Influence of the opening size on the air velocity through the capsule in the capsule based Dry Powder Inhaler's (cDPI's)

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Capsule based Dry Powder Inhalers (cDPI‘s)

Frictional forces between material

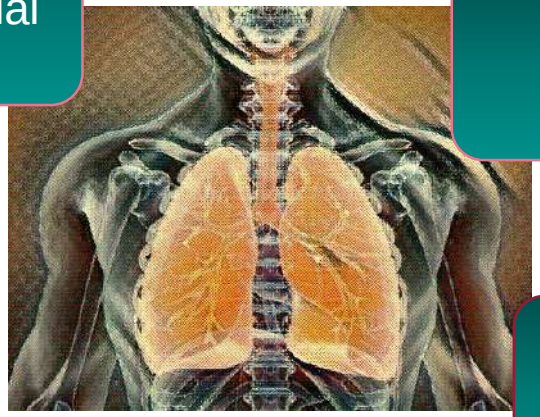
Capsule filling process

Filling material

Material-material interactions

Device

- Geometry of the mouthpiece
- The capsule chamber volume
- Position of the capsule in the chamber
- Structure of grids



Capsule shell

- Piercing/puncture properties
- Elasticity of the shell
- Lubrication

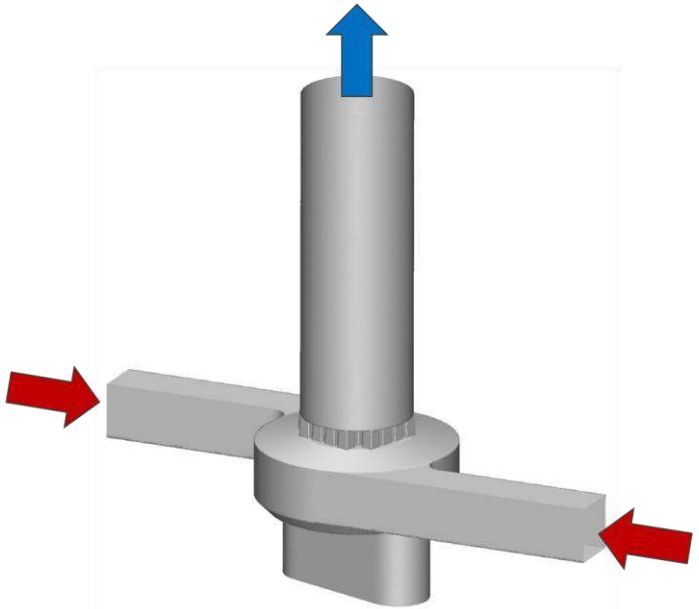
Patient inspiratory flow

Ambient temperature and humidity

Geometry of the airways

Computational Fluid Dynamics (CFD) simulations

- Experimental observation of processes within small inhaler device (the air flow, breakage of agglomerates, drug detachment during wall impact, inertial effects, impact velocity and angle) is very difficult.
- CFD simulations are tools used for numerical analysis of dry powder inhalers to allow understanding of flow structures and the resulting transport of drug particles.



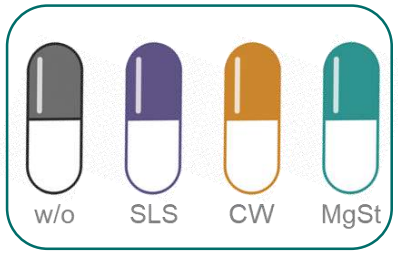
Aim of our work

- To compare the sizes of the openings (punctures) of differently stored and lubricated gelatin capsules pierced using Plastiape RS01 inhaler.
- To compare the size of the openings to the emission of fine particle dose (FPD) delivered through the given opening.
- To understand the air flow circulation through the capsules opening in relation to the size of the opening area and relate it to the delivery of the FPD.

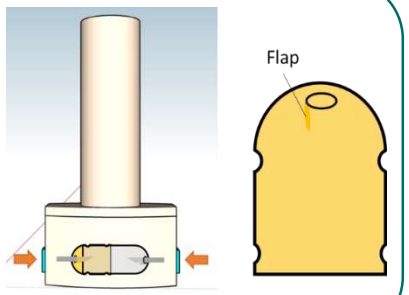
Materials and methods

Capsule puncturing, evaluation of the openings; capsule filling process & aerodynamic performance

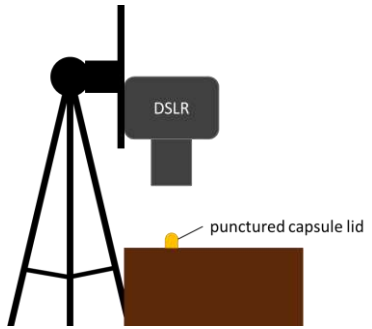
Gelatin capsules (size 3)

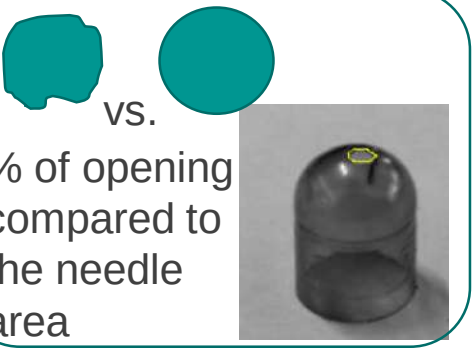


7 days
22%RH
51% RH



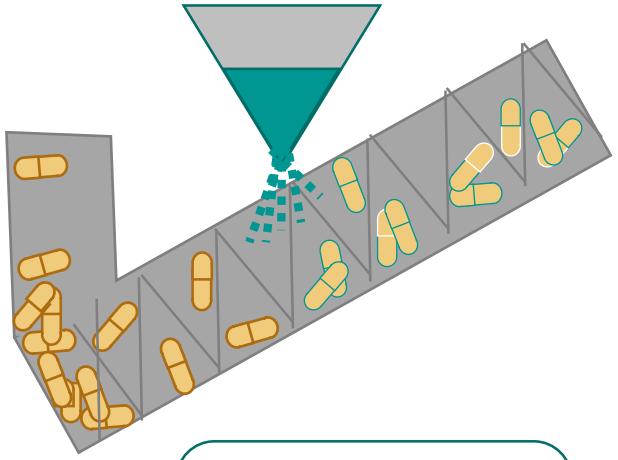
Plastiape RS01



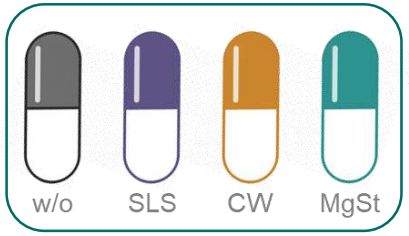


vs.

% of opening compared to the needle area



- without lubricant [w/o]
- Sodium lauryl sulfate [SLS]
- Carnauba wax [CW]
- Magnesium stearate [MgSt]

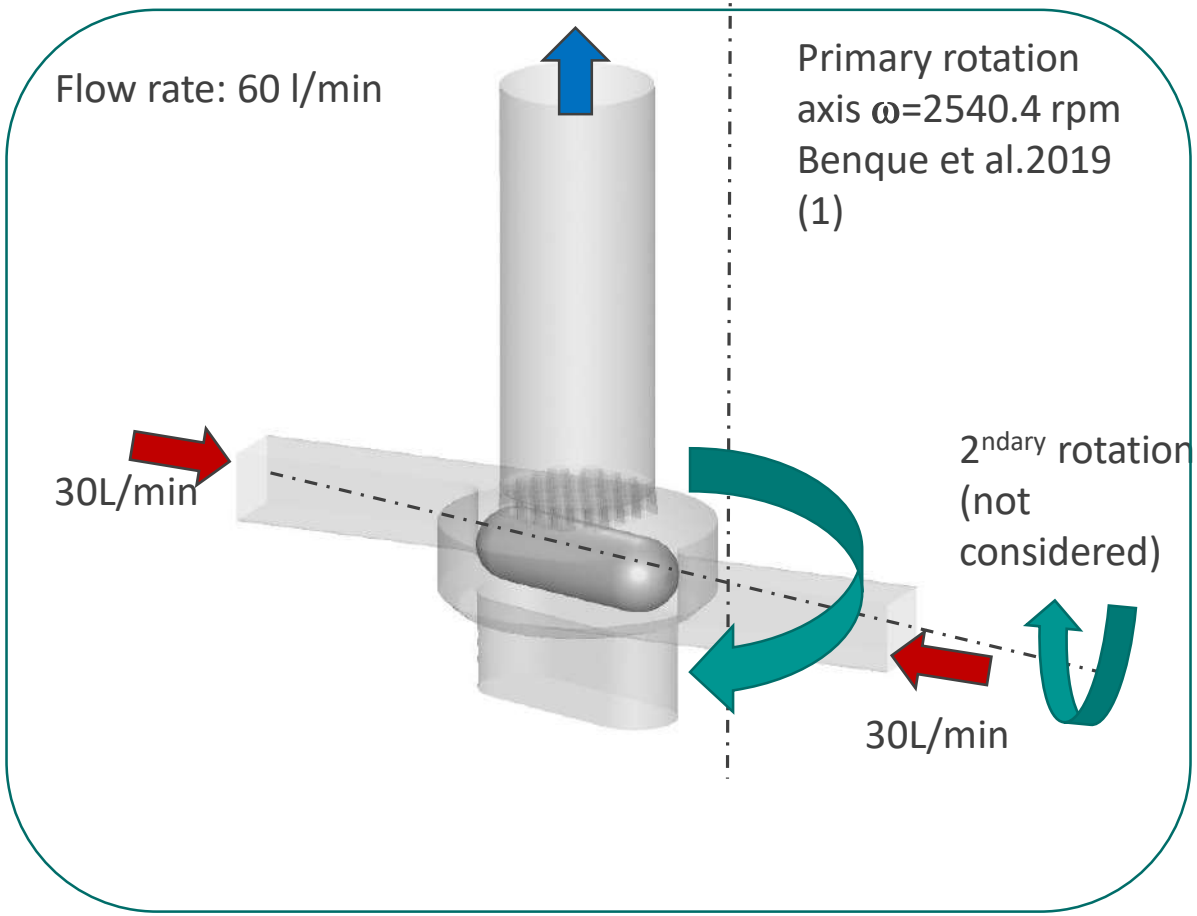


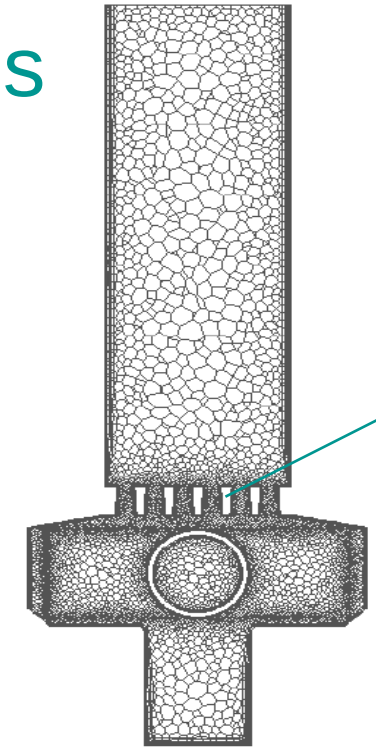
1 wt% Budesonide
99 wt% Inhalac230
25mg blend /capsule

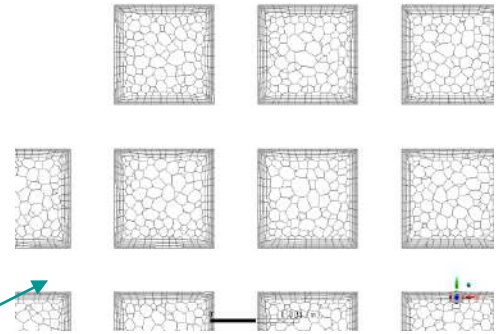
Capsule filling via Flexalab (MG2) at 22% & 51% RH, 1500 cph

Aerodynamic performance- Fast Screening Impactor (FSI)

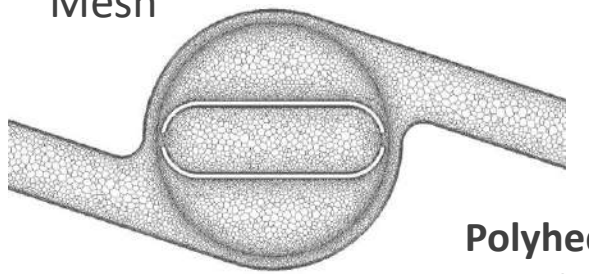
Simulation of flow and rotation rates



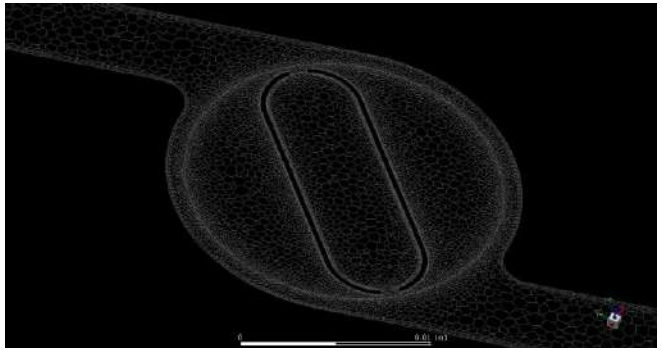




Mesh



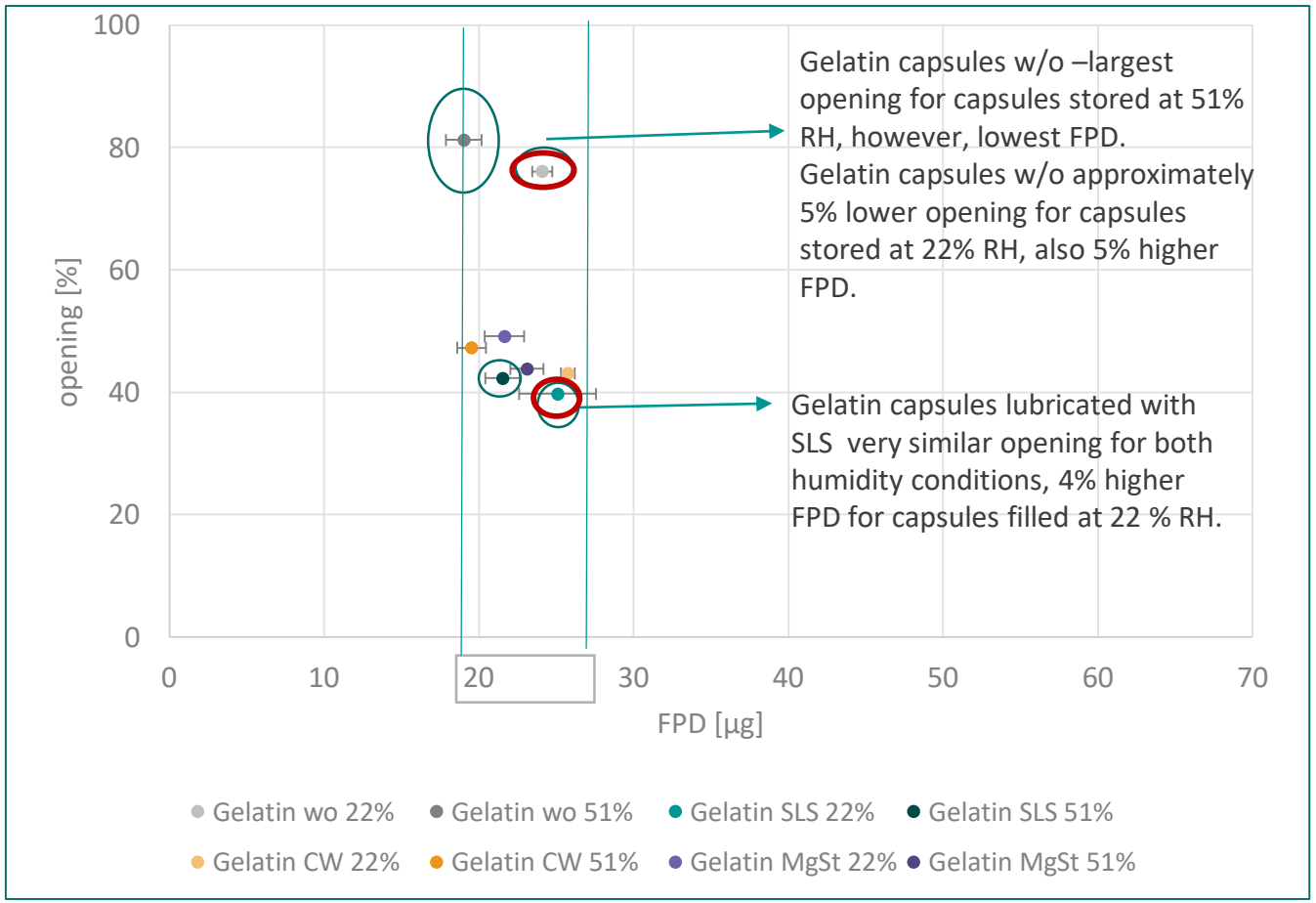
Polyhedra, 1.2Mio Cells



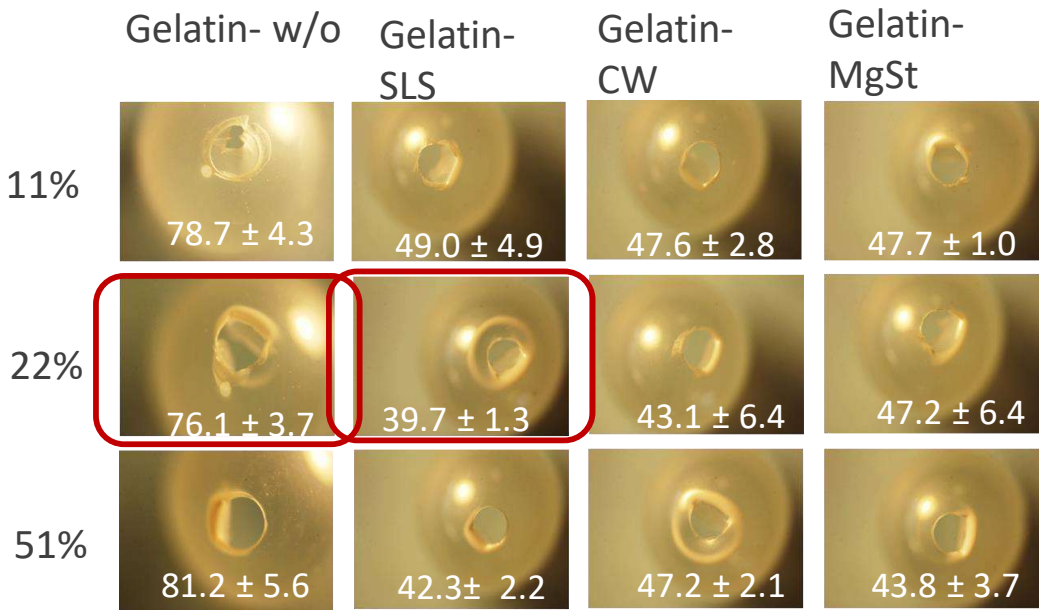
1. Benque et al. “Understanding motion of hard shell capsules in DPI’s.” vol.567 *Int.Journ.Pharm 2019*

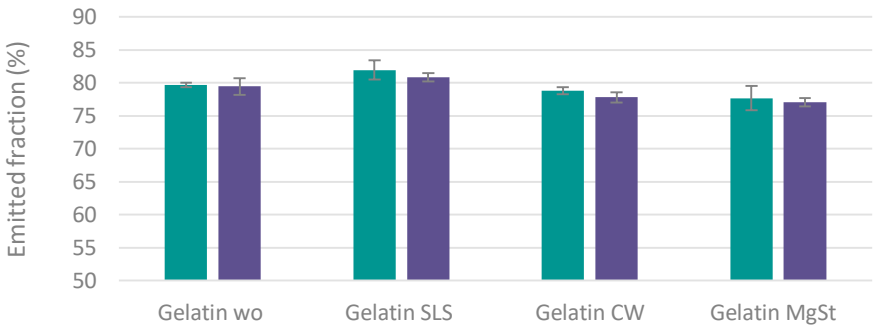
Results

Aerosolization properties of differently lubricated gelatin capsules in relation to the opening size



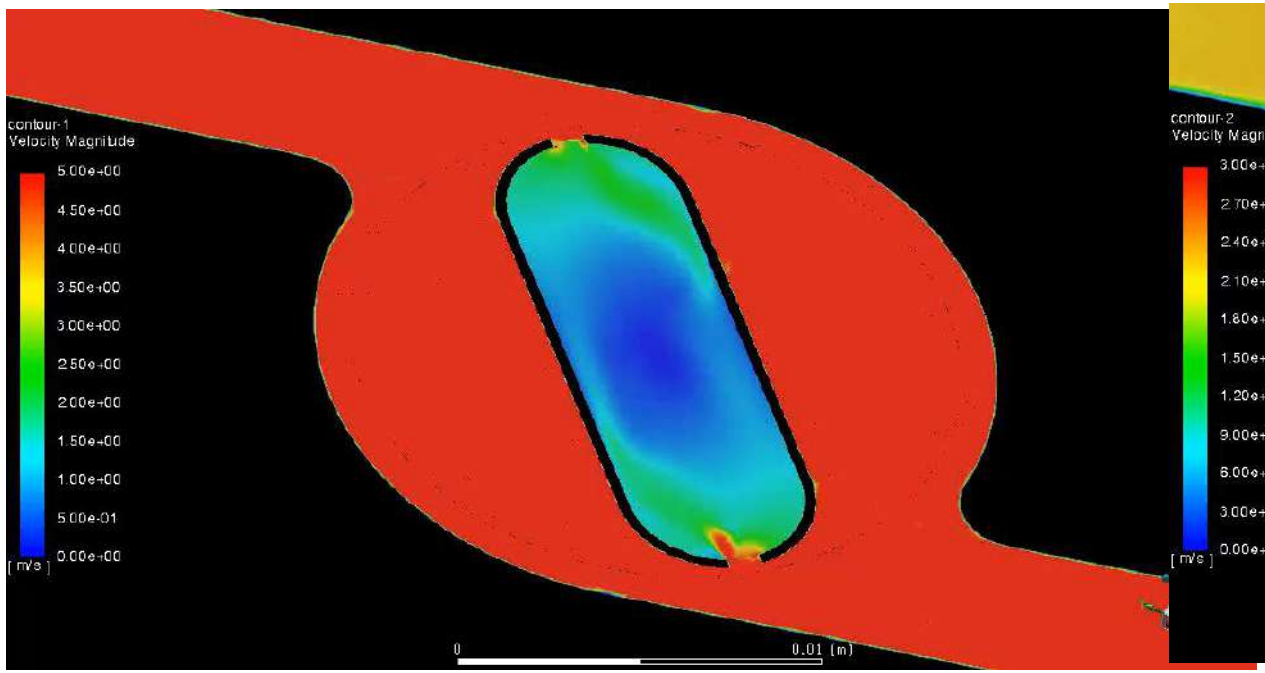
250 µg Budesonide / capsule



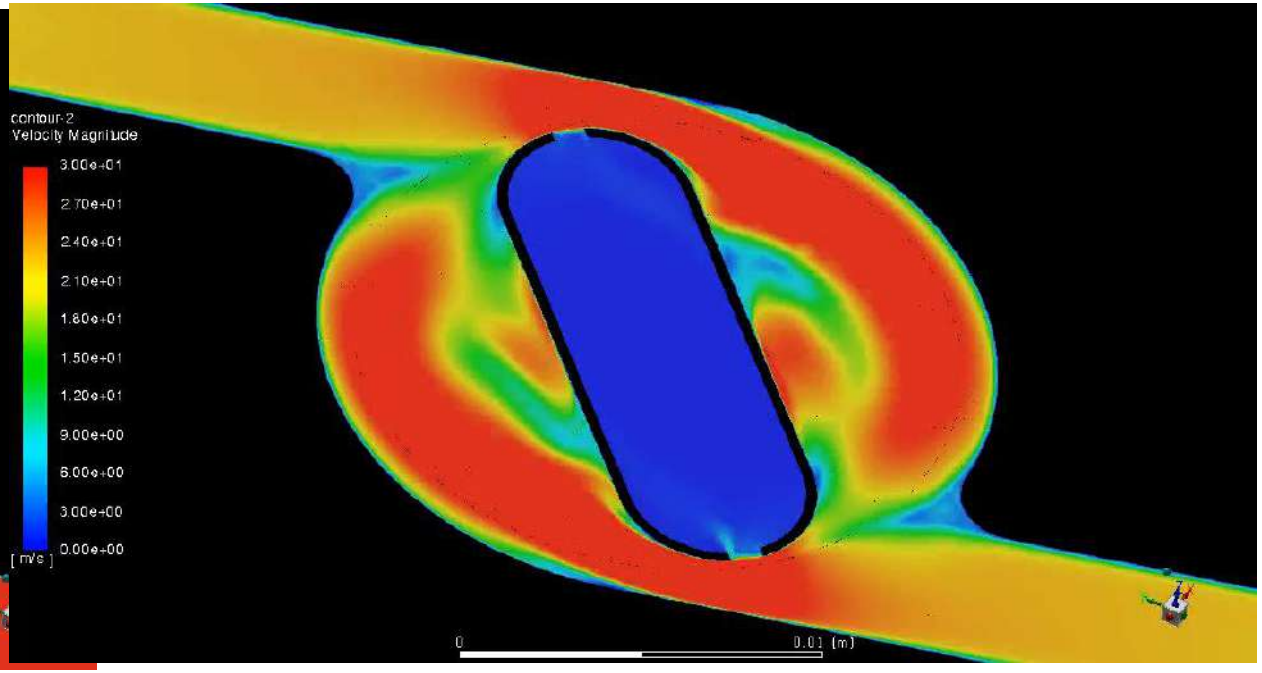


1. Wutscher et al. AAPS, 2020
2. Wutscher et al. AiCHE, 2020

Moving domain and velocity, Gelatin w/o opening area 76.1 %

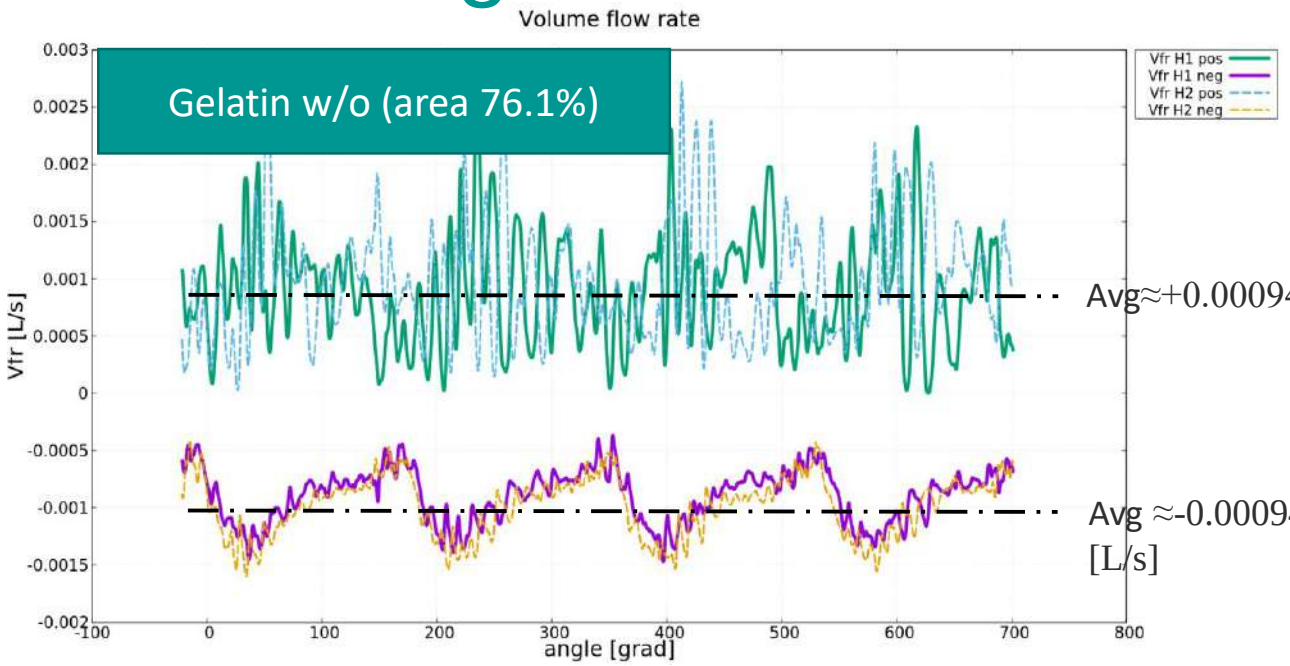


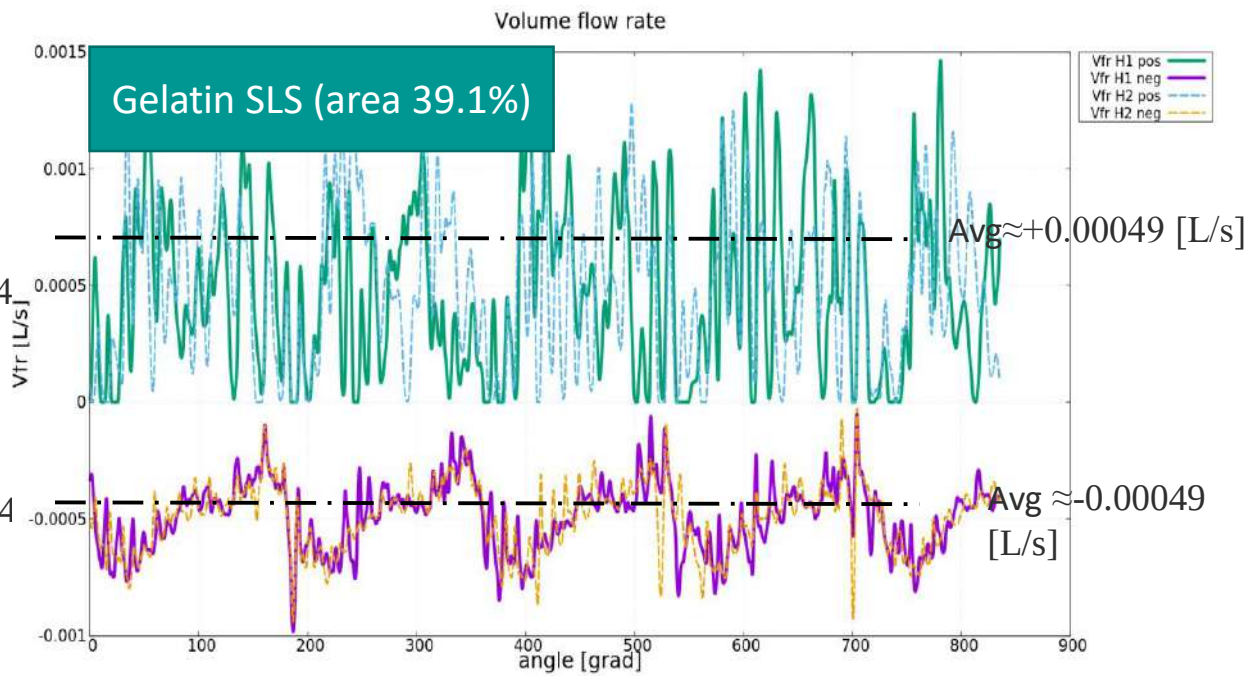
Air velocity in the capsule



Air velocity out of the capsule

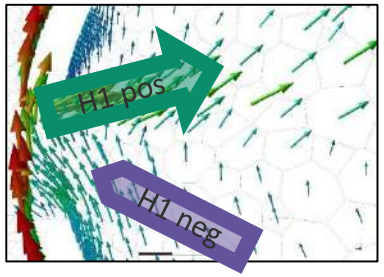
Monitoring in-/out- Volume flow rate

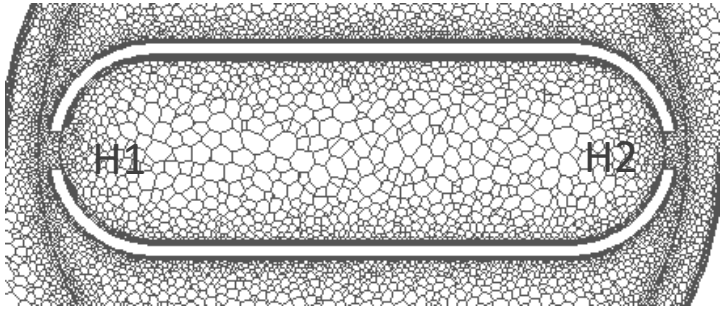


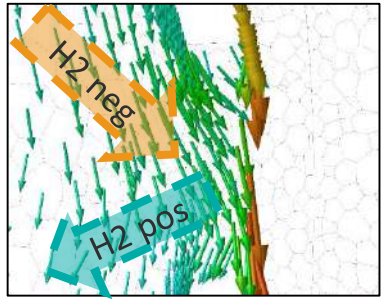


Air flowing through the gelatin w/o:
9.4e-4 L/s * 60 s/min * 2 = 0.1128 L/min (**0.19%** of total flow)

Air flowing through the Gelatin SLS:
4.9e-4 L/s * 60 s/min * 2 = 0.0588 L/min (**0.10%** of total flow)







Conclusions

- Larger opening area was observed for non lubricated capsules compared to lubricated.
- FPD was not directly related to the opening size, nonetheless more to the RH during capsule filling process.
- Very visible effect of the opening area on the air circulation through the capsule.
- Even though the opening size of the lubricated capsules appeared lower and exhibited lower air circulation, the FPD and the ED was not necessarily lower. This could indicate better disaggregation and de-attachment of the API particles from carrier as a consequence of higher air speed through smaller opening.
- CFD simulation was proven to be a powerful tool to predict changes in air velocity through different opening sizes. Even though these changes did not have a drastic effect on the ED of the formulation studied, using carrier free formulations, the ED is expected to be strongly affected by the air velocity inside the capsule.
- As a next step, numerical Discrete Element Method (DEM) simulation with inclusion of particles will be performed to correlate better the behaviour of particles with the air velocity within DPI's.

Thank you!

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