The development of a robust methodology to evaluate inhalation capsule puncture performance

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PURPOSE

• Two-piece gelatin capsules have been used traditionally as an oral dosage form and as unit dose containers for a powdered drug for use in dry powder inhalers (DPI).
• Hypromellose is an alternative capsule material that has been shown to possess better functional properties than gelatin when used in DPI.
• Both materials are currently used in DPI but a standardised methodology to evaluate capsule puncture performance, which is an essential property, does not exist.
• This study aimed to develop a robust methodology to determine potential differences in the puncture characteristics of different capsule materials, to assist in the development of hard capsules for this application.

METHODS

• A steel conical tipped pin from a commercial DPI device (Plastiape S.p.a., Monodose Mod.7, 2 x 1 pin), see Fig. 1, was mounted in a bespoke miniaturised materials testing machine (Zwick® Testing Machines Ltd, UK), attached to an XForce P 50N load cell, see Fig. 2. The equipment is designed to measure small changes in force (accuracy ±1% of the measured value) during a measurable displacement.
• A stainless steel bushing from a capsule-filling machine (Qualicaps), held a size 3 capsule in a fixed position directly below the steel pin.
• Hypromellose and gelatin capsules (n=10 per each test), conditioned over saturated solutions of Calcium chloride (33% RH) and Lithium Chloride (11% RH) at 22ºC for 1 week, to simulate poor storage conditions.
• Capsules were punctured by the pin at a speed of 10 mm/s and the displacement of the pin and the resulting forces were recorded on a force-displacement curve.
• Punctured capsules were subsequently removed from the bush for visual inspection, see Fig. 3.

RESULTS

• Repeated force-displacement profiles were highly reproducible for each of the capsule materials. However, HPMC and gelatin capsules possessed different signature profiles, characterised by differences in the penetration event, see Figure 4.
• Gelatin capsules: showed a rapid drop in force after puncture indicating that the pin had lost contact with the shell wall; the force then increased as the flap regained contact. This was more marked after lower RH conditioning indicating particles of the shell wall had become detached.
• Hypromellose capsules: compared to gelatin the drop in force after puncture was less rapid and declined less; there was a much reduced second peak compared to gelatin. The difference probably being due to a lower elasticity of these puncture flaps compared to the gelatin ones.
• The force required to puncture hypromellose capsules was lower than for gelatin and occurred at a shorter deformation distance, see Table 1.

CONCLUSIONS

• A rapid and robust methodology has been developed that is able to characterise penetration of a hard shell capsule by the pins that are employed in DPI.
• The sensitivity and reproducibility of the methodology enables users to describe differences in the capsule materials. This could have a significant impact on the design, development and quality assurance of hard shell capsules for use in DPI.

BIBLIOGRAPHY


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