

Does water impact capsule roughness and DPI aerodynamic performance?

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Introduction

- ⊕ Capsule-based dry powder inhaler (DPI) is one of the most widespread inhalation delivery devices used for the treatment of a diverse range of pulmonary diseases.
- ⊕ The moisture content of the hard capsules used in these devices depends on the environmental relative humidity (RH) to which they equilibrate. Different moisture contents often affect formulation performance.
- ⊕ The present work intends to study if water absorption by two capsules with different color may impact their inner surface roughness and the fraction of API released.

Methods

For this study, two HPMC capsules with different colors (clear and orange) were stored at different conditions (1%RH/RT, 75%RH/RT, 75%RH/40°C) with and without a powder formulation. Empty and filled capsules were tested by atomic force microscopy (AFM), water content (coulometric Karl-Fisher) and aerodynamic PSD (by NGI).



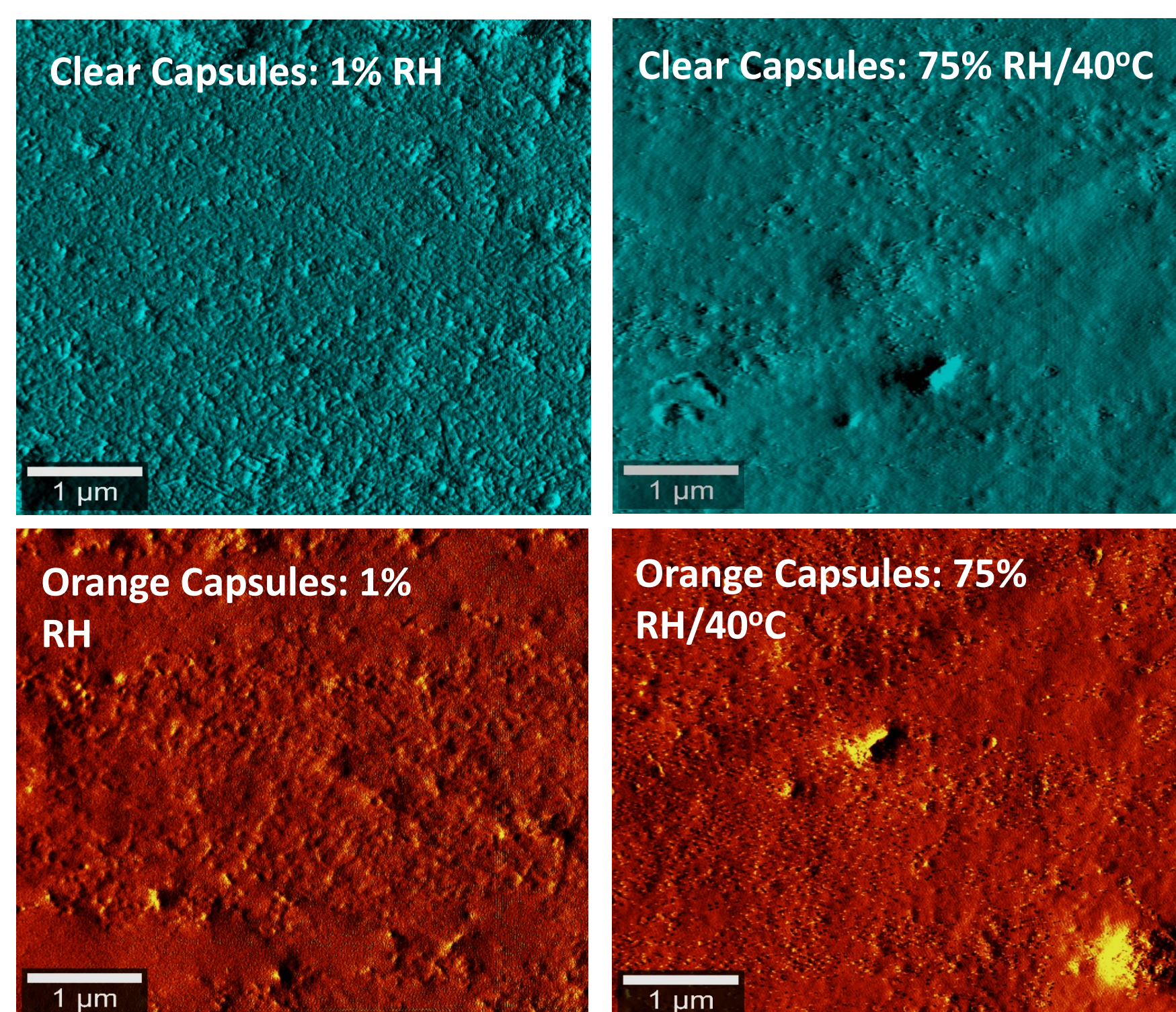
Results

KF analysis

Capsule type	Test type	Water content (% w/w)			
		Room Rel. Humidity (46-49 %)/Room Temp (RT)	1% RH/ RT	75 % RH/ RT	75 % RH/ 40°C
Clear Capsules HPMC #3	Empty capsule	5.5	0.5	11.0	9.2
	Powder inside the capsule	5.0	4.9	5.1	5.0
Orange Capsules HPMC #3	Empty capsule	5.1	0.9	9.6	8.4
	Powder inside the capsule	4.9	5.1	5.1	4.8

- Both clear and orange capsules showed to be highly affected by the RH in which they were stored:
- RH of 1% led to a reduction of the water content to levels below 1% in both clear and Orange capsules;
 - Slightly lower water content was found for empty capsules stored at the same RH (75%RH) but higher temperature (40°C);
 - The water content of the powder formulation inside the different capsules showed to not be affected by the different humidity conditions in which the capsules were exposed. However, 98% of the formulation contains lactose monohydrate, which is a stable and non-hygrosocopic excipient with about 5% w/w of water content.

AFM analysis



Capsule type:	Roughness SA (nm), mean (n=3)		
	Conditions: 1%RH/ RT	Conditions: 75 % RH/ RT	Conditions: 75 % RH/ 40°C
Orange Caps.	131.5	120.4	94.6
Clear Caps.	137.9	55.0	30.9

- AFM showed that clear capsules stored at 1% RH had higher roughness in the inner shell surface than the ones stored at 75%/RT and 75°C/40°C probably due to the plasticization of the HPMC capsule by the water and temperature.
- The same roughness reduction extent was not observed in orange capsules, which could be explained by the presence of the pigment that reduces the ability of water to interact directly with the capsule polymer.

NGI analysis

% of ED vs H₂O (%w/w)

Clear capsules: Fraction of API released remain constant regardless of the capsule water content

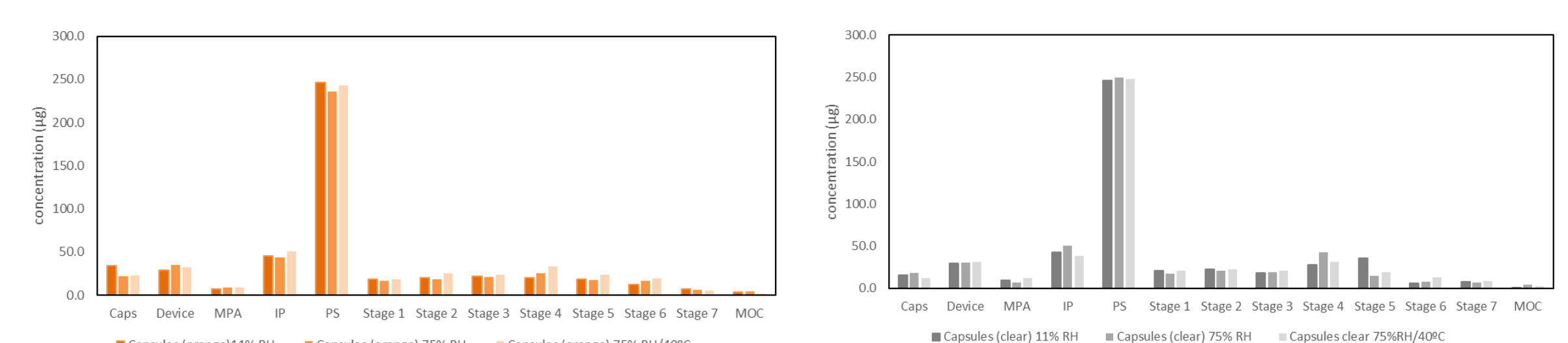
Orange capsules: Higher capsule water content led to lower drug release (r=0.99)

% of ED vs roughness

Clear capsules: The reduction of inner capsule roughness surface seems not to affect drug release in both capsules

Orange capsules:

% of Emitted Dose (ED)	Capsule type	1%RH/ RT	75 % RH/ RT	75 % RH/ 40°C
		Orange	91	83
Clear	87	88	87	



Conclusions

- ⊕ Storage conditions led to a modification in capsule's water content and roughness, which was different for the two capsules under study;
- ⊕ For the formulations studied, no major impact in % ED was seen with the modification of capsule roughness observed during storage at different RH conditions;
- ⊕ Although capsules shells showed to be physically affected by an increase of RH, the water content of the powder formulations remained constant regardless of the RH in which they were stored. Nevertheless, orange capsules showed reduced ED % when stored at higher RH conditions (75% RH);
- ⊕ The extent of water exchange between the capsule shell and the powder blend and how it impacts formulation performance, needs further study;