Particle Engineering Research from the NSF ERC Research Experience for Teachers (RET) Program at NJIT (Paper #44d)

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Structured Organic Particulate Systems ...an Engineering Research Center (C-SOPS)

NJIT New Jersey's Science & Technology University

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Background

- NJIT's Research Experiences for Teachers (RET) program in collaboration of the NSF Engineering Research Center for Structured Organic Particulate Systems (ERC-SOPS) and the Center for Pre-College Programs

- 14 high school teachers for 6-week summer research on various particulate materials and processes relevant to pharmaceutical products collaborating with graduate student mentors under the guidance of professors

- Workshops on technical writing, best research practice, effective collaboration in a team, pharmaceutical industry and process–formulation development, educational module development delivered by various faculty/CPCP experts

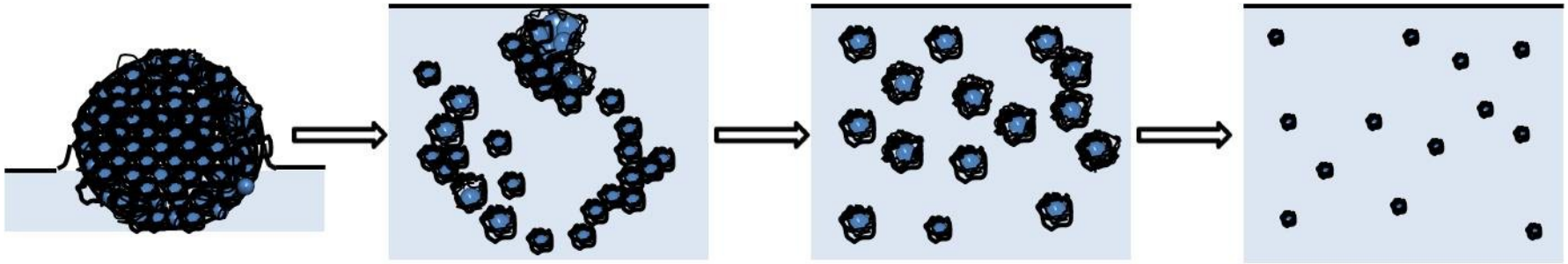
- Finally, in the educational component, the teachers came up with a professional development plan and prepared "educational modules", which were delivered to high school students.

Summer Research Topic I

The bioavailability enhancement of poorly water-soluble drugs via drug nanoparticle composites

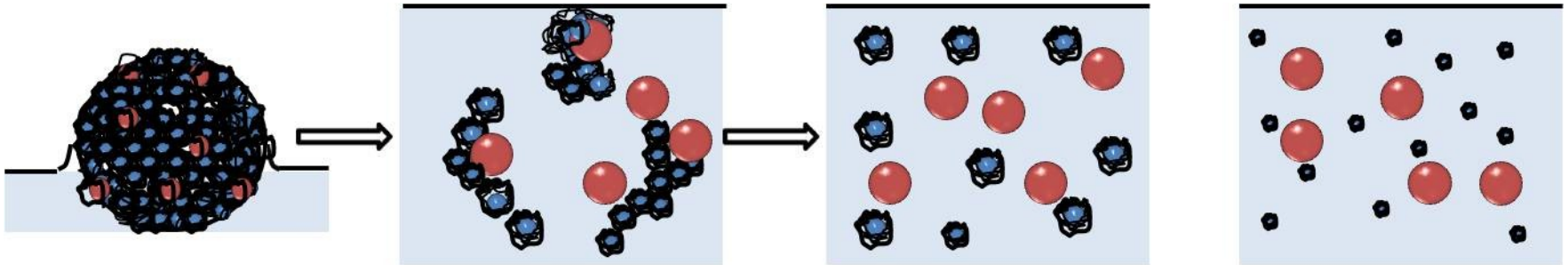
Background: Nanocomposite Microparticles

NCMPs with conventional soluble dispersants: soluble polymers, sugars, surfactants, etc.

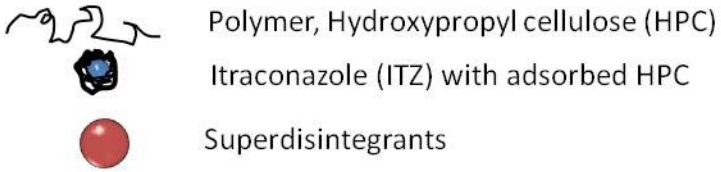


Wetting Aggregate breakage Dissolution

NCMPs with co-milled superdisintegrant (crosslinked polymer) & soluble polymer

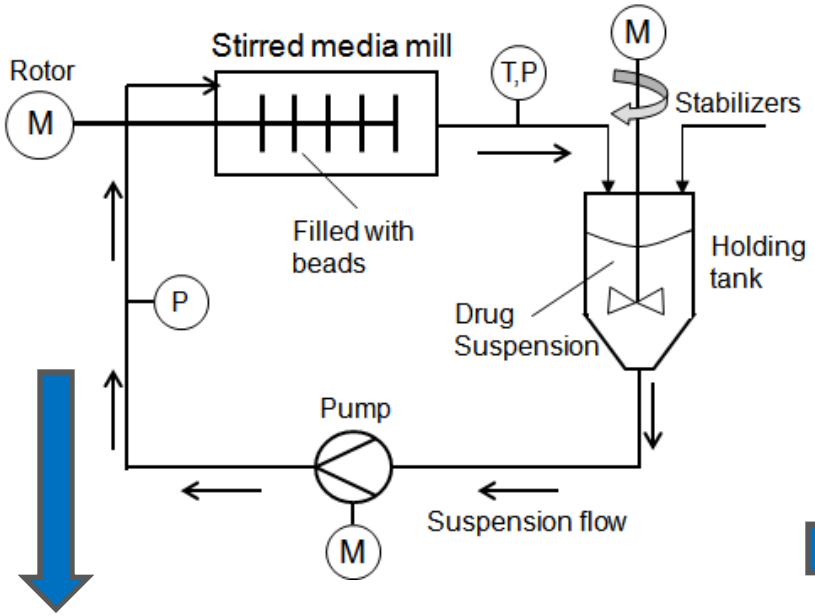


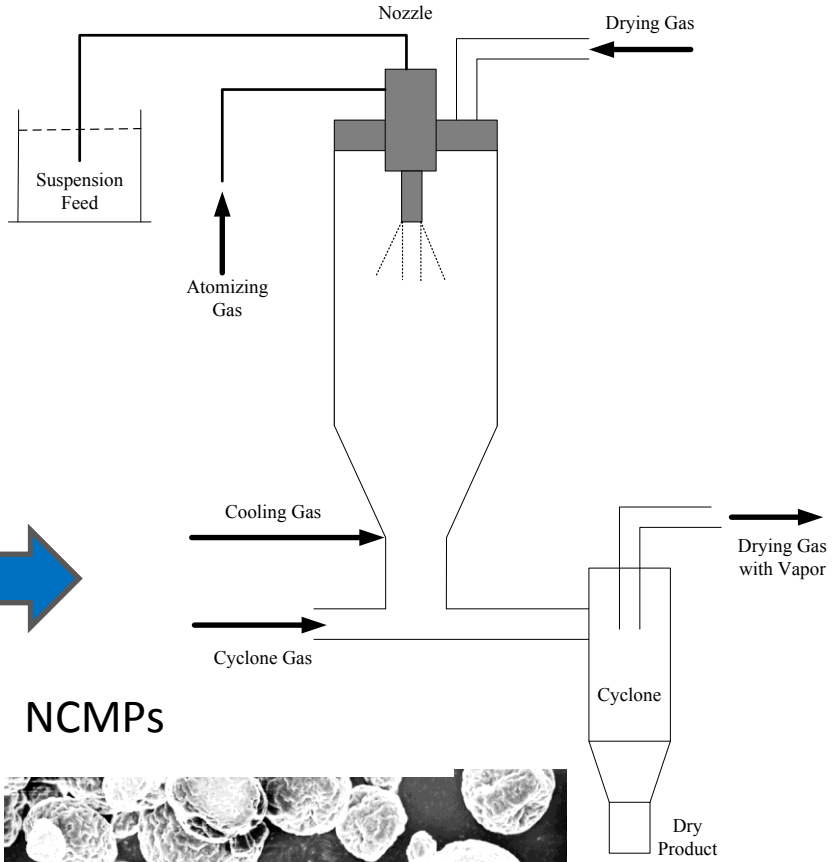
Wetting Swelling Aggregate breakage Dissolution



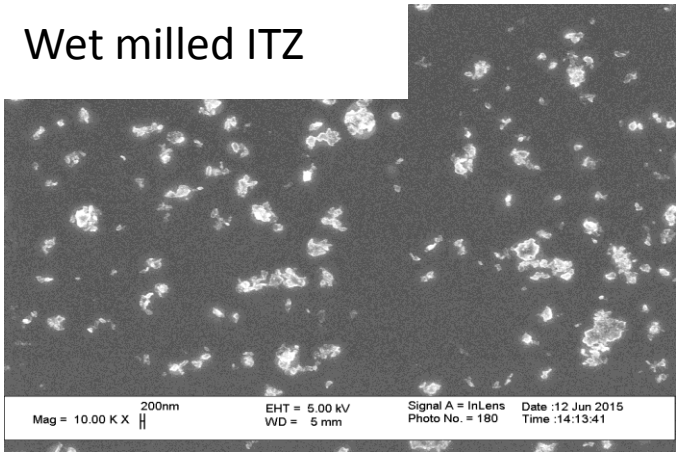
NCMP: nanocomposite microparticle comprising drug nanoparticles + dispersants

Preparation of Drug Nanocomposites

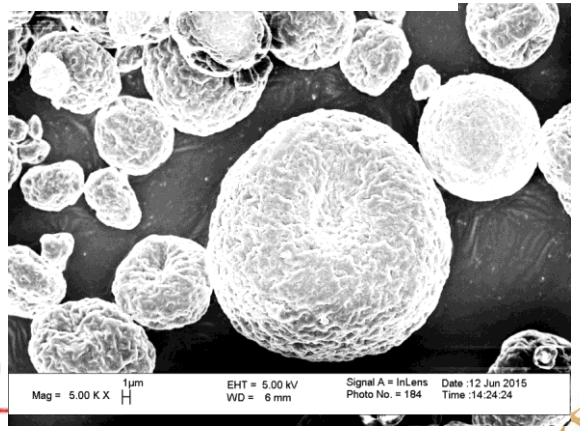




Wet milled ITZ



NCMPs



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Characterization Methods

- Drug nanosuspensions
  - **Particle size analysis** (laser diffraction, Coulter LS 12 320)
- Nanocomposites
  - **Drug content:** 100 mg nanocomposite dissolved in 20 ml dichloromethane.
  - **Dissolution** (USP II paddle method): 20 mg ITZ dose, 1000 ml dissolution medium, i.e., 3 g/L aq. SDS solution.
  - **UV spectroscopy:** the absorbance was measured at a wavelength of 260 nm.

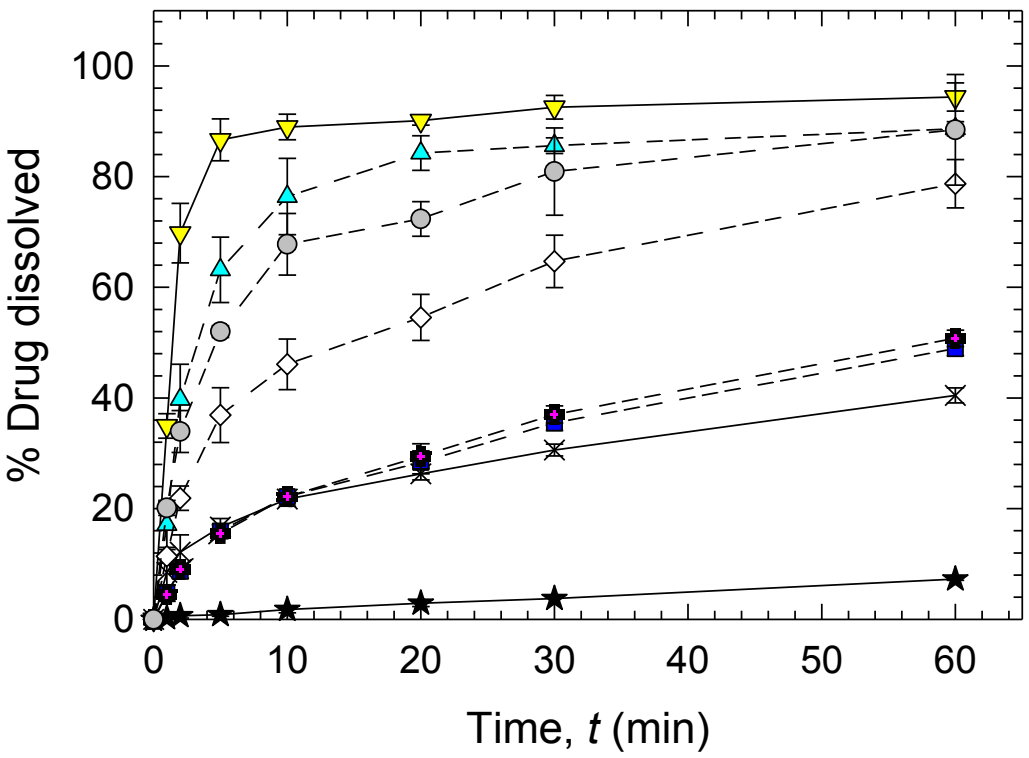
Formulations and Drug Content

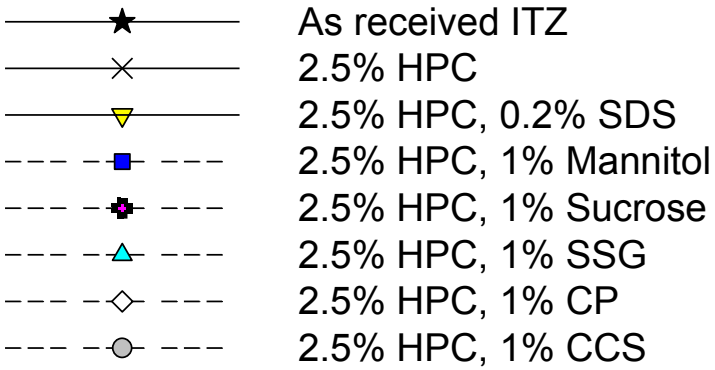
Run no	HPC (% w/w)[a]	SDS (% w/w)[a]	Other additives (% w/w)[a]	Theoretical drug content (%)	Drug content and RSD in nanocomposites (% w/w)[b]
1	2.5	0	–	80.0	78.9 (5.19)
2	0	0.2	–	98.0	N/M
3	2.5	0.2	–	78.7	78.3 (4.66)
4	2.5	0	1 (Mannitol)[c]	74.1	72.4 (5.59)
5	2.5	0	1 (Sucrose) [c]	74.1	70.3 (4.20)
6	2.5	0	1 (SSG)[d]	74.1	74.0 (2.73)
7	2.5	0	1 (CP)[d]	74.1	72.8 (4.30)
8	2.5	0	1 (CCS)[d]	74.1	74.0 (3.69)

[a]Drug loading in suspensions is 10%. % w/w is with respect to the weight of deionized water, 200 g.
[b]% w/w is the weight of ITZ with respect to the weight of NCMPs.
[c]Added after milling.
[d]Co-milled for 15 min.

➢**High drug loaded NCMPs: 70-80% with RSD < 6%.**

Dissolution Profiles with Sugars/Sugar Alcohols/Superdisintegrants as Dispersants





➢**Fastest drug dissolution was obtained from the HPC–SDS-based nanocomposites.**

➢**Superdisintegrants (SSG > CCS > CP) are more effective dispersants than sugar and sugar alcohol.**

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Summer Research Topic II

Effect of film thickness & superdisintegrants on strip film disintegration time

Background – Why Oral Strip Film?

- **Demand:**
  - Some patients cannot swallow pills
    - Very young, elderly, dysphagic
  - Fast drug release improved bioavailabili
    - Faster relief for patients
    - No need to administer with water
  - Personalized dosage

- **Issues:**
  - Strip films for oral applications need to disintegrate in the oral cavity to deliver active therapeutic agents.
  - No standard disintegration test method for ODFs: USP1, petri dish, and frame methods used.
  - Disintegration time affected by the thickness of the film besides the formulation.

Objectives

- Comparative assessment of the reliability of various disintegration test methods

- Investigate the effect film thickness and two different superdisintegrants on the disintegration time of strip films

Process Summary & Equipment

Polymer solution

API dry powder

Shear mixing

Film casting and drying

Characterization

Test films:

Disintegration
- Petri Dish
- Film Frame
- USP1

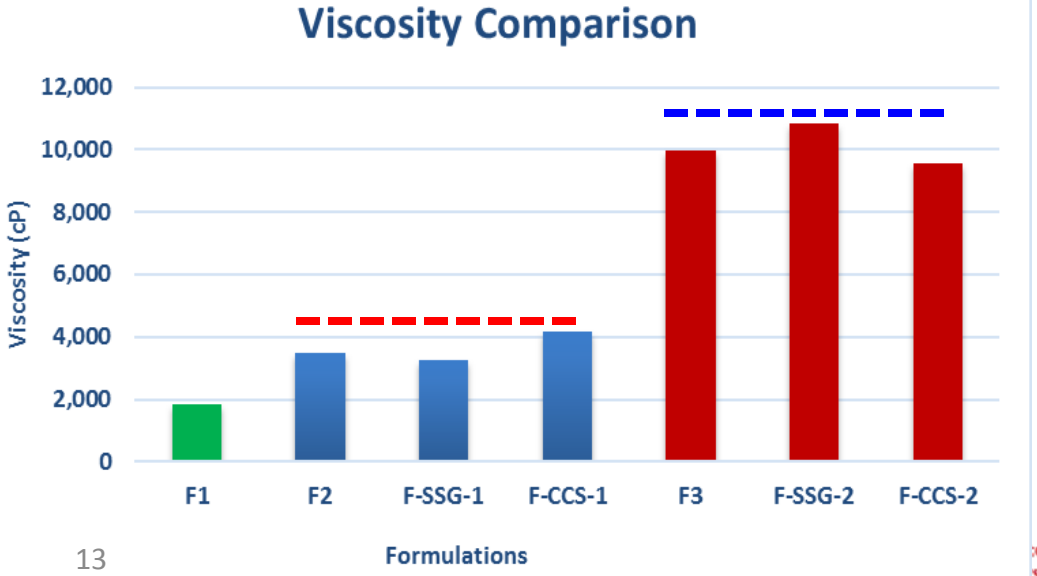
Dissolution
- USP IV

Drug assay

Formulations for Fenofibrate-Loaded Films

Formulations	HPMC-E15 (g)	Glycerin (ml)	API amount (g)	DI water (ml)	Superdisintegrants (g)
F1	10	3	2.5	100	0.00
F2	10	3	2.5	80	0.00
F3	10	3	2.5	70	0.00
F-SSG-1	10	3	2.5	100	0.75
F-CCS-1	10	3	2.5	100	1.40
F-SSG-2	10	3	2.5	100	1.75
F-CCS-2	10	3	2.5	100	2.75

API is fenofibrate (BCS II)

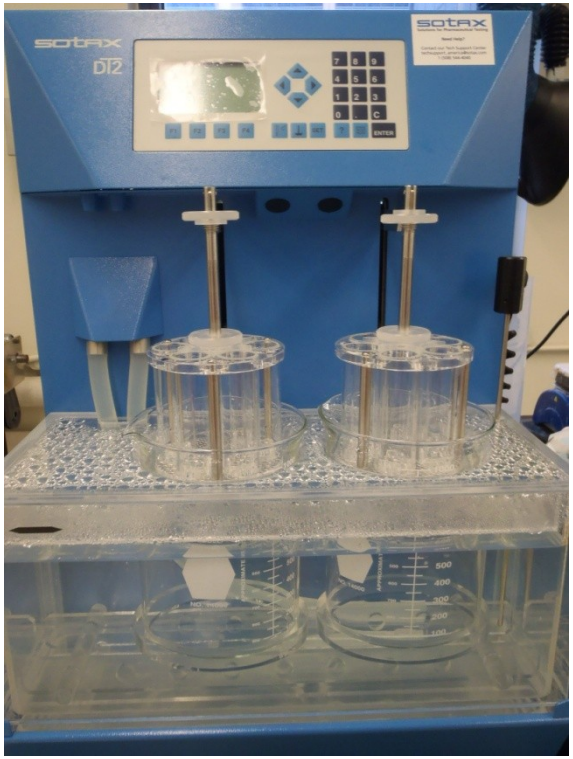


F2 = F-SSG-1 = F-CCS-1 = Viscosity ~4000 cP
F3 = F-SSG-2 = F-CCS-2 = Viscosity ~10,000 cP

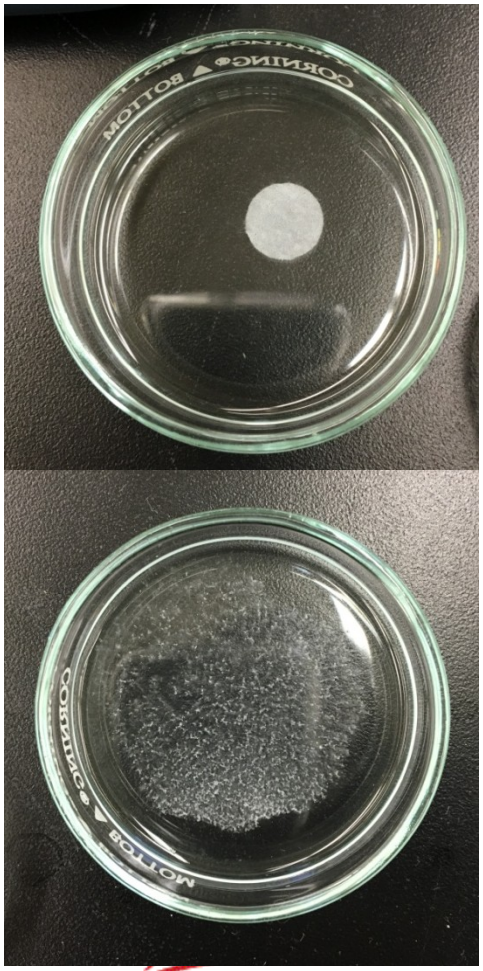
- Superdisintegrants increased the viscosity of the polymer solution
- SSG was able to achieve the same viscosity of CCS at lower concentrations

Characterization Equipments of Disintegration Time

USP1



Petri Dish



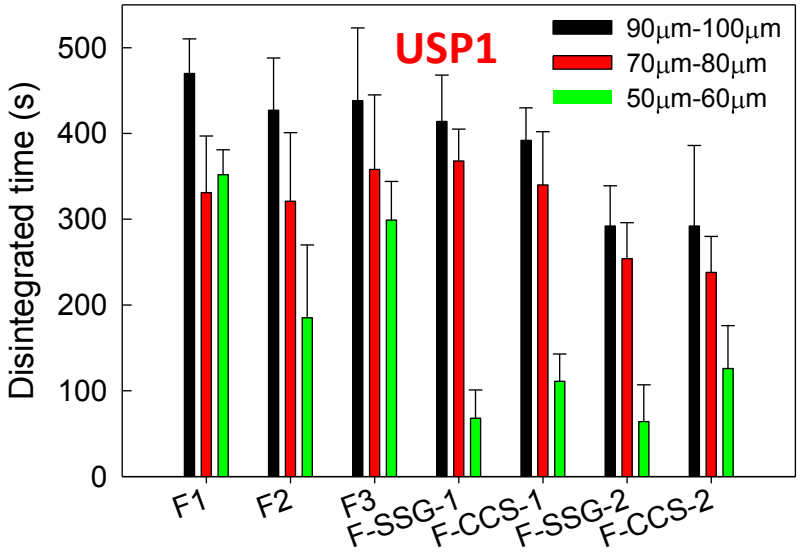
Slide Frame

Content uniformity of 50-60 µm films

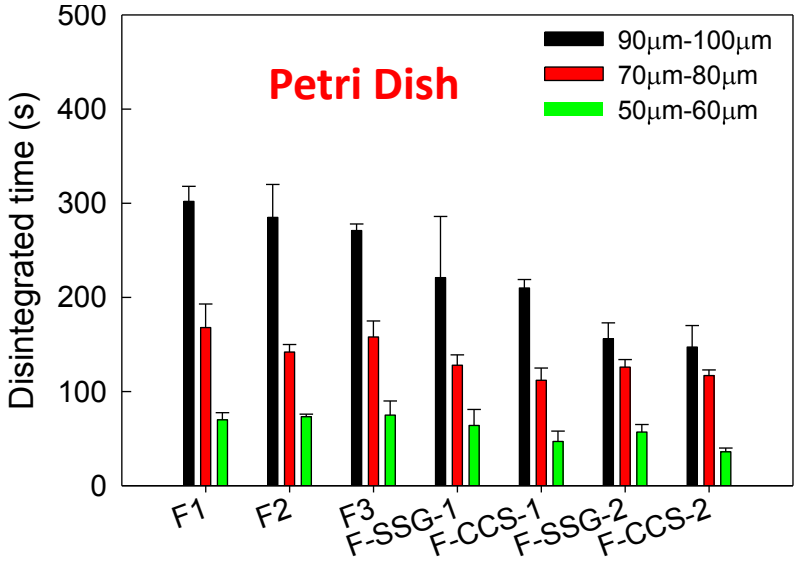
Formulations	Film mass (mg)	RSD (%)	Film thickness (µm)	RSD (%)	API loading (mg/cm²)	wt% API	RSD (%)
F1	4.69	6.21	54.7	5.17	1.01	15.29	5.87
F2	5.50	3.74	60.1	4.53	1.14	14.78	0.69
F3	5.31	5.45	59.3	4.89	1.14	15.28	1.43
F-SSG-1	4.71	5.05	51.7	7.13	0.92	13.94	5.22
F-CCS-1	4.11	6.09	52.5	5.09	0.77	13.35	5.09
F-SSG-2	3.97	2.79	50.7	5.29	0.79	14.13	2.36
F-CCS-2	3.28	2.16	59.5	3.48	0.62	13.44	3.18

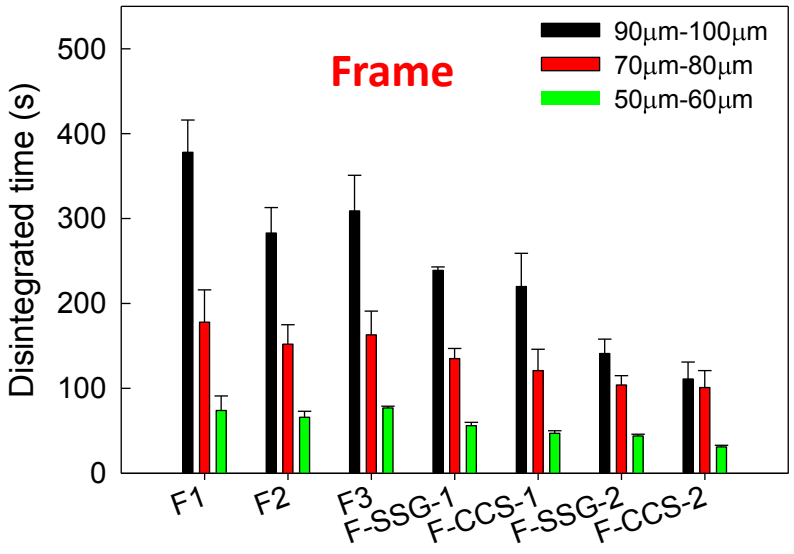
- **Target film thickness of 50-60 µm achieved, with 13-15% drug loading**
- **Low drug RSD (all < 6%). Higher viscosity helps; lower RSD at higher HPMC/additive concentrations.**

Disintegration Time via Different Methods



- USP1 method predicts longer disintegration time with much larger RSD than the other two methods.
- Thickness effect was better discriminated by Petri Dish and Frame methods than the USP1.
- Thicker films disintegrated more slowly. Presence of superdisintegrants reduced the time.





Q&A