Excellent CU of Low Dose Direct Compression Tablets Achieved Using Co-processed API

Changquan Calvin Sun, Ph.D.

Pharmaceutical Materials Science and Engineering Laboratory

University of Minnesota

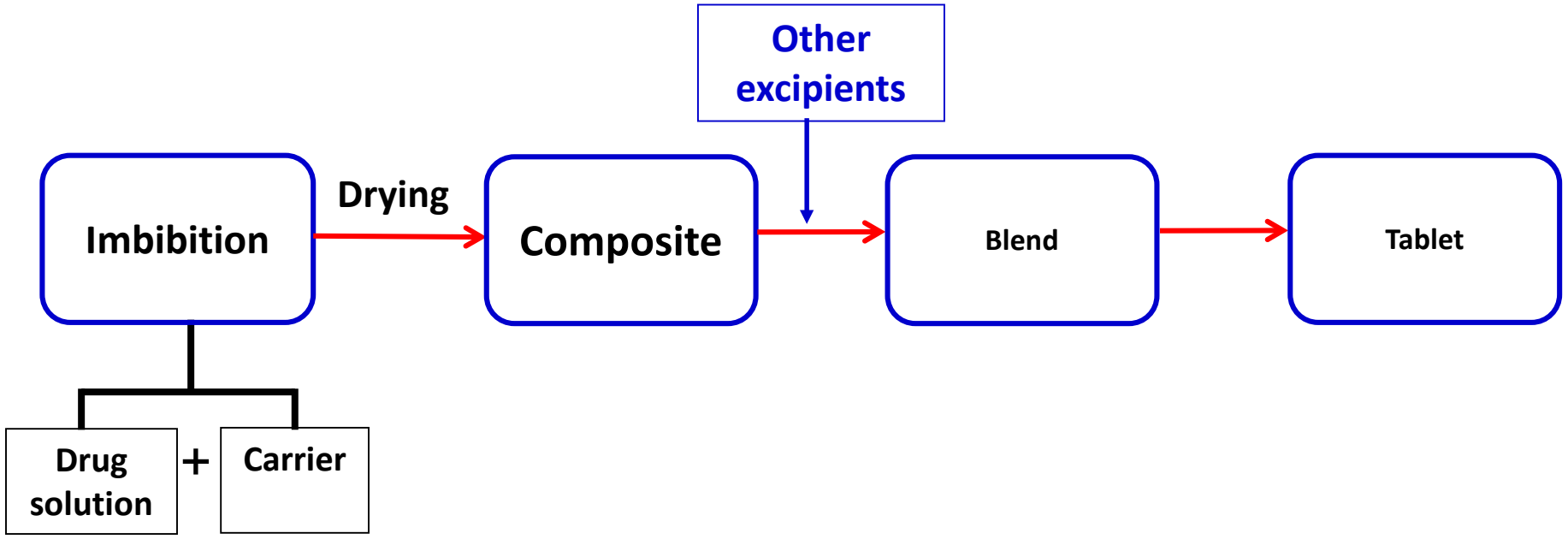
Challenges in Tablet Manufacturing

1. **Powder flowability**
2. **Powder tabletability**
3. **Tablet dissolution**
4. **Content uniformity**
5. **Tablet friability**
6. **Speed sensitivity**
7. **Punch sticking**
8. **Stability**

For **Low** dose drugs

For **High** dose drugs

Co-Processing Approach 1: Mesoporous Carriers



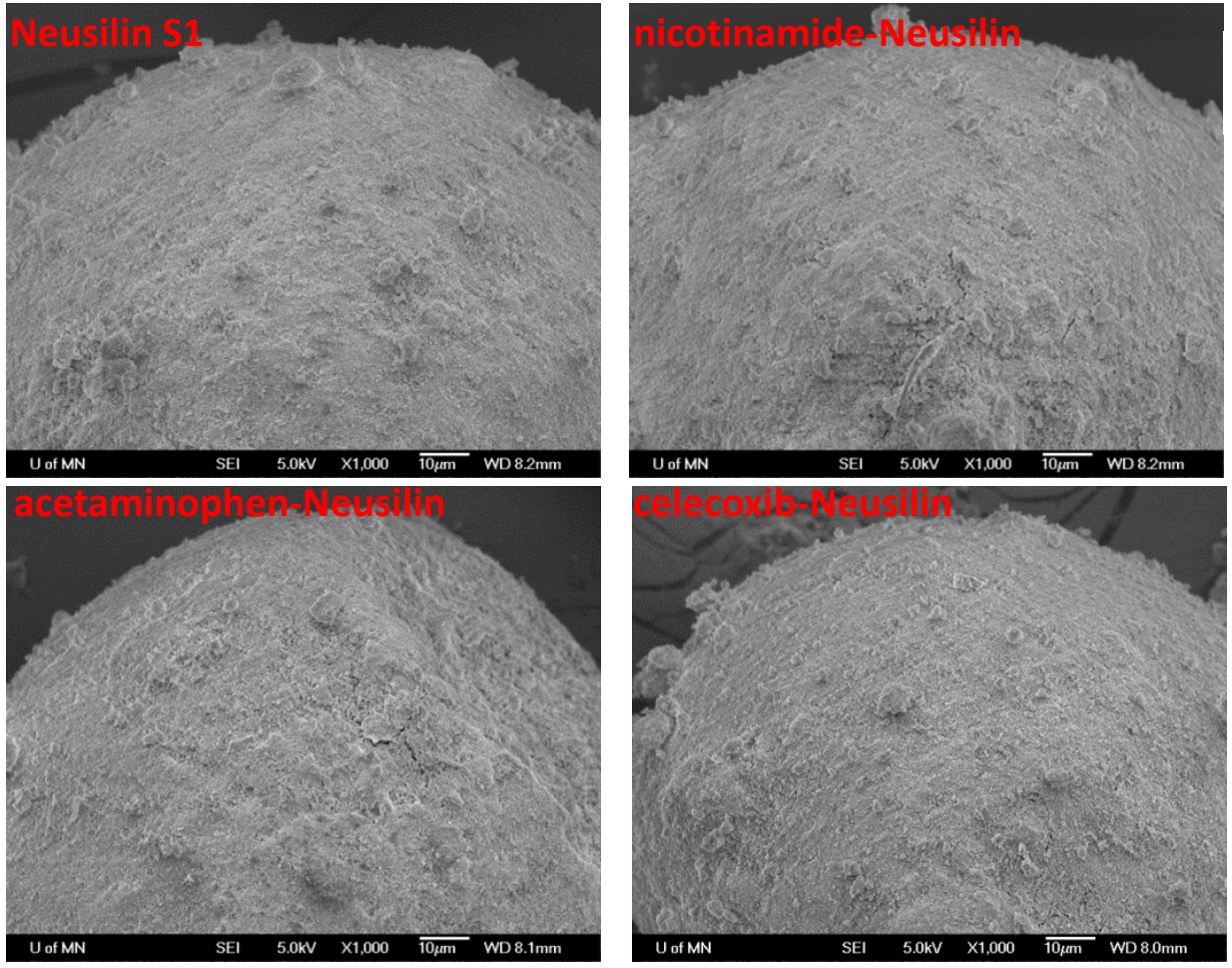
10% drug loading in a composite can be routinely achieved, up to 40% (w/w)

Potential advantages:

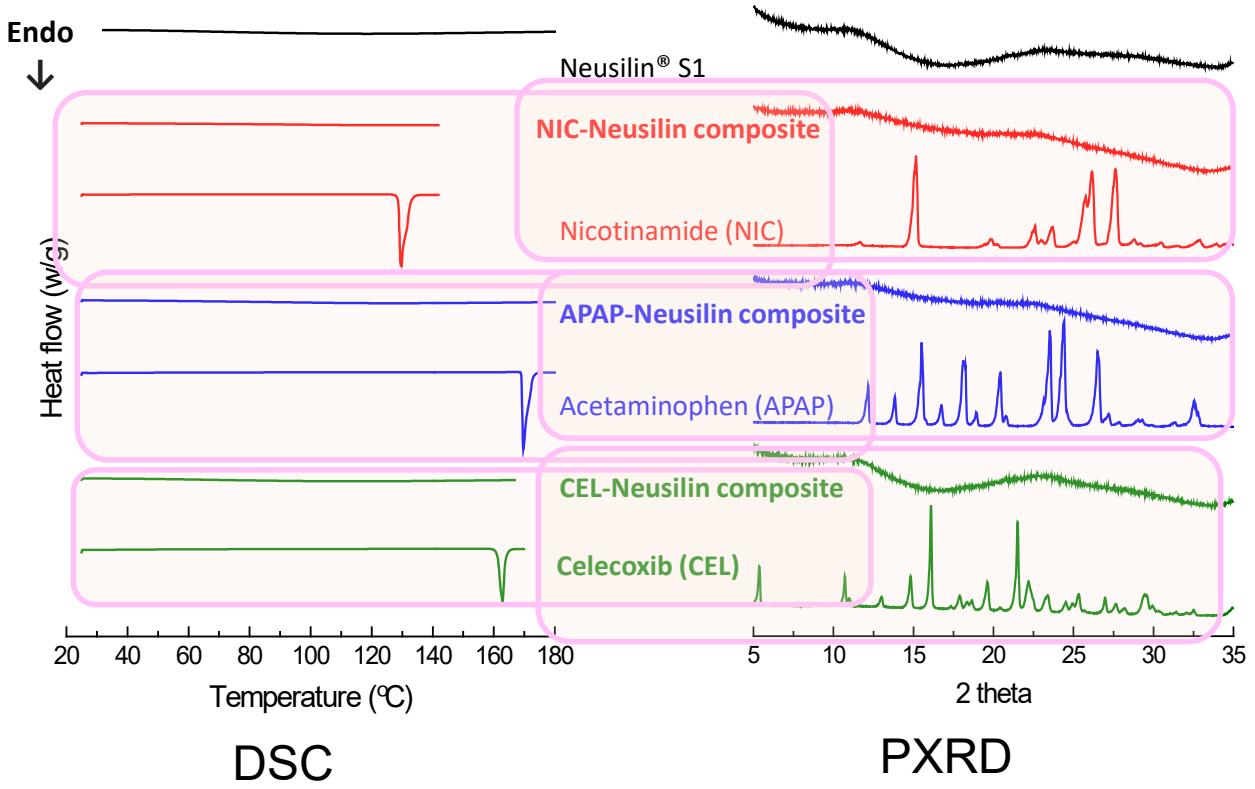
1. Uniform distribution of drug - independent of drug type and loading
2. Properties of the composite - insensitive to drug type and drug loading
3. Possibility for developing a platform formulation

Characterization of Co-Processed APIs

SEM (5% drug loading)



Solid-state Properties (10% Drug Loading)



Sun, et al., 2019, *Powder Technol, 342, 856-863*

Sun et. al., 2017, *J. Pharm. Sci.*, 106:1772-1777

IR Tablet Platform Formulation (Low Dose)

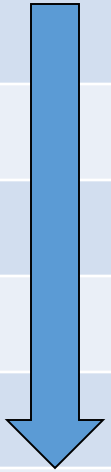
Component	wt %
Drug [a] - Neusilin® S1 composite	20.0
Microcrystalline cellulose (Avicel PH102)	49.5
Lactose monohydrate (Fast-Flo)	25.0
Croscarmellose sodium (Ac-Di-Sol)	5.0
Magnesium stearate	0.5
Total	100

[a] **model drugs:** nicotinamide (NIC), sulfacetamide (SFA), phenylepherine HCl (PE), acetaminophen (APAP), theophylline (Theo), and griseofulvin (GRS)

Sun et. al., 2017, *J. Pharm. Sci.*, 106:1772-1777

Model Drugs: A Wide Span of Solubility

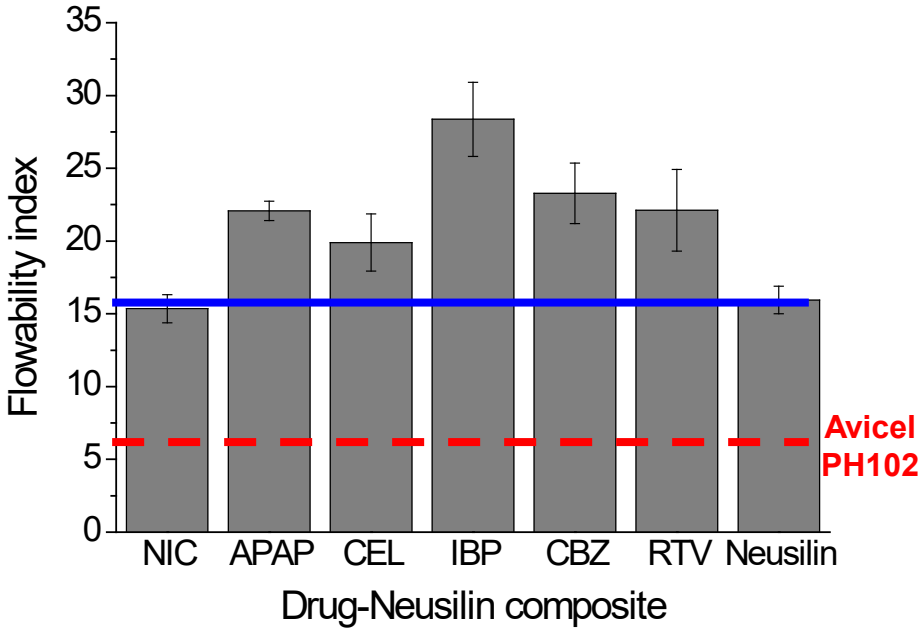
Drug	abbreviation	Aq. Solubility (mg/mL)
nicotinamide	NIC	1000
phenylephrine HCl	PE	100
acetaminophen	APAP	12.8
sulfacetamide	SFA	8.3
theophylline	THEO	8.0
griseofulvin	GRS	0.0077

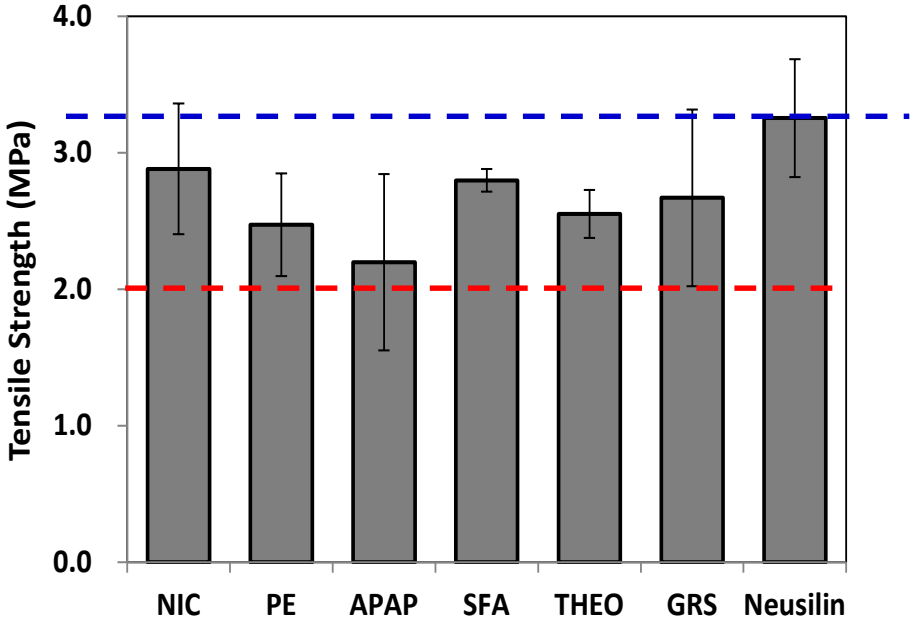


Solubility spans a range of **5** orders of magnitude!

Manufacturability of Co-Processed APIs

(5% drug loading)





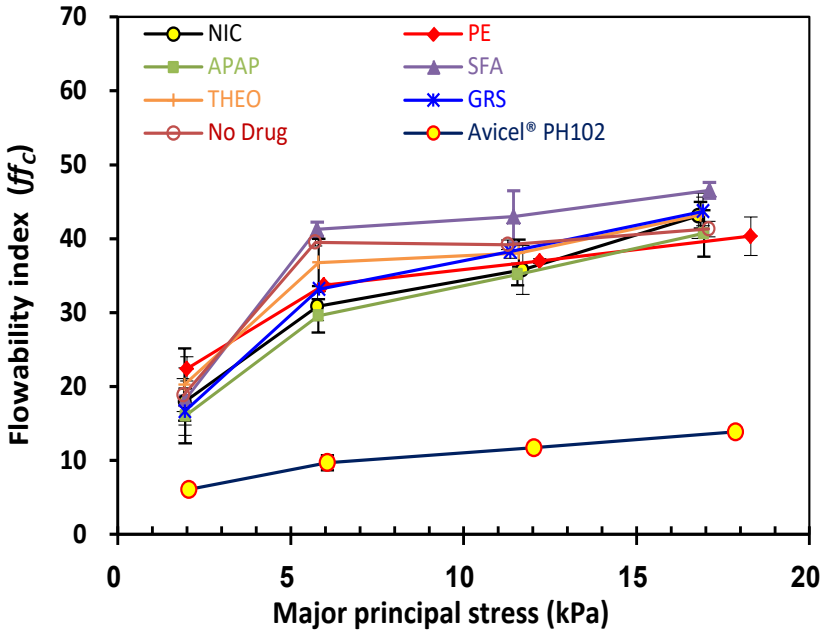
Flowability

Tabletability

Sun et. al., 2017, *J. Pharm. Sci.,* 106:1772-1777

Performance of Formulation

Flowability



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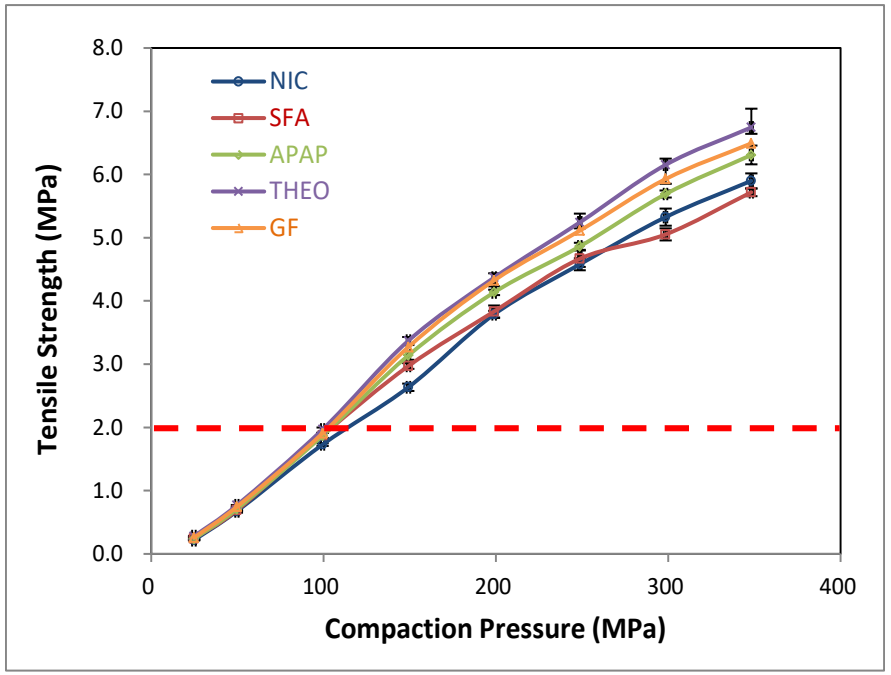
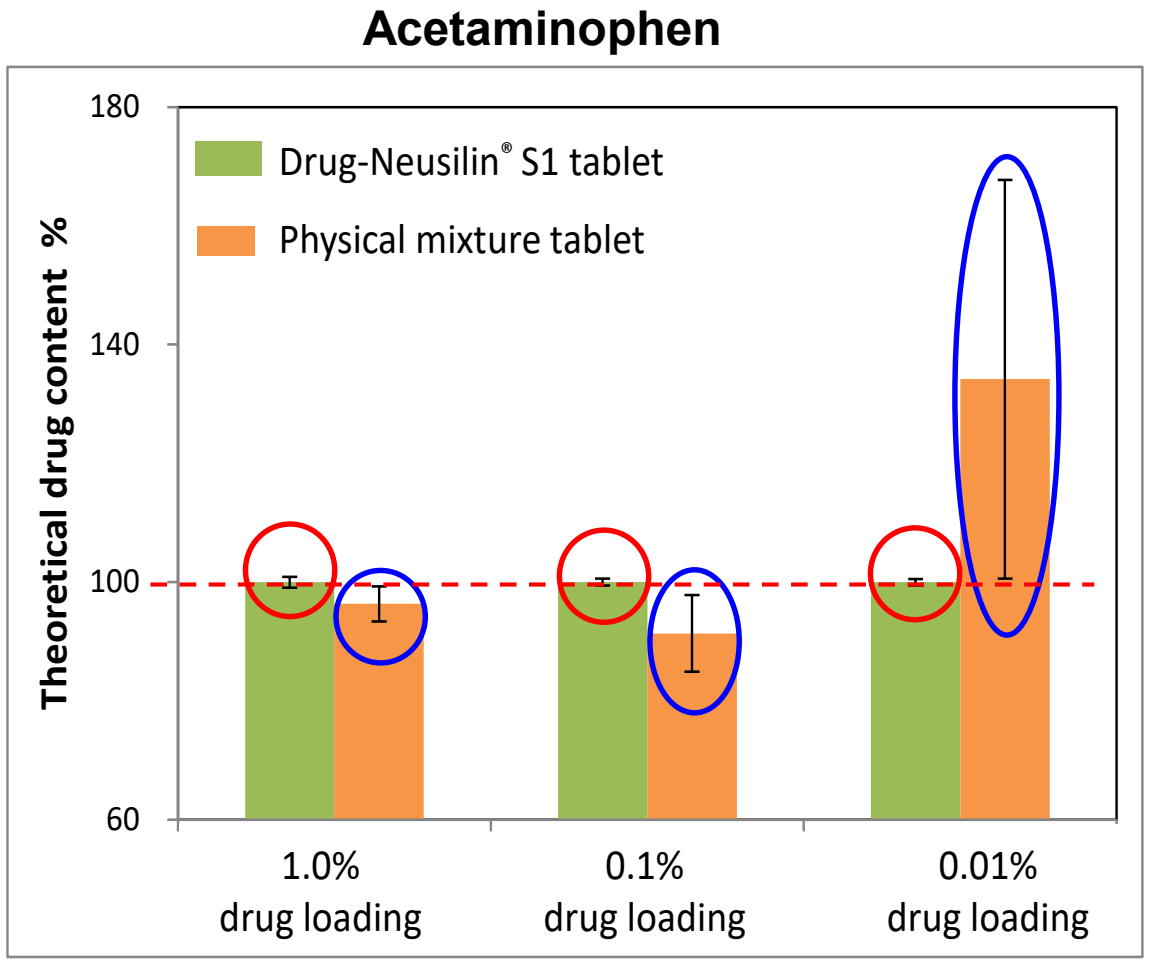
Tabletability



	NIC	SFA	APAP	THEO	GF
Tablet friability (%)	0.58	0.05	0.20	0.13	0.18
Disintegration time (s)	30-40 s for all tablets				

Tablets were compressed at 150 MPa

Tablet Content Uniformity



1% drug loading						
	NIC	PE	APAP	SFA	THEO	GRS
Mean (%) N = 6	98.0	100.2	99.3	99.6	98.3	99.6
RSD (%)	0.45	0.77	0.89	0.67	0.99	0.67

The uniformity of drugs in mesoporous carriers is at least as good as tablet CU.

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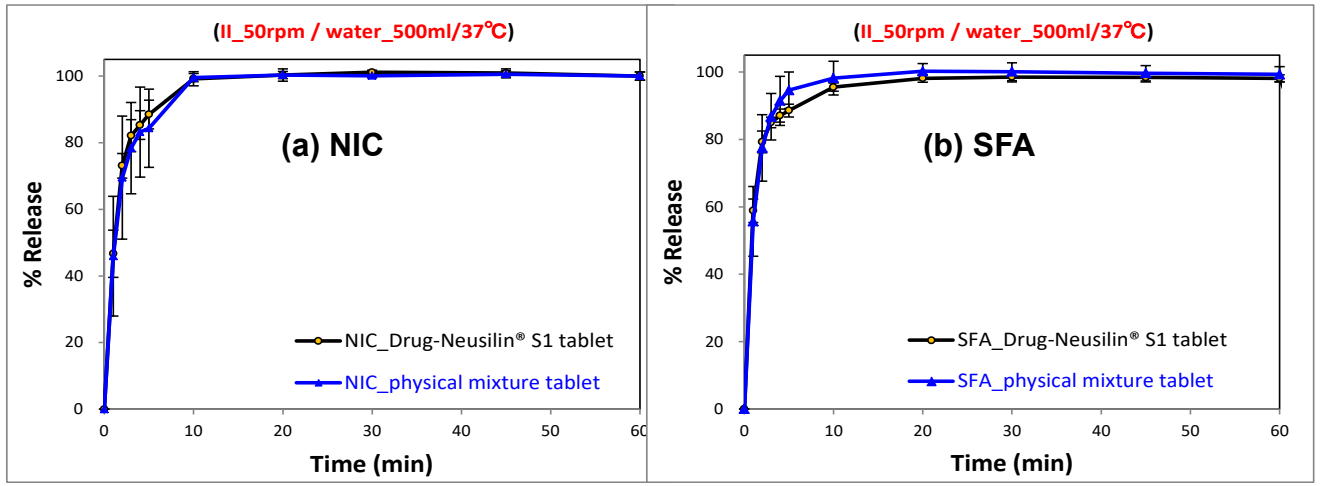
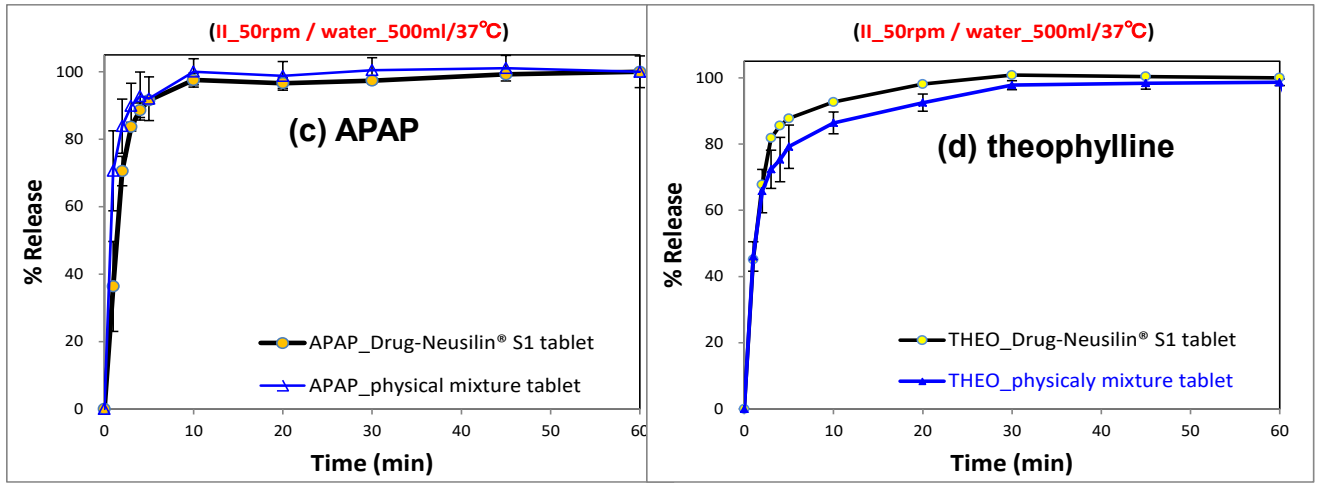
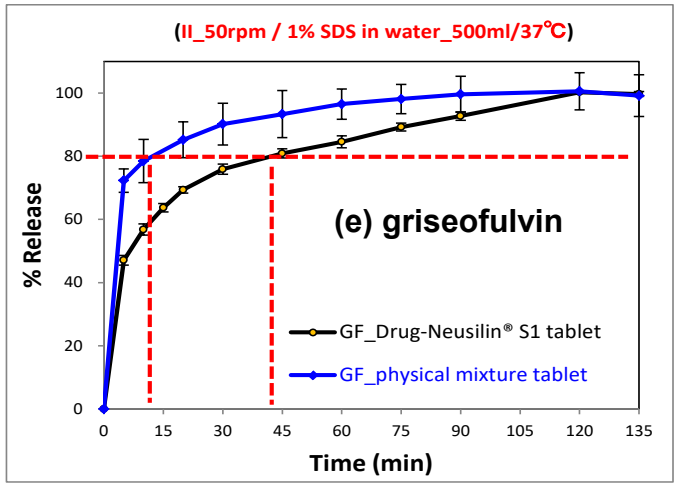
Tablet Dissolution







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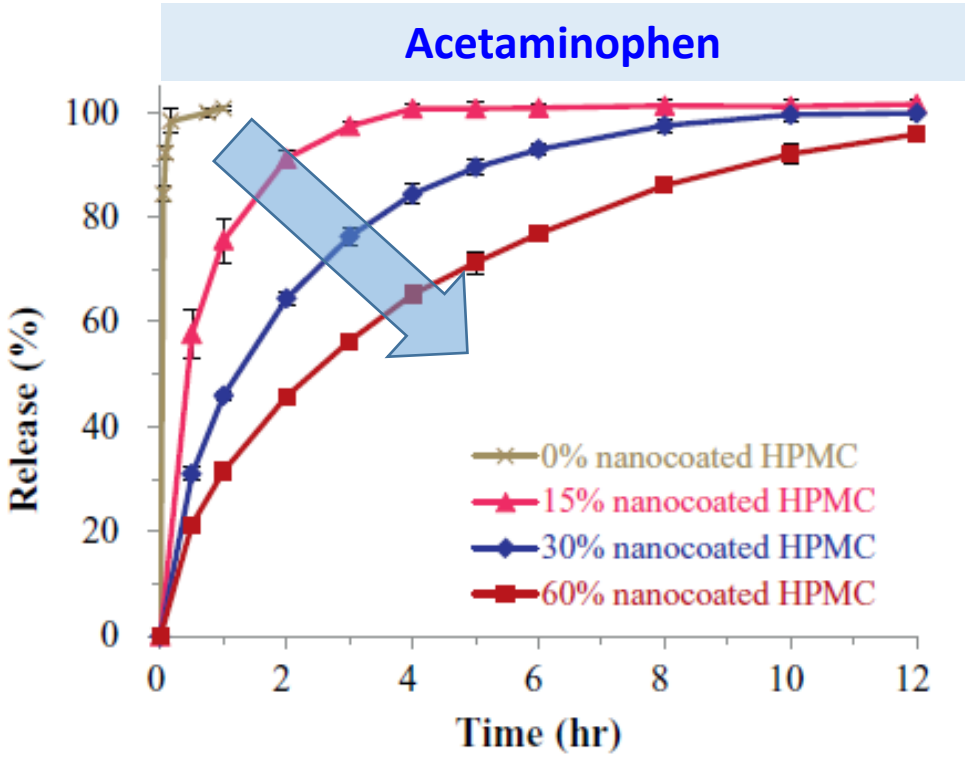
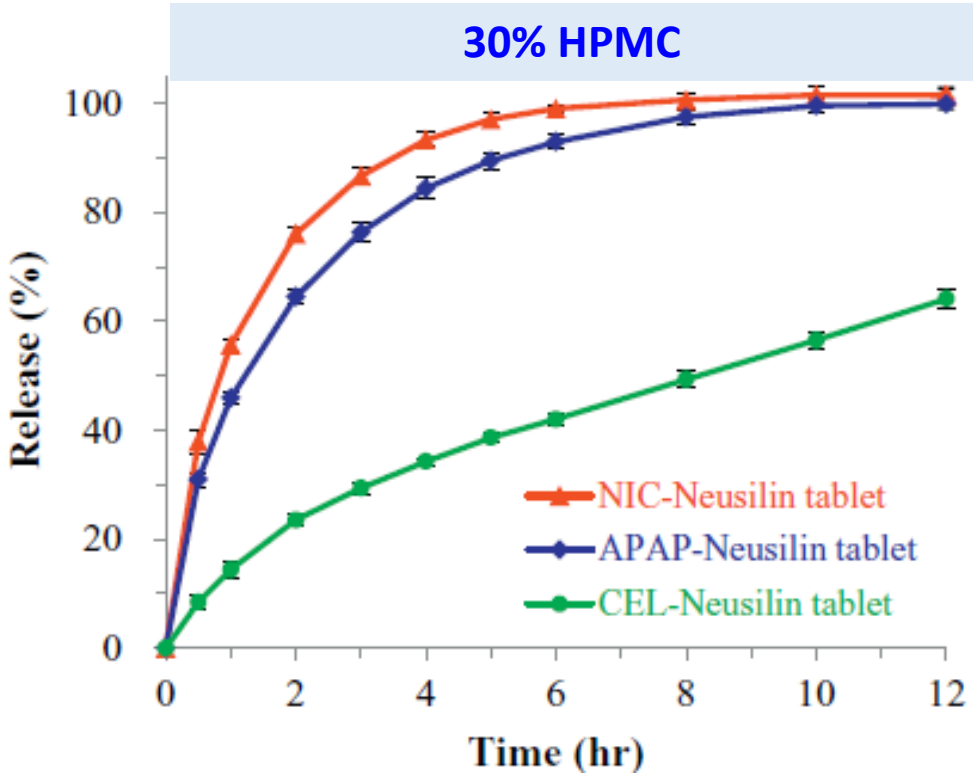
SR Tablet Platform Formulation



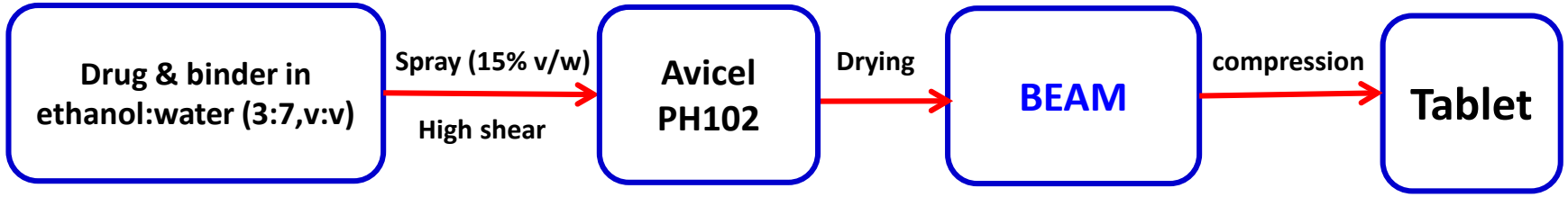


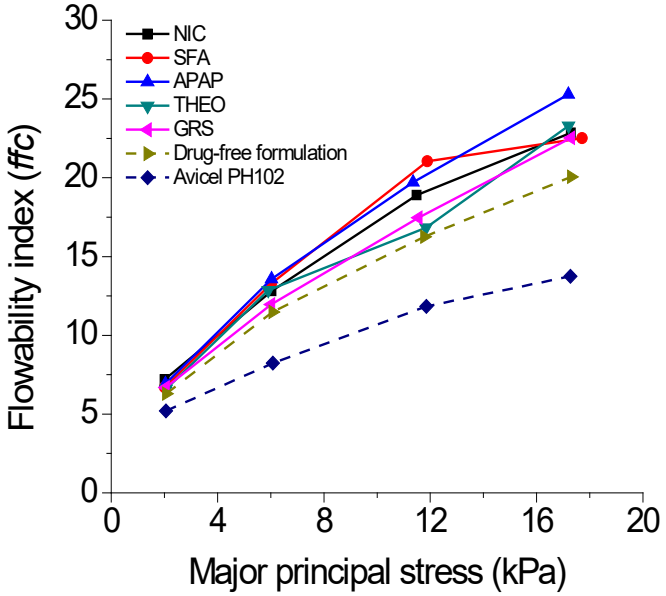
Sun et. al., *Powder Technol,* 342 (2019) 856–863

Co-Processing Approach 2: Binder Enhanced API-MCC (BEAM)

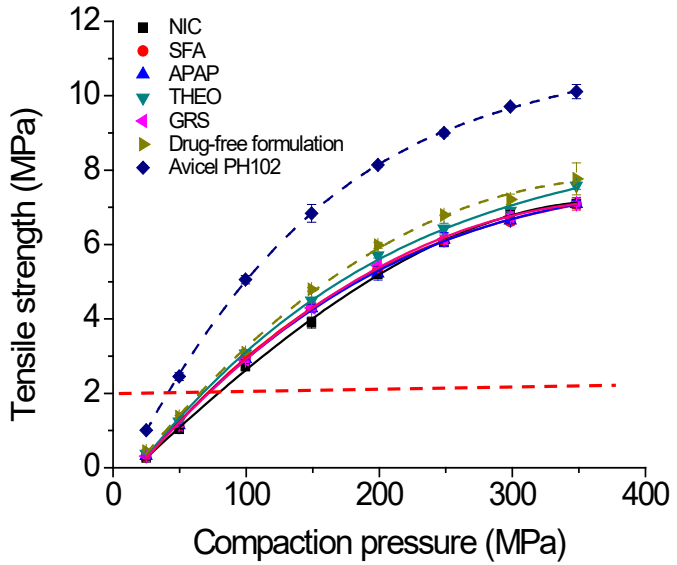
Known properties of MCC (Avicel PH102)

1. Good flowability
2. Excellent tabletability
3. Low ejection force
4. Self-disintegrating
5. HSWG improves flowability





Excellent flowability



Excellent tabletability

Tablet properties (0.1% drug loading, 100 MPa)

	NIC	SFA	APAP	THEO	GRS
Friability (%)	0.01	0.02	0.04	0.02	0.02
Disint. time (s), n = 3	< 40	< 40	< 40	< 40	< 40
EJ force (N), n = 3	104 ± 6	106 ± 5	114 ± 4	102 ± 1	113 ± 4
CU (RSD%), n = 6	0.8	0.6	0.9	0.8	1.6

Conclusions

1. Excellent content uniformity was obtained using a carrier approach for very low dose drugs

2. Drug-carrier composite approach enables the development of DC formulation platforms (IR and SR) for low dose tablets

3. Co-processed API is a powerful approach to address problems encountered in tablet formulation and manufacturing

Acknowledgements

Dr. Wei-jhe Sun

Dr. Aktham Aburub

Many other colleagues, former students, postdocs, and visiting scholars for contributions in other projects

AAPS
Abbott Laboratories
BASF
Boehringer Ingelheim
Celgene
Cima Labs
DFE Pharma
Eli Lilly
Huadong Pharmaceutical
Merck
NSF
NSF - CPPR
Pfizer
PhRMA Foundation
Univ. of Minnesota
US FDA

Sun Lab
https://www.pharmacy.umn.edu/departments/pharmaceutics/changquan-calvin-sun-lab