Understanding intra- and inter-individual differences in capsule puncture following actuation of a dry powder inhaler

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RESULTS & DISCUSSION

• Inhalation grade hard capsules size 3, clear/clear, gelatin and hypromellose (Quali-V®-I) were supplied by Qualicaps Europe.
• Before use capsules, closed manually to the locked position, were conditioned in desiccators at a saturated solution of lithium chloride (c. 11% RH) and calcium chloride (c. 34% RH) for 10 days at room temperature. The RH were chosen to represent sub-optimal storage conditions and give moisture contents below and at the lower end of the moisture specification limit. Their moisture content was determined by loss on drying tests4.
• Four types of capsules were tested: gelatin & hypromellose (at the lower end of moisture specification) and gelatin & hypromellose (below the moisture specification).
• Each participant punctured 12 capsules, 3 of each type, in a randomised order and were blinded to the capsule type.
• Participants were then given a questionnaire to comment on their experiences.
• Punctured capsules were positioned in steel holder, cap facing up, and were imaged using an AmScope stereo-microscope before being analysed using ImageJ® software.

METHODS, continued

• Approval for a study using volunteers was obtained from Cardiff School of Pharmacy and Pharmaceutical Sciences Research Ethics Committee.
• Participants were recruited by convenience sampling and data was collected from each volunteer on their age, gender, occupation and experience of using a DPI.
• Sampling aimed to recruit equal numbers of men and women across five different age groups between 18 and 65. Exclusion criteria included previous experience of using or witnessing a DPI being used.
• An information sheet was provided to volunteers and consent was obtained before the study.
• A standard script was used to provide a brief description of study and an instruction sheet was explained to explain how to use the DPI. No additional verbal information was given. Standardised answers to questions that participants could ask were prepared in advance.
• A questionnaire was given to each participant to rate how easy or difficult it was to load capsule and press the buttons.
• DPI naïve participants (n=34) were selected: gender: 18 female and 16 male; ages, 7 in groups 18-24, 25-34, 35-44, 45-54, and 6 in 55-64.
• A two-pin Monodose DPI supplied by Plastiape S.p.A. (Milan, Italy) was used in the study, see Fig.1.

CONCLUSIONS

• A small number of capsules failed to be punctured by the DPI user; hypromellose (n=6) and gelatin (n=3). The difference was not statistically significant (Z-test for comparing proportions, p=0.3124). Hesitancy, observed in some participants at the beginning of the experiment, may account for some non-punctures.
• Results indicate that the greatest variability in the area of the puncture was in gelatin capsules with normal moisture specification. However the inter-individual variability in puncture area was significantly different between gelatin and hypromellose capsules with normal moisture specification. The intra-individual variability was also greater for gelatin capsules than hypromellose capsules at both moisture levels.
• The shape of the punctures in hypromellose capsules at both moisture contents were predominately circular (80%).
• Puncture shapes in gelatin capsules were more variable, particularly at low moisture content, see Fig. 5B, and flaps were also detached (74.5%), compared to the gelatin capsules with normal moisture content (97.1%).
• The majority of participants rated the process of loading the capsules and pressing the buttons as very easy (27/34) and the remainder as easy.

BIBLIOGRAPHY

4. Qualicaps, Chemical and microbiological test methods for Quali-V® capsule and Quali-V®-I capsule, 2013, p.26, "Test, loss on drying"