

Influence of internal lubricant on powder aerosolization properties from inhalation grade hypromellose capsules (Quali-V®-I)

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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^{1,2,3}.
- A method to measure the amount of mould lubricant has been developed for Qualicaps by Complutense University in Madrid⁴.

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 (Respirose, supplied by SMB Technology) was fractionated by sieving, using 250, 125, 90, 63 and 45 µm sieves, at vibration amplitude of 40 for 10 min and particles were collected on the 90 µm 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 ± 1 mg of blended powder was filled into size 3 hypromellose capsules (Quali-V®-I) manufactured using three different lubricant levels; low (10.81 µg/capsule), medium (15.97 µg/capsule) and high (23.23 µg/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 (Plastiapipe) 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, Emittted Dose, Fine Particle Dose, Fine Particle Fraction and the Mass Mean Aerodynamic Diameter (MMAD) were measured.

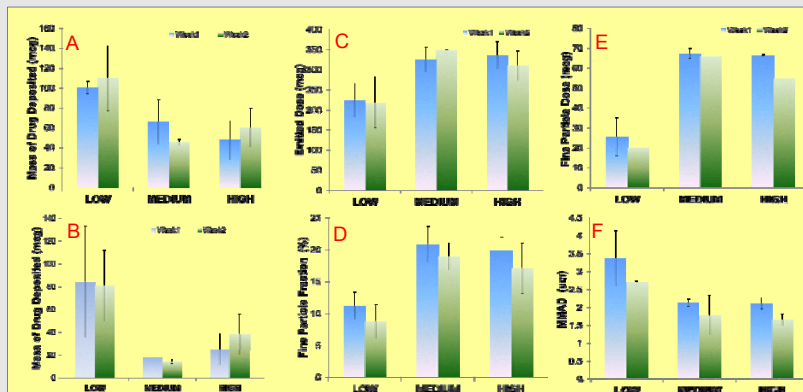


Figure 2. Effect of capsule lubricant level & storage on Mass of Drug Deposited, Capsule(A) & Device (B), Emittted Dose (C), Fine Particle Fraction (D), Fine Particle Dose (E) and Mass Mean Aerodynamic diameter (F).

RESULTS

- Results clearly indicate significantly lower Emittted 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 lubricant². 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 µg are beneficial as there is a decrease in drug deposition in capsules, whilst more than doubling the fine particle dose and fraction.

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