

Extemporaneous preparation of fixed-dose combination orodispersible films by hot melt ram extrusion 3D printing

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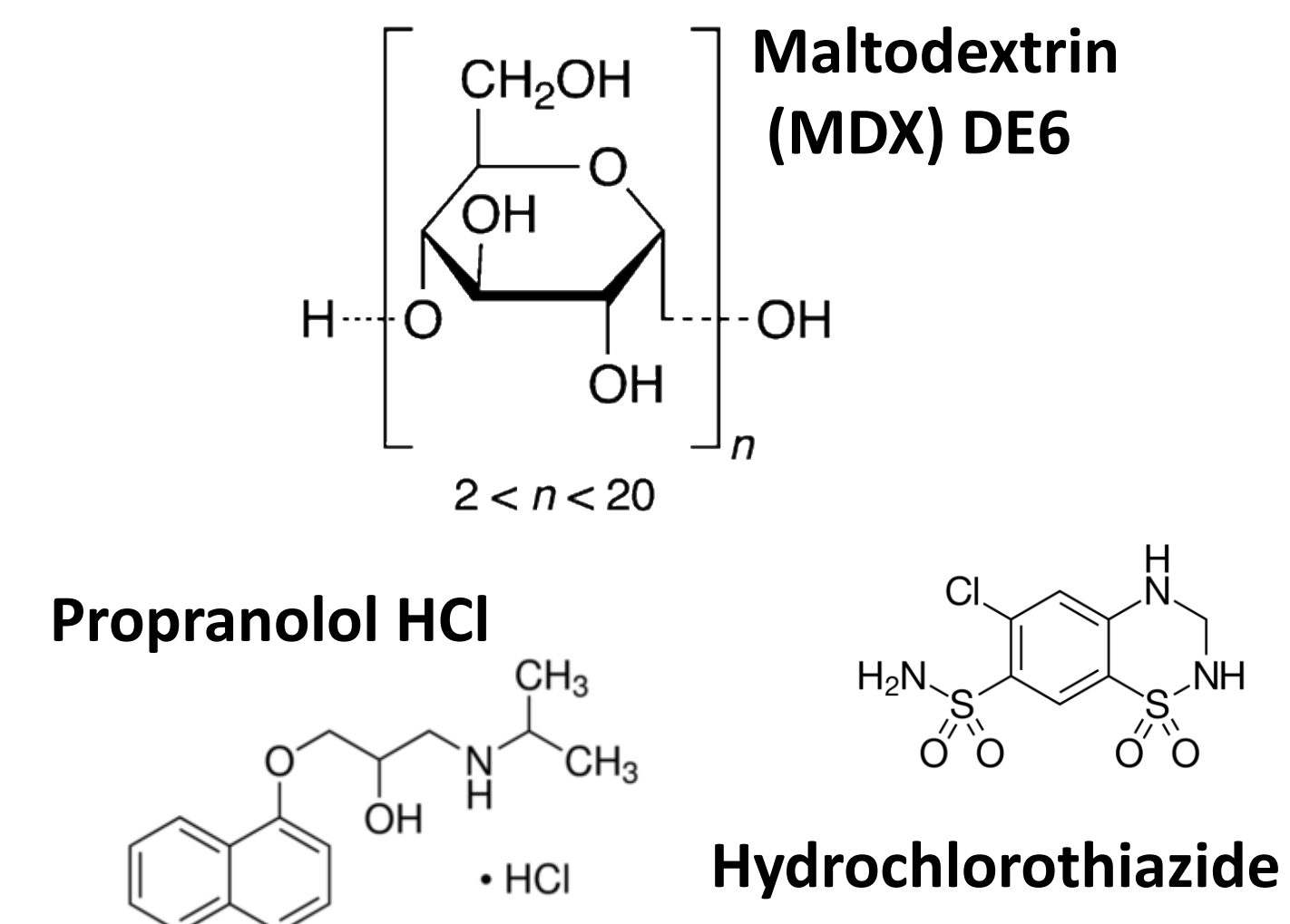
Background

- Orodispersible films (ODF) are a valuable option for the administration of drugs to patients affected by dysphagia, children and elders [1].
- To extemporaneously compound ODF in personalized dosing, few methods have been developed. Among these, hot melt ram extrusion printing has proven suitable for obtaining ODF with high drug loading [2].

Aim

- To prepare propranolol HCl (PRH) single dose ODF for personalized treatment by hot melt ram extrusion printing
- To evaluate the feasibility of the extemporaneous compounding of ODF loaded with a fixed-dose combination of PRH and hydrochlorothiazide (HCTZ).

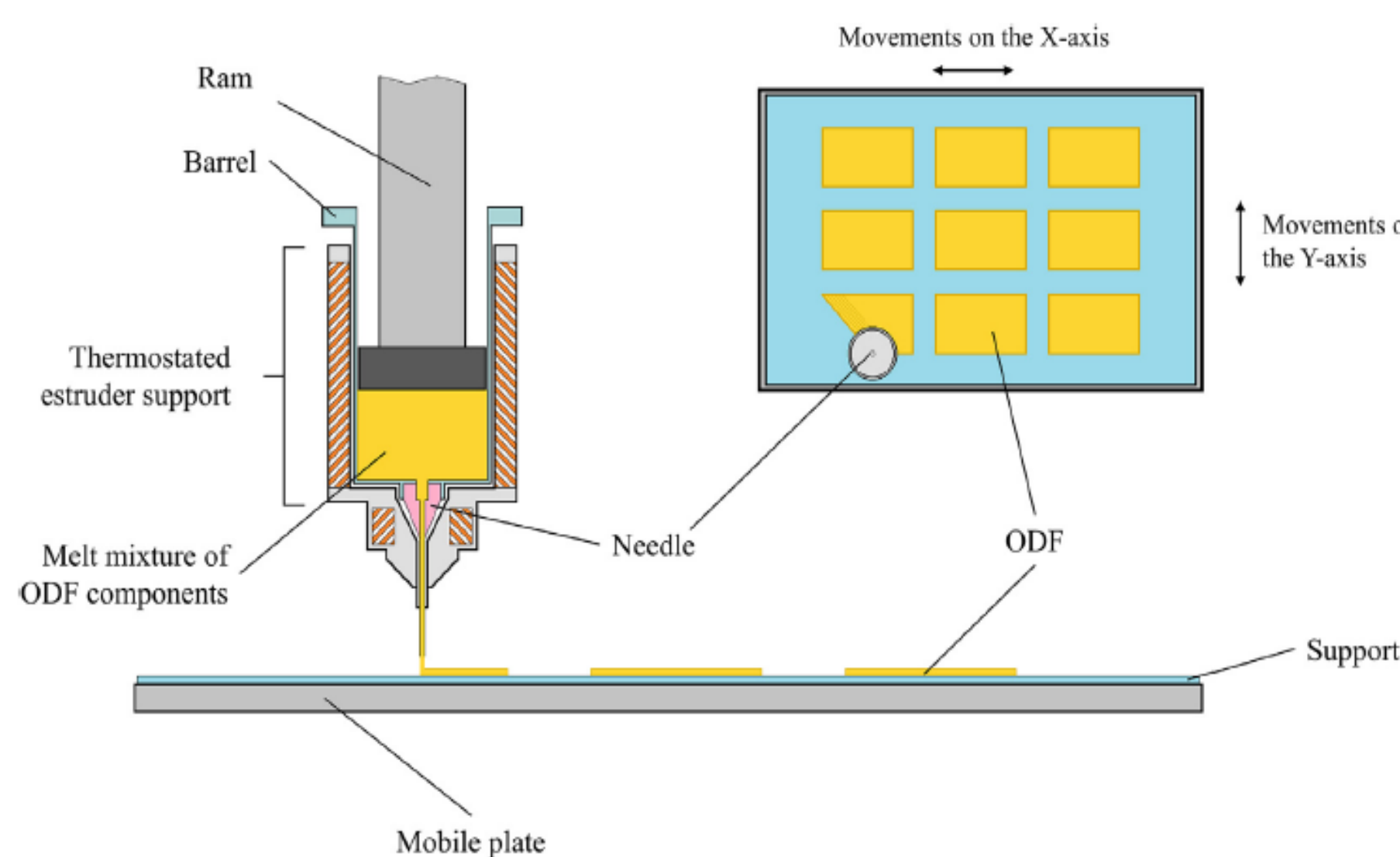
Materials



Preparation of ODF by hot-melt ram extrusion

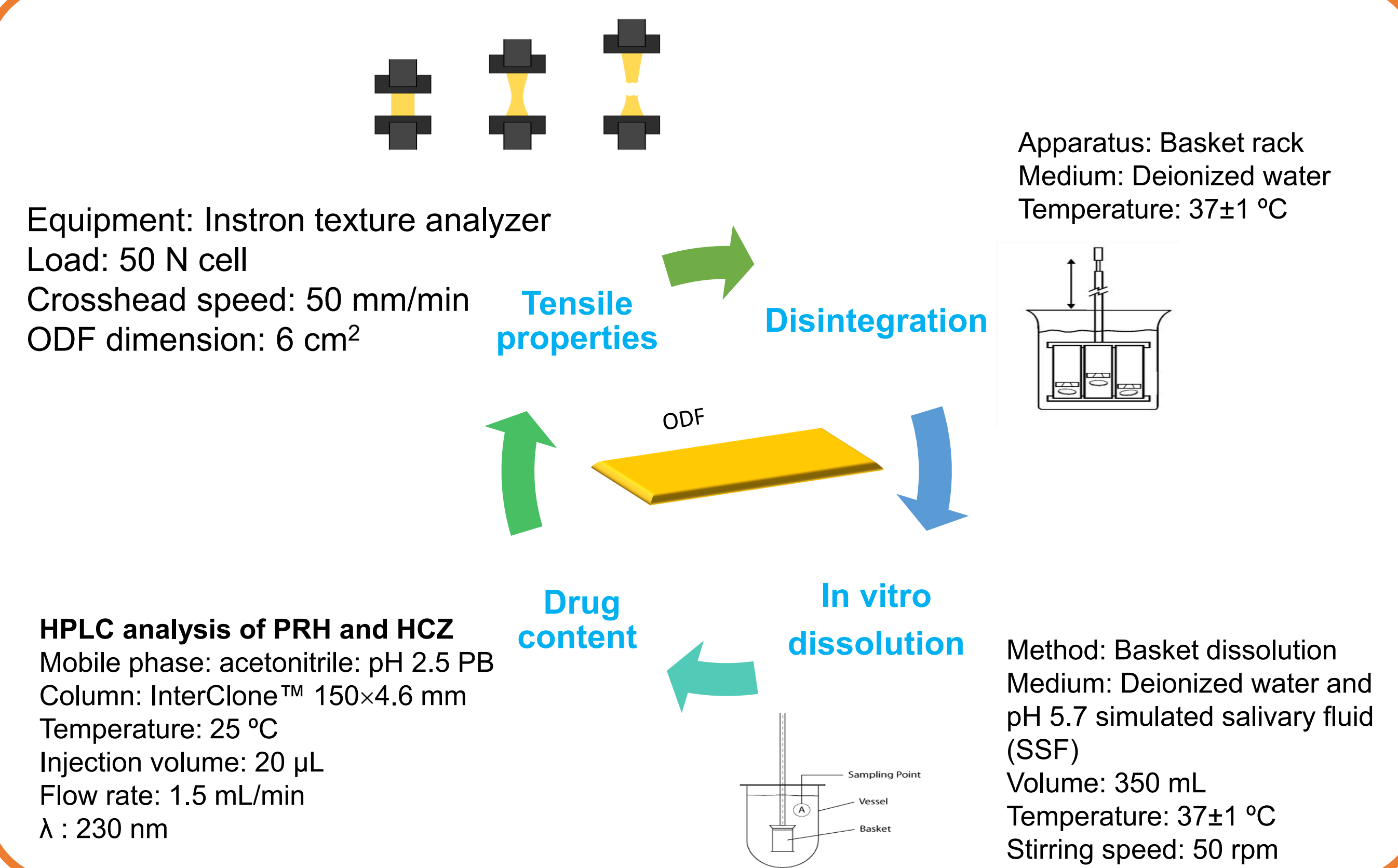


- Mixture preparation:** MDX plasticized with glycerol and drug(s) were mixed in a mortar.
- Melting of the mixture:** The mixture was loaded into a barrel and melted at 95 °C.



- Printing of ODF**
 - Printing speed: 20 mm/s
 - Infill angle: 120 °
 - Plate speed: 10 mm/s
- Packaging** The printed ODF were immediately packaged in aluminum foil and stored at 25 °C

ODF characterization

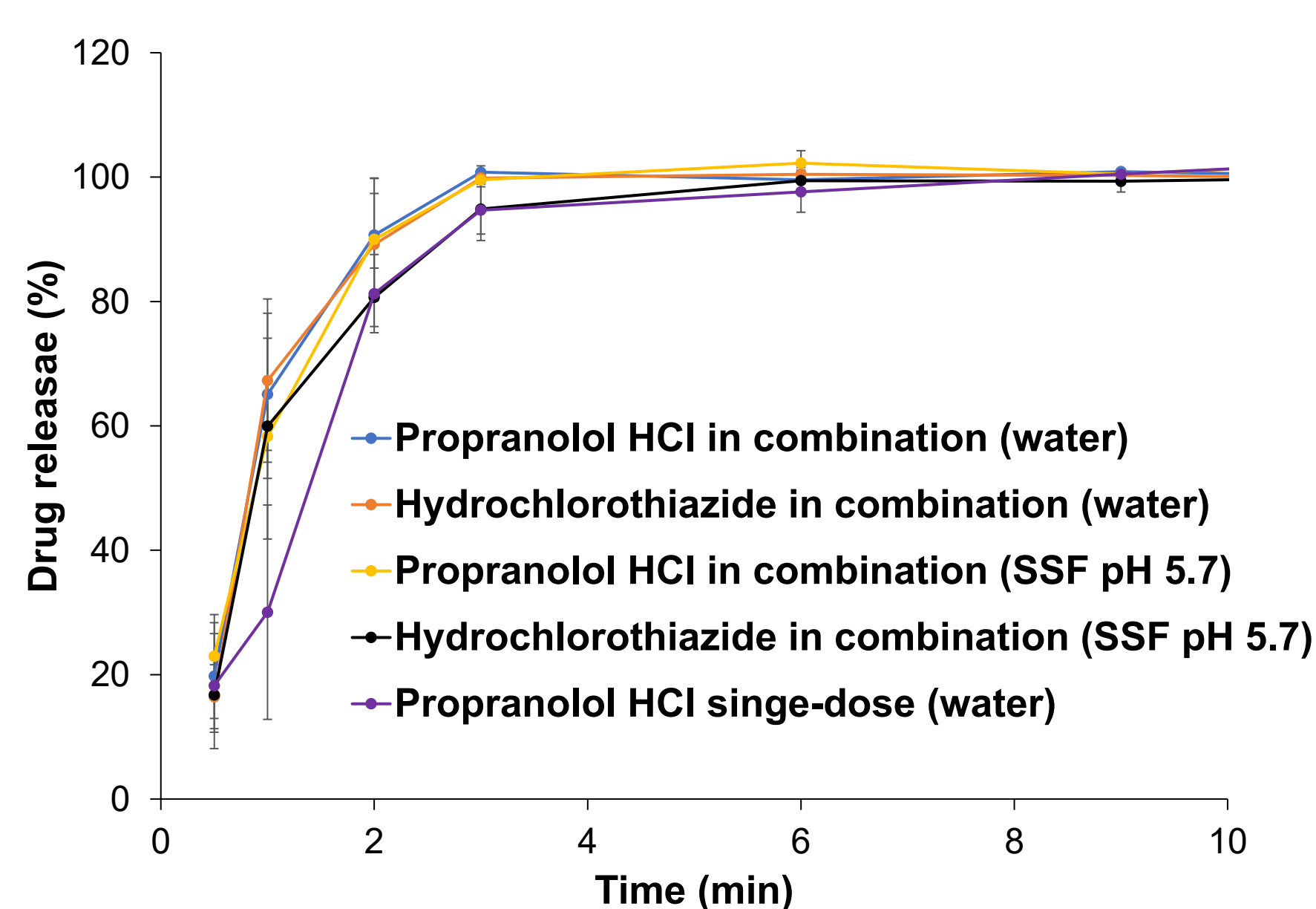


Results and Discussion

ODF characteristics	Placebo	Propranolol single dose ODF					Fixed dose combination ODF	
		F1	F2	F3	F4	F5	PR	HCTZ
ODF area (cm ²)	1	1	1.5	2	6	6	6	
Theoretical drug content (mg)	-	5	10.48	13.20	25.00	40.00	40	25
Drug content (mg)	-	4.95±0.27	10.78±0.46	13.78±1.00	25.43±0.51	40.62±2.79	40.74±0.58	25.17±0.30
ODF weight (mg)	51.6±3.1	50.0±3.8	105.0±3.4	132.0±2.7	250.0±2.4	252.3±1.4	253.6±0.5	
Thickness (µm)	318±14	403±9	398±7	403±16	318±12	329±30	363±4	

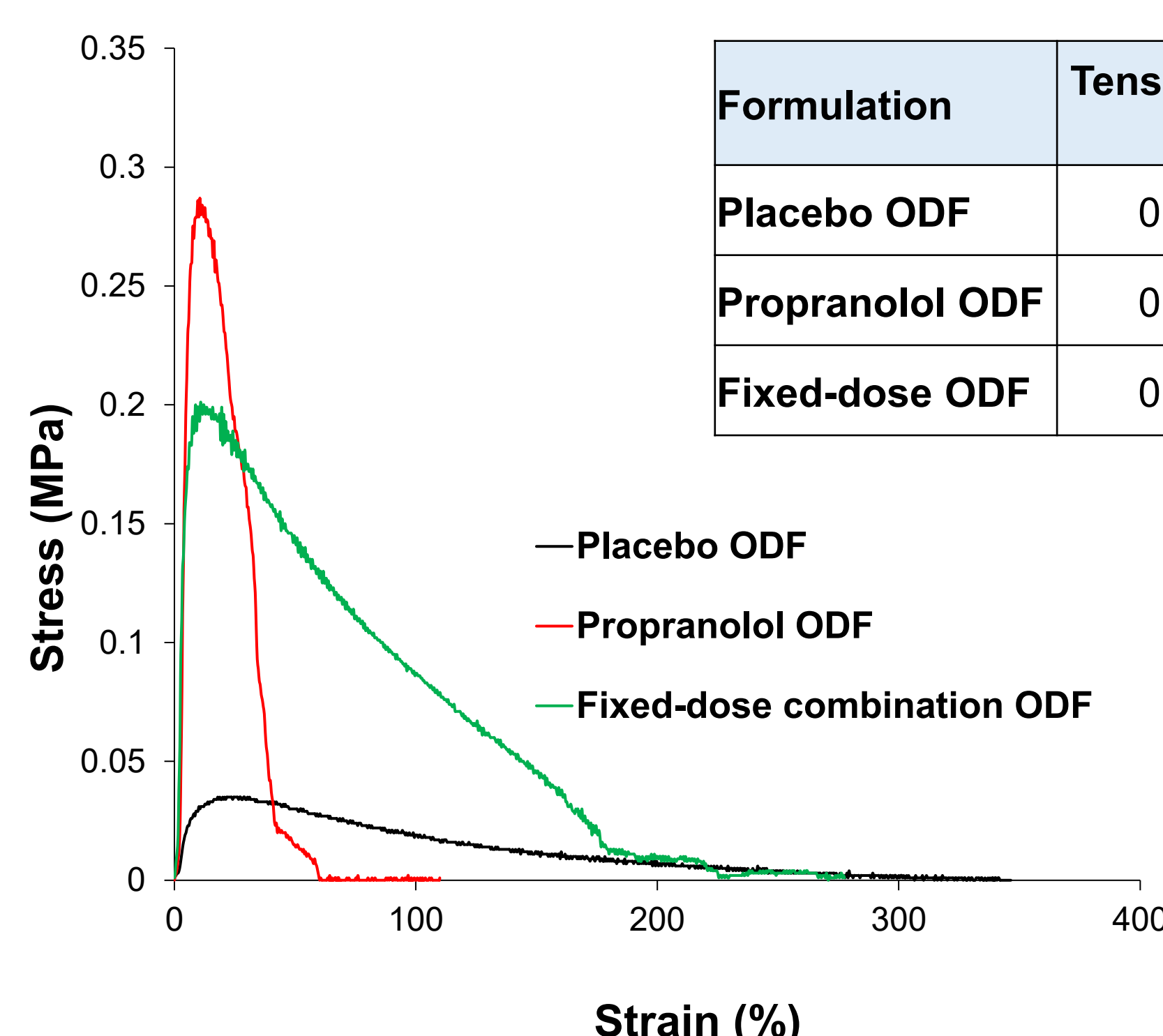
- The average printing time per single ODF ranges between 47 to 150 s depending on the ODF area.
- ODF appeared whitish, homogenous, non-sticky, and easy to handle without fracture.
- In all ODF, no impurities or degradation products were evidenced by HPLC analysis.
- ODF disintegrated within 3 min, in compliance with Ph. Eur. specifications.

In vitro dissolution of 6 cm² ODF



✓ For ODF with area of 1, 1.5 and 2 cm², one point sampling were made with 100% drug release within 3 min.

Tensile properties



Formulation	Tensile Strength (MPa)	Young modulus (MPa)	Elongation (%)	Tensile Energy (MJ/m ³)
Placebo ODF	0.03±0.01	0.23±0.15	323.04±27.34	0.03±0.01
Propranolol ODF	0.32±0.15	7.93±4.87	153.89±91.13	0.16±0.07
Fixed-dose ODF	0.15±0.04	2.52±0.95	172.57±68.65	0.10±0.05

Addition of the two drugs (fixed-dose) enhanced the films' tensile strengths and tenacity with respect to placebo ODF

Conclusions

- ✓ This study demonstrated the feasibility of using hot melt ram extrusion printing for the extemporaneous preparation of ODF of different sizes for personalized dosing.
- ✓ Furthermore, this technology can also be exploited to prepare extemporaneous fixed-dose combination ODF which would allow to reduce polypharmacy and medication errors.

References

- Cilurzo et al., Drug Discov. 2018;23:251–9.
- Musazzi et al., Int. J. Pharm. 2018;551:52–9.