The role of mechanical properties in DPI carriers

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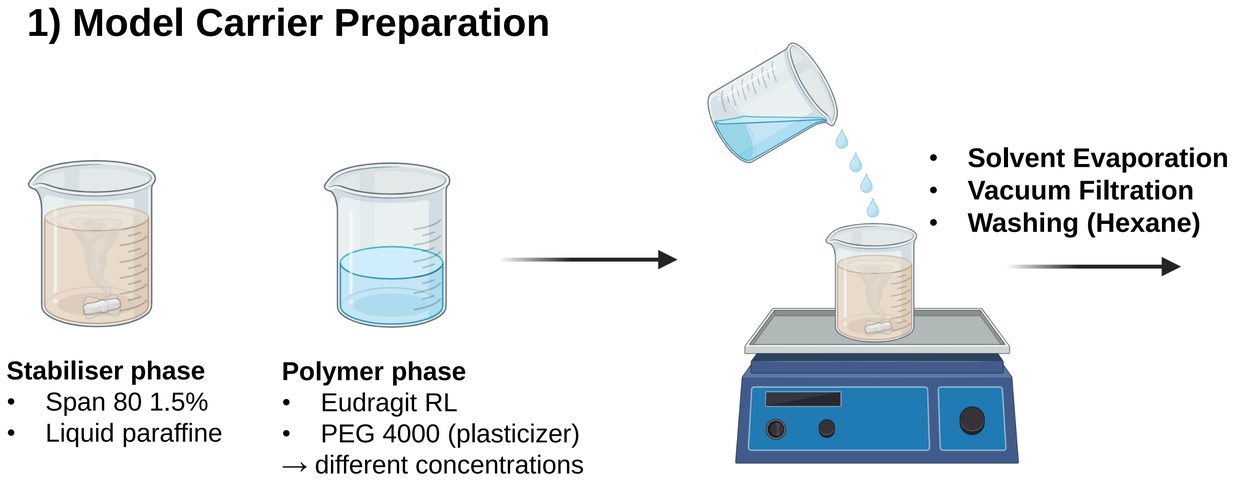
Introduction

- Aerodynamic performance of interactive blends depends on mixing time/energy [1]
- Leading hypothesis assumes the effect of so called press-on-forces (i.e deformation of particles during mixing) [2,3]
- Mechanical properties of particles should predict the behaviour of fine particle fraction (FPF) with respect to mixing time if the hypothesis holds true

Methods

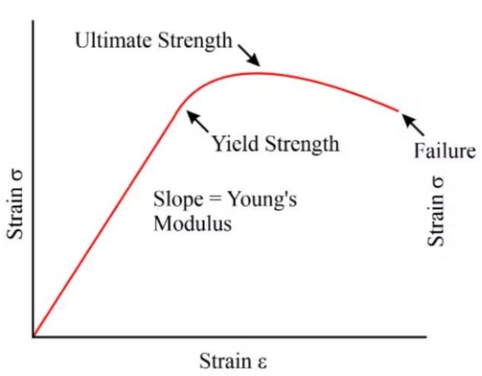
1) Model Carrier Preparation



2) Analysis of Mechanical Properties

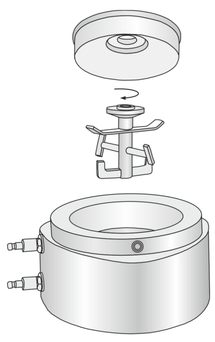
Polymer film preparation
- Solvent casting in MeOH
- Dispersion spread across Non cohesive surface
- Film thickness 0.5 mm
- Drying period 24h

Texture Analysis
- **Young's Modulus**
- **Yield Strength**



3) Aerodynamic Performance (laser diffraction)


Microspheres


High Shear Mixing


2% API (Glycopyrrolate)

- **Batch size 20 g**
- **500 rpm**
- **1 – 15 min mixing time**

Blends F1

Blends F2

Blends F3

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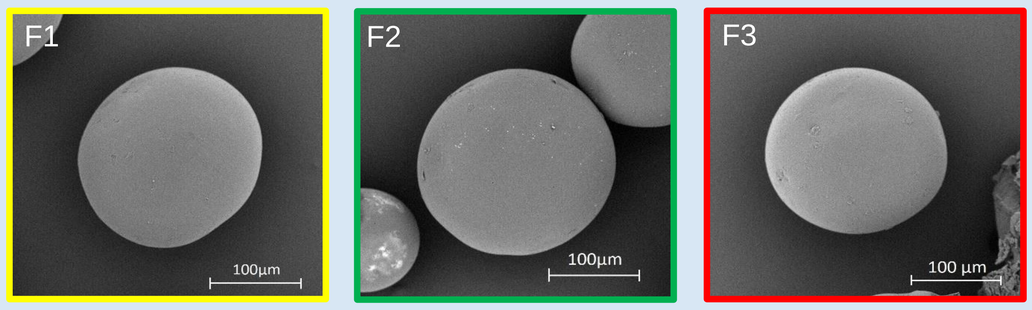
- **4 kPa pressure drop**
- **Novolizer as device**
- **FPF% = fraction < 5µm**

Aim

Verify the relationship between mechanical properties and FPF
1) Create model carriers with varying plasticity
2) Evaluate their mechanical properties
3) Investigate aerodynamic performance
4) Link mechanical properties and aerodynamic performance

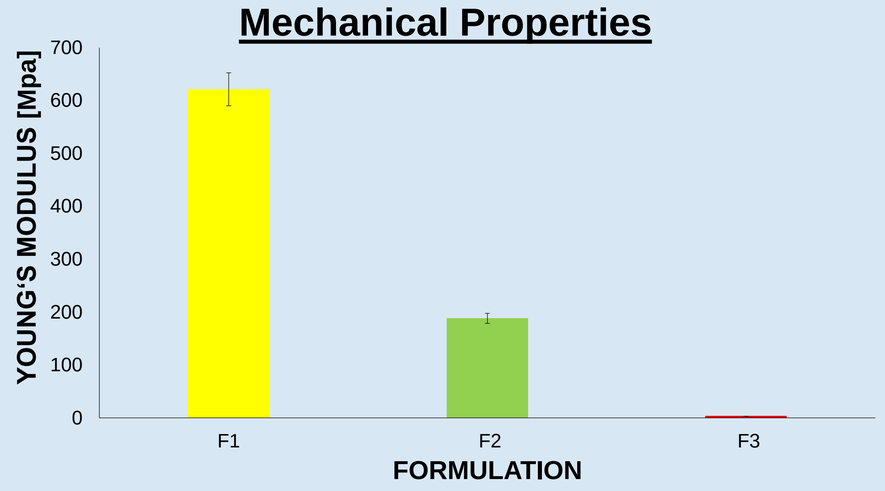
Results

Model Carriers with varying plasticity

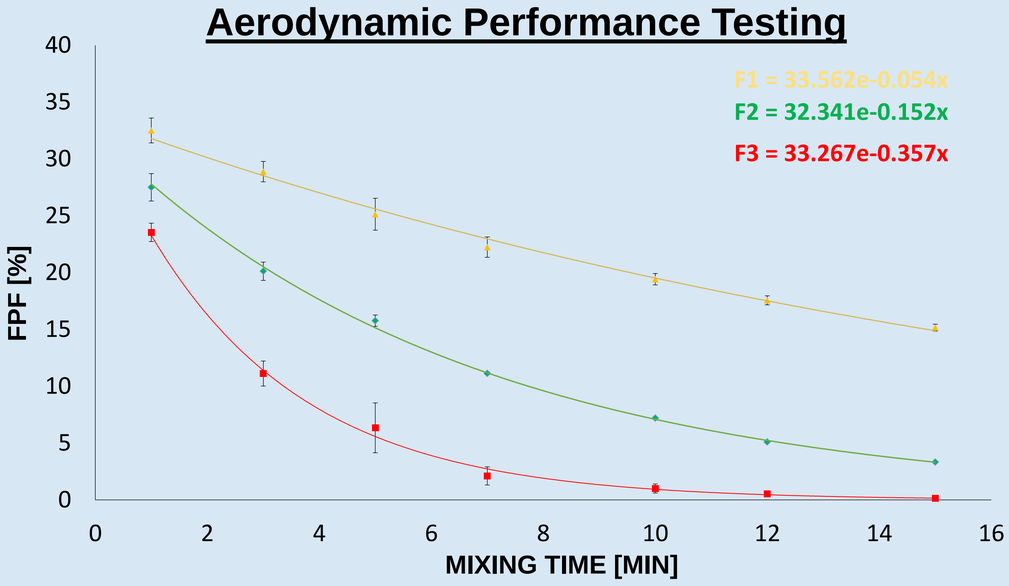


	0% PEG	10% PEG	25% PEG
Formulation	x10 [µm]	x50 [µm]	x90 [µm]
F1	219.85 ± 1.11	297.51 ± 0.93	352.28 ± 1.14
F2	220.18 ± 0.88	299.01 ± 0.99	351.51 ± 1.16
F3	219.55 ± 1.41	298.13 ± 1.01	351.77 ± 1.77
API*	0.609	3.25	6.91

Mechanical Properties



Aerodynamic Performance Testing



n=3, error bar = SD for all measurements; *supplier data

Conclusion and Outlook

- **There is a clear correlation between the course of the fine particle fraction as a function of the mixing time and the mechanical properties of the carrier particles**
- **The next steps include repeating the tests using impactor analysis (Fast Screening Impactor)**
- **The relevance of mechanical properties for interactive powder mixtures will be further investigated with excipients relevant for inhalation.**

References

[1] *Thalberg K, Åslund S, Skogevall M, Andersson P. Dispersibility of lactose fines as compared to API in dry powders for inhalation. Int J Pharm. 2016;504:27–38*
[2] *Podczeck F, Newton JM. Development of an ultracentrifuge technique to determine the adhesion and friction properties between particles and surfaces. J Pharm Sci. 1995;84(9):1067–1071*
[3] *Hertel M, Schwarz E, Kobler M, Hauptstein S, Steckel H, Scherließ R. The influence of high shear mixing on ternary dry powder inhaler formulations. Int J Pharm. 2017;534(1–2):242–250*

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