

## PURPOSE

- Hard capsules are made by a dipping process and a surface lubricant for the mould pins is an essential processing aid for removing dried capsule shells from manufacturing pins, see **Figure 1**.
- This lubricant has been shown to have an effect on powder retention in capsules that are used for inhalation of medicines<sup>1,2,3</sup>.
- A method to measure the amount of mould lubricant has been developed for Qualicaps by Complutense University in Madrid<sup>4</sup>.

## AIM

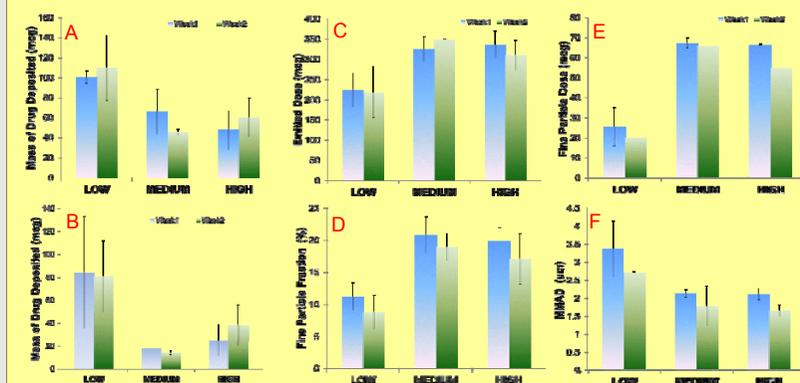
- To investigate aerosolization properties of a model inhalation powder formulation, lactose and micronized salbutamol, from hypromellose capsules with different levels of internal lubricant when used in dry powder inhaler (DPI).
- Good quality capsules, with visual properties and filling machine performance, were manufactured with each level.



**Figure 1.** Diagram of hard capsule manufacturing machine to show machine sequence and where point mould lubricant is applied.

## METHODS

- Inhalation grade lactose (Respitose, supplied by SMB Technology) was fractionated by sieving, using 250, 125, 90, 63 and 45  $\mu\text{m}$  sieves, at vibration amplitude of 40 for 10 min and particles were collected on the 90  $\mu\text{m}$  sieve.
- Micronised salbutamol sulphate and lactose were mixed in ratio of 1 : 50 (w/w) via geometric dilution to obtain a 2 % binary blend.
- Once blend uniformity was achieved,  $20 \pm 1$  mg of blended powder was filled into size 3 hypromellose capsules (Quali-V®-I) manufactured using three different lubricant levels; low (10.81  $\mu\text{g}/\text{capsule}$ ), medium (15.97  $\mu\text{g}/\text{capsule}$ ) and high (23.23  $\mu\text{g}/\text{capsule}$ ).
- The capsules were stored in a humidity chamber (Sanyo Atmos Chamber) at 22 °C and 40 % RH for 2 weeks (n=3).
- The stored capsules were emptied using an 8-pin DPI (Plastiapi) into a next generation cascade impactor. This was repeated at weekly intervals and the drug content was assessed via HPLC method.
- Mass of Drug remaining in capsule/device, Emitted Dose, Fine Particle Dose, Fine Particle Fraction and the Mass Mean Aerodynamic Diameter (MMAD) were measured.



**Figure 2.** Effect of capsule lubricant level & storage on Mass of Drug Deposited, Capsule(A) & Device (B), Emitted Dose (C), Fine Particle Fraction (D), Fine Particle Dose (E) and Mass Mean Aerodynamic diameter (F).

## RESULTS

- Results clearly indicate significantly lower Emitted Dose from capsules with the low lubricant level. For the medium and high level of lubricant the Fine Particle Dose & Fine Particle Fraction were almost twice that obtained with the low level of lubricant. The MMAD was significantly lower.
- Similar result was reported by Saim & Horhota in 2002 who proposed a method for overcoming drug retention in hard gelatin inhalation capsules by washing closed empty capsules with supercritical carbon dioxide to remove the internal lubricant<sup>2</sup>. They found the greatest powder retention occurred at a low level.

## CONCLUSIONS

- The study clearly indicates that lubricant level within capsules has influence on deposition profiles and amount of drug remaining in capsule and inhaler device after actuation.
- The results obtained suggest lubricant levels greater than 10.81  $\mu\text{g}$  are beneficial as there is a decrease in drug deposition in capsules, whilst more than doubling the fine particle dose and fraction.

## BIBLIOGRAPHY

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