

How important is internal lubricant in capsules for inhalation?

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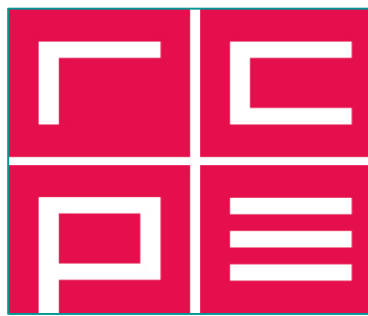
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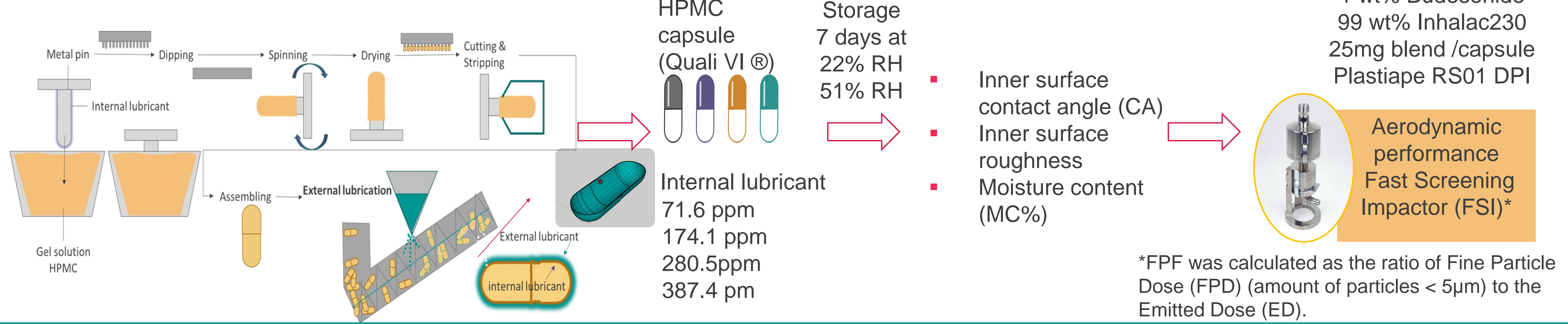
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Introduction

Hypromellose (HPMC) inhalation grade capsules are made by dipping stainless steel mold pins into the warm polymer solution, polymer drying and film formation. To safely remove capsule from pins, pins are previously coated with a surface lubricant. In this study, we addressed the hypothesis that the remaining internal lubricant may influence the delivery of API from capsule-based dry powder inhaler (DPI) due to the different surface roughness, storage conditions and surface energy of the capsules surface and lipophilicity of the formulation used for inhalation.

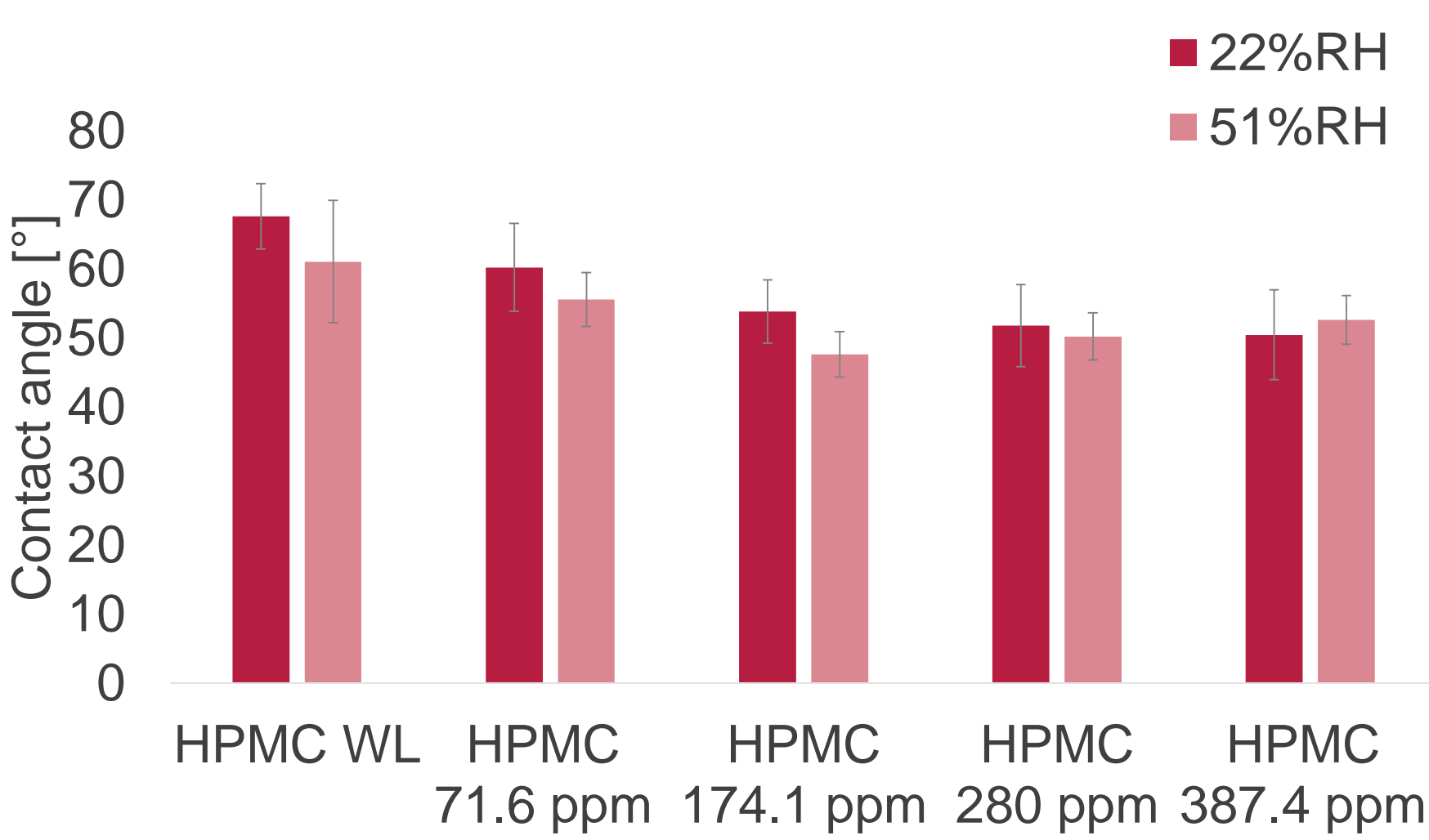
Materials and Methods



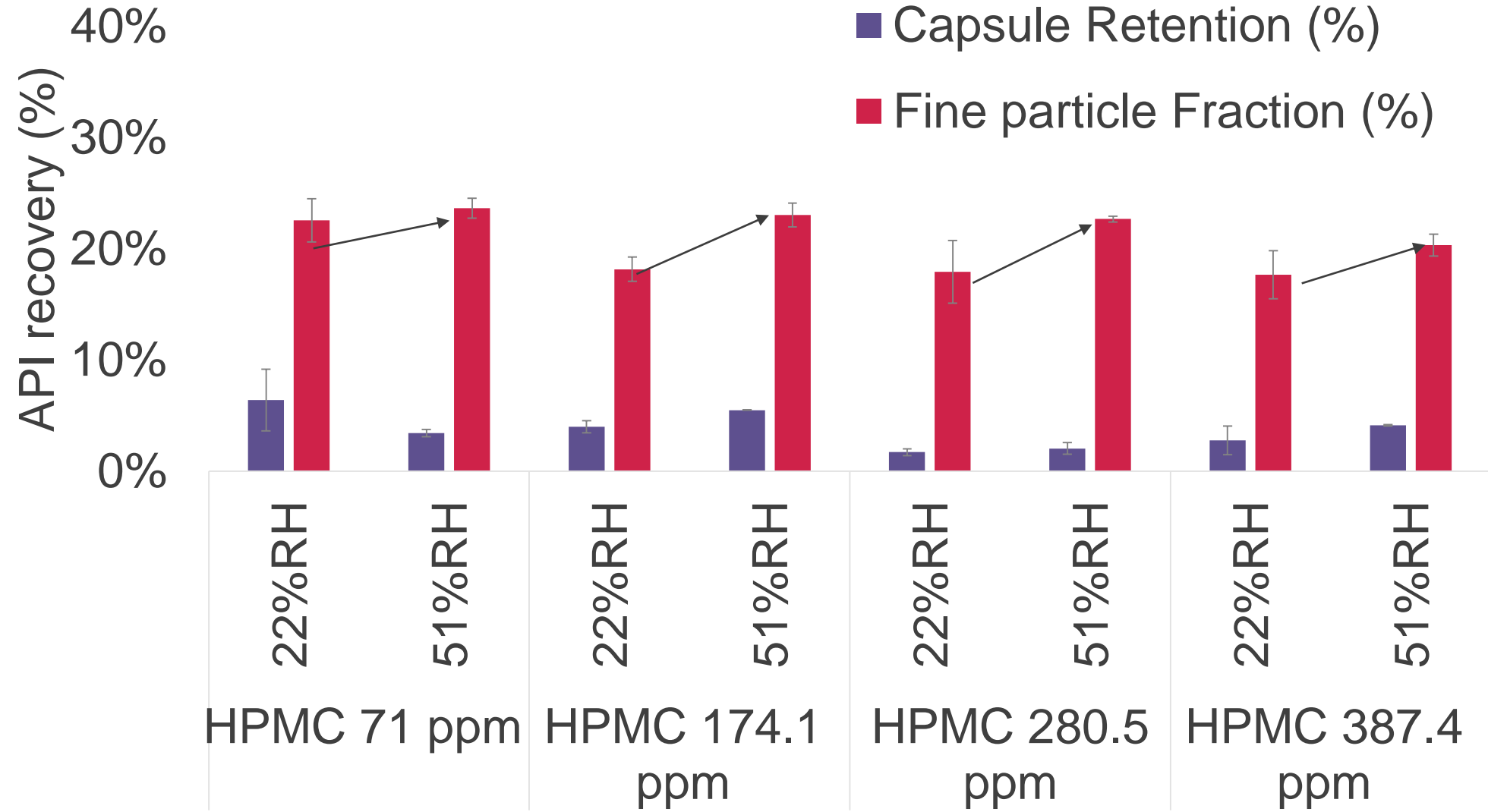
Results

Lubricant content (ppm)	Ra (nm), initial samples at T=0	MC (%) for capsules at T=0
HPMC 71.6	86.13 ± 5.97	5.3 ± 0.15
HPMC 174.1	57.07 ± 10.85	5.25 ± 0.35
HPMC 280.5	66.5 ± 16.50	5.18 ± 0.18
HPMC 387.4	59.60 ± 6.12	4.98 ± 0.42

Surface roughness and MC (%) of the capsules as received (no storage). Surface roughness: Ra (nm)-arithmetic mean height of the assessed profile. n=3±SD



CA of the inner surface of the capsules stored at 22 %RH and 51 %RH using water as a polar solvent. HPMC without lubricant (WL). n=3±SD



API fraction retained in the capsules and fine particle fraction (FPF) delivered from the capsules stored at 22% RH and 51% RH, n=2-4±SD

- Roughness (Ra) decreased with increasing internal lubricant amount from 71.6 ppm → 174.1 ppm; further increase in lubricant amount less affected the Ra.
- Lowered Ra of capsules with higher lubricant → better inner surface coverage by lubricant and fewer asperities on the inner surface.
- CA<90 : hydrophilic inner capsule surface; higher CA of non lubricated (WL) compared to lubricated capsules might imply increased hydrophilicity after lubrication.

At 22 %RH, API capsule retention decreased with increasing lubricant amount and seemed to be less affected for capsules with higher lubricant content (280.5 ppm - 387.4 ppm). At both RHs, FPF decreased from capsules with 71.6 ppm to capsules with 174.1 ppm lubricant and seemed to be less affected for capsules with higher lubricant content. FPF seemed more influenced by the storage conditions, as higher FPF was delivered from capsules stored at higher RH.

Conclusion and outlook

- Lubricant still present on the inner capsule surface may influence the roughness, hydrophilicity and API capsule retention.
- Different polarity and quantity of remaining lubricant might contribute to the interaction of API with capsule surface causing variable aerosolization. The lipophilicity of API might be important for the API retention in differently lubricated capsules.
- The interplay of different factors (roughness, humidity, hydrophilicity) of capsule material but also formulation used in inhalation need to be taken into account when formulating DPI based formulations and will be focus of our further work.