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Numerical analysis of the density distribution within scored tablets

Moulay Saddik Kadiri[1], and Hanafi Moussaoui[1]

[1]Process engineering and optimization of industrial systems laboratory (LIPOSI)
National school of applied sciences, Khouribga, Morocco

ABSTRACT

Scored tablets provide dose flexibility, ease of swallowing and cost savings. However, some problems with scored tablets can be confronted like difficulty of breaking, unequally breaking and loss of mass upon breaking. This paper investigates the effect of score lines on the density distribution using continuum modelling. In keeping with previous work in the pharmaceutical field, a modified Drucker Prager Cap model is described briefly and used in the simulations. Coulomb friction is included between powder and tools. The microcrystalline cellulose (MCC) Vivapur® 102 was used to identify the model parameters using experimental tests with instrumented die, shear cell and diametrical crushing. The obtained results indicate that simulations may be useful not only to determine density distributions within tablets, but also may provide indications about performance of score lines.

Keywords— *scored tablets; density distribution; Drucker Prager Cap; finite element modelling; die compaction.*

I. Introduction

Tablets that can be broken in half or quarters will be scored by the manufacturer to make the process easier. The scored tablets present some advantages. The most important advantage is the dose flexibility. Ease of swallowing is another important advantage of scored tablets especially for big sized tablets [1,2,3]. Moreover, the scored tablets may reduce the costs of medication. Scored tablets reduce the number of tablets needed. Thus, we can reduce costs for both the producing industry as well as the pharmacy and the patient. When a tablet is broken in half, there is no guarantee that the drug dosage contained in each half. Scoring a tablet improves the chances that the drug dosage may be divided equally if the tablet has been cut exactly in the scored indentation. If this does not occur the tablet will fragment, and a proportion of the tablet will be lost. For more details about advantages, problems and performance indicators of score lines, see the review published by E. van Santen et al. [1].

In this work, numerical simulation was used to analyze the effect of score lines on the density distributions. The compaction behavior of pharmaceutical powders can be studied using the principles of continuum mechanics at a macroscopic level, i.e. phenomenological models. In continuum mechanical modelling, the powder is considered macroscopically as continuous and porous medium. The media is characterized by overall parameters such as cohesion, interparticle friction and mechanical properties such as Young's modulus and Poisson ratio which are depending on density during the compaction. In addition, as the applied load increases, the admissible stress in the tablet must be bounded in a domain which is bounded by one or a set of surfaces in the pressure and deviatoric space. This domain defines the yield surface. However, to describe mechanisms such as hardening and softening resulting from the loading and unloading of the powder, the domain expands or contracts as the volumetric strain decreases or increases. This evolution is defined a flow function or flow potential.

A variety of continuum models from the soil mechanics literature have been developed from experiments on different geo-materials as described by Drucker et al. [4], Schofield and Wroth [5], Di-Maggio and Sandler [6], Gurson [7] and Green [8].

In this paper, the response of the powder behavior using the Drucker-Prager Cap model during die compaction with scored punches was studied. DPC model have been used for pharmaceutical powders by A. Michrafy et al. [9], S. Kadiri et al. [10, 11], J.C. Cunningham [12], and recently by L.H. Han et al. [13], T. Sinha et al. [14, 15].

The main objective in this work is to analyze the effect of the score lines on the pharmaceutical powder compaction using continuum modelling. This paper is organized as follows: Section 2 presents the materials and methods; parameters identifications are introduced in section 3. Results and discussions are in section 4. Finally, section 5 summarizes the conclusions.

II. Materials and methods

A. The used powder

The microcrystalline cellulose (MCC) Vivapur® 102 is often used as a pharmaceutical excipient. Characteristics of the powder MCC 102 provided by JRS (J. Rettenmaier and Sohne) is shown in Table 1. This powder having good flowability, compressibility and compactability, was used to identify the model parameters.

TABLE I. PROPERTIES OF MCC VIVAPUR® FROM J. RETTENMAIER AND SOHN

Powder	***Mean Particle Size***	***True density***	***Bulk density***
MCC Vivapur 102	90 μm	1.59 +/-0.002g/cm^3	0.31 +/-0.02g/cm^3

B. Drucker Prager Cap model

The template The Drucker Prager Cap (DPC) model was described in several papers [9, 10, 11, 12, 13, 14, 15]. This model is implemented in the Abaqus Software. The yield function is defined with three surfaces represented in Fig. 1: the shear failure surface F_s defining the correlation between the cohesion d and the internal friction angle β, the elliptical surface (or Cap surface) F_c which can expand or contract according to the volumetric strain and the transition surface F_t between F_s and F_c. The evolution of the Cap surface is described with the hardening function pb which is the position of the Cap on hydrostatic pressure axis for each density state.

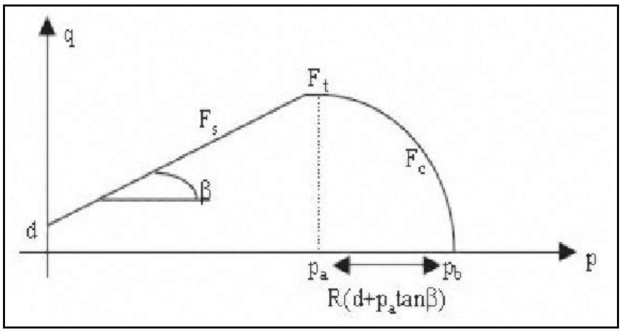

Fig. 1. Drucker-Prager Cap model presented in the (p,q) plane.

$p = -1/3\ tr(\sigma)$ is the hydrostatic pressure, and $q = (3/2\ (S{:}S))^{1/2}$ is the Mises equivalent stress in which S is the stress deviator, defined as:

$$S = \sigma + pI$$

Where σ is the stress tensor, and I is the identity matrix.

Six parameters are required to define the yield surface of the modified DPC model: d, β, p_a, R, p_b and α and two elastic parameters, Young's modulus E and Poisson's ratio ν, are required for describing the elastic behavior of powders. Experimental tests with instrumented die, shear cell and diametrical crushing was used to identify these parameters.
The powder is characterized by mechanical properties (d, β, E) which evolve with the relative density of the powder, a constant Poisson's ratio ν and an evolution of the hardening function p_b with volumetric plastic strain during compression.

III. Material parameter indentification for the dpc model

A. Cohesion and angle of inetrnal friction

Diametral and uniaxial compression tests were used to identify the cohesion and the internal friction using the approach based on the shear failure surface of the DPC model [10, 13]. The evolutions of cohesion and friction angle are shown in Fig. 2 and Fig. 3. These results are similar to results obtained by Han et al.[10] for MCC Avicel PH101 having similar properties (mean particle size and true density) as MCC Vivapur 102. The results of the friction angle are rare and sometimes contradictory in literature. Stanley et al. [16] estimated the angle of internal friction of Titanium Dioxide using a shear cell. His results show that with increasing pressure, friction angle decreases.
Nevertheless, another result of Sinka et al. [17] shows rather a growth of the angle of internal friction and an exponential evolution of cohesion. However, our results are like those obtained by Han et al. [13] for Avicel PH101.

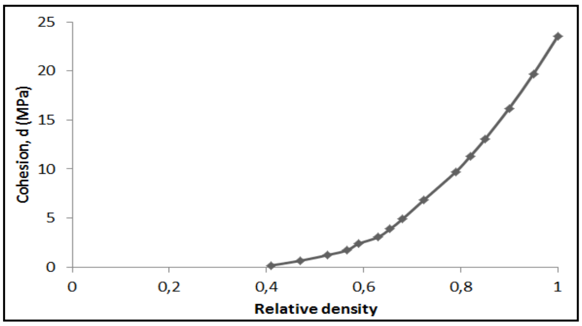

Fig. 2. Cohesion of MCC 102 estimated by axial and diametral tests with Drucker-Prager Cap model (fitted to zero porosity).

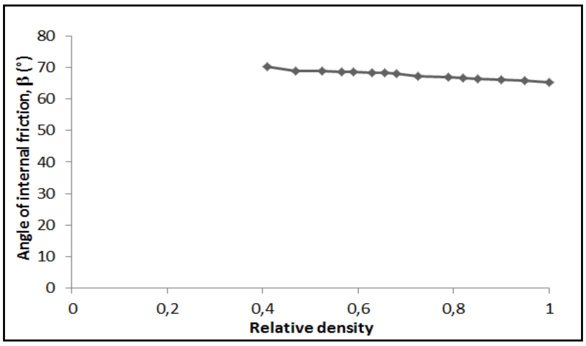

Fig. 3. Friction angle of MCC 102 estimated by axial and diametral tests with Drucker-Prager Cap model (fitted to zero porosity).

B. Cap shape parameter R and hardening function p_b

The position of the cap shape is determined by the cap shape parameter R and hydrostatic compression yield stress (hardening function) p_b. The parameter R is the eccentricity of the ellipse which defines the cap (Fig. 1). The hardening behavior in the model and the variation of the relative density is defined in terms of the volumetric plastic strain:

$$\varepsilon_p^{vol} = \ln(\rho/\rho_0) \quad (1)$$

Where ρ is the current relative density, and ρ_0 is the initial relative density on filling of die.

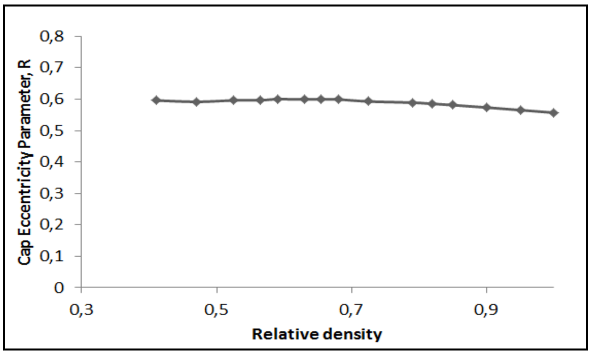

Fig. 4. Cap eccentricity parameter R.

From the experimental data of the compaction cycle, the hardening function pb and the eccentricity R were calculated and plotted versus the volumetric strain and relative density respectively (Fig. 4 and 5).

The trends are comparable with those published in the literature. Recently, Diarra et al. found similar trend of R and pb [18]. Han et al. found the same trend for pb, but the eccentricity R increases with relative density [13].

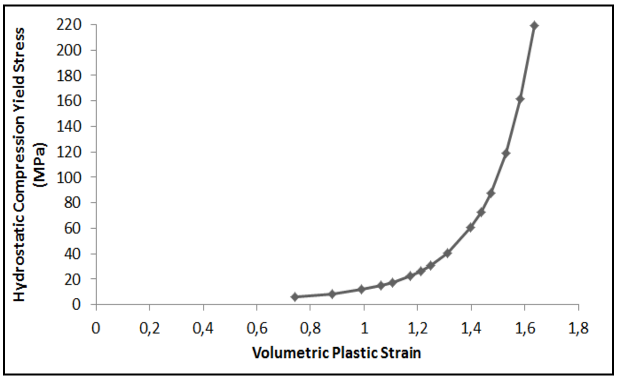

Fig. 5. Hydrostatic compression yield stress p_a.

C. Elastic parameters (Poisson's ratio and Young's modulus)

For Poisson's ratio ν, we use the relationship obtained by Long [19, 20]:

$$\nu = \alpha/(1+\alpha) \quad (2)$$

Where α is the transfer ratio (ratio of the radial stress to the axial stress). Compaction of the MCC 102 powder in a cylindrical die at the ambient temperature gave a transfer ratio in the range 0.4 - 0.45 [21]. For $\alpha = 0.4$ in Eq. (2), the Poisson's ratio ν is 0.29.

The Young modulus E was estimated from the simple compression test (without die). We use the macroscopic response of tablet that is given by the stress-strain curve. A cylindrical tablet of MCC Vivapur 102 is placed between two punches. To limit a deformation by bloc that lead generally to a non-uniform stress state, the contact between tablet and punches was lubricated. The obtained values are increasing with the relative density as plotted in Fig. 6.

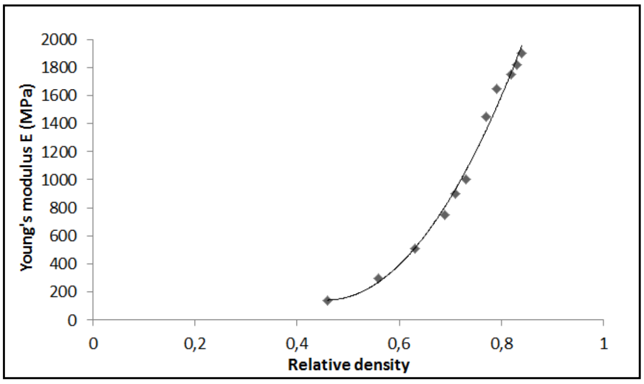

Fig. 6. Young's modulus E plotted as function of relative density.

D. Powder-die wall friction

To complete the boundary problem of the compaction, the die wall friction coefficient is needed. During compaction, the powder friction at the die wall induces non-uniform axial stress and produces density gradients within the compact. The friction effect could be quantified by the wall friction coefficient. The friction coefficient can be determined by an indirect method based on Janssen-Walker theory [22]. This approach was applied by Michrafy et al. [23] to three pharmaceutical powders MCC 101, 102 and 105. We use the result obtained for MCC 102 that shows a decreasing of the friction coefficient in the first stage of densification (relative density < 0.55) and tends towards an asymptotic value approximately equal to 0.4. For the simulation, a mean constant value of 0.4 was taken.

IV. Results and discussions

The simulation of the uniaxial single-ended die compaction process of MCC Vivapur® 102 powder was conducted using the software Abaqus® (Simulia). The user subroutine (USDFLD) was used to update the elastic parameters and the parameters of the failure curves when the relative density changed using the visual FORTRAN compiler. The powder was modelled as a deformable continuum, while the punches and die were modelled as analytical rigid bodies without any deformation. The wall friction effect was considered by adopting a Coulombic boundary condition on the interfaces powder/wall and powder/punch. A constant friction coefficient equal to 0.4 was taken.

The numerical simulations correspond to two different geometries: flat-face and concave face. Due to the axial symmetry, half of the powder bed was meshed with elements of type "CAX4R" four-node axisymmetric elements and with a mirror effect we can see the whole tablet in Fig. 7. These simulations were conducted by imposing a displacement to the upper punch as in the experimental test. The model was validated by observing a good agreement between finite element prediction and experimental measurement of loading-unloading curves and by a comparison between predicted density distribution and experimental axial density presented in [11].
Numerical simulation produces a gradient of density distribution throughout the height of the tablet (Fig. 7). The friction prevents the powder from sliding along the interfaces of punches and die. As a result, very dense regions are developed on the upper edges of the tablet and low-density regions on the lower edges. These results are similar to those obtained by Aydin et al. [24] and Michrafy et al. [9]. Also, similar results were obtained by Han et al. [13] for MCC powder and recently by Diarra et al. [18] for ceramic powder.

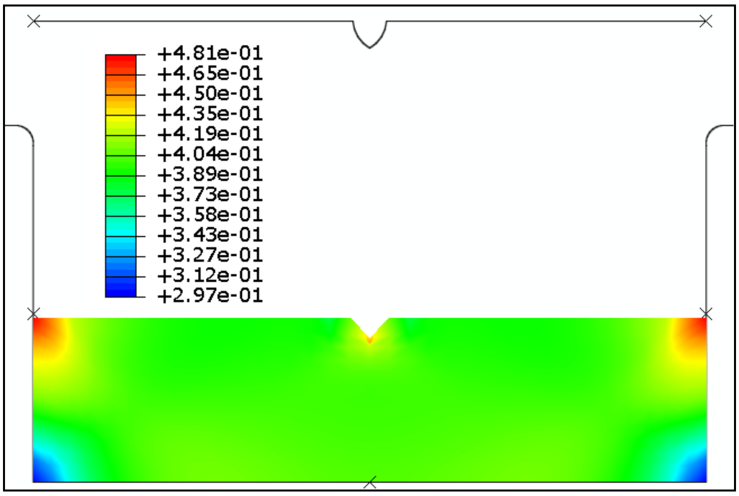

Fig. 7. Density distribution of scored flat-tablet after decompression.

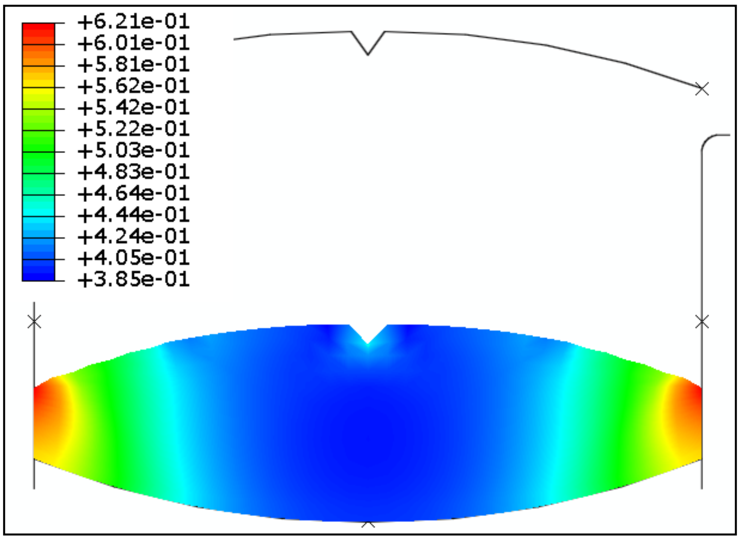

Fig. 8. Density distribution of scored concave-face tablet after decompression.

The punch geometry could also cause heterogeneity of density distribution. Fig. 8 shows a non-uniform density distribution of concave tablet. High density regions are developed at the edges of the concave tablet with low density regions near the tablet apex. The consequence of low and high-density regions is that the local properties of the powders are affected.

The strength of a porous material generally increases with density. From this point of view, low density regions may influence adversely the performance of the tablets during post compaction operations such as coating, packaging, transport and use. In addition, the localized disintegration and dissolution may be affected [25]. For flat and concave face punches, we have a dense region at the bottom of the score line. Fig. 9 and Fig. 10 show the evolutions of the relative density at the upper part from the die wall to the tablet apex for flat-face and concave face punches respectively. This result is qualitatively similar to X-rays tomography measurements obtained Sinka et al. [25].

The presence of the score line lead to particular effects. The tablet can break at the least dense region near the tablet apex. This situation may lead to a difficulty of breaking exactly at the score line; the tablet will be broken unequally. The risk of dose variability may be very dangerous for the patient because of the risk of taking subsequently light or heavy halves. Another problem can be met is loss of mass, due to powdering and fragmentation at the score line when a tablet is broken. Loss of mass leads to loss of dosage, contamination and health hazards for others than the patient [1].

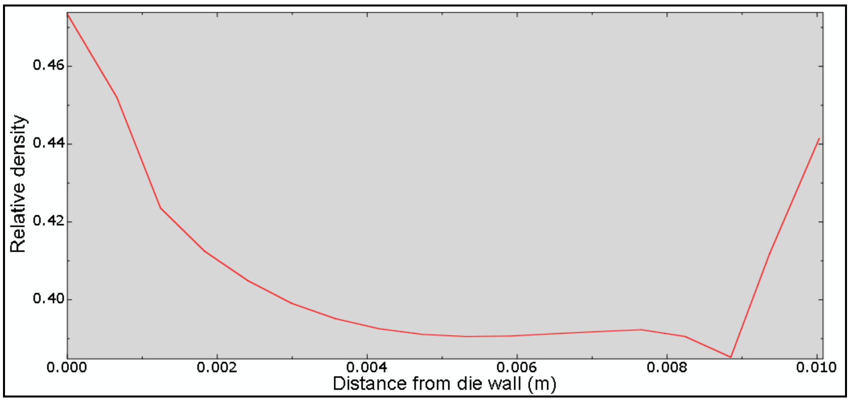

Fig. 9. Relative density evolution at the upper flat face from the die wall to the tablet apex.

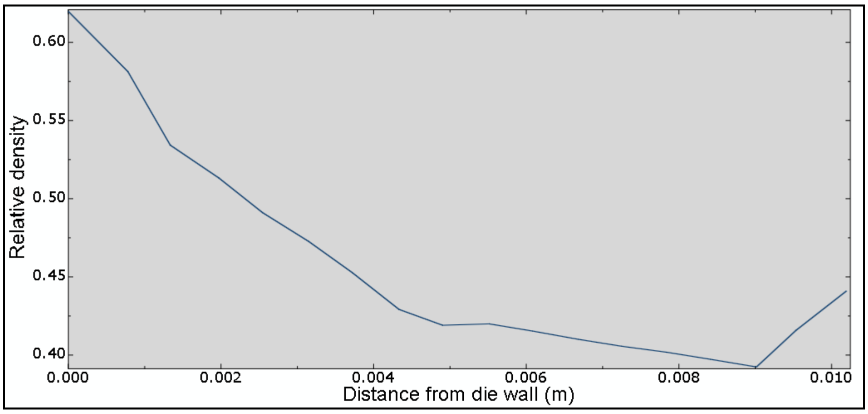

Fig. 10. Relative density evolution at the upper concave face frome the die wall to the tablet apex.

V. Conclusions

The Drucker Prager Cap model was successfully implemented for tablet compaction simulations in a commercial finite element software. The parameters governing the yield surfaces were estimated by experimental tests. The simulation reproduces the density distribution during compaction powder process. For both cases, flat and concave face punches, the obtained results show heterogeneity of the density distribution on the scored tablet at maximum compaction. Moreover, this heterogeneity continues developing during the decompression phase. For flat-face punches, very dense regions are developed on the upper edges of the tablet and low-density regions on the lower edges. However, high density regions are developed at the edges of the concave tablet with low density regions near the tablet apex. But, for both cases, flat and concave, we have a dense region at the bottom of the score line.

The tablet can break at the least dense region near the tablet apex and not exactly at the score line. This can lead to dose variability that may be very dangerous for the patient because of the risk of taking subsequently light or heavy halves. Moreover, the heterogeneity of density may lead to loss of mass, due to powdering and fragmentation at the score line when a tablet is broken.

The obtained result indicates that finite element simulations may predict not only density and stress distributions within tablets, but also may provide indications about performance of score lines. Finite element simulation can be an important tool to analyze factors influencing the performance of score lines like shape, size, curvature and thickness of the tablet and the form and deepness of the score line.

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