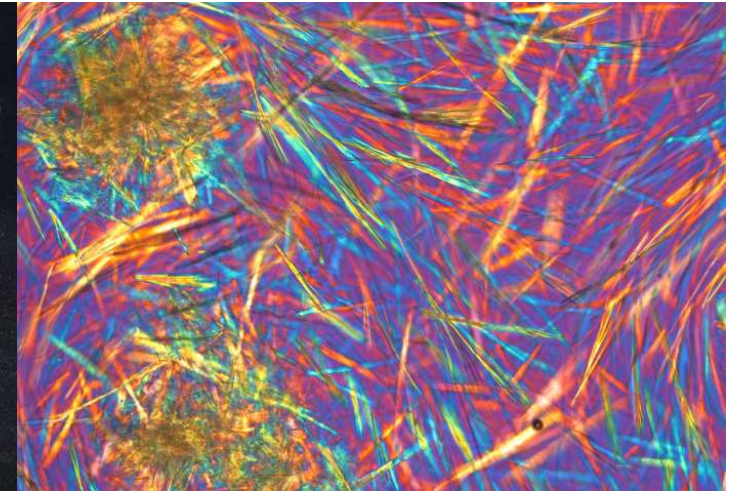
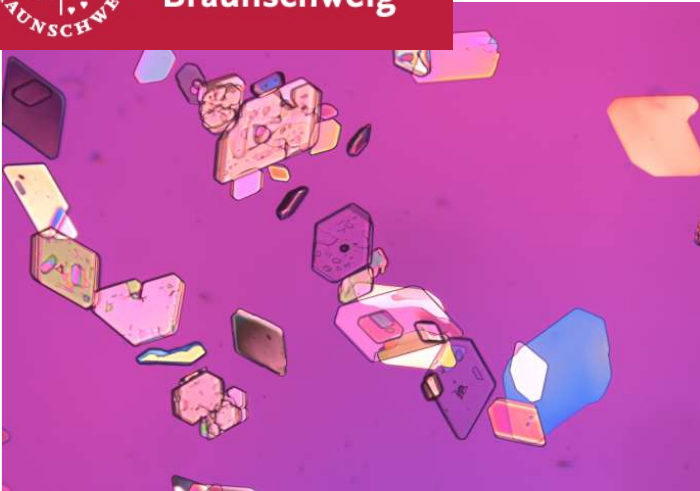




Technische
Universität
Braunschweig



Institut für Pharmazeutische Technologie
und Biopharmazie
pharmazie in braunschweig



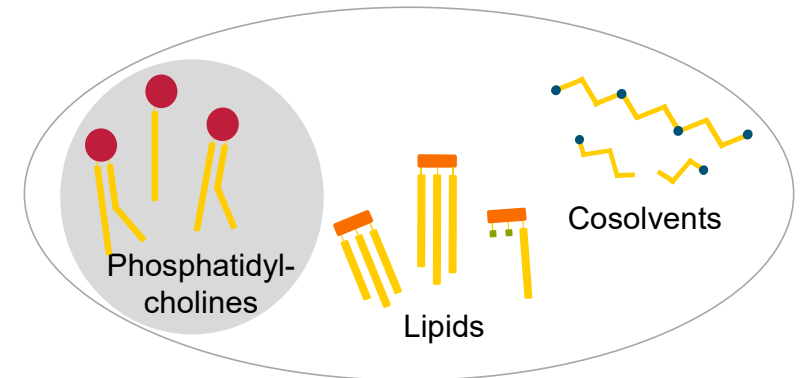
Phospholipid-based self-dispersing formulations for the delivery of poorly water-soluble drugs via hard capsules

Heike Bunjes, Linda Grüne

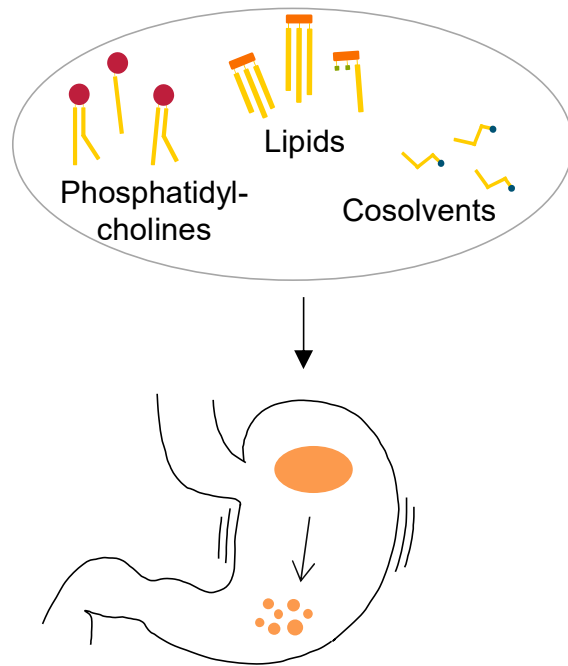
PRC Webinar, May 20, 2026

Background & rationale

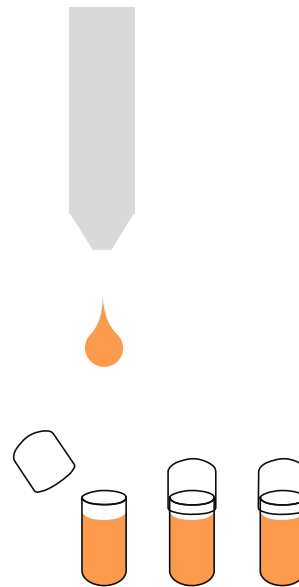
- Poor aqueous solubility of many modern drugs
- Lipid-based formulations → oral bioavailability ↑
- Self-dispersing drug delivery systems
→ 30 - 60 % synthetic surfactants and cosolvents
- Phospholipids as alternative?
- Diacyl phosphatidylcholines (PC)
→ Monoacyl phosphatidylcholines



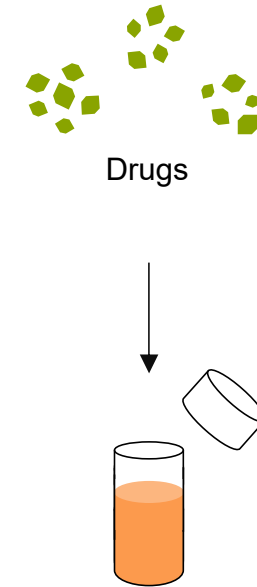
Specific approach: Development of phospholipid-based formulations



Self-dispersing
drug delivery systems



Liquid filling in
(hard) capsules



Loading with
lipophilic drugs

Aims



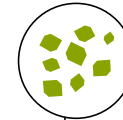
Miscibility

- Homogeneous, stable formulations
- High content of phospholipids
- Good dispersibility
- Clarification of underlying structures



Capsule filling

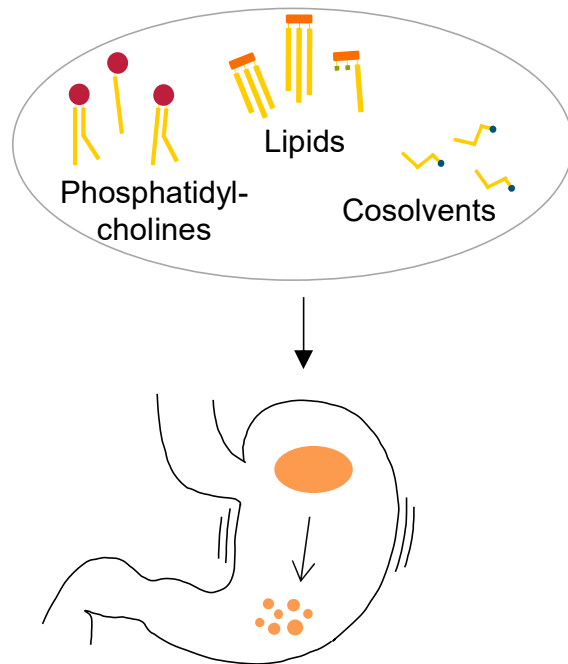
- Suitable filling behavior
- Compatibility with hard capsules



Drug loading

- High loading capacity for lipophilic drugs
- In bulk as well as dispersion
- Influence of composition on drug load
- Good dispersibility

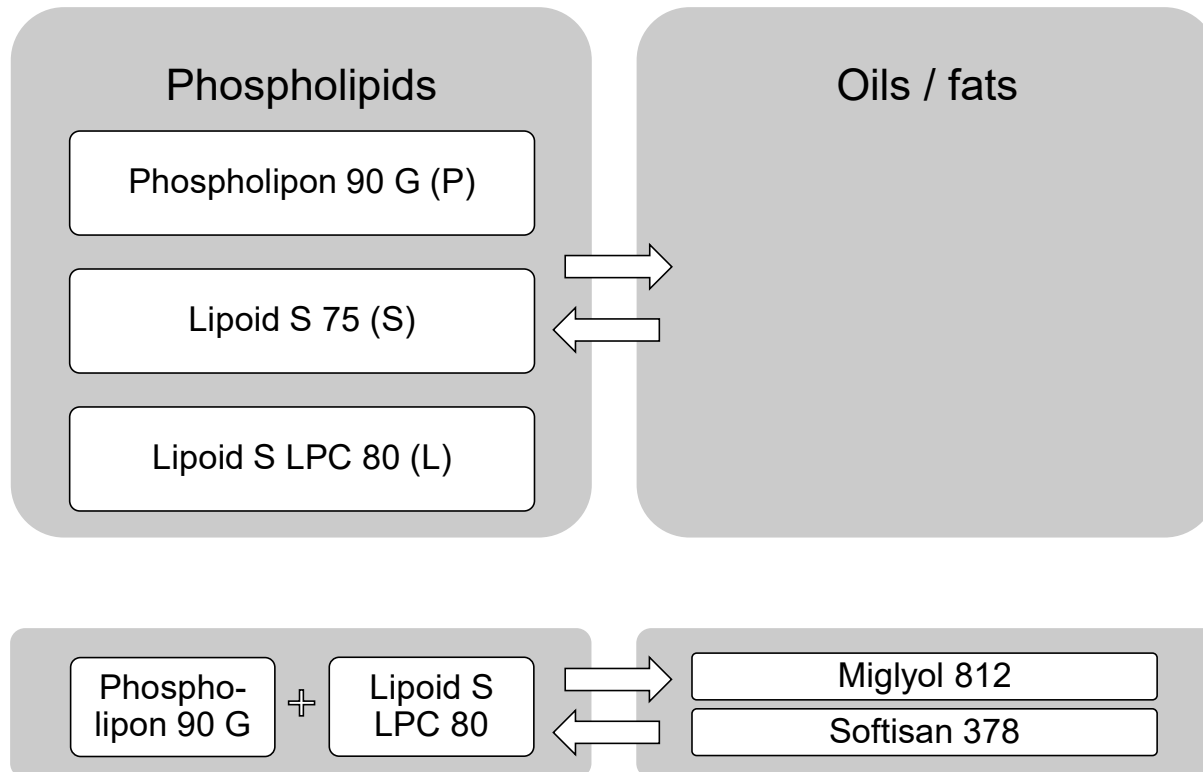
Miscibility & Dispersibility



Self-dispersing
drug delivery systems



Miscibility study



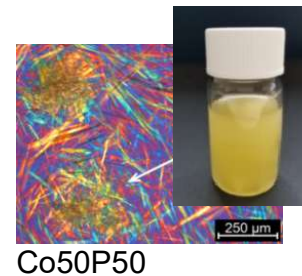
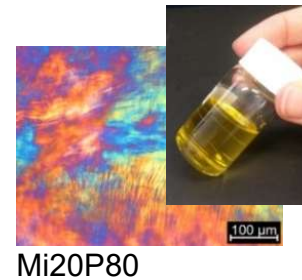
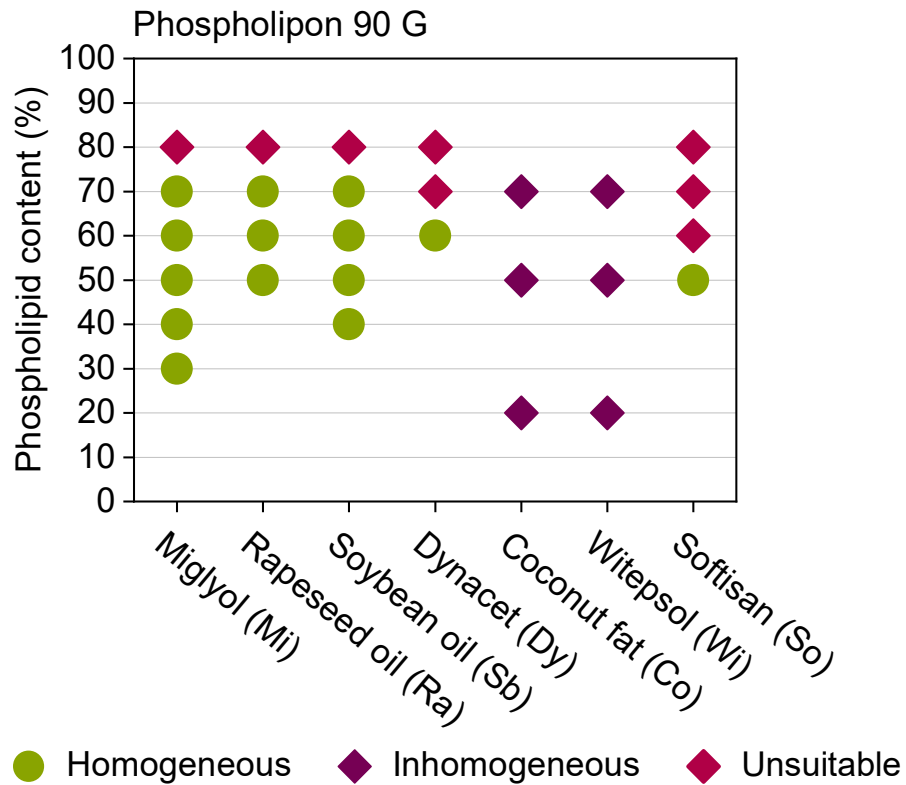
- Oils → liquid mixtures
- Fats → semisolid mixtures
- Combination PL90G + LPC80 → better dispersibility?
- Formulations with 5% ethanol
- Favorable processability with dual centrifugation (65°C)



[1]



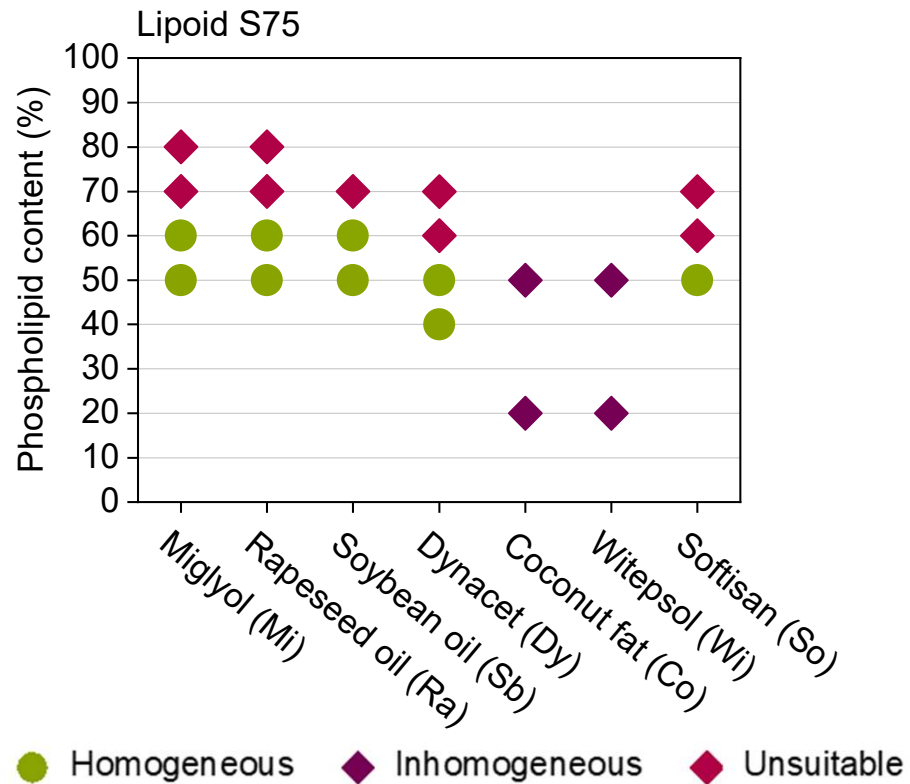
Miscibility: PL90G and S75



- Oils: max. 60 - 70% PL90G
- Softisan: max. 50% PL90G, inhomogeneous with other fats



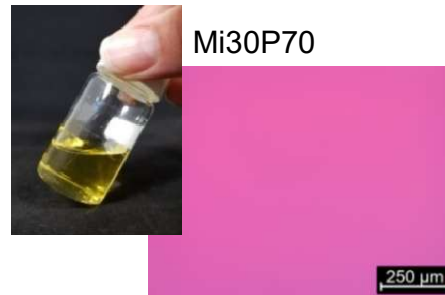
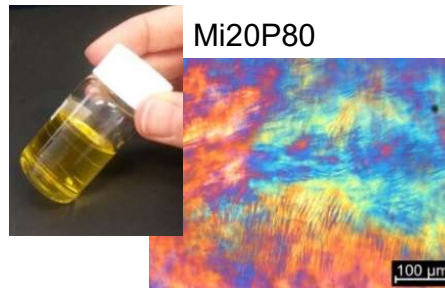
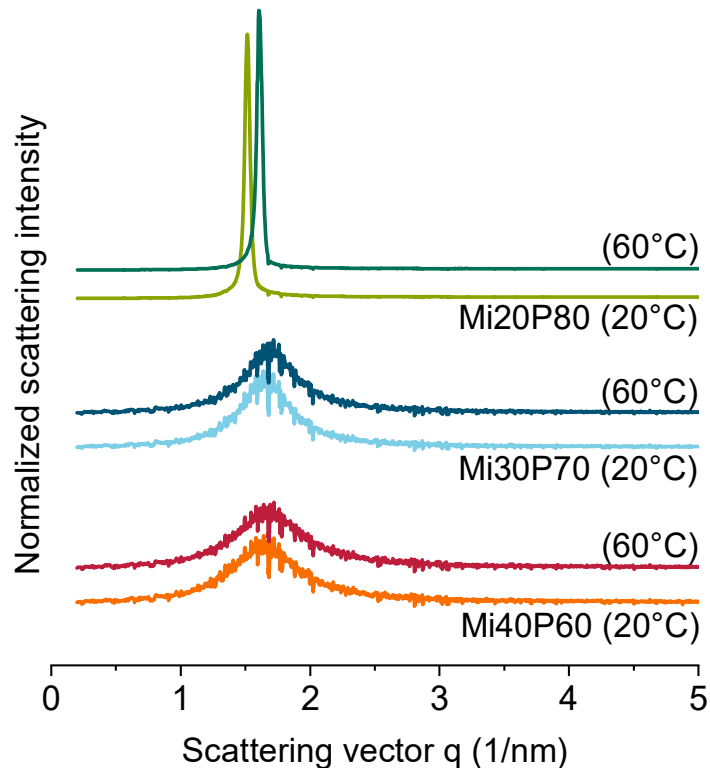
Miscibility: PL90G and S75



- Oils: max. 60 - 70% PL90G
- Softisan: max. 50% PL90G, inhomogeneous with other fats
- S75 similar but 10% less in oils

Structural investigations

SAXS (no reflections in WAXD)



Homogenous mixtures:

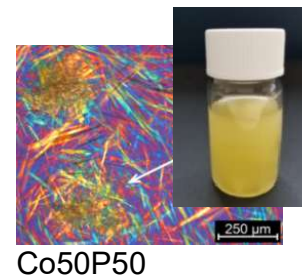
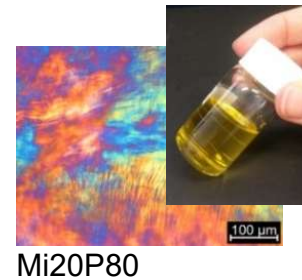
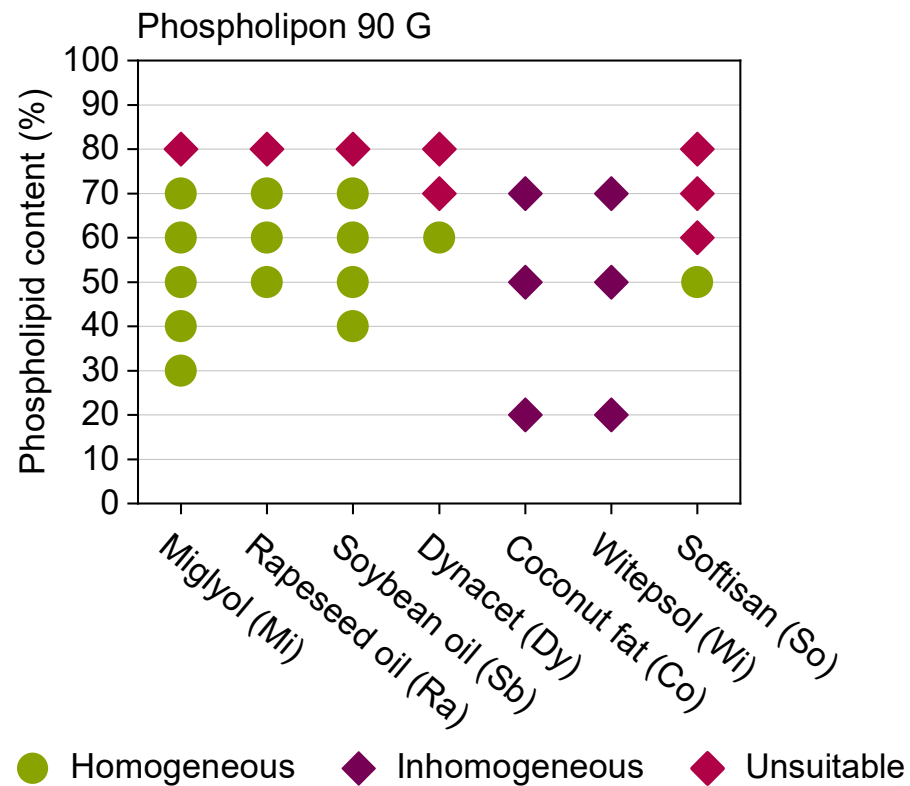
- Isotropic
- Broad reflection
→ reverse micelles

„Unsuitable“ mixtures:

- Anisotropic
- Sharp reflection
→ liquid crystals



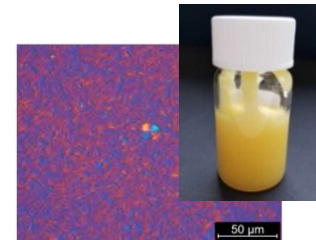
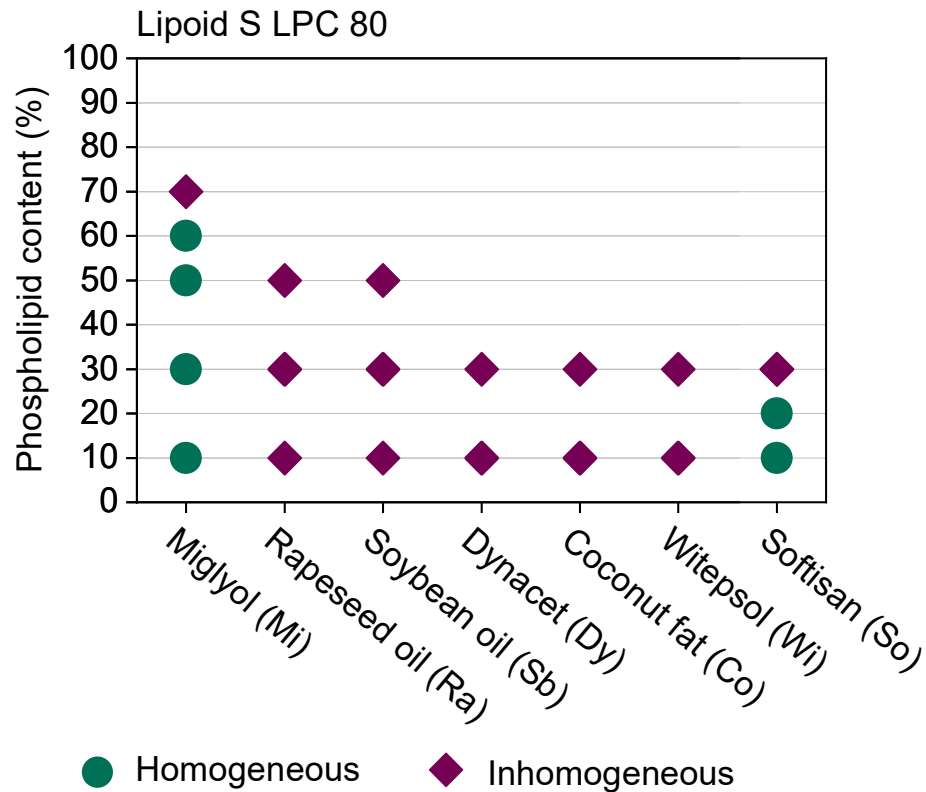
Miscibility: PL90G and S75



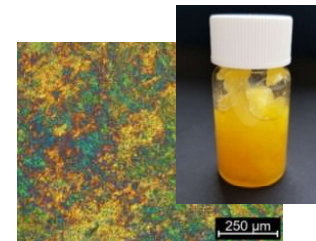
- Oils: max. 60 - 70% PL90G
 - Softisan: max. 50% PL90G, inhomogeneous with other fats
 - S75 similar but 10% less in oils
 - Reverse micellar or liquid-crystalline structures
- ⇒ Mixtures with high phospholipid content
- ⇒ More PL90G than S75 possible



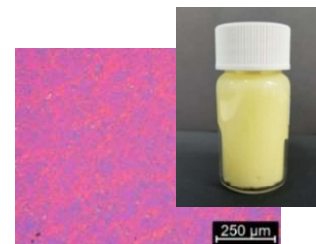
Miscibility: LPC80 and ternary mixtures



Mi50L50



Sb50L50

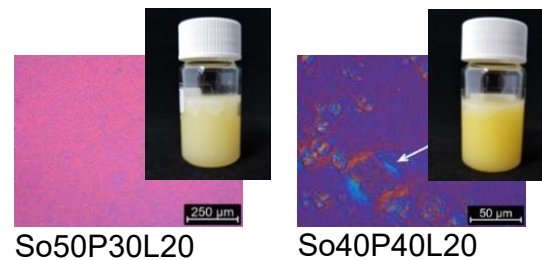
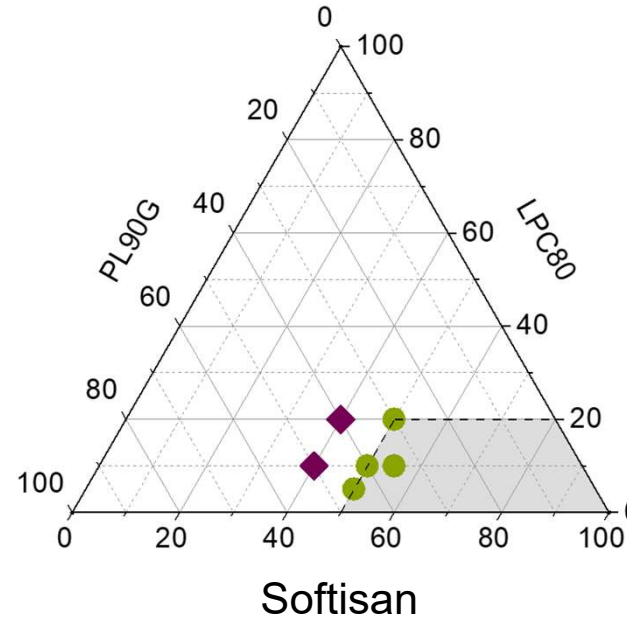
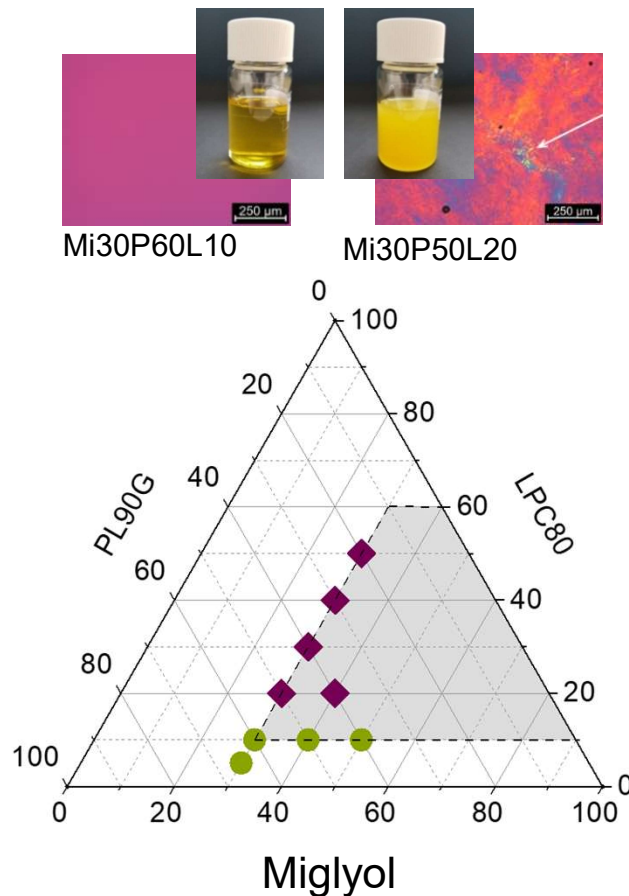


So80L20

- LPC80 only miscible with Miglyol & Softisan
- Miglyol: max. 60% LPC80, lamellar (liquid) crystals
- Softisan: max. 20% LPC80, liquid-crystalline structures



Miscibility: LPC80 and ternary mixtures



- LPC80 only miscible with Miglyol & Softisan
- Miglyol: max. 60% LPC80, lamellar (liquid) crystals
- Softisan: max. 20% LPC80, liquid-crystalline structures
- Ternary mixtures:
max. 10 - 20% LPC80

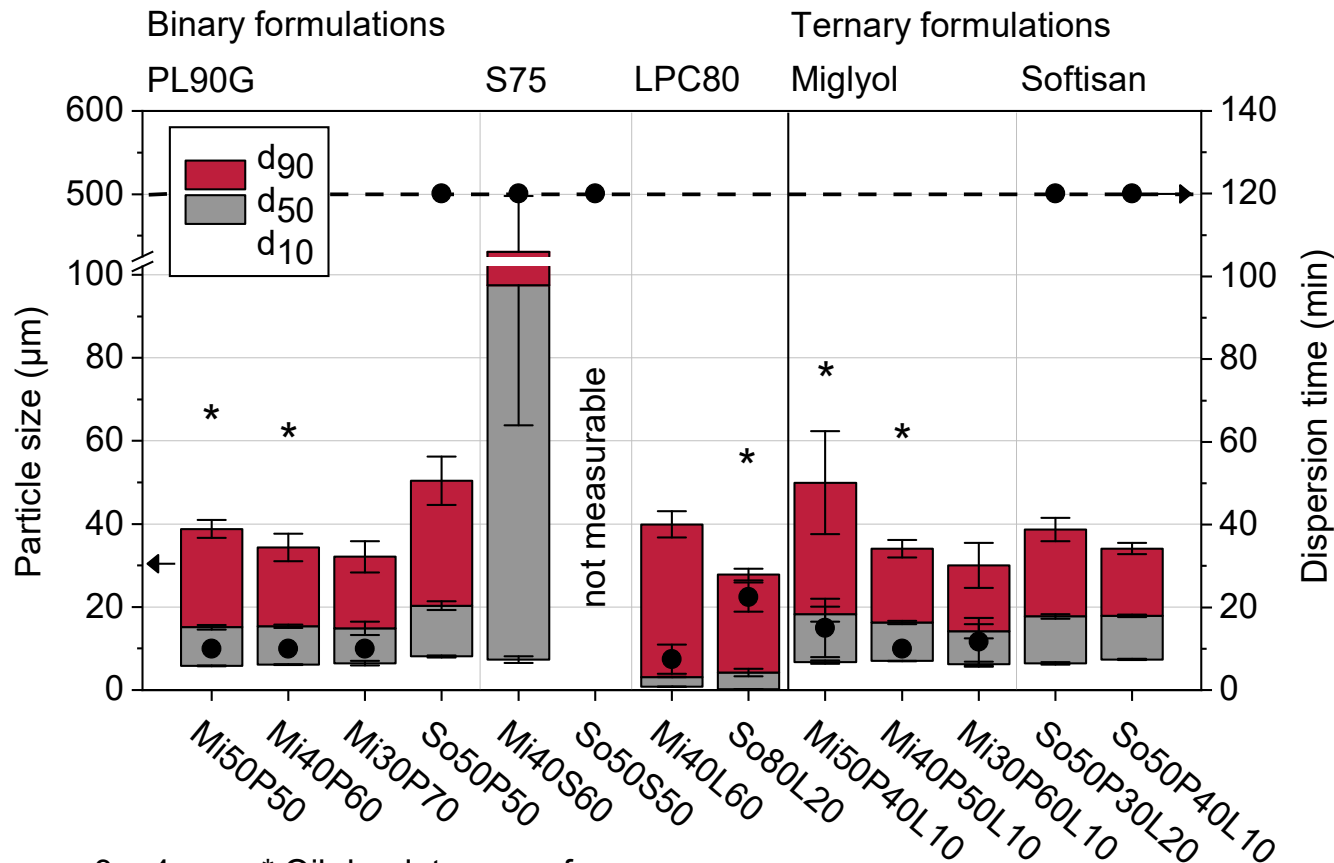
⇒ LPC80: different miscibility and structures

⇒ Ternary mixtures with little LPC80

● Homogeneous ◆ Inhomogeneous



Dispersibility



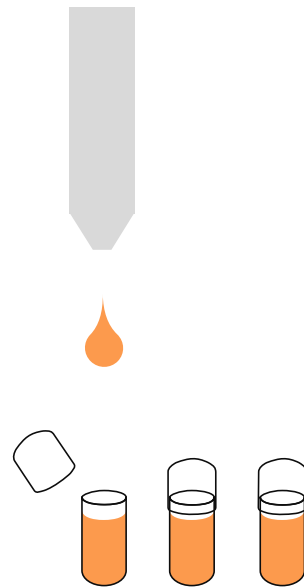
- Short dispersion time: PL90G + Miglyol, LPC80
 - Long dispersion time: PL90G + Softisan, S75
 - Ternary mixtures: no improvement
- ⇒ Miglyol + PL90G (+ LPC80) advantageous properties

n = 3 – 4

* Oil droplets on surface

Artificial gastric fluid, 37°C, 100 UpM

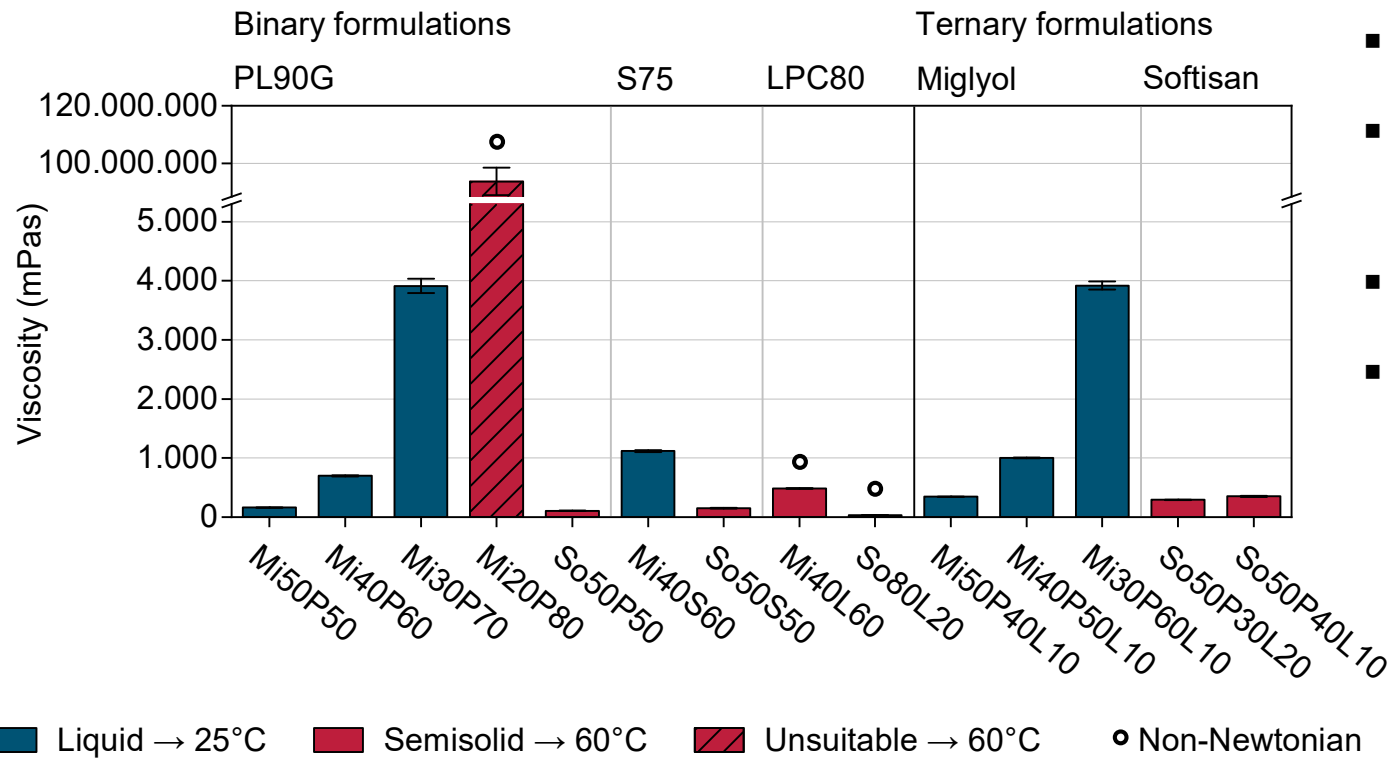
Capsule filling properties



Liquid filling in
(hard) capsules



Filling behavior – viscosity

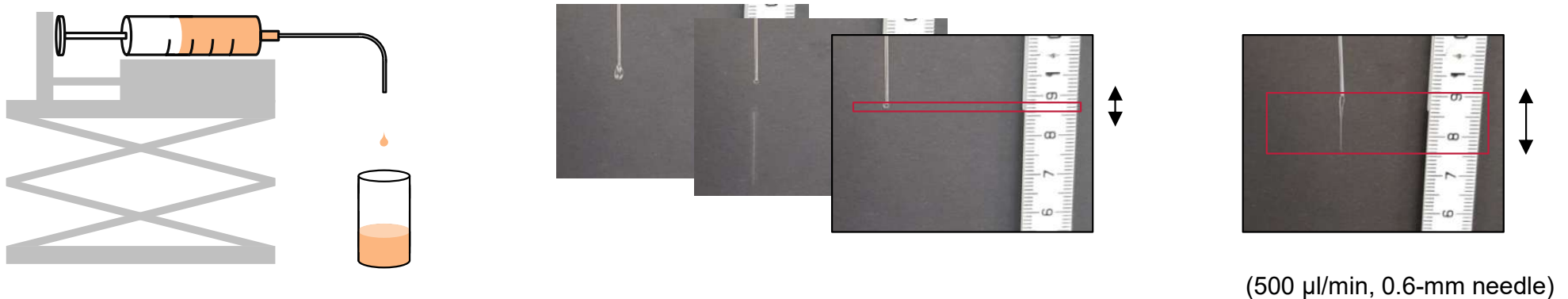


n = 3

Viscosity at 100 Pa

- Homogeneous: low viscosity
 - Unsuitable: viscosity > 25.000 mPas [1]
 - More PC → viscosity ↑
 - LPC80: non-Newtonian
- ⇒ Most formulations „pumpable“

Filling behavior – setup for stringing test

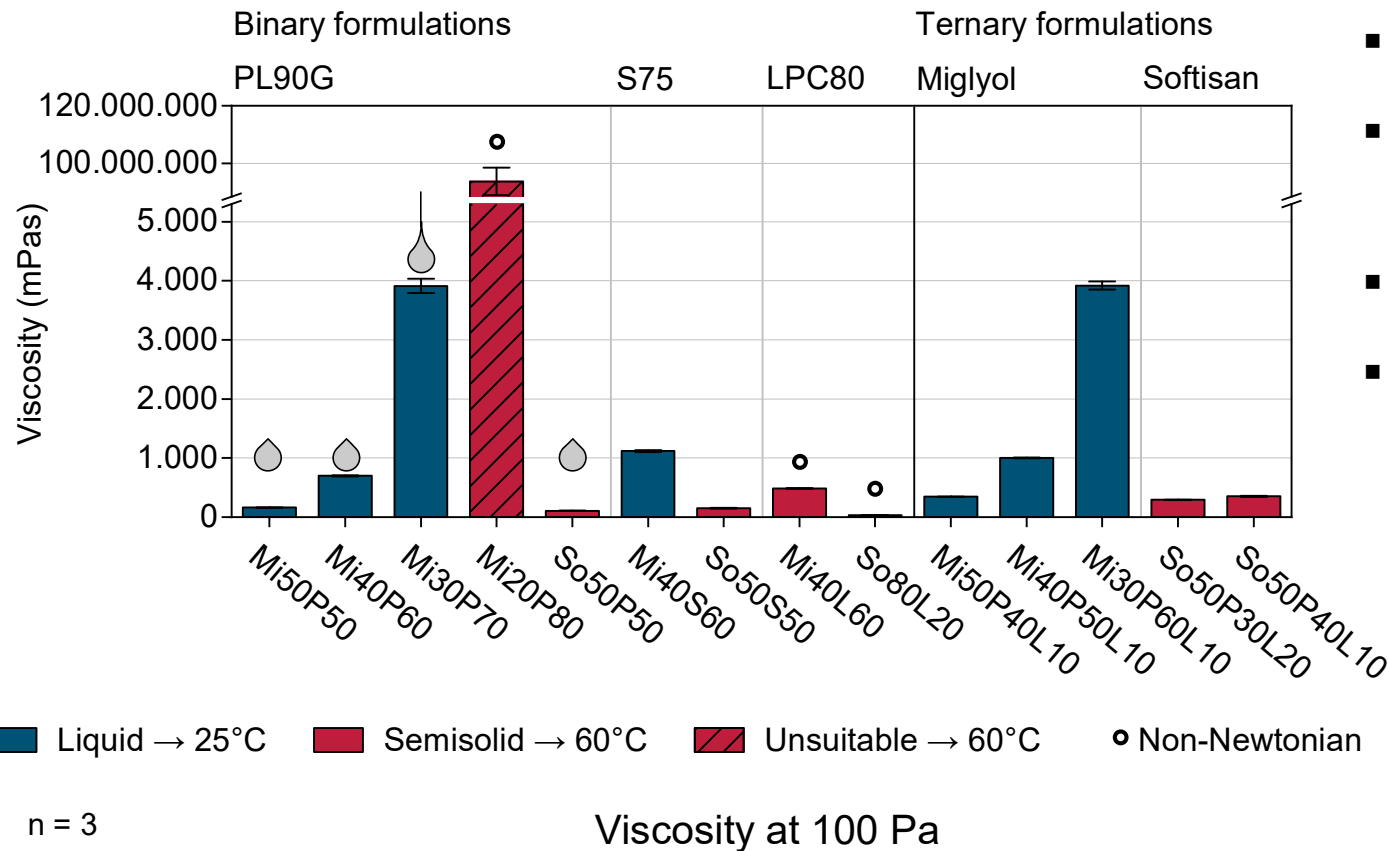


➤ Setup for small-scale experiments

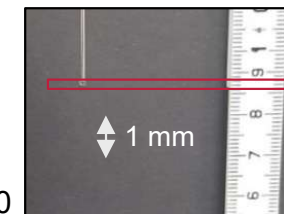
- Syringe pump for dosing at defined rates
- In case of stringing, string length determined after dripping



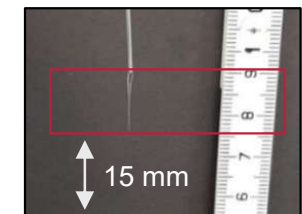
Filling behavior – stringing



- Homogeneous: low viscosity
- Unsuitable: viscosity > 25.000 mPas [1]
- More PC → viscosity ↑
- LPC80: non-Newtonian
- ⇒ Most formulations „pumpable“
- ⇒ Clean drip-off up to 60% PL90G



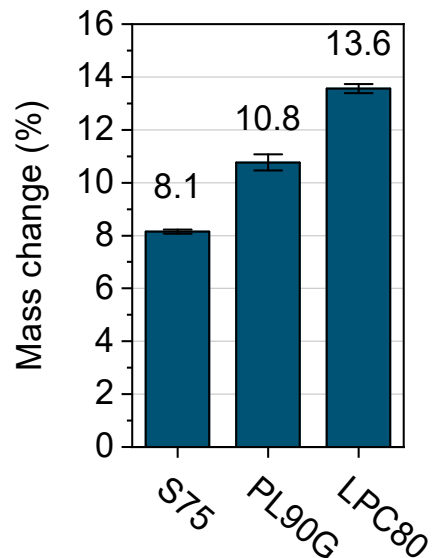
Mi50P50



Mi30P70

(500 µl/min, 0.57 mm cannula)

Compatibility with capsule material – hygroscopicity



1.0 H₂O_{Uptake}

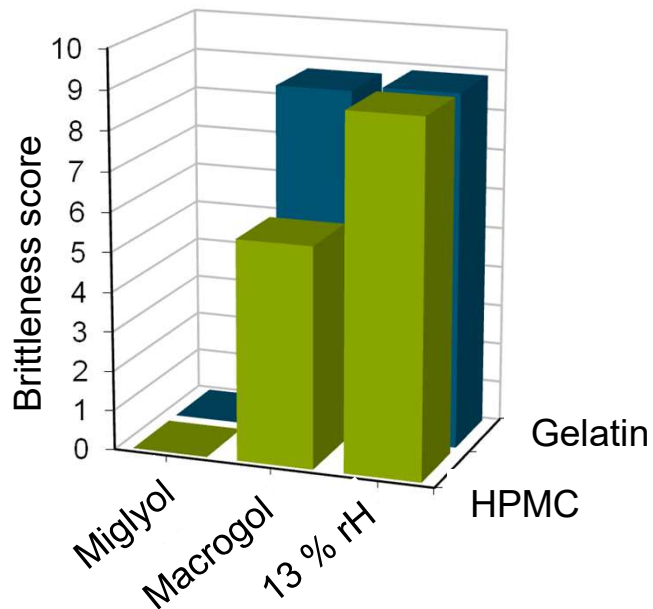
■ Mass_{Max}

■ Mass_{Min}

n = 3 – 4

- Open storage, 25°C, 60% rH
- Raw materials:
 ~ 8 – 14 % water uptake
- S75 < PL90G < LPC80
- Mixtures: lower water uptake
- More PL: Water uptake↑,
 ethanol loss↓

Compatibility with hard capsules – mechanical stability

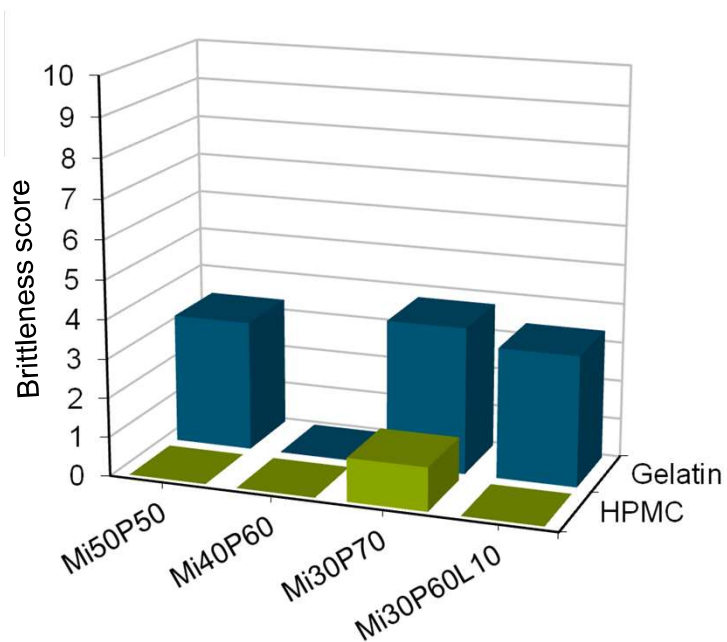


- Controls: Miglyol, Macrogol, 13% rH
- Miglyol: Capsules elastic
- Macrogol, 13% rH: Capsules brittle
 - HPMC: Brittleness not expected
 - Distinguishing between compatible and hygroscopic substances

0 = no splintered capsule
10 = all capsules splintered
n = 8 – 12

25°C, closed containers, tablet hardness tester

Compatibility with hard capsules – mechanical stability



- More PC: hygroscopicity \uparrow , ethanol evaporation \downarrow
 - Gelatin capsule: Certain brittleness
 - Exception: Mi40P60 \rightarrow Optimum
 - HPMC capsule: very low brittleness
- \Rightarrow HPMC preferable material

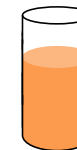
0 = no splintered capsule
10 = all capsules splintered
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25°C, closed containers, tablet hardness tester

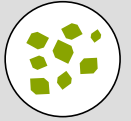
Drug loading



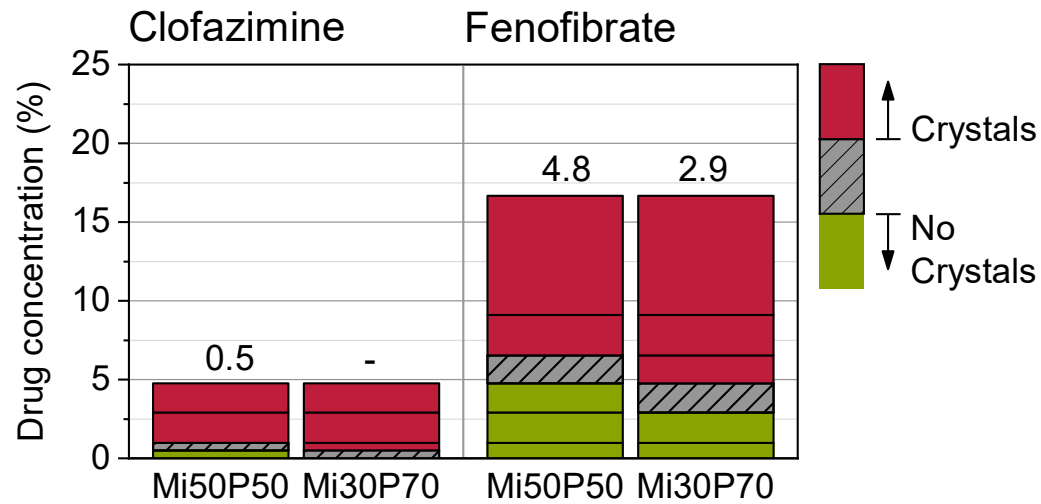
Drugs



Loading with
lipophilic drugs

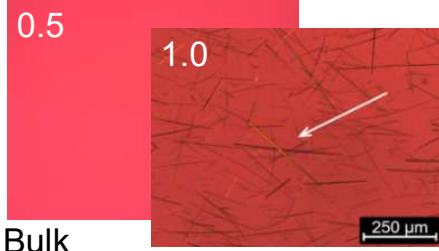


Drug loading – clofazimine & fenofibrate

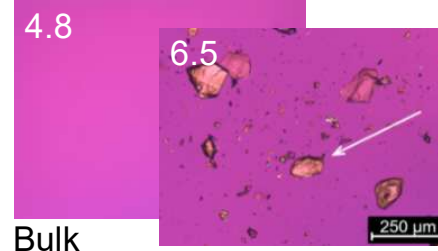


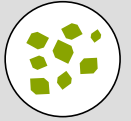
- Drugs with different physicochemical properties
- Loading screening with dual centrifugation at 23°C
- Clofazimine (T_M : ~211°C): very low drug load, needle-shaped crystals
- Fenofibrate (T_M : 81°C): medium drug load

Mi50P50-clofazimine

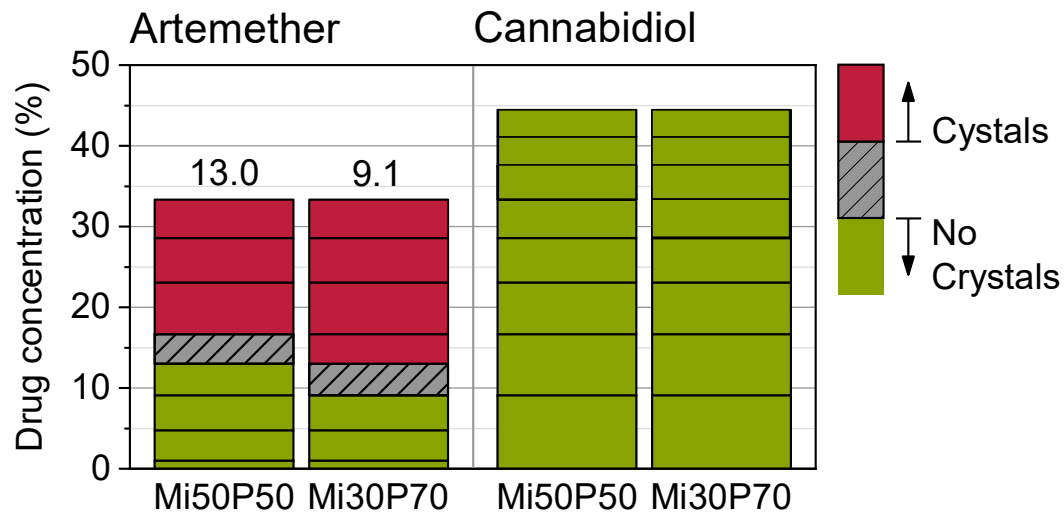


Mi50P50-fenofibrate

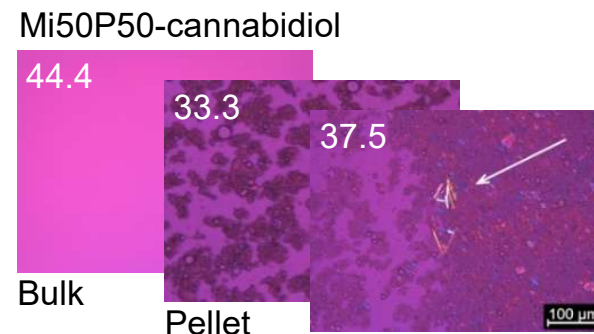


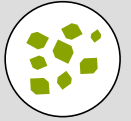


Drug loading – artemether & cannabidiol

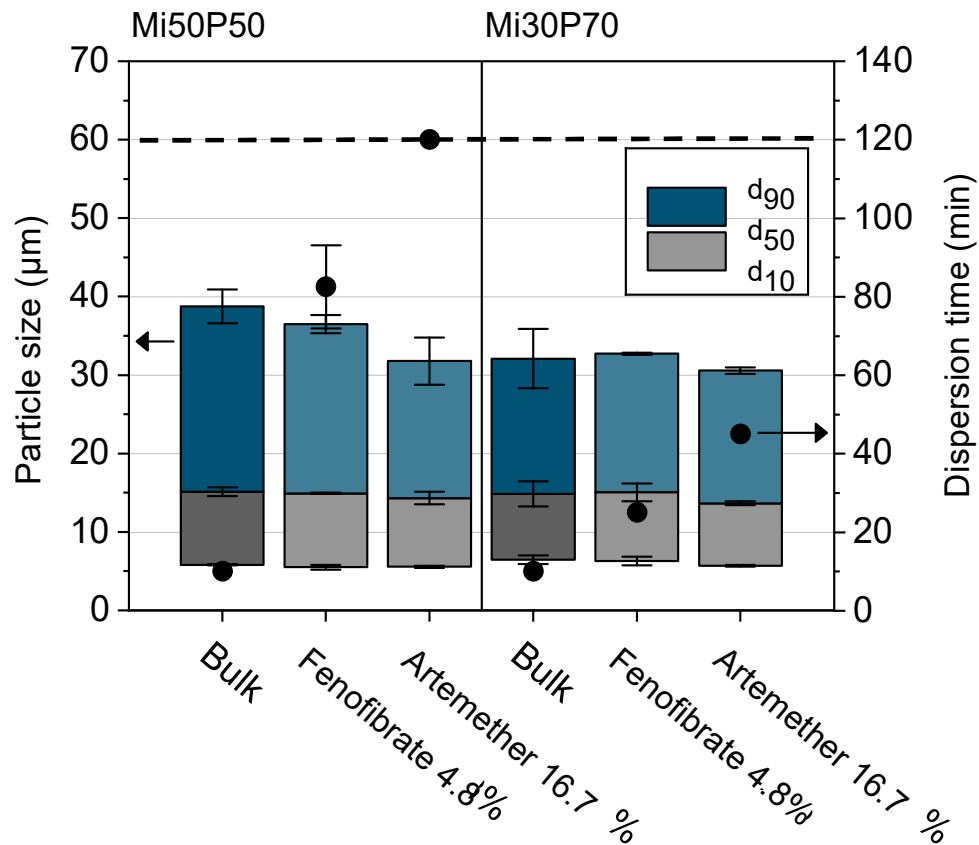


- Artemether (T_M : $\sim 87^\circ\text{C}$): high drug load, platelet-shaped crystals
- Cannabidiol (T_M : 67°C): Crystals only after dispersion, very high drug load
 - ⇒ Higher solubility in Mi50P50 than in Mi30P70
 - ⇒ Lower solubility when $T_M > 150^\circ\text{C}$ [1]
 - ⇒ Artemether and cannabidiol: Unusually high solubility





Dispersibility of drug-loaded formulations



- Similar particle sizes
- Drugs prolong dispersion time
 - ⇒ Higher dispersion time with
 - lower phospholipid content
 - Higher drug load
 - ⇒ High oil content → higher loading capacity
 - ⇒ High PC content → better dispersibility

Summary



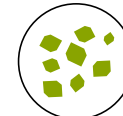
Miscibility

- Homogenous mixtures, high phospholipid content
- Miglyol + PL90G (+ LPC80) best properties
- Reverse micelles or (liquid-)crystalline structures



Capsule filling

- Homogenous formulations “pumpable“
- Clean drip-off up to 60% PL90G
- Higher compatibility with HPMC capsules



Drug loading

- High loading with low-melting drugs
- High phospholipid content decreases solubility
- Drug load increases dispersing time

Thank you!



Dr. Linda Grüne



Phospholipid
Forschungszentrum / Research Center
Heidelberg

Dr. Peter van Hoogevest



Prof. Dr. Ulrich Massing

