



Leiden University
Medical Center

3D printing tablets for individual pediatric patients

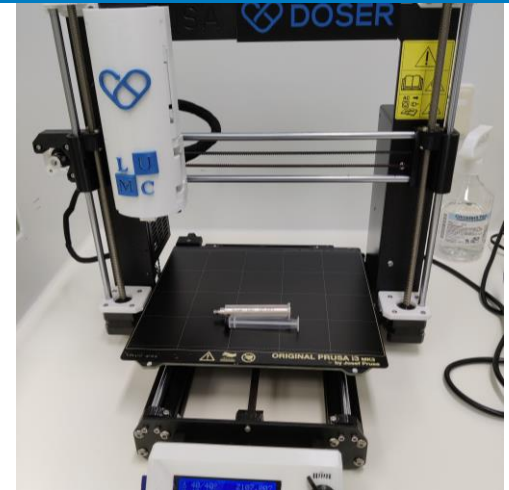
Development of furosemide and sildenafil tablets

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Pharmacist - PhD candidate

3D PHARMA PRINTING CONFERENCE

30TH MARCH 2022



Pediatric medicine – the unmet medical need



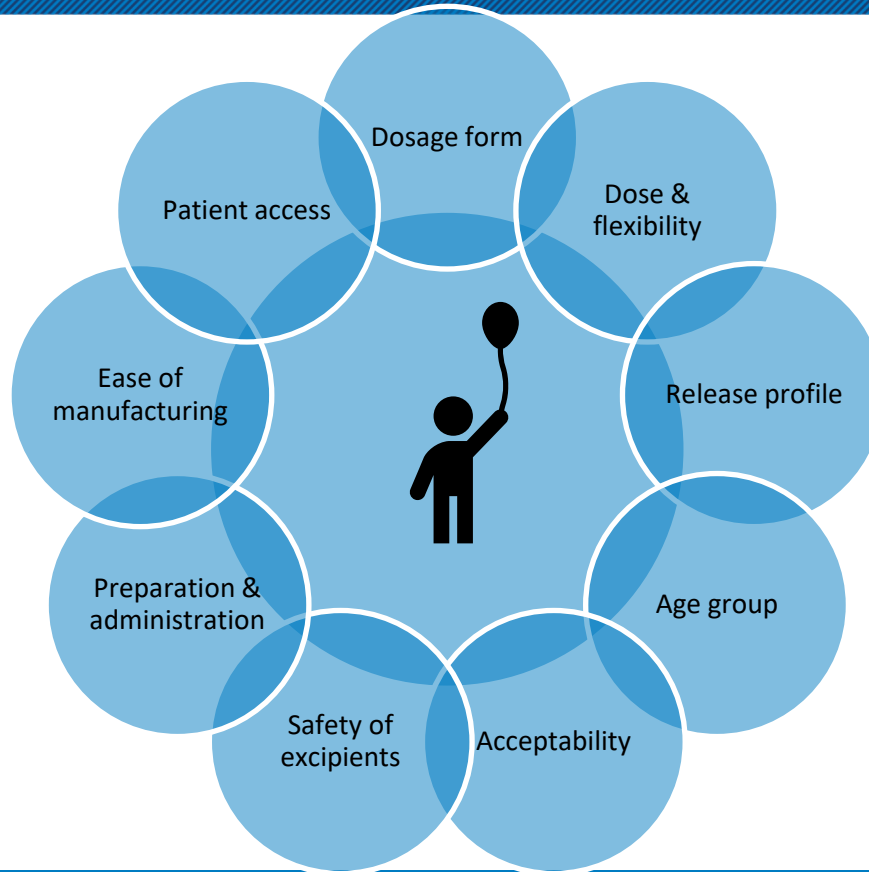
- Treated as small adults
- Commercial tablets are often:
 - Too big
 - Wrong dose
 - Manipulation leads to dosing errors
- Oral liquids
 - Poor palatability → poor acceptability
 - Unsuitable excipients
- Children prefer small tablets!

Van Riet-Nales et al. Acceptability of different oral formulations in infants and preschool children. Arch Dis Child 2013 Sep;98(9):725-731

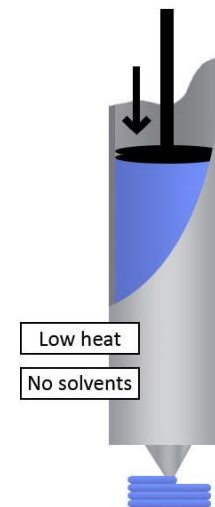
Examples of unmet medical need

Furosemide	Sildenafil
1 – 4 mg/kg in 2 – 4 doses	1,5 – 6 mg/kg in 3 doses
Tablets 20 – 500 mg	Tablets 20 – 100 mg
Injection fluid not suitable for oral intake (pH ~9)	Suspension 10 mg/mL
Dutch formulary oral liquid 2 mg/mL <ul style="list-style-type: none">• Contains propylene glycol	LUMC oral liquid 1 mg/mL <ul style="list-style-type: none">• Poor acceptability

Pediatric-centered formulation design

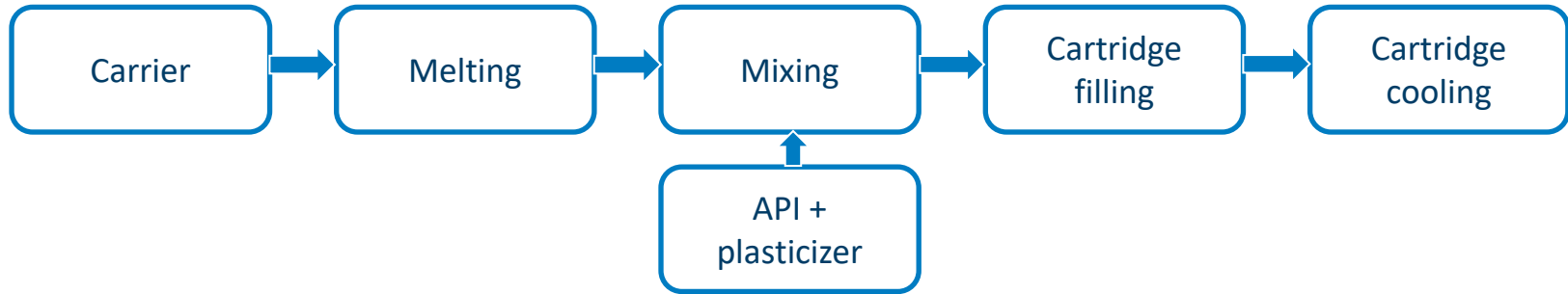


Semi-solid extrusion @ LUMC



Production process

Cartridge preparation



Printing process



Composition

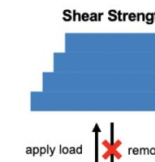
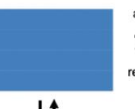
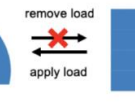
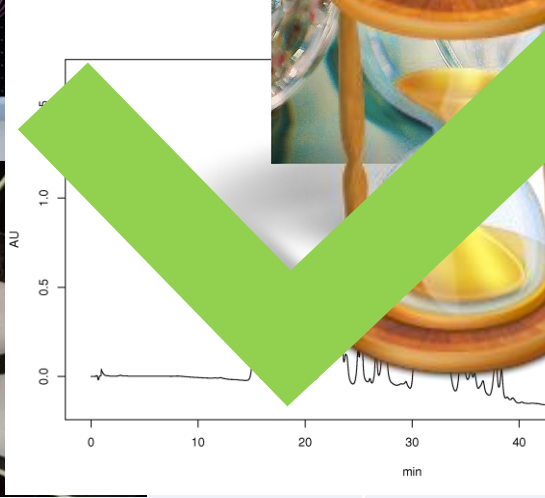
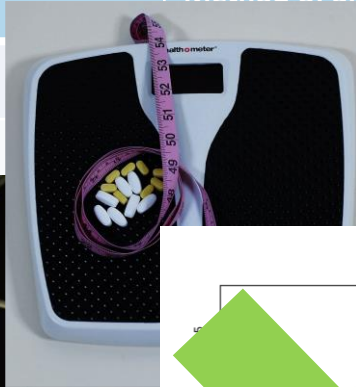
API	Furosemide		Sildenafil	
Dose	2 mg	10 mg	4 mg	10 mg
Carrier	Macrogol monostearate			
Plasticizer	Polysorbate 80			Glycerol 100%

Quality control

Specification	Method of analysis	Acceptance criteria
Appearance	Visual observation	Off-white, wax-like tablet, layered structure, diameter 7 mm
Tablet weight	Weighing	RSD $\leq 4.0\%$ Mean weight vs. expected weight $\leq 3.0\%$
Identification API (including impurities)	HPLC-UV	Chromatogram of standard solution and sample has to be equal
Content uniformity	HPLC-UV	EP requirement: Acceptance value ≤ 15
Dissolution rate	Basket method coupled with UV-spectrophotometer	EP requirement: $\geq 80\%$ of labelled content dissolved at 45 min
Mechanical strength	Visual observation	No signs of mechanical stress or splitting of layers
Microbiological quality	EP 2.6.12 and 2.6.13	TAMC $< 10^3$ CFU per tablet TYMC $< 10^2$ CFU per tablet Absence of E. coli

Quality control

Specification	Method of analysis	Acceptance criteria
Appearance	Visual inspection	Visual inspection
Tablet weight	Weight measurement	Weight measurement
Disintegration	Disintegration test	Disintegration test
Mechanical strength	Shear strength test	Shear strength test
Microbial growth	Microbial growth test	Microbial growth test



3D-printed tablets are ready for use in clinical practice

With great thanks to...



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