Solid-state stability of advanced lipid-based excipients upon processing via extrusion and 3D-printing

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Lipids: Enormous potential impaired with tough challenges

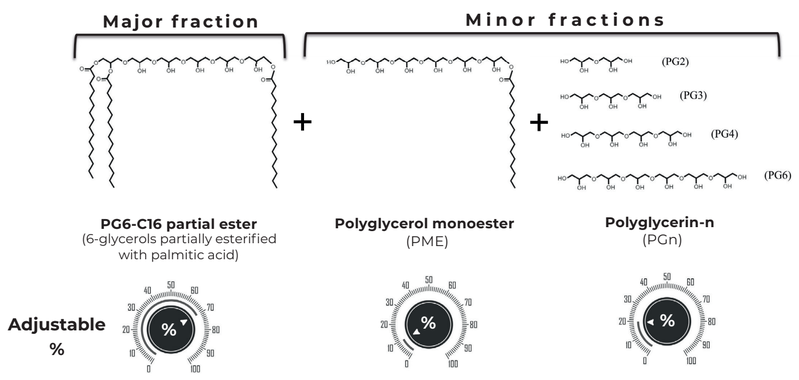
Conventional Lipid-based excipients + Down streaming via Extrusion and 3D-printing » Major challenges

1 lack of 3D-printing-associated properties
- ! Mechanical properties
- ! Viscosity

2 Complex solid-state behaviors
- ! Upon aging
- ! Upon API-loading
- ! Upon heat-treatment

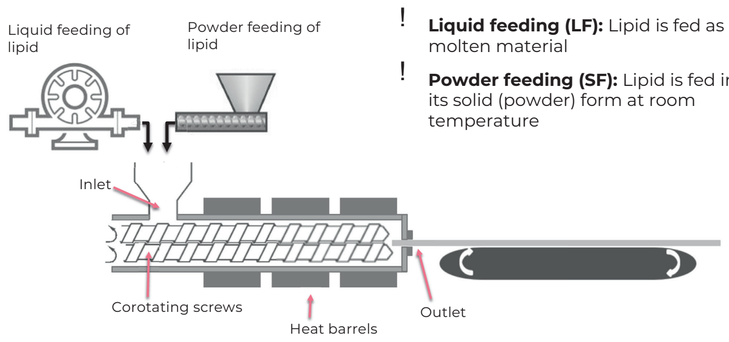
This work investigates the solid-state stability of polyglycerol ester of fatty acids (PGFAs), as next generation lipid-based excipients (LBE), upon variation in their composition, different extrusion approaches, and when loaded with active pharmaceutical ingredient (API).

Composition tuning



- ! Tuning composition via increasing minor fractions in the system
- ! Enhanced filament's mechanical properties for 3D-printing
- ! Controlled physicochemical properties required for drug release

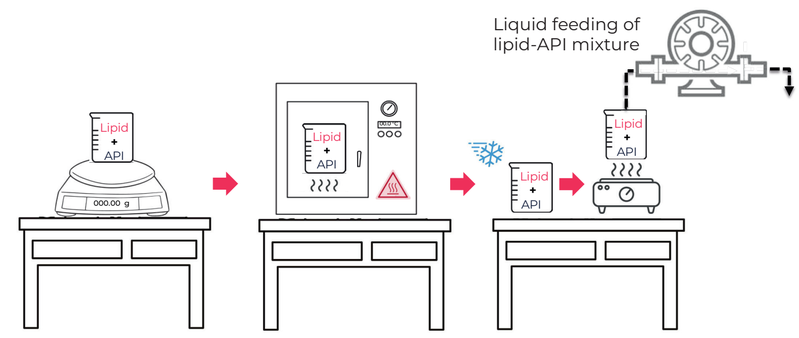
Extrusion approaches [3]



- ! **Liquid feeding (LF):** Lipid is fed as molten material
- ! **Powder feeding (SF):** Lipid is fed in its solid (powder) form at room temperature

- ! Enhanced filament mechanical properties for 3D-printing
- ! Reduced filament porosity

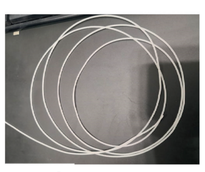
API-loading



- ! API in molten lipid
- ! Feeding of molten mixture (liquid feeding)

Results

+ liquid feeding

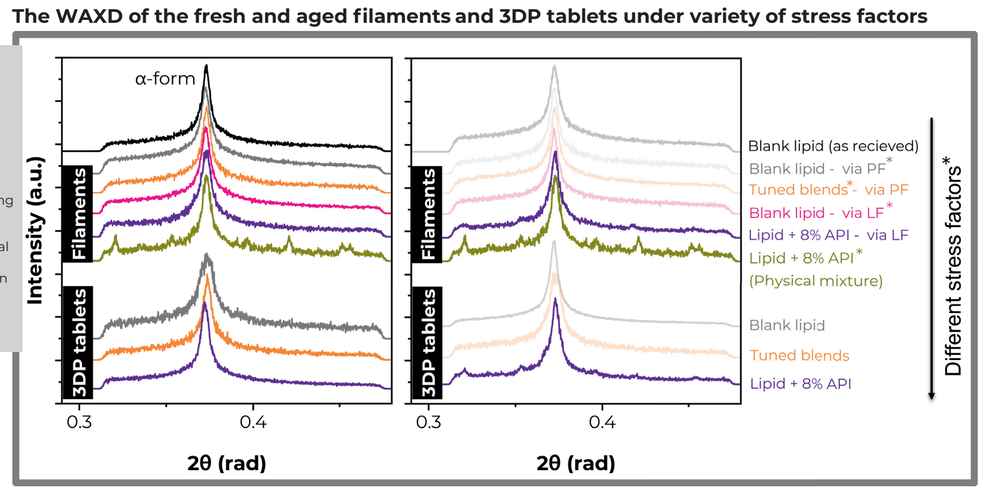


+ composition tunning

API-loaded 3DP tablet

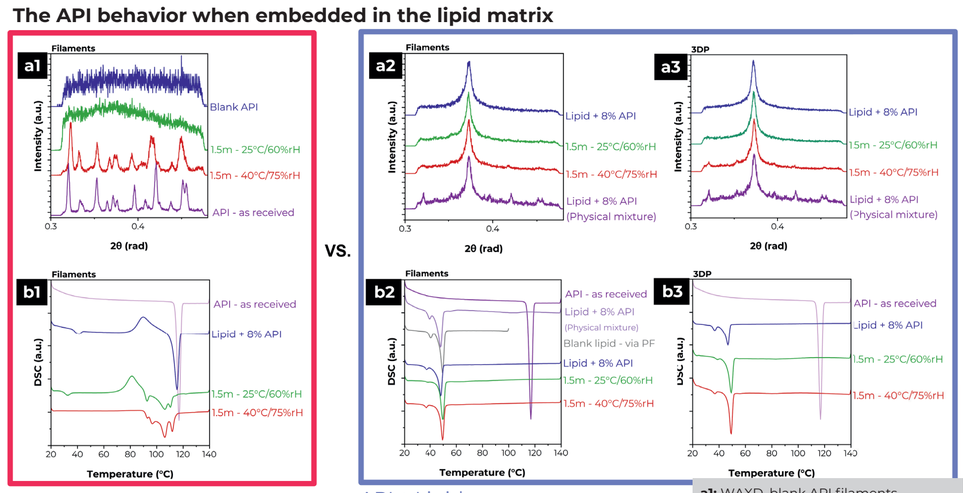
* **WAXD:** Wide angel X-ray diffraction
Stress factors:
.Shear stress
.Shear stress + heat
.Chemical (Indigenous)
.Chemical (Exogenous)
Aged: 1.5m, 40°C/75%rH
3DP: 3 dimensional printing
PF: Powder feeding
LF: Liquid feeding
API: Active pharmaceutical ingredient
Tuned blend: Composition tunning via adding minor fractions in the system

The WAXD of the fresh and aged filaments and 3DP tablets under variety of stress factors



- ! ! -form is always given under all stress conditions
- ! ! -form is always given after storage → No polymorphism
- ! API remains in amophous state for 1.5 month

The API behavior when embedded in the lipid matrix



Blank API
- x Fast recrystallization
- x polymorphsim

API + Lipid
- ✓ Amorphous status maintained for longer
- ✓ No polymorphsim

a1: WAXD, blank API filaments
a2: WAXD, API + Lipid filaments
a3: WAXD, API + Lipid 3DP tablets
b1: DSC, blank API filaments
b2: DSC, API + Lipid filaments
b3: DSC, API + Lipid 3DP tablets

WAXD: Wide angel X-ray diffraction
DSC: Differential scanning calorimetry

Possibility to overcome the challenges!

PGFAs ...as next generation LBE + Down streaming via Extrusion and 3D-printing »

- ✓ **Extrudable**
- ✓ **3D-printable**
- ✓ **Prolonged amorphous state of API**
- ✓ **Stable upon processing and storage**

References

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