3D printing of Personalized Dosage Forms: A Clinical Framework for Quality Control Using Pure API and Reformulated Crushed Tablets

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1. CLINICAL CHALLENGES

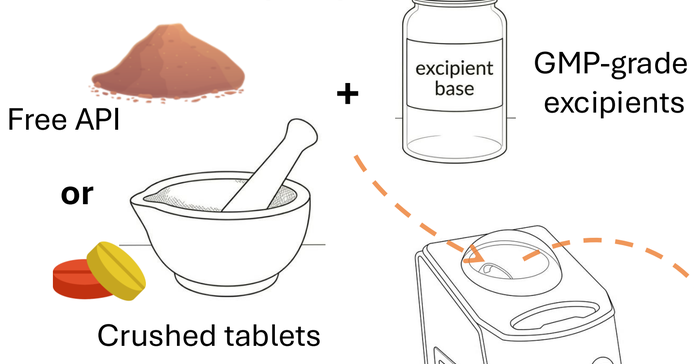
- **Inter-Patient Variability:** differences in pharmacokinetics, pharmacodynamics and swallowability restrictions.
- **Pediatric Treatment :** frequent dose adjustments based on patient tolerance, clinical response, and growth.
- **Manual Compounding:** tablet splitting, crushing, or dilution, introducing risks of dosing errors, cross-contamination, and variable quality.
- **Lack of Bulk APIs:** difficult access to API powders, requiring crushed commercial tablets (CRT) as drug source for dose reformulation.

2. AIM of the STUDY

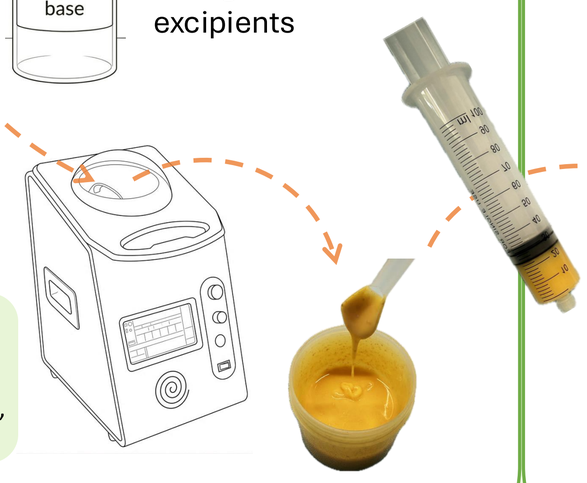
Validate a standardized, GMP-aligned framework for chewable dosage forms 3D printed directly into blister packaging using reformulated crushed tablets and systematic evaluation of the critical quality attributes

3. METHODS

OLANZAPINE (OLZ)

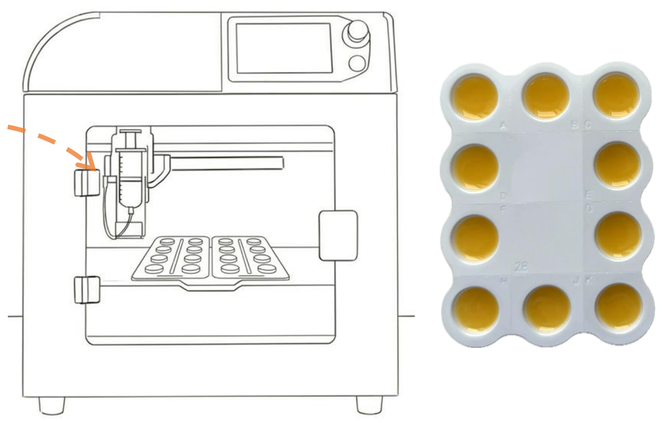


- Antiemetic drug in pediatric chemotherapy protocols,
- accurate low-dose titration (1.5-9.0 mg) to prevent sedation,
- poorly soluble BCS Class II drug



A. CONTROLLED PREPARATION OF THE PHARMA INK

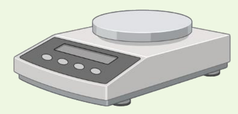
- on-demand and customizable dosing, high reproducibility, and reduced operator dependency.
- brings digital traceability, software-driven control, and in-line quality verification



B. VALIDATION OF THE 3D PRINTING PROCESS

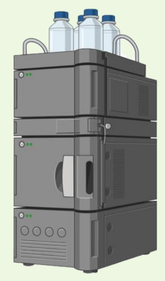
C. CRITICAL QUALITY ATTRIBUTES ASSESSMENT

- Mass uniformity



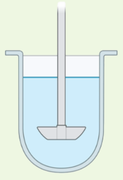
Ph. Eur. 12th ed. 2.9.5

- Content uniformity



Ph. Eur. 12th ed. 2.9.6 and 2.9.40

- Dissolution tests



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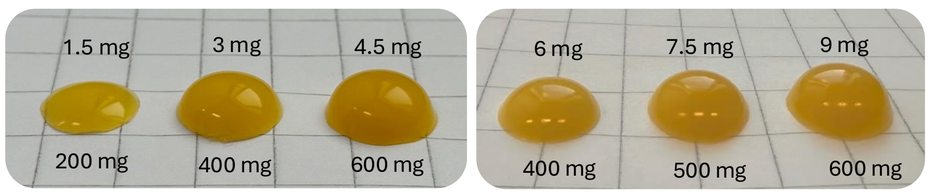
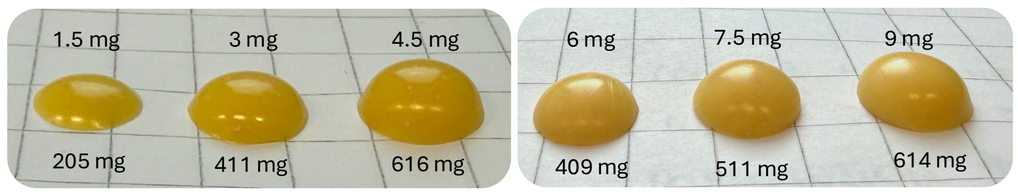
- Stability studies

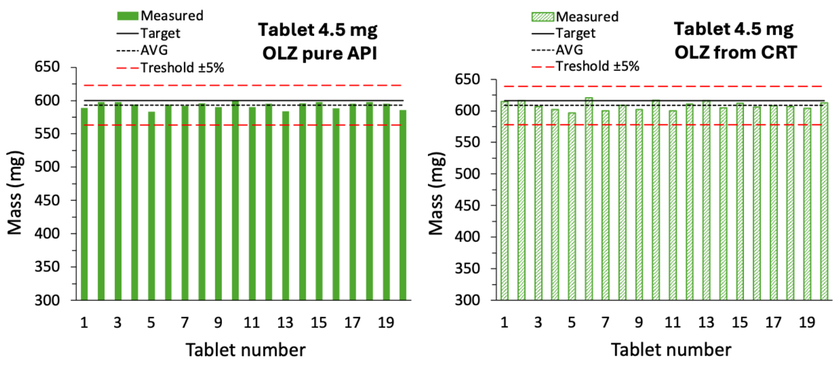
4. RESULTS





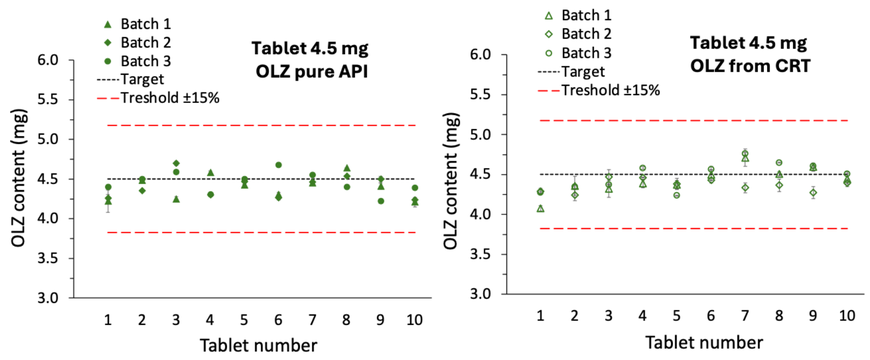
Dosages (1.5-9 mg) containing OLZ as PURE API (from formulations 0.75% and 1.5% w/w) on the left and dosages containing OLZ as CRT (from formulations 0.73% and 1.46% w/w) on the right

Mass Uniformity



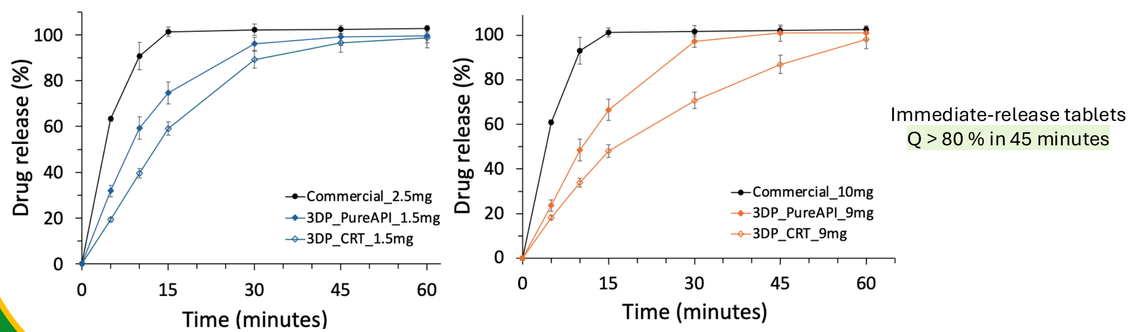
OLZ source		Target (mg)	Batch 1
Pure API	0.75 %	200	196.4±7.1
		600	589.9±8.0
	1.5 %	400	396.5±6.9
		600	595.9±6.3
CRT	0.73 %	205	204.1±8.5
		616	605.9±7.2
	1.46 %	409	413.5±8.2
		614	613.7±10.2

Content Uniformity



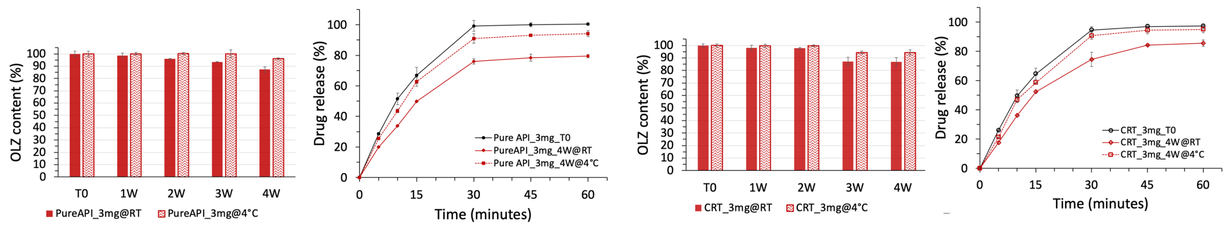
OLZ source		Dosage (mg)	Batch 1 Content (%)	Batch 1 AV
Pure API	0.75 %	1.5	100.5±0.9	2.4
		4.5	100.5±2.7	6.5
	1.5 %	6	97.9±2.7	7.2
		9	101.0±1.7	4.2
CRT	0.73 %	1.5	97.6±3.2	8.7
		4.5	99.5±2.8	6.7
	1.46 %	6	100.1±1.5	3.8
		9	99.0±1.9	4.6

Dissolution Studies



Immediate-release tablets
Q > 80 % in 45 minutes

Stability Studies



OLZ as pure API

OLZ as CRT

Pictures of representative tablets after 4 weeks of storage undergoing brown discoloration: on the left, the tablet stored at RT, and on the right, the tablet stored at 4°C

5. CONCLUSIONS

Successfully validated both pure API and CRT as starting materials, solving the issue of bulk API unavailability in hospitals
Gelatin-based matrix ensured high dosing accuracy across the full therapeutic range despite low drug concentration and poor solubility
All batches met Ph. Eur. Standards and immediate-release dissolution profiles
A GMP-aligned digital workflow that reduces manual workload, minimizes human error, and enables safe, on-demand compounding was established

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