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Research paper

Investigation and modelling approach of the mechanical properties of compacts made with binary mixtures of pharmaceutical excipients

V. Busignies [a], B. Leclerc [a], P. Porion [b], P. Evesque [c], G. Couarraze [a], P. Tchoreloff [a,*]

[a] Centre d'études Pharmaceutiques de l'Université Paris XI, Châtenay-Malabry, France
[b] Université d'Orléans, Orléans, France
[c] Ecole centrale de Paris, Châtenay-Malabry, France

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Abstract

Three pharmaceutical excipients (microcrystalline cellulose, lactose, anhydrous calcium phosphate) and their binary mixtures were compacted to form compacts of various mean porosities. Some mechanical properties (Young's modulus, tensile strength and Brinell hardness) were studied on these compacts. The mechanical properties of the binary mixtures were not proportional to the mixture composition expressed in mass. More, for all the properties, a negative deviation was always observed from this linear relationship. In reference to a composition percolation phenomenon, critical mass fractions were detected from the graph mechanical property vs. mass composition of a mixture. The results obtained with Brinell hardness differed from the results of the Young's modulus and the tensile strength, i.e. the most plastic material in the binary mixture controlled the mixture behaviour. Secondly, a predictive model based on a statistical approach was proposed for the Young's modulus and the tensile strength. The validity of this model was verified on experimental data, and an interaction parameter used to characterize the affinity of the two compounds was calculated. Finally, the X-ray tomography technique was applied to the compacts of cellulose/phosphate mixtures to obtain cross-sections images of the compacts. The analysis of the cross-sections images allowed explaining the no linear relationship of the different mechanical properties results observed on these binary mixtures.

Keywords: Binary mixtures; Compactibility; Tensile strength; Young's modulus; Brinell hardness; Modelling; X-ray tomography; Percolation

1. Introduction

Tablets produced in pharmaceutical industry are generally made with a number of components. However, the study of the properties of compacted mixtures has received little attention. Data of single materials are generally available and the right formulation is generally obtained after lots of trials. Whereas, it must be useful to predict the tablet properties from the data obtained with the mixture components. Numerous workers have investigated the compaction of binary mixtures [1–8]. In most cases, no simple relationship is found from the compaction properties of the single materials and their proportions in the mixture, and the mechanical properties of tablets compressed from binary mixtures are in general not linearly related to the properties of tablets obtained from single materials. Many studies show three possibilities for this relationship, a positive/negative effect or a linear relationship [8]. These results are attributed to the degree of magnitude of the bonds between particles of different materials. In that case, the aim of all studies of tableting powder mixtures will be to use the known properties of single materials in order to predict the compaction behaviour of mixtures. Due to the variety and the complexity of tableting properties, there

* Corresponding author. IFR-141, "Innovation thérapeutique: du Fondamental au Médicament", Centre d'études Pharmaceutiques de l'Université Paris XI, 5 rue Jean-Baptiste Clément, 92296 Châtenay-Malabry, France. Tel.: +33 1 46 83 56 11; fax: +33 1 46 83 58 82.
E-mail address: pierre.tchoreloff@cep.u-psud.fr (P. Tchoreloff).

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Nomenclature

V: microcrystalline cellulose, Vivapur 12®
F: partly amorphous lactose, Fast Flo®
A: anhydrous calcium phosphate, A TAB®
VA: Vivapur 12®/TAB® mixtures
VF: Vivapur 12®/Fast Flo® mixtures
AF: A TAB®/Fast Flo® mixtures
ε: mean compact porosity
P_y: mean yield pressure
σ_c: compaction pressure
σ_r: tensile strength
E: Young's modulus
H_b: Brinell hardness
F_m: maximal load applied in microindentation and Young's modulus measurement
F_r: maximal load applied in tensile strength measurement
p: distance between the two support of the three point single beam test
δ: central deflexion in the three point single beam test
h and l: thickness and width of the parallelepipedical compacts
D: indentor diameter
D: diameter of the indentation imprint
n: number of experimental trials used in the calculus of the average values
Y_{AA}, Y_{BB}: properties of the single materials (A and B) in the 1st approach of the statistical model
Y_{AB}: property resulting from the binary interaction {AB} in the 1st approach of the statistical model
Y_{ww}: interaction parameter in 1st approach of the statistical model
Y_{AAA}, Y_{BBB}: properties of the single materials (A and B) in the 2nd approach of the statistical model
Y_{ABB}, Y_{BAA}: properties resulting from the triplet interaction {ABB} and {BAA} in the 2nd approach of the statistical model
Y_{ww1}, Y_{ww2}: interaction parameters in 2nd approach of the statistical model
x and $(1-x)$: mass proportions of the two components of a binary mixture in the statistical model (Section 3.3)

are few studies in the literature which propose a model for mechanical properties of compacted mixtures [9,10]. A satisfactory theory enabling the prediction of the mixture properties does not exist at present. Recently, the percolation theory was used to explain the change of properties of compacted binary mixtures [11,12]. In the case of powder mixtures, it is a composition percolation phenomenon and the important parameter is the phase fractions. Binary mixtures of powders can be considered as systems made of three phases: two particles phases and pore space. According to a composition percolation phenomenon and at a constant porosity, the mixture can be in three situations [12–14]. If an A/B mixture is considered, when the fraction of B is small, these particles are isolated inclusions and form a dispersed phase. The component in a greater proportion (A) and/or with the smaller particle size forms a continuous phase. The presence of a dispersed phase changes the behaviour of the continuous phase due to the localization of tensions. When the fraction of B increases, the particles of B form aggregates. At last, when the fraction of B particles is high, a percolating B particle network appears for a B concentration corresponding to the percolation threshold, p_{c1}. The phase A ceases to exist as an infinite cluster for a B concentration corresponding to the upper percolation threshold, p_{c2}. Between the two thresholds, the two components form two interpenetrating percolating networks. To know in which situation the mixture is could be helpful to understand the behaviour of powder mixtures. More, in binary mixture containing particles of both components A and B, three kinds of interactions may occur [15]: (1) A bonds preferentially with A and B bonds preferentially with B, (2) the affinity of A (B) for A (B) is the same as the affinity of A for B, (3) A bonds preferentially with B. Thus, the percolation thresholds in a compact of a binary mixture depend on the relative concentrations and the relative bond-forming properties [14].

The present work was performed to analyse the compaction behaviour of single materials (microcrystalline cellulose, lactose and anhydrous calcium phosphate) and their binary mixtures. This analysis was based on the measurement of some mechanical properties like Young's modulus, tensile strength and Brinell hardness. The three pharmaceutical excipients were chosen because of their different compaction behaviour [16,17]. The single materials and the binary mixtures were compacted and their mechanical properties were studied. First, the variations of these properties with the mixture composition are presented. Secondly, the objective of this study is to define the behaviour and to propose a model for the tensile strength and the Young's modulus of compacted binary mixtures using the mechanical properties obtained with the single excipients. X-ray microtomography technique was also performed with one of the binary mixtures to obtain cross-sections images of the compacts. These images were analysed to characterize and study the heterogeneity in the compacts. It was also correlated to the different mechanical properties observed.