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The intrinsic nature and the coherence of compacted pure pharmaceutical tablets

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Abstract

The paper describes methods to define the intrinsic mechanical nature, and the coherence of various pure compacted tablets using both the nanoscopic indentation and the confined die compaction results. Data for seven different kinds of pharmaceutical drugs and excipients, composing alpha lactose, microcrystalline cellulose (Avicel PH 102), acetylsalicylic acid (Aspirin), dicalcium phosphate, magnesium carbonate, acetaminophen (Paracetamol) and pre-gelatinized starch are reported. The powders were compacted to various ultimate normal stresses ranging between 25 and 246 MPa in instrumented (force/displacement) singled ended axial compression in a cylindrical die with planar punch. The planar surfaces of these compacted tablets were nano-indented. The results clearly show that the coherence and the intrinsic nature of the tablets may be defined in a more comprehensive manner using interpretations of the nano-indentation rather than the uniaxial compaction data. The various data are consistent with the magnitude of the tensile strength of the compacts.

Keywords: Intrinsic mechanical nature; Coherence; Nanoscopic; Alpha lactose; Avicel PH102; Aspirin; Dicalcium phosphate; Magnesium carbonate; Paracetamol; Pre-gelatinized starch

1. Introduction

The compaction of powders is widely used in the pharmaceutical industry to convert drugs, in the form of small particles, into coherent and tough metered solid dosage forms. This has proven to be a very effective and economic means of drug delivery. Producing drugs in the tabletted form is, in fact, the most common means of drug delivery. It is, in volume terms, by far the most frequently adopted means of drug and food supplement delivery.

The process of tabletting can be described as the route "whereby a loose natural or prepared powder is placed in some form of die and pressed between punches to form a coherent mass" [15]. The ability of a powder mass to reduce in volume when compressed does not, however, ensure the formation of a mechanically coherent tablet. It is important that the powder particles cohere, or adhere, into a suitable form after removal of the applied tabletting load and the ejection from the die [7].

Practically this requires the formation of tablets of appropriate size and shape with the required incorporation of the chosen drug. At a pilot stage this would normally require the production of a large number of tablets, and consequent use of significant amount of the drug. The tablets would then be fractured using the Brazilian Test Method [6].

A different technique is to employ a nano-indenter. This apparatus, which is highly sensitive and precise, can probe a very small volume of material; perhaps a single particle but certainly the junctions between a few particles. The compliance response produced as a result of indenting material constitutes some characteristics, such as the creep response and the elastic recovery, by which the coherence of the compacted material may be interpreted or rationalised.

Nano-indenters have been employed in the characterisation of materials for some years [16]. Oliver and Pharr [12] describe in detail the use of nano-indentation to determine the hardness and elastic modulus of materials such as fused silica and soda

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lime glasses and for single crystals of aluminium, tungsten, quartz and sapphire. Liao and Wiedmann [10] used nano-indentation to characterise the surface hardness of pharmaceutical solids such as paracetamol and potassium chloride.

The loading and unloading curve (schematically presented in Fig. 1) to some extent characterises the nature of the intrinsic deformation of the material under test, is subdivided into several sub-sections, i.e., the induction phase, the mean slope, and the smooth or discontinuous, linear/hardening later phases. The strain relaxation noted during the holding segment is a reflection of the material's duration dependent flow or creep response. The unloading curve, from which most of the mechanical properties of a material can be deduced, gives a good indication of the stored elastic strain.

The final segment, to complete a cycle of a nano-indentation test, is the unloading segment. During this segment the indenter tip is removed. The reaction of removing the indenter tip is graphically recorded as the reaction load versus the imposed penetration depth. This segment is also a significant means to characterise the mechanical response of the material under test and to sense and quantify the stored elastic strain, which is a major factor in defining the cohesion of the materials utilised in this study. The extent of the stored elastic strain was deduced from the elastic work of the material under test, and calculated by integrating the area underneath unloading curve as was suggested by Briscoe, Fiori and Pelillo [3]. However, it suffices to say, that the material with a high elastic recovery has an advantage during the ejection process, as the die walls cannot form plastic junctions with the compacted material, and the material in turn does not greatly adhere to the die walls.

This current paper will illustrate that the mechanical coherence of a particular tablet may be tentatively established using a nano-indenter system. Nano-indentation data are reviewed and compared with the force/displacement characteristics observed during the compaction of the tablet and with the tensile strength determined by diameteral compression.

2. Materials and experimental methods

2.1. Material

Seven different types of excipients and drugs, as tabulated in Table 1, were investigated at both the macroscopic and the nanoscopic level. The powders were all of pharmaceutical quality and representative of the grades typically used in industrial compaction.

2.2. Preparation

The mass of each tablet was kept constant at 1 g, and the powder for each tablet was weighed using a Sartorius electronic balance, Model MC1 (Sartorius AG, Goettingen, Germany), with the accuracy range of ±0.001 g, and poured into a hardened stainless steel cylindrical die 16 mm diameter using a plastic funnel with a large tube diameter to facilitate the flowability of the powder; stage I in Fig. 2.

2.3. Uniaxial compaction

The tablets were uniaxially compacted, between a mirror-polished platen and a single acting upper punch, in a cylindrical 16 mm diameter hardened stainless steel die manufactured by Specac, UK; stage II in Fig. 2. The compactions were carried out using a commercial universal testing machine (Lloyds EZ 50, UK), at a cross-head speed of 0.1 mm/s for loading and 0.0167 mm/s for unloading; stage III in Fig. 2. The applied force and the cross-head displacement were recorded by a compatible computer software programme, termed "Nexygen Ondio"

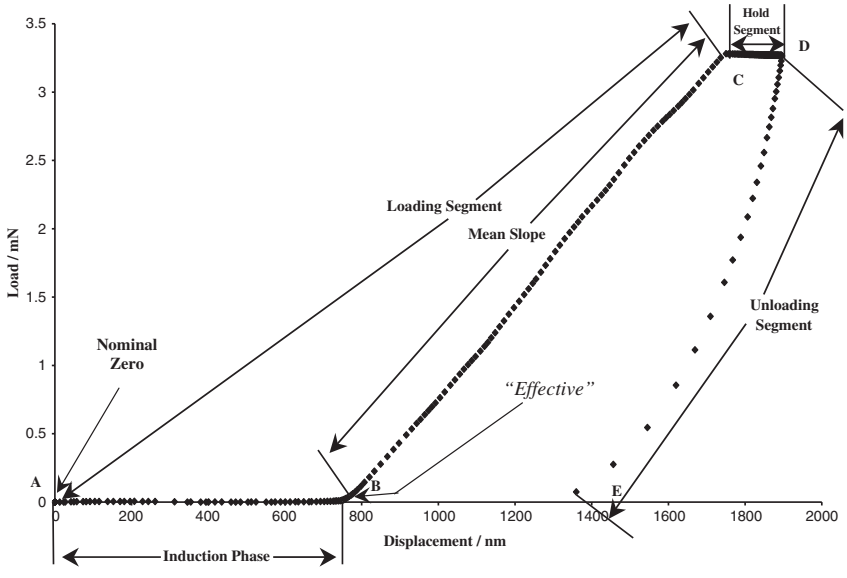

Fig. 1. Schematic of a complete cycle of a nano-indentation test and its various segments; AB is the induction, BC is the points selected to find the mean slope, AC is the loading segment, CD is the holding segment, and DE is the unloading segment.