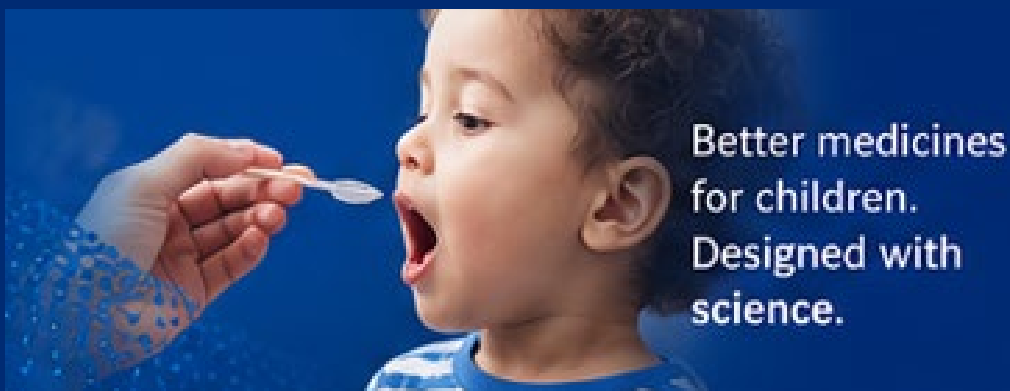


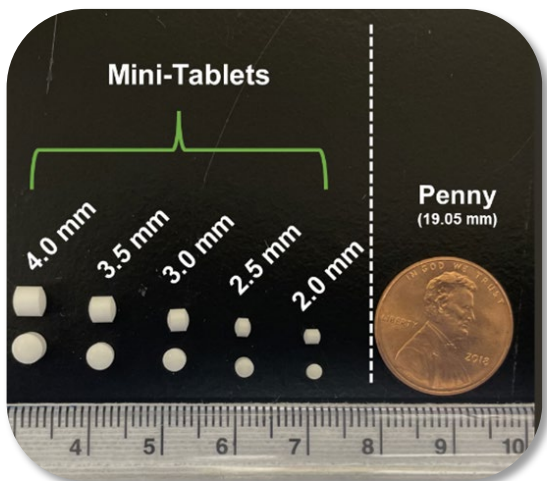
Predicting Weight Variability in Mini-Tablets: Impact of Particle Size and Tablet Punch Size

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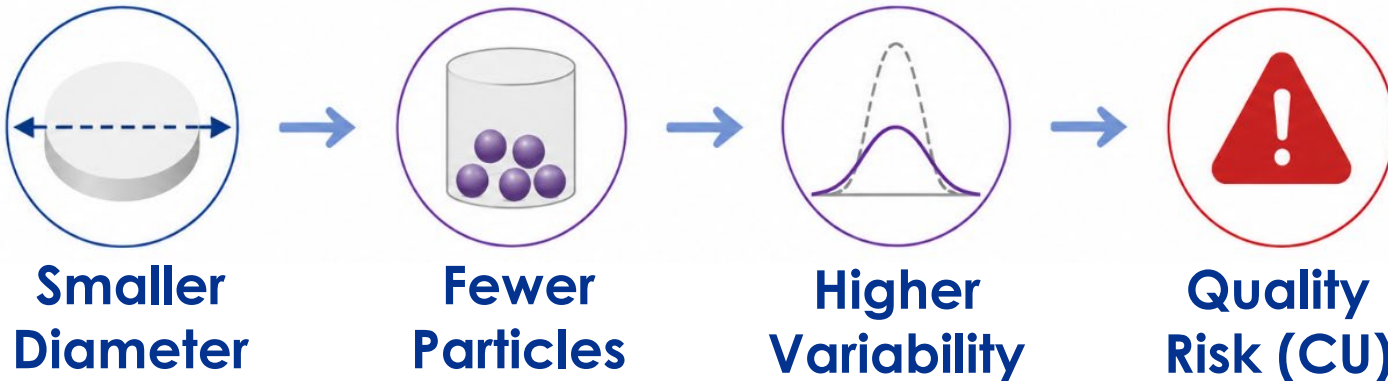
1 Mini-tablets: Patient-Centric Dosage Forms For Children

Mini-tablets: Small tablets (1 – 4 mm) administered as multiple units



- Dose Flexibility**
Age/weight-based dosing
- Dose accuracy**
Precise titration
- Stability**
Better than liquids
- Ease of administration**
Can be sprinkled onto solid or liquid food

2 Challenges with mini-tablets



★ Highlights

- ✓ First-principles, physics-based model
- ✓ Predicts mini-tablet weight variability from tablet punch diameter and blend PSD
- ✓ Verified using 50 experimental runs on rotary press
- ✓ Strong agreement ($R^2 = 0.93$; NRMSE=0.05) and robust model
- ✓ Guides selection of blend PSD targets

3 Our Approach: From First-Principles to Model Verification

Derive Model



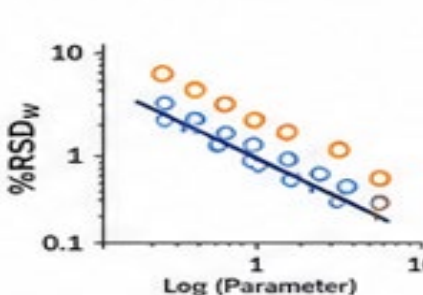
Particle sampling statistics + packing considerations

Experimental Design

Unimodal Suglets® as Surrogate Granules Compressed on Rotary Press

- 5 PSDs (430 – 1150 μm)
- 5 Punch Sizes (3 – 13 mm)
- 2 Fill Heights (3.8 & 9 mm)
- = **total 50 runs**

Verify Scaling Relationships



Verify full model

Compare predicted vs experimental



First-Principles Model

Tablet weight variability (%RSD) as a function of punch diameter and blend PSD

$$w_{RSD}(\%) = 100 \times \sqrt{\frac{2}{3} \times \frac{d_{50}^3}{D^2 h_d} \times \frac{\rho_t}{\rho_b} \times \exp[4.5(\ln(\sigma_g))^2]}$$

1 Packing efficiency PSD spread correction

Parameter	Definition
D	Tooling diameter
d_{50}	Mean blend diameter
h_d	Fill height
ρ_b	Bulk density of blend
ρ_t	True density of blend
σ_g	Spread of PSD ($\frac{d_{90}}{d_{50}})^{0.78}$
w_{RSD}	Weigh variability (%RSD)

4 High-level Results and Data Analysis

Experimental Data Weight Variability (%RSD)

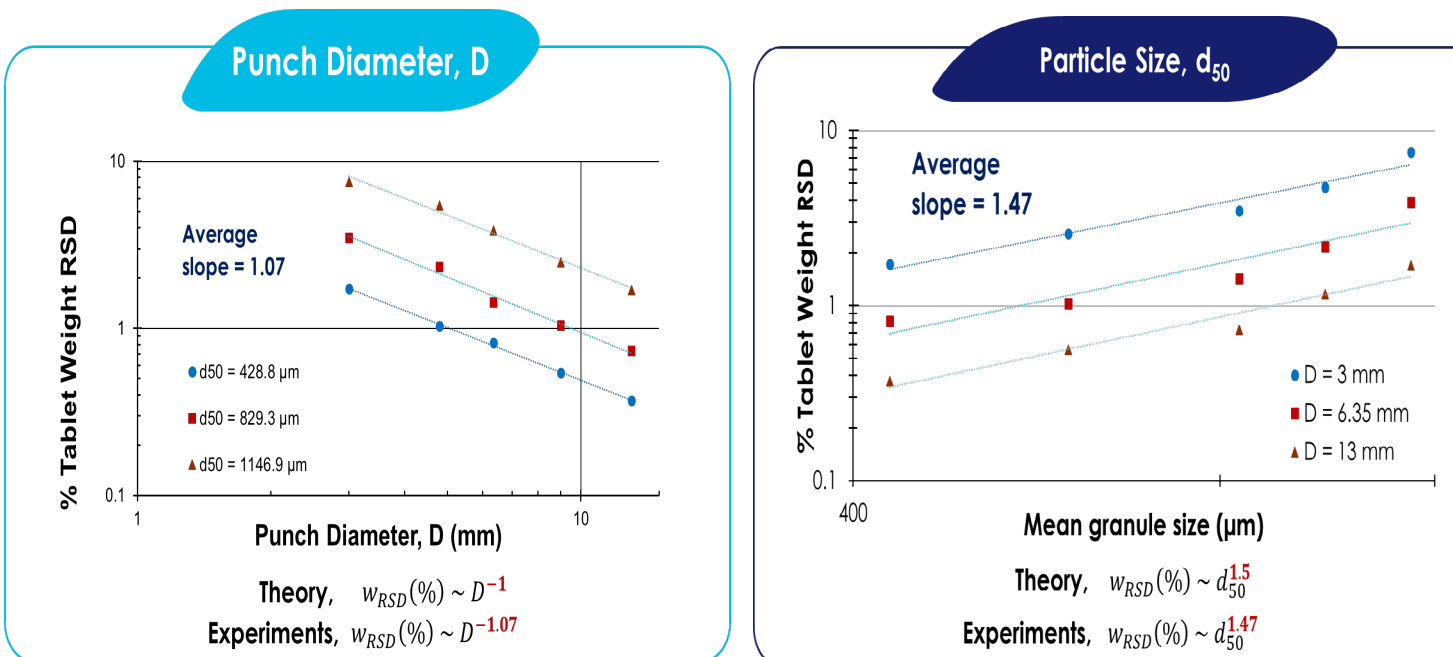
Blend PSD (d_{50} , μm)	3	4.8	6.3	9	13
430	1.73	1.03	0.82	0.54	0.37
600	2.57	1.31	1.03	0.64	0.56
830	3.49	2.34	1.43	1.04	0.73
975	4.77	3.65	2.18	1.56	1.17
1150	7.53	5.46	3.88	2.48	1.70
	3	4.8	6.3	9	13

Tooling Size (mm)



3 mm mini-tablets showed highest variability imply greater CU risk

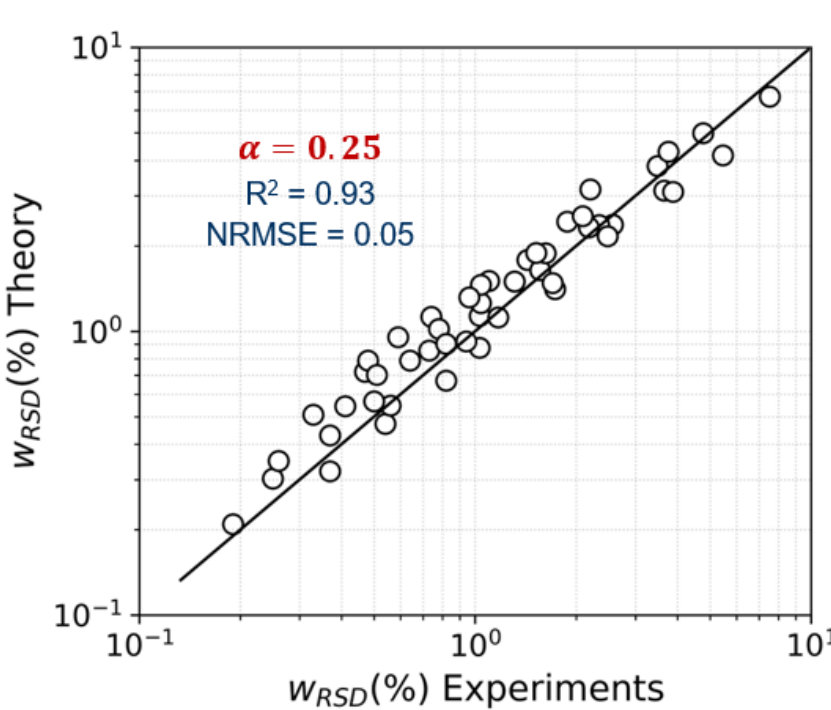
Scaling Verification



Experimental scaling matches first-principles predictions

5 Model Verification

$$w_{RSD}(\%) = \alpha \times 100 \times \sqrt{\frac{2}{3} \times \frac{d_{50}^3}{D^2 h_d} \times \frac{\rho_t}{\rho_b} \times \exp[4.5(\ln(\sigma_g))^2]}$$



- Single fitter parameter** (α)
- Robust** (bootstrap resamples)
- Accurate Prediction** (cross-validation)

6 Relevance for Pediatric Mini-Tablets

- Developed a model which quantitatively predicts that smaller particles (d_{50}) reduce tablet weight variability
- The model provides a starting point for PSD and tablet punch size selection during mini-tablet development

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Scan to view our manuscript (J. Pharm. Sci.)

This work provides a mechanistic framework to advance pediatric mini-tablet development