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Mechanics of pharmaceutical pellets – Constitutive properties, deformation and breakage behavior[☆]

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Abstract

To ensure robust manufacturing of unit-based oral solid dosage forms with minimal structural imperfections and high mechanical reliability across subsequent processing unit operations (for e.g. withstanding mechanical stresses during coating, optional axial compression, handling, packaging, storage and transport conditions), process design should include consideration of precise limits of accurate micro, macro and bulk properties of the constituent pellets.

This communication presents a comprehensive intricate database of micro-mechanical properties' and breakage probability distribution functions of pellets, illustrating the stiffening and strengthening effects of coatings and the softening and weakening effects of structural moisture. Further insights such as the (contact) history-dependent softening during decompression, strain hardening upon repeated stressing, strength recovery by drying and the fragmentation pattern by cracking are also presented.

The contents herein are based on conveniently performable lab-scale diametrical compression measurements on model microcrystalline cellulose pellets – demonstrating feasibility of the approach and validity of the contribution.

Keywords

compression, excipients, fluid-bed, image analysis, mechanical properties, microcrystalline cellulose, physical characterization, powder technology, solid dosage form, water in solids

1 Challenges and a pragmatic approach to a comprehensive solution

As of today, at least 80% of all pharmaceutical products involve oral solid dosage forms (OSDs). Tablets (generally $3 \leq h \leq 6$ mm and $5 \leq d \leq 10$ mm) and capsules (generally $14 \leq h \leq 25$ mm and $5 \leq d \leq 8$ mm) account to approximately 50% and 18% respectively of today's global OSDs. If the manufacturing of the drug substance and end-units containing them are put together – the manufacturing throughput can range from 1-5000 kg/h and can cost from 1 to 10,00,000 $ US per gram. With the increasing medicinal efficacy and multi-dimensional quality, these traditionally consumption-easy products are only going to be increasing.

Often powdery raw, in-process materials and intermediates suffer from low bulk density, poor flowability, caking effects at storage, segregation at handling and poor compressibility. For such reasons, powders may often be first processed to form granules/pellets multiple unit pellet systems (MUPS®)[1], which may then subsequently be used to manufacture OSDs;

[☆]in memory of Prof. Dr.-Ing. habil. Jürgen Tomas (1953-2015)