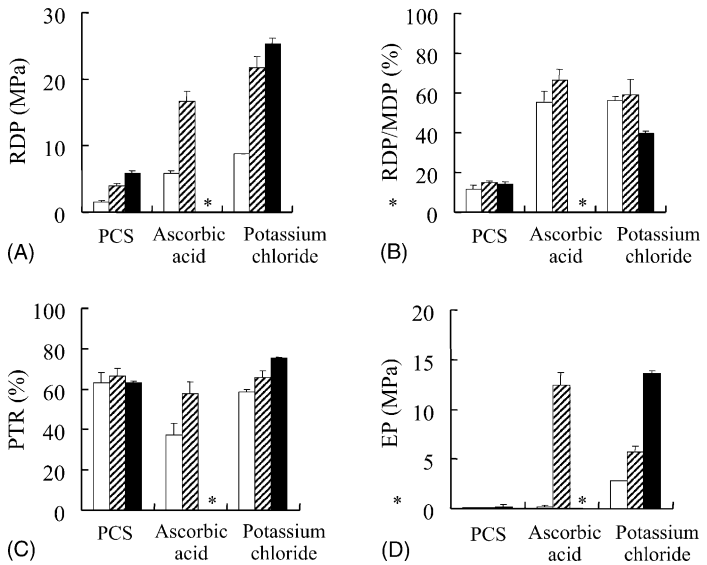

Fig. 5. Effect of compression pressure on the compaction parameters of PCS, ascorbic acid and potassium chloride: 50 MPa (□), 100 MPa (▨), 200 MPa (■). The data are the average values of four runs. * Tabletting was impossible because of higher ejection pressure at 200 MPa. (A) RDP; (B) RDP/MDP; (C) PTR; (D) EP.

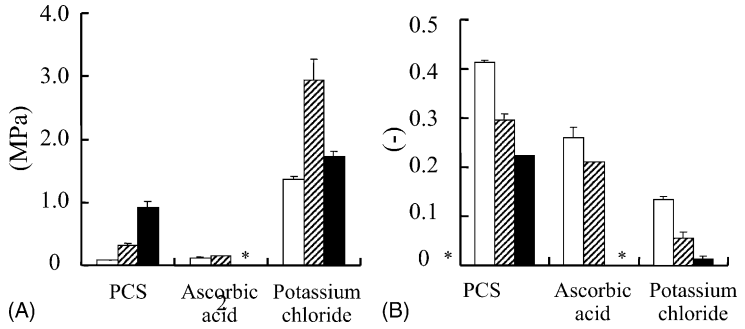

Fig. 6. Effect of compression pressure on the tensile strength and porosity of tablet prepared with PCS, ascorbic acid and potassium chloride: 50 MPa (□), 100 MPa (▨), 200 MPa (■). The data are the average values of four runs. * Tabletting was impossible because of higher ejection pressure at 200 MPa. (A) Tensile strength and (B) porosity.

of PCS may also be attributed to its strong elastic property.

If the friction coefficient is same regardless of compression pressure, EP depends on the RDP at each compression pressure. The higher RDP leads to increasing EP. EP was very small when RDP was less than 5 MPa. The small EP values of PCS may be attributed to its elastic property of the particle. EP of potassium chloride depended on the compression pressure. This tendency well reflected the observed RDP values. It is presumed that plastic particles such as potassium chloride deformed with increasing compression pressure. This may lead to increasing contact area at the die wall, which increase the resultant RDP and EP. On the other hands, the high EP of ascorbic acid can be explained by its sticky property. As ascorbic acid particles are less compactable, a hard compact was not obtained at lower compressing pressure such as 50 MPa. Therefore, ascorbic acid showed the low EP although its RDP value was high.

Tensile strength and porosity of tablet on each compression pressure were shown in Fig. 6. PCS shows a typical tendency, where tensile strength increased and porosity decreased with increasing the compression pressure. The increased compression pressure causes the increase in contact area of particles. Ascorbic acid has very small tensile strength because bonding force of ascorbic acid particles is weak. Potassium chloride has a large tensile strength at any compression pressure. However, tensile strength did not increase with increasing the compression pressure, although its porosity decreased with increasing compression pressure. It may be attributed to its large particle size. The higher compression pressure may cause dislocation between particles producing a crack to weaken the particle bonding in tablet.

4. Conclusions

We established an evaluation method for compaction property of pharmaceutical materials by measuring the die wall force in the process. It was also found that the profile of the die wall force in tabletting was closely related to the tabletting troubles such as capping and sticking. The profile of die wall force reflects the plasticity and friction property of pharmaceutical materials. In case of crystalline lactose, a large residual die wall pressure and the sharp peak observed in the profile of die wall force at ejection process was well correlated to its capping tendency. Maximum die wall pressure was also found to be a useful parameter for compaction property of powder as well as pressure transmission ratio. Both of RDP and MDP can be calculated by measuring the die wall force profile in tabletting. We propose the use of a parameter of RDP/MDP instead of RDP as a convenient parameter in comparing the compaction property of pharmaceutical materials regardless of compression pressure.

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