

On the Links Between Elastic Constants and Effective Elastic Behavior of Pharmaceutical Compacts: Importance of Poisson's Ratio and Use of Bulk Modulus

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ABSTRACT: The elastic properties of pharmaceutical powders and compacts are of great interest to understand the complex phenomena that occur during and after the tableting process. The elastic recovery after compression is known to be linked with adverse phenomena such as capping or delamination of tablets. Classically, the elastic behavior is modeled using linear elasticity and is characterized using only Young's modulus (E), often by using a value extrapolated at zero porosity. In this work, four pharmaceutical products were studied. The elastic behavior of compacts obtained using a large range of applied pressure was characterized. First, it was found more suitable to use apparent elastic moduli than extrapolations at zero porosity. Then, the results indicate that there was not always a good correlation between the values of Young's modulus and the actual elastic recovery of the compacts. Poisson's ratio (ν), which differs from one product to another and is porosity-dependent, must be taken into account. Finally, the bulk modulus (K), which combines E and ν , was shown to be well correlated with the elastic recovery of the compacts and can be considered as a relevant parameter to characterize the elastic behavior of pharmaceutical compacts. © 2013 Wiley Periodicals, Inc. and the American Pharmacists Association *J Pharm Sci*

Keywords: mechanical properties; compression; tableting; tablet; powder technology

INTRODUCTION

The elastic properties of pharmaceutical powders and compacts are of great interest to understand the complex phenomena that occur during the tableting process. Adverse phenomena like capping were linked to the elastic properties of the compact that can be evidenced during the unloading part of compaction cycle and the ejection.^{1–3} The elastic properties are also involved in the problems of delamination of multilayers compacts.^{4,5}

To model the elastic behavior of the compacts, linear elasticity based on Hook's law has been used for a long time in the pharmaceutical field.^{6,7} Young's modulus (E) was mainly considered and was extensively studied in the literature for a great number of pharmaceutical products.^{8–11} On the contrary, only few studies were focused on Poisson's ratio (ν),^{12–14} certainly because of the difficulty to perform a precise measurement of its value. Thus, in most of the cases, Poisson's ratio is not taken into account or considered as constant and equal to 0.3.

One of the specificity of a pharmaceutical compact is to be a porous medium with porosity depending on the pressure applied to produce it. Mechanical properties such as elasticity are porosity dependent, which means that the elastic constants measured on the compacts must be considered as apparent parameters, that is, not only dependent on the product but also on the porosity of the compact. The characterization of the elastic properties of a pharmaceutical product must thus be performed as a function of the density. To overcome this problem

and obtain a single value that makes it possible to compare the products to one another, mathematical equations giving the evolution of Young's modulus were used.^{15–17} Thanks to these equations, a value of E_0 (Young's modulus at zero porosity) can be derived and was used to build an elasticity scale to compare the products.⁸

Nevertheless, this approach is questionable. The first reason is that, for some products, the value of E_0 depends on the chosen mathematical model.^{7,11} This point was already discussed in the literature but for the moment no satisfactory answer was provided. The value E_0 must then be taken with caution. The second reason is that the zero porosity level is, most of the time, very far from the actual porosity found in pharmaceutical tablets. If for high pressures some products give compacts with very small porosity (e.g., cellulose), some others always keep a high porosity level even for high compaction pressure (e.g., some calcium phosphates).¹⁸ This means that the value of E_0 is not always representative of the elastic behavior of compacts obtained with the actual industrial loads.

In a previous article,¹⁴ we presented an original method to measure Young's modulus and Poisson's ratio of pharmaceutical compacts. In the present work, this methodology was applied to four pharmaceutical products. In a first part, it was intended to account for the advantage of using the apparent elastic moduli instead of extrapolations at zero porosity. Then, the role of Poisson's ratio in the elastic deformation during die compaction was emphasized, to confirm whether or not, Young's modulus was a suitable parameter to study the elastic behavior of the powders under compaction. For this purpose, the apparent elastic moduli were compared with the experimental consequence of elasticity, that is, the total elastic recovery (%ERt) of the compacts.

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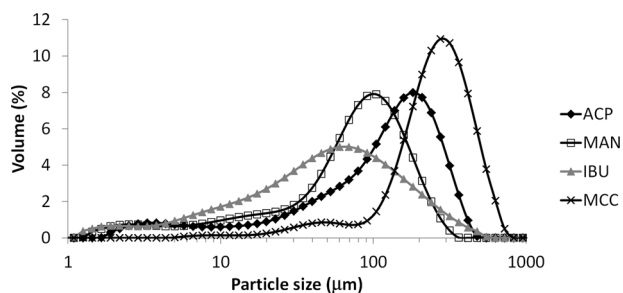


Figure 1. Particle size distribution in volume of the different powders.

MATERIAL AND METHOD

Powders

Four pharmaceutical powders were studied in this work: microcrystalline cellulose (MCC; Avicel® PH-200; FMC Biopolymer, Newark, Delaware), anhydrous dicalcium phosphate (ACP; A TAB®; Rhodia, Courbevoie, France), ibuprofen (IBU; Ibuprofen DTP; BASF, Ludwigshafen, Germany), and mannitol (MAN; Pearlitol®, Roquette Pharma, Lestrem, France). The particle size distribution in volume (V%) was obtained by laser diffraction (Mastersizer 2000; Malvern Instruments, Malvern, UK) using the Fraunhofer's theory. The measurement was performed on dry powders with a dispersion pressure of 2 bar. The results can be seen in Figure 1. For the compression, all the powders were lubricated with 1% magnesium stearate MF3V (Peter Greven, Bad Munstereifel, Germany). The blending was performed at 50 rpm for 5 min using a turbula mixer (Type T2C; Willy A Bachofen, Muttenz, Switzerland).

The particle density was determined using a helium pycnometer (AccuPyc 1330; Micromeritics, Norcross, Georgia) with measurements performed in triplicate (10 purges and 10 runs each time).

Compression

The compaction experiments were performed using a Stylcam® 200R (Medelpharm, Bourg en Bresse, France) compaction simulator. This device is a single-punch tableting press. Two rotating cams with inserts control the displacement of the two punches. The rotation of the cams is controlled electronically, and the two punches have a symmetrical movement during the compaction process. The height of the precompression insert can be adjusted to change the precompression pressure (from 0% to about 90% of the main compaction pressure). The pressure level during the main compaction is controlled through the thickness of the compact.

The pressure on the upper punch, the lower punch, and the die wall are measured with strain gauges. The die-wall pressure was calibrated using an elastomer with a Poisson's ratio of 0.5. The accuracy on the axial force was 10 N and 0.5% on the radial pressure. The punch displacements were monitored with potentiometric displacement transducers with a precision of 0.01 mm. During the acquisition, the sampling rate was 1000 Hz. We used standard Euro B round and flat-faces punches with a diameter of 11.28 mm. All the experiments were performed in the direct cam mode with a speed of 2 cpm.

For the measurement of the distance between the punches, the deformation of the machine was taken into account. This deformation was determined using a stainless steel calibration

disc (40CMD8S; Deville rectification, Pont-Salomon, France) with a Young's modulus of 205 GPa. The calibration disc was compressed under the conditions mentioned above. The strain of the disc was calculated using Hooke's law and was taken into account for calculation of the elastic deformation of the press.

To measure a value of the die-wall pressure as accurate as possible, the compacts were made in order to have, during the compression, the middle of the compact height as near as possible to the center of the strain gauge. The pressure level was fixed by simultaneously adjusting the filling height and the distance between the punches to always have a thickness at the compression peak around 3.50 mm. It means that the mass of compacted powder changed during the experiments.

The values of Young's modulus and Poisson's ratio were obtained using double compaction experiments as described elsewhere.¹⁴ In this methodology, the first compaction is used to obtain the compact and the elastic properties are measured during the beginning of the second compaction. To obtain the evolution of the porosity with the compaction pressure and the final volume of the compact, single compaction experiments were performed, and the compacts were measured immediately (i.e., within 1 min) after the ejection using a micrometer (Mitutoyo, Kawasaki, Japan).

RESULTS AND DISCUSSION

Evaluation of the Apparent Young's Modulus

The apparent Young's modulus was measured for all the products as a function of the pressure used to produce the compact (i.e., the precompression pressure in the double compaction experiments). By measuring the evolution of the porosity with the applied pressure, the apparent Young's modulus could then also be studied as a function of the porosity. The results are presented in Figure 2. In Figure 2a, the values are presented as a function of the porosity; and in Figure 2b, they are presented as a function of the compaction axial pressure (P_{ax}) needed to obtain the compact. The mean value between the pressure on the upper punch and the pressure on the lower punch was taken as P_{ax} . The values of E_0 were calculated as often done in the literature, using the Spriggs equation,^{7,9,11,16,19} and the results are presented in Table 1.

Anhydrous dicalcium phosphate had a much higher E_0 than other products, MAN had an intermediate value, and IBU and MCC had a rather low E_0 . These results are consistent with the existent literature.^{8,11} Classically, these results are interpreted saying that ACP is a hard material, whereas IBU and MCC are soft elastic material, MAN being intermediate.⁸ Nevertheless, these results reflect only the behavior at zero porosity. Figure 2a shows that for the pressure range used in this experiment, the porosity levels were very different from one product to another. For example, for ACP, the lowest porosity was

Table 1. Values of E_0 Calculated by Using the Spriggs Equation: $E = E_0 e^{-b\phi}$ with ϕ the Porosity

Products	E_0 (GPa)	b	R^2
ACP	190	10.7	0.9855
MAN	11.1	7.2	0.9948
IBU	4.3	16.7	0.9949
MCC	3.2	5.7	0.9897

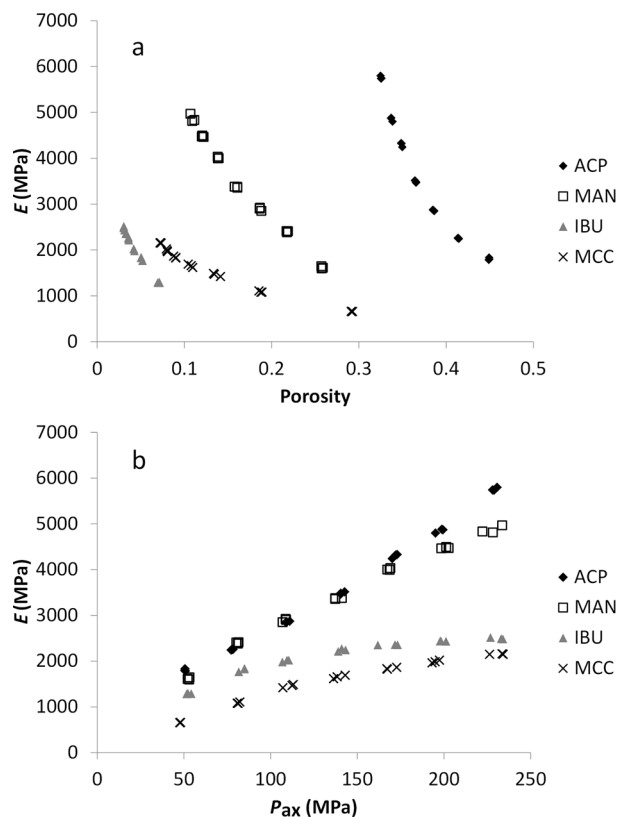


Figure 2. Evolution of the apparent Young's modulus for the four products as a function of (a) the porosity and (b) the applied pressure.

0.32 ($P_{ax} = 230$ MPa). The value at zero porosity is then of little interest for the compacts of ACP obtained under the used pressure range. Instead of using the porosity, the apparent Young's modulus can be compared as a function of the P_{ax} used to produce the compact (Fig. 2b). In this case, the results indicated that until 150 MPa, MAN and ACP gave compacts that had approximately the same Young's modulus when obtained at the same pressure level, even if the E_0 of MAN was almost 20 times lower than the ACP one. So finally, by looking at the apparent Young's modulus at the same P_{ax} , there was no great difference between the elastic properties of compacts of MAN and ACP obtained at the same pressure. These results emphasize that E_0 is maybe not the right parameter to judge the elastic behavior during compaction. Thus, in the following sections, apparent Young's moduli were used instead of E_0 .

The second point of this work was to verify whether the apparent Young's modulus is a suitable parameter to predict elastic behavior under compaction. For this purpose, it would be interesting to study whether it is well linked to the experimental consequence of elasticity, that is, the elastic recovery.

Relation Between Elastic Recovery and Elastic Moduli: The Role of Poisson's Ratio and the Use of the Bulk Modulus

The principal experimental consequence of the elasticity during compression experiment is the elastic recovery of the compact after the compaction. Part of this recovery occurs immediately after compaction and ejection, and for some products, the volumetric expansion still continues several hours after compaction because of viscous phenomena.^{20,21} The elastic moduli represent

the immediate elastic recovery, so only the expansion immediately after the ejection will be considered in this work.

The immediate elastic recovery is a complex phenomenon.²² It can be divided into two steps.²³ There is a first recovery during the unloading part of the compaction cycle. Nevertheless, because of the presence of the die and of the frictions between the die and the compact, this relaxation is not complete and a second step of volumetric expansion occurs when the compact is ejected from the die. Some classical approaches only consider the first step to evaluate elasticity, especially when using energetic approach.^{24–27} The approach considering only “in-die” recovery does not require any extra handling of the compact which can be convenient particularly for products with very low cohesion after the ejection. In certain cases, authors showed that there was a good correlation between “in-die” elastic recovery and %ERT.²³ Nevertheless, “in-die” elastic recovery is influenced by the frictions between the powder and the die that are not linked to the elastic properties of the compact. As the products studied in this work did not present problems of cohesion, the use of the elastic recovery including the two steps was chosen to evaluate the experimental elastic behavior.

In the literature, the elastic recovery was calculated using the compact height, its radius, or its volume.^{11,20,23,24,28} In this study, the volume was selected as it makes it possible to measure the %ERT. For this purpose, the compacts were measured directly after ejection, giving the final volume, V_f . The %ERT was then classically calculated using the minimal volume under compaction (V_{min}) by using Eq. 1:

$$\%ERT = \frac{V_f - V_{min}}{V_{min}} \times 100 \quad (1)$$

This parameter was calculated for each product as a function of the compaction pressure during single compaction experiments. The results are presented in Figure 3. Different trends can be seen depending on the product. For MCC, %ERT initially decreased and then increased for higher pressure. The other products globally showed a slight increase of %ERT with the pressure. These results are consistent with already published ones.²⁵

At all pressures, MCC had the greatest %ERT. On the contrary, IBU showed the lowest %ERT for all the pressure levels, with a %ERT equal to the one of MAN for the two highest pressures. ACP showed a greater %ERT than MAN. If we compare these results with the apparent Young's modulus presented

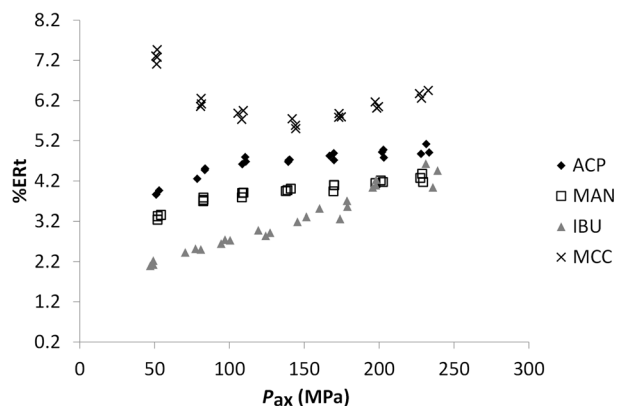


Figure 3. Evolution of %ERT versus P_{ax} for the four products.

in Figure 2b, there is no clear correlation between the values of %ERt and the values of the apparent Young's modulus. For example, for compacts produced at $P_{ax} = 110$ MPa, the apparent Young's moduli can be sorted in the following order: E (MCC) < E (IBU) < E (MAN) = E (ACP), whereas for %ERt the order is: %ERt(IBU) < %ERt(MAN) < %ERt(ACP) < %ERt(MCC). Thus, in this case, the use of Young's modulus is clearly inappropriate to describe the elastic behavior and there is no direct correlation between elastic recovery and Young's modulus.

To understand these results and find which elastic parameter would be suited to represent the elastic deformation, it would be interesting to look at the equations of linear elasticity. For homogeneous and isotropic solid, the general formulation giving the elastic strains (ϵ) as a function of the stresses (σ) can be written as²⁹:

$$\epsilon_{ij} = \frac{1+\nu}{E} \sigma_{ij} - \frac{\nu}{E} \sigma_{kk} \delta_{ij} \quad (2)$$

where δ_{ij} is the Kronecker delta. In the case of die compaction, there is a cylindrical symmetry and the stresses and the strains can be divided into two kinds: the axial ones and the radial ones. Equation 2 gives then the two following equations³⁰:

$$\epsilon_{ax} = \frac{1}{E} (\sigma_{ax} - 2\nu\sigma_{rad}) \quad (3)$$

$$\epsilon_{rad} = \frac{1}{E} [\sigma_{rad} - \nu(\sigma_{ax} + \sigma_{rad})] \quad (4)$$

where ϵ_{ax} and ϵ_{rad} are the axial and the radial strains, respectively, and σ_{ax} and σ_{rad} are the axial and the radial stresses, respectively. In the experiments, the axial stress is equal to the P_{ax} , and the radial stress is equal to the radial pressure (P_{rad}). During die compaction, the compact undergoes both axial and radial strains. Both strains are linked to the stresses and to both E and ν . Thus, to characterize the elastic deformation, E cannot be considered alone and Poisson's ratio must be taken into account.

In the pharmaceutical literature, Poisson's ratio was often not taken into account when studying elasticity. The reason for this fact seems to be that authors considered that there are no great differences between the Poisson's ratio of the different pharmaceutical products. In such a case, it would then be justified to consider only Young's modulus. Nevertheless, it was reported in a previous work that this approximation is not always justified.¹⁴

Poisson's ratio was measured as a function of the compaction P_{ax} for all the products. The results can be seen in Figure 4. The results show that the products had different Poisson's ratio and that Poisson's ratio had not a constant value. For example, IBU had a very high Poisson's ratio compared with other products. The evolution of Poisson's ratio differed from one product to another. This evolution is linked to the evolution of the porosity of the compact when varying the P_{ax} . For example, the limited variations of Poisson's ratio for IBU and ACP could be linked to the narrow porosity range explored (Fig. 2). Moreover, the correlation between Poisson's ratio and porosity was discussed previously in the literature, and different trends were observed depending for example on the bulk value of Poisson's ratio.^{31–34} Referring to these works, the large changes of Poisson's ratio

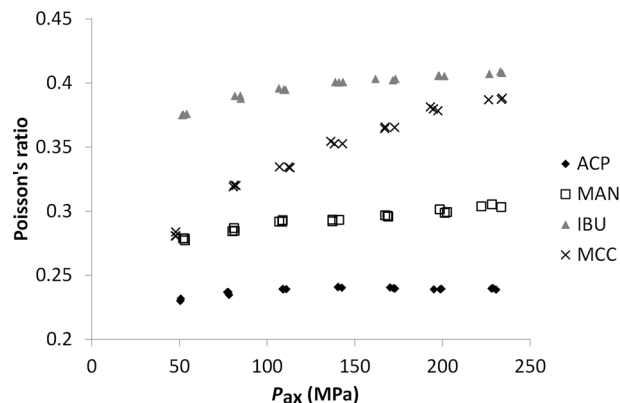


Figure 4. Evolution of Poisson's ratio versus P_{ax} for the four products.

for MCC could be linked to the large variation of porosity and to a high bulk value of Poisson's ratio.

These differences between the Poisson's ratios of the studied products explain why Young's modulus was not well correlated with the elastic recovery. To study the elastic behavior of the compacts, both Young's modulus and Poisson's ratio must be taken into account.

By combining Eqs. 3 and 4, it is possible to obtain the total volumetric elastic strain ($\epsilon_v = \epsilon_{ax} + 2\epsilon_{rad}$):

$$\epsilon_v = \frac{(1-2\nu)}{E} (\sigma_{ax} + 2\sigma_{rad}) \quad (5)$$

Equation 5 is classically rewritten as:

$$\epsilon_v = \frac{p}{K} \quad (6)$$

where p is the hydrostatic pressure and K is the bulk modulus. These two parameters have the following expression^{29,30}:

$$p = \frac{\sigma_{ax} + 2\sigma_{rad}}{3} = \frac{P_{ax} + 2P_{rad}}{3} \quad (7)$$

$$K = \frac{E}{3(1-2\nu)} \quad (8)$$

The volumetric elastic strain is closely related to %ERt defined earlier but is not exactly equal to it. In fact, the elastic strain is calculated, taking as a reference the relaxed state. ϵ_v is thus defined as:

$$\epsilon_v = \frac{V_f - V_{min}}{V_f} \quad (9)$$

From Eq. 6, two conclusions can be drawn regarding the study of the elastic recovery of the pharmaceutical compacts after compaction. First, the elastic strain, and as a consequence, the elastic recovery is directly linked to the bulk modulus, which thus should be used instead of Young's modulus. Second, apparent moduli should be calculated as a function of the hydrostatic pressure to make it possible to compare one product with another.

To test the two previous conclusions, ϵ_v and K were calculated for all the products as a function of p using Eqs. 8 and 9. The results can be seen in Figure 5. Contrary to the results obtained

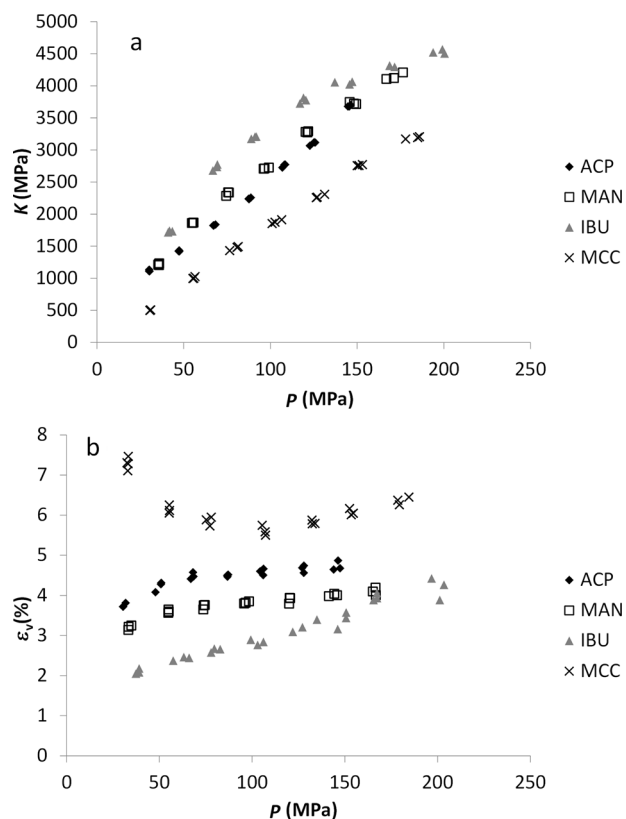


Figure 5. Evolution of (a) K and (b) ϵ_v versus p for the four products.

previously with Young's modulus, there is a good correlation between the values of bulk modulus and of ϵ_v . As expected according to Eq. 6, for a given hydrostatic pressure, the higher ϵ_v the lower K . This trend was obtained on the whole domain of hydrostatic pressure. The influence of Poisson's ratio and the usefulness of the bulk modulus were well seen for the case of IBU. Even if IBU had a lower E than MAN and ACP, because of the high values of ν , it had a highest K on a large domain of p and this corresponded to the lowest elastic deformation. Thus, the bulk modulus made it possible to obtain the good trend for the evolution of the elastic deformation under compaction and should be considered as a relevant parameter to study the elastic deformation of pharmaceutical powders under compaction.

CONCLUSIONS

The use of elastic moduli is an interesting way to describe the elastic behavior of the pharmaceutical powder under compaction. Nevertheless, it was proved in this study that the value of the moduli extrapolated at zero porosity must be taken with caution when using products that gives compacts of very different porosity levels for the same pressure range.

Because of the variations of Poisson's ratio between the different products studied, it was seen that it was difficult to link Young's modulus to the elastic recovery of the compact after compression. The use of the bulk modulus, which is a combination of E and ν , was proposed and made it possible to obtain the good trend for the variation of the elastic recovery. To be able to compare the different products, all the parameters were

calculated as a function of the hydrostatic pressure, which takes into account both the axial and radial pressures.

This study showed that Poisson's ratio, which was used to calculate the bulk modulus, must be taken into account to correctly understand the elastic behavior of pharmaceutical powders under compaction. The bulk modulus is an interesting parameter to study the elastic recovery of pharmaceutical compacts during compression. As such, it could be used, in the quality by design approach, as a material attribute representative of the elastic behavior of the powder that could be linked to critical quality attributes like capping.

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REFERENCES

- Garr JSM, Rubinstein MH. 1991. An investigation into the capping of paracetamol at increasing speeds of compression. *Int J Pharm* 72(2):117–122.
- Nakamura H, Sugino Y, Watano S. 2012. In-die evaluation of capping tendency of pharmaceutical tablets using force-displacement curve and stress relaxation parameter. *Chem Pharm Bull* 60(6):772–777.
- Wu CY, Hancock BC, Mills A, Bentham AC, Best SM, Elliott JA. 2008. Numerical and experimental investigation of capping mechanisms during pharmaceutical tablet compaction. *Powder Technol* 181(2):121–129.
- Vaithiyalingam SR, Sayeed VA. 2010. Critical factors in manufacturing multi-layer tablets—Assessing material attributes, in-process controls, manufacturing process and product performance. *Int J Pharm* 398(1–2):9–13.
- Podczec F. 2011. Theoretical and experimental investigations into the delamination tendencies of bilayer tablets. *Int J Pharm* 408(1–2):102–112.
- Kerridge JC, Newton JM. 1986. The determination of the compressive Young's modulus of pharmaceutical materials. *J Pharm Pharmacol* 38(S12):79P.
- Roberts RJ, Rowe RC. 1987. The Young's modulus of pharmaceutical materials. *Int J Pharm* 37(1–2):15–18.
- Bassam F, York P, Rowe RC, Roberts RJ. 1990. Young modulus of powders used as pharmaceutical excipients. *Int J Pharm* 64(1):55–60.
- David SE, Ramirez M, Timmins P, Conway BR. 2010. Comparative physical, mechanical and crystallographic properties of a series of gemfibrozil salts. *J Pharm Pharmacol* 62(11):1519–1525.
- Busignies V, Tchoreloff P, Leclerc B, Hersen C, Keller G, Couraze G. 2004. Compaction of crystallographic forms of pharmaceutical granular lactoses. II. Compacts mechanical properties. *Eur J Pharm Biopharm* 58(3):577–586.
- Kachrimanis K, Malamataris S. 2004. "Apparent" Young's elastic modulus and radial recovery for some tableted pharmaceutical excipients. *Eur J Pharm Sci* 21(2–3):197–207.
- Ketolainen J, Oksanen M, Rantala J, Storpellinen J, Luukkala M, Paronen P. 1995. Photoacoustic evaluation of elasticity and integrity of pharmaceutical tablets. *Int J Pharm* 125(1):45–53.
- Roberts RJ, Rowe RC, York P. 1994. The Poisson ratio of microcrystalline cellulose. *Int J Pharm* 105(2):177–180.
- Mazel V, Busignies V, Diarra H, Tchoreloff P. 2012. Measurements of elastic moduli of pharmaceutical compacts: A new methodology using double compaction on a compaction simulator. *J Pharm Sci* 101(6):2220–2228.
- Spinner S, Knudsen FP, Stone L. 1963. Elastic constant porosity relations for polycrystalline thoria. *J Res Natl Bur Std* 67(1):39–46.

16. Spriggs RM. 1961. Expression for effect of porosity on elastic modulus of polycrystalline refractory materials, particularly aluminum oxide. *J Am Ceram Soc* 44(12):628–629.
17. Phani KK, Niyogi SK. 1987. Young modulus of porous brittle solids. *J Mater Sci* 22(1):257–263.
18. Busignies V, Leclerc B, Porion P, Evesque P, Couarraze G, Tchoreloff P. 2006. Compaction behaviour and new predictive approach to the compressibility of binary mixtures of pharmaceutical excipients. *Eur J Pharm Biopharm* 64(1):66–74.
19. Hancock BC, Clas SD, Christensen K. 2000. Micro-scale measurement of the mechanical properties of compressed pharmaceutical powders. 1: The elasticity and fracture behavior of microcrystalline cellulose. *Int J Pharm* 209(1–2):27–35.
20. Picker KM. 2001. Time dependence of elastic recovery for characterization of tableting materials. *Pharm Dev Technol* 6(1):61–70.
21. York P, Baily ED. 1977. Dimensional changes of compacts after compression. *J Pharm Pharmacol* 29(2):70–74.
22. Anuar MS, Briscoe BJ. 2009. The elastic relaxation of starch tablets during ejection. *Powder Technol* 195(2):96–104.
23. Haware RV, Tho I, Bauer-Brandl A. 2010. Evaluation of a rapid approximation method for the elastic recovery of tablets. *Powder Technol* 202(1–3):71–77.
24. Patel S, Kaushal AM, Bansal AK. 2007. Effect of particle size and compression force on compaction behavior and derived mathematical parameters of compressibility. *Pharm Res* 24(1):111–124.
25. Antikainen O, Yliruusi J. 2003. Determining the compression behaviour of pharmaceutical powders from the force-distance compression profile. *Int J Pharm* 252(1–2):253–261.
26. Aburub A, Mishra D, Buckner I. 2007. Use of compaction energetics for understanding particle deformation mechanism. *Pharm Dev Technol* 12(4):405–414.
27. Pontier C, Champion E, Viana M, Chulia D, Bernache-Assollant D. 2002. Use of cycles of compression to characterize the behaviour of apatitic phosphate powders. *J Eur Ceram Soc* 22(8):1205–1216.
28. Armstrong NA, Haines-Nutt RF. 1972. Elastic recovery and surface area changes in compacted powder systems. *J Pharm Pharmacol* 24:Suppl:135P–136.
29. Srinath LS. 2009. *Advanced mechanics of solids*. 3rd ed. New Delhi, India: Tata McGraw-Hill.
30. Brewin PR, Coube O, Doremus P, Tweed JH, Eds. 2008. *Modelling of powder die compaction*. London, UK: Springer.
31. Arnold M, Boccaccini AR, Ondracek G. 1996. Prediction of the Poisson's ratio of porous materials. *J Mater Sci* 31(6):1643–1646.
32. Kovacik J. 2006. Correlation between Poisson's ratio and porosity in porous materials. *J Mater Sci* 41(4):1247–1249.
33. Phani KK. 2008. Correlation between ultrasonic shear wave velocity and Poisson's ratio for isotropic porous materials. *J Mater Sci* 43(1):316–323.
34. Ramakrishnan N, Arunachalam VS. 1990. Effective elastic-moduli of porous solids. *J Mater Sci* 25(9):3930–3937.