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FEM simulation of the die compaction of pharmaceutical products: Influence of visco-elastic phenomena and comparison with experiments

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ABSTRACT

This work studies the influence of visco-elastic behavior in the finite element method (FEM) modeling of die compaction of pharmaceutical products and how such a visco-elastic behavior may improve the agreement between experimental and simulated compression curves.

The modeling of the process was conducted on a pharmaceutical excipient, microcrystalline cellulose (MCC), by using Drucker–Prager cap model coupled with creep behavior in Abaqus® software. The experimental data were obtained on a compaction simulator (STYLCAM 200R). The elastic deformation of the press was determined by performing experimental tests on a calibration disk and was introduced in the simulation. Numerical optimization was performed to characterize creep parameters.

The use of creep behavior in the simulations clearly improved the agreement between the numerical and experimental compression curves (stresses, thickness), mainly during the unloading part of the compaction cycle. For the first time, it was possible to reproduce numerically the fact that the minimum tablet thickness is not obtained at the maximum compression stress.

This study proves that creep behavior must be taken into account when modeling the compaction of pharmaceutical products using FEM methods

1. Introduction

Numerical modeling of powder behavior is increasingly used in the pharmaceutical field to complete experimental tests. In the case of die compaction, which is one of the most important processes in the pharmaceutical industry, finite element method (FEM) was introduced to better understand the powder behavior under high pressure. This numerical approach, when properly controlled, is an excellent tool for predicting powder densification, design space qualification and could also be useful for process scale-up.

Many studies were carried out using the Drucker–Prager cap (DPC) model and gave interesting results about the distribution of global variables (stress, strain and density) (Han et al., 2008; Michrafy et al., 2002, 2004, 2011; Sinka et al., 2003, 2004; Wu et al., 2005, 2008). Studies were also conducted to improve the DPC model (Frenning, 2007) and the characterization of its parameters (Brewin et al., 2008; Hentschel and Page, 2007; Mazel et al., 2012; Shang et al., 2012; Sinha et al., 2010) for a suitable simulation of powder behavior. Comparisons between experimental compression curves and simulated curves were done and showed that the hardening behavior of powder is generally well predicted (Diarra et al., 2012; Han et al., 2008). On the other hand, the simulation of the part of elastic recovery (decompression phase) highlighted some discrepancies between experimental and numerical curves (Diarra et al., 2012). Moreover, some well-known experimental features are not reproduced by the numerical simulations. For example, during experimental compression tests, the maximum pressure is not reached at the minimum tablet thickness. This phenomenon is due to the viscous behavior of the powder (Müller and Caspar, 1984) that was, until now, never taken into account to simulate the compaction of pharmaceutical powders. The objective of this article was to study the influence of visco-elastic behavior in the FEM modeling of die compaction of pharmaceutical products and how such a visco-elastic behavior may improve the agreement between experimental and simulated compression curves.

To obtain useful comparison it is important to set a numerical model that emulate as precisely as possible the experimental test. In our case, as creep behavior is a time dependent phenomena, the real kinetic of the compaction test had to be used in the simulation. From an experimental point of view, the kinetics can be obtained by using sensors that measure the displacements of the punches as a function of time. The time–displacement curves can thus be entered in the numerical modeling. Nevertheless, in the experiments, the sensors cannot be placed on the active surface of the punch and

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Nomenclature

d	powder cohesion [MPa]
E	Young's modulus [MPa]
F_c	cap surface [–]
F_s	failure surface [–]
p	hydrostatic stress [MPa]
p_a	evolution parameter [MPa]
p_b	hydrostatic compression yield stress [MPa]
$\tilde{p}^{cr}$	effective creep pressure [MPa]
q	mises equivalent stress [MPa]
R	cap eccentricity [–]
t	compression time [MPa]
β	friction angle [°]
$\tilde{\epsilon}^{cr}$	equivalent creep strain [–]
$\dot{\tilde{\epsilon}}^{cr}$	equivalent creep strain rate [–]
ϵ_v^p	volumetric inelastic strain [–]
ν	Poisson's ratio [–]
$\tilde{\sigma}^{cr}$	equivalent creep stress [MPa]
σ_{lo}	lower punch stress [MPa]
σ_r	die-wall stress (radial stress) [MPa]
σ_{up}	upper punch stress [MPa]
σ_{ax}	axial stress [MPa]

due to elastic deformation of the whole device the measured displacement is not exactly the displacement of the active surface of the punch (Shang et al., 2012). The elastic deformation of the press must then also be taken into account in the simulation.

In this paper, we first present the method used to experimentally determine the elastic deformation of the whole press and to implement this deformation in the numerical model. In a second time a numerical modeling approach is performed to include the viscous response of powder when compressed. Finally, numerical results obtained from the simulation of creep behavior of powder are compared to the experimental ones.

2. Materials and methods

2.1. Powder

A classical pharmaceutical excipient, microcrystalline cellulose, MCC (Avicel® PH-200, FMC Biopolymer, USA), was used in this study. This choice is motivated by the fact that MCC powder is well known for its plastic and visco-elastic behavior. The powder was lubricated with 1% (w/w) of magnesium stearate MF3V® (Peter Greven, Bad Münstereifel, Germany).

2.2. Tableting press

The experimental compaction tests were performed using a compaction simulator Stylcam 200R (Medelpharm, Bourg en Bresse, France). This press is equipped with sensors to measure the upper, the lower and the radial compaction forces, and the upper and lower punch displacements. The running of this single station press and the experimental conditions were previously described in details (Diarra et al., 2012; Michaut et al., 2010). For these experiments, the precompression pressure was deleted and a direct cam profile was chosen with a compaction speed of 1 tablet per minute. The axial force was monitored with an accuracy of 10 N and the displacements of the punches with a precision of 0.01 mm. The sampling rate was 1 kHz.

To take into account the global elastic deformation of the whole press when high pressure is applied, an un-deformable calibration disk of 5 mm height was compacted. The deformation-stress curve obtain from this experiment was used to calculate the exact experimental thickness under pressure.

2.3. Drucker–Prager cap model parameters

The mechanical behavior of the powder was modeled using Drucker–Prager cap model. The parameters required to conduct the simulation were determined as already described in the literature (Brewin et al., 2008; Diarra et al., 2012; Han et al., 2008; Mazel et al., 2012) and the experimental data are plotted in Fig. 1.

The friction angle β determined from uniaxial and diametrical compression tests did not vary much (Diarra et al., 2012; Han et al., 2008, 2011; Shang et al., 2012) and had a magnitude of about 69° for microcrystalline cellulose powder. In this study, this constant value was used for the simulation. The DPC model parameters (d, β, R and p_b) found for MCC ph200 powder are comparable to those used by Han et al. (Han et al., 2011) for the study of another cellulose powder.

2.4. Numerical method

The Finite Elements Method modeling was performed using Abaqus software (Dassault Systèmes, Vélizy-Villacoublay, France). The set-up of the numerical modeling can be seen on Fig. 2.

2.4.1. Modeling of the press

In the simulation, the press is represented by a die and two punches (Fig. 2). The die was considered as a deformable material with constant elastic properties. To simulate the elastic deformation of the whole press, the two punches were represented by a deformable material with variable elastic properties that were calculated using the experimental curve of the compression of the calibration disk, as described below in the results section. The punches displacements were introduced in the simulation by adding the Abaqus key word "Amplitude" in the program.

2.4.2. Creep behavior

The powder bed was considered as a continuum media meshed with axisymmetric elements.

To take into account the creep behavior in the simulation, the cap creep model was used. This creep model is associated to the Drucker–Prager/cap model plasticity. The representation of the models in the p–q plan (p: hydrostatic pressure, q: mises equivalent stress) is given in Fig. 3. Depending on the type of loading, two creep mechanisms are active: cohesion creep and consolidation creep. The cohesion creep mechanism follows the type of plasticity active in the shear-failure plasticity region, whereas the consolidation creep mechanism follows the type of plasticity active in the cap plasticity region. As it can be seen in Fig. 3 there is an area in which both mechanisms are active. For the case of cohesion creep mechanism and for a given stress state, the equivalent creep stress $\tilde{\sigma}^{cr}$ is calculated as:

$$\tilde{\sigma}^{cr} = \frac{q - p\tan\beta}{1 - \tan\beta/3}$$

This stress is replaced by the effective creep pressure $\tilde{p}^{cr} = p - p_a$ when consolidation creep mechanism is used. In the die compression process, the consolidation creep mechanism is predominant.

Generally, creep behavior can be divided in three parts: primary, secondary and tertiary (Yang et al., 1999). The primary and tertiary creep behaviors are non-proportional when the secondary is proportional and easy to model. Creep laws are defined in Abaqus with "user subroutine" because of the complex form of creep curve. In this study, the standard power laws proposed in Abaqus/Standard