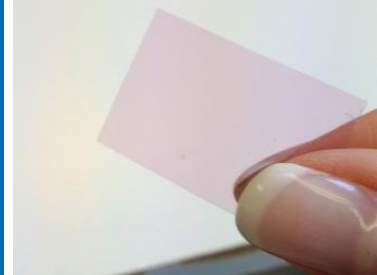


Printing technologies for individualized medicines

Prof. Dr. Jörg Breitzkreutz
Institute of Pharmaceutics and Biopharmaceutics
Heinrich Heine University Düsseldorf, Germany
joerg.breitzkreutz@hhu.de



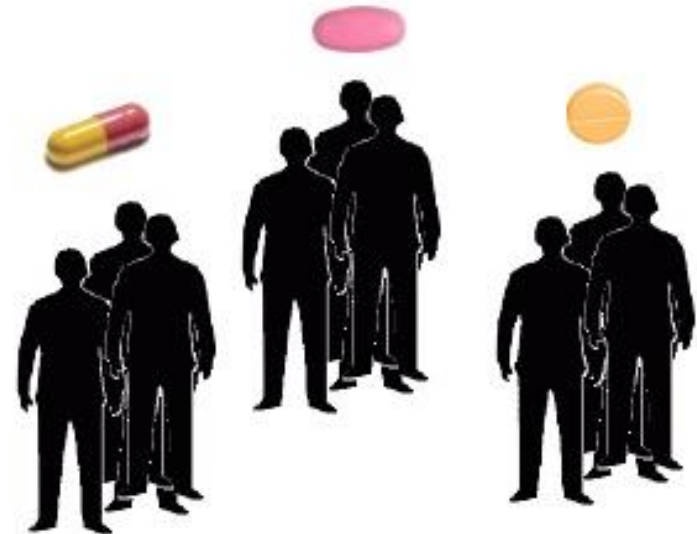
Losan Pharma, 4th Scientific DDC, Binzen, 15.02.2022

Current Practice



Trial and error

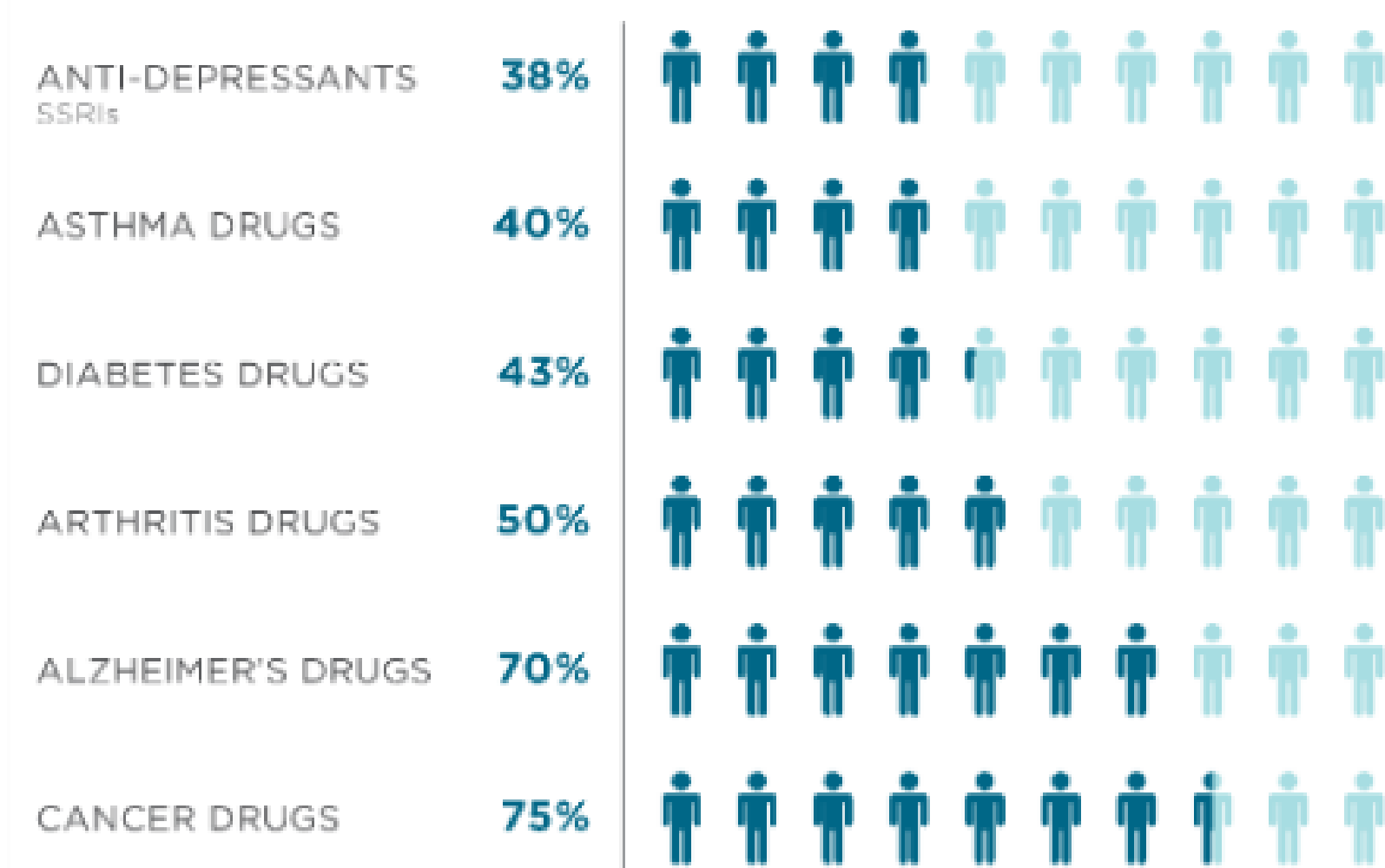
Personalized Medicine



**The right treatment
for the right person
at the right time**

*A. Miller, Personalized Medicine Coalition
www.personalizedmedicinecoalition.org*

Lack of Treatment



*B.B. Spear, M. Heath-Chiozzi, J. Huff,
Clinical Trends in Molecular Medicine 7: 201-204 (2001)*



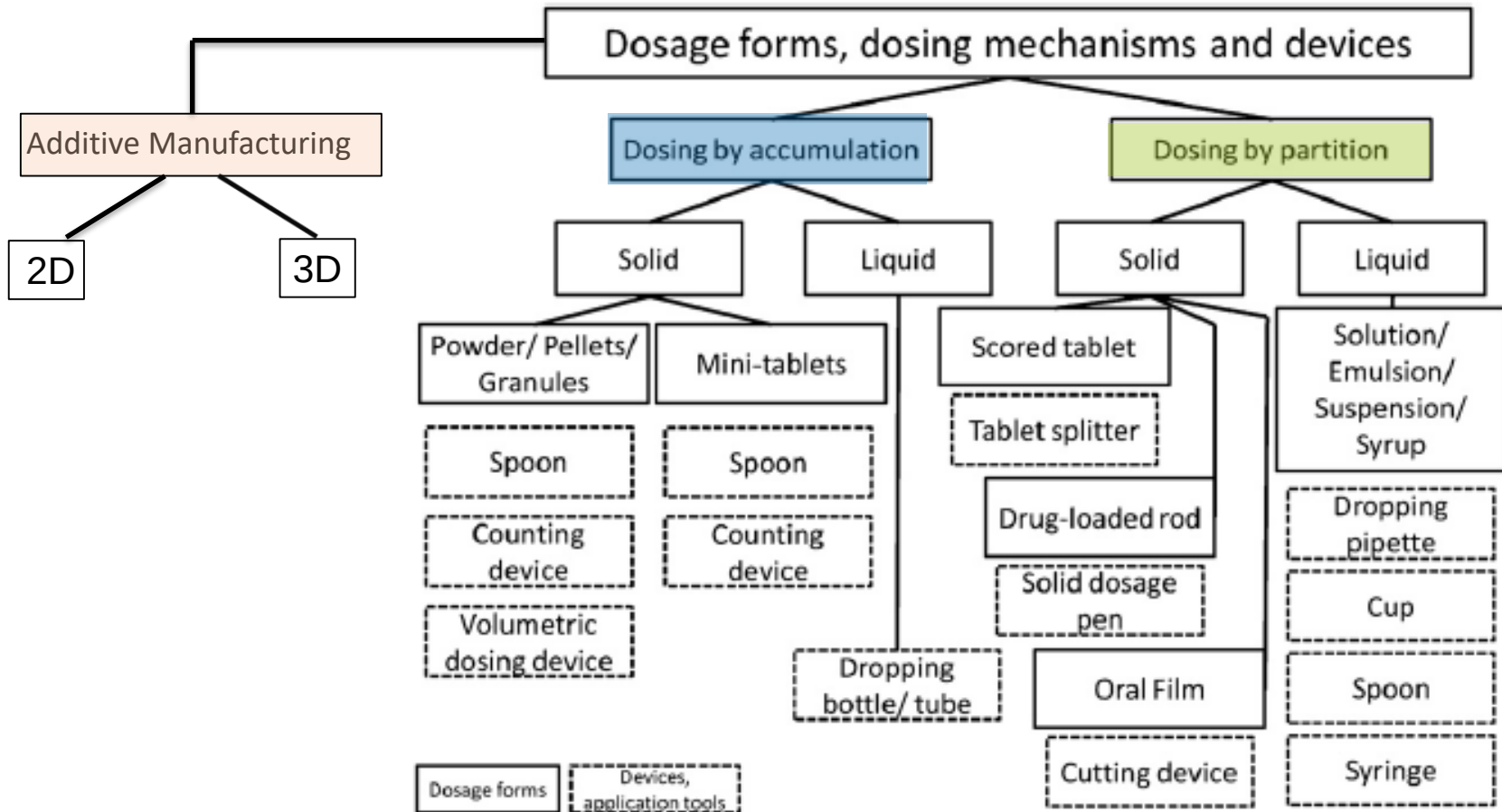
Roche



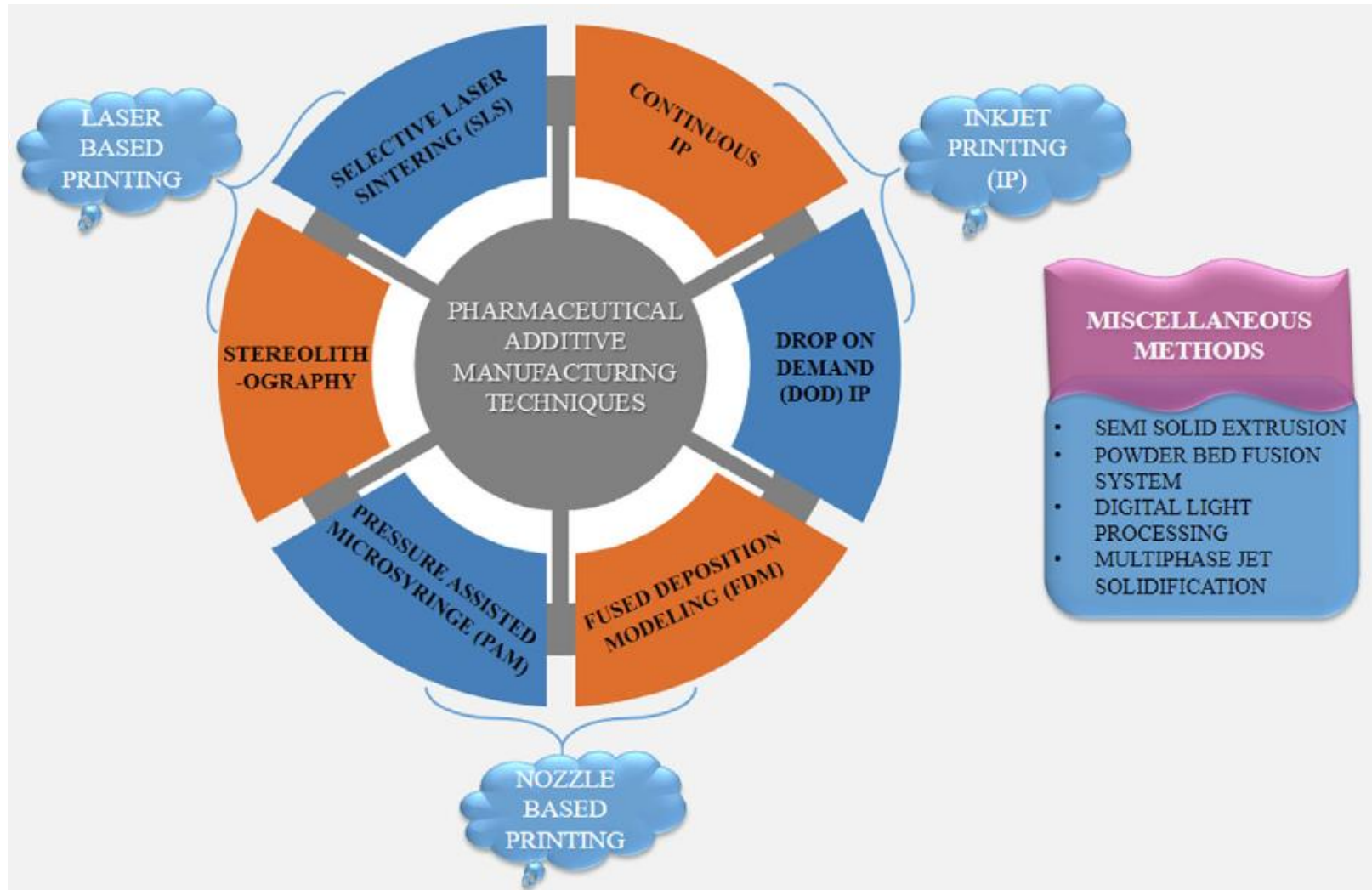
div.



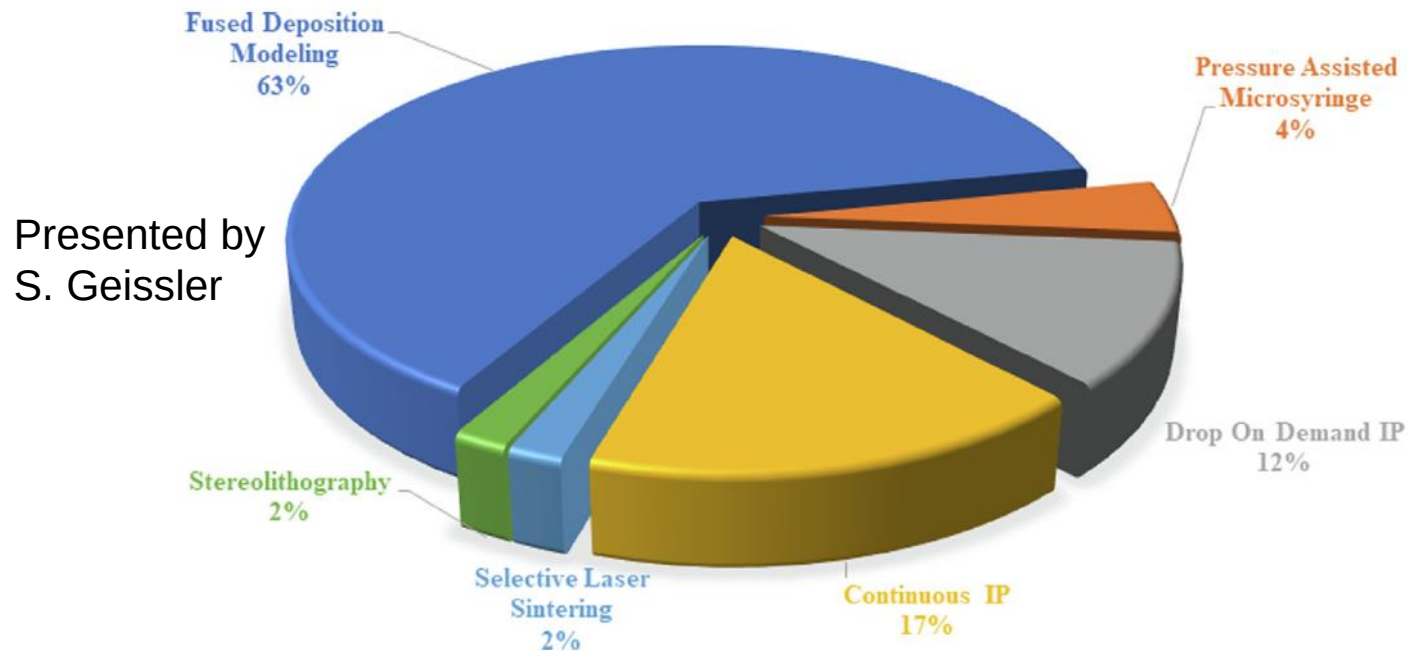
Dose adjustment by...



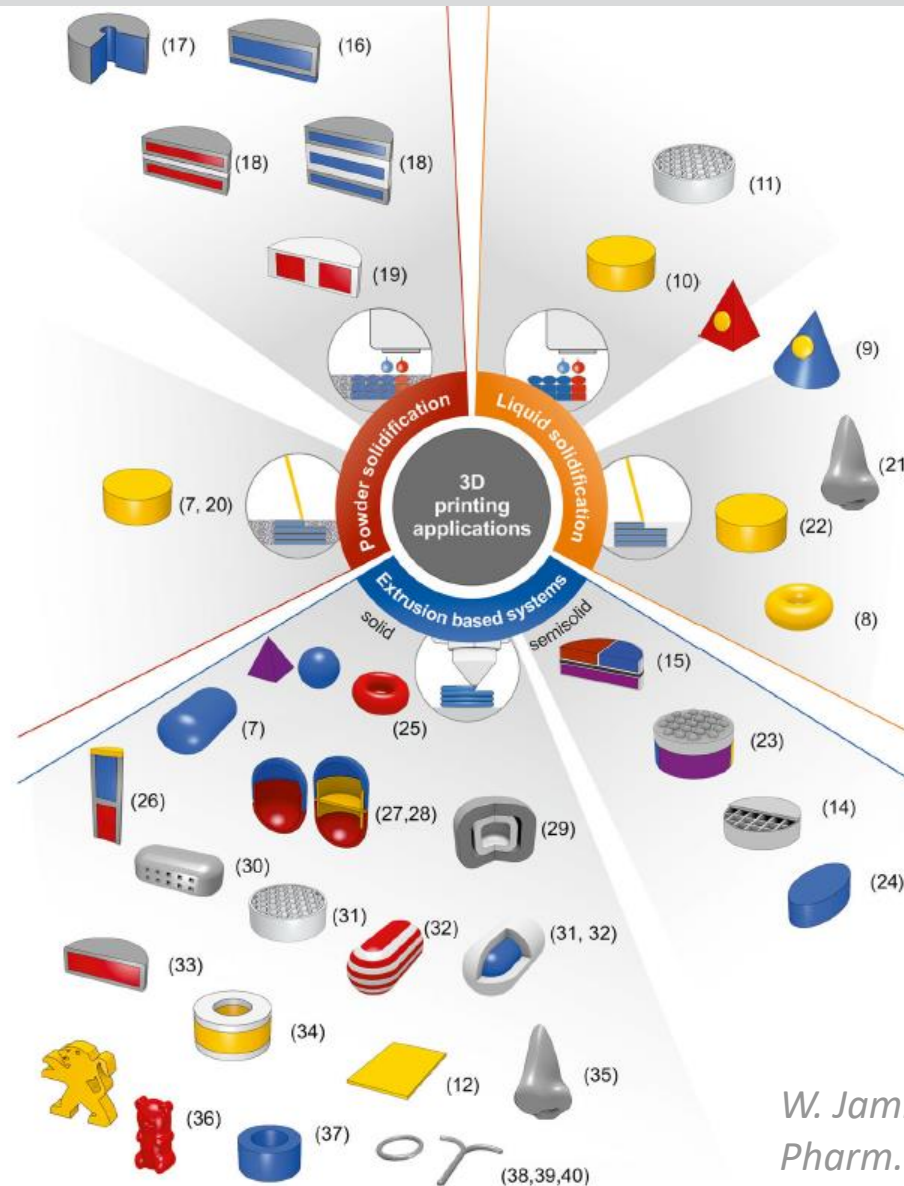
Modif. from K. Wening, J. Breitkreutz, Int. J. Pharm. 404: 1-9 (2011)



S. Bandari et al. , Adv. Drug Deliv. Rev. 172: 52-63 (2021)



S. Bandari et al. , Adv. Drug Deliv. Rev. 172: 52-63 (2021)



W. Jamróz et al. ,
Pharm. Res. 35: 178 (2018)

Drug Printed Objects

1 substrate



*A. Melocchi al. ,
J. Pharm. Sci.
109: 2943-57
(2020)*

≥2 substrates



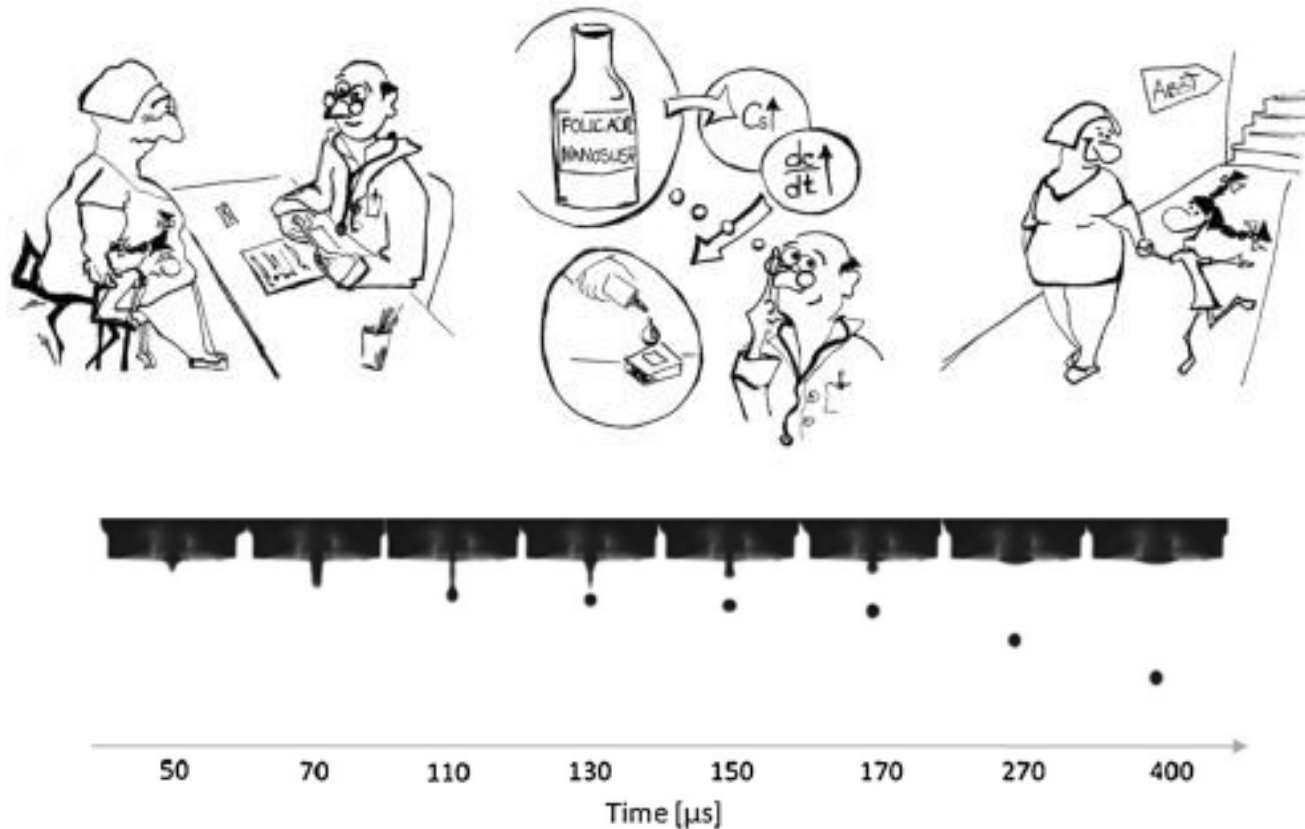
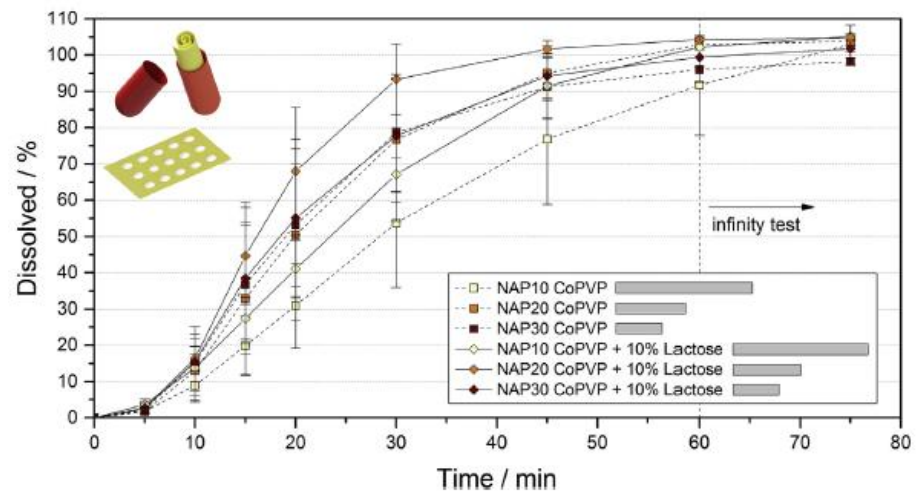
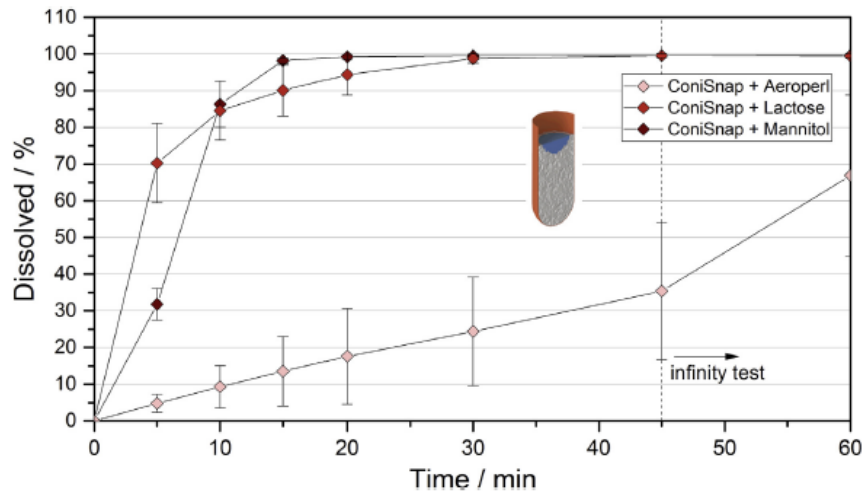
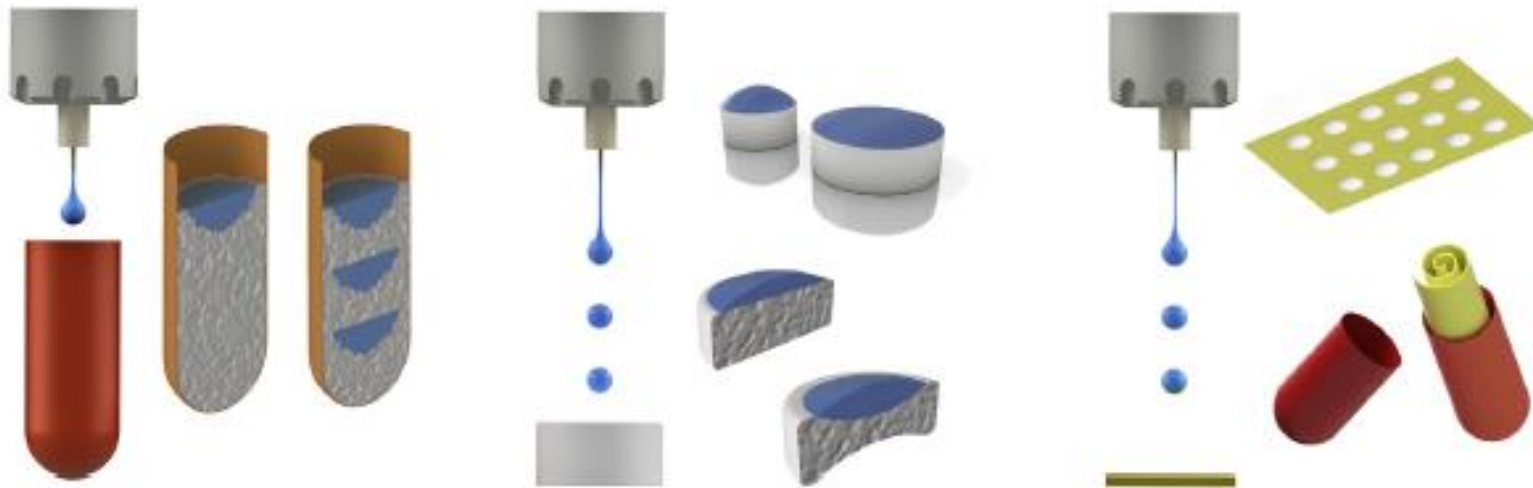


Fig. 7. Visualization of the drop formation. The pulse width is 25 μs , the pulse amplitude 100 V and the frequency 200 Hz. The final droplet size is 68.4 μm .

*J. Pardeike, D.M. Strohmeier, N. Schrödl, C. Voura, M. Gruber, J.G. Khinast, A. Zimmer
Int. J. Pharm. 420, 93-100 (2011)*



B. Bonhoeffer, A. Kwade, M. Juhnke, J. Pharm. Sci. 106:1102-1110 (2017)

1. Drug printing into pre-filled capsules

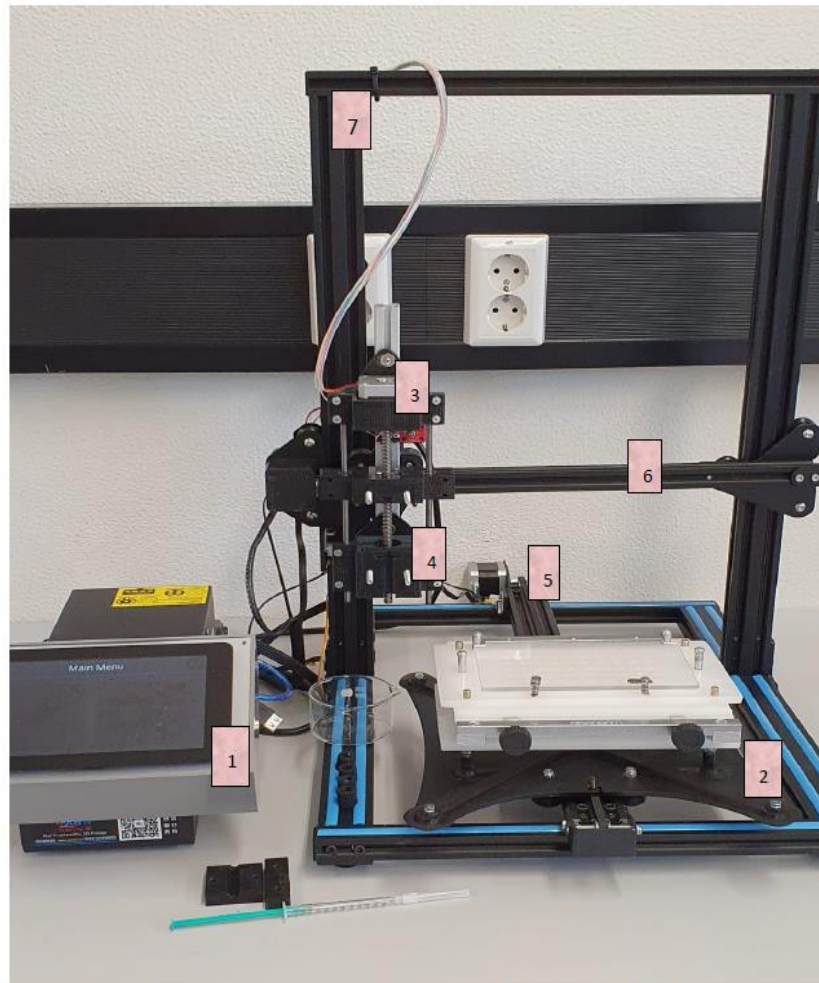


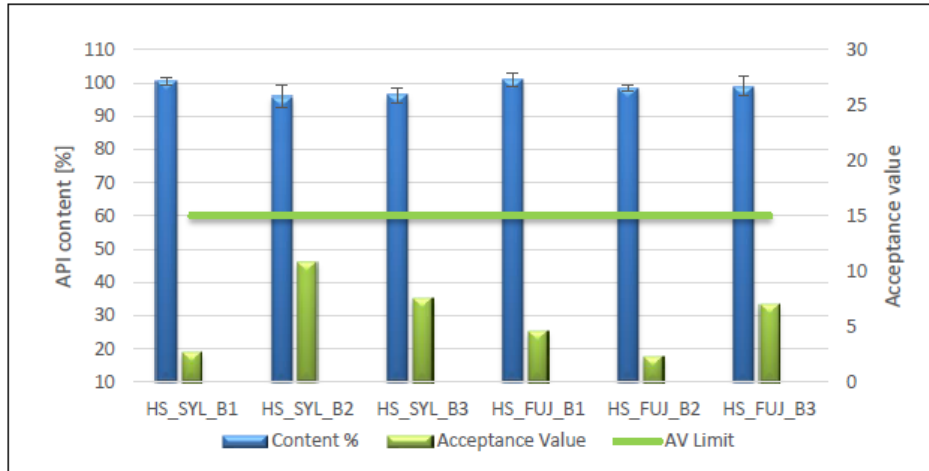
Figure 1: Electronic liquid dosing system consists of 1) Control unit, 2) Capsule board holder, 3) Liquid dosing unit, 4) Syringe holder, 5) Capsule board travel rail, 6) Dosing unit travel rail for x-axis 7). Dosing unit travel rail for the z-axis.

Electronic Liquid Dispensing System (ELDS)

Saar & Waldeck (2020), cooperation with ZL, Eschborn

1. Drug printing into pre-filled capsules

5 mg Metoprolol tartrate



*Naming: Dosing device_Excipient_batch number; HS= Hamilton syringe, SYL= Syloid®244 FP, FUJ= Fujicalin®, B= Batch
Figure 22: Content and Acceptance value (AV) for capsules with 5 mg Metoprolol tartrate made with different excipients, dosing system used: Hamilton syringe, $\bar{X} \pm sd$, n=10

B. Sarker, MSc thesis HHU Düsseldorf (2021)

1 mg Enalapril maleate

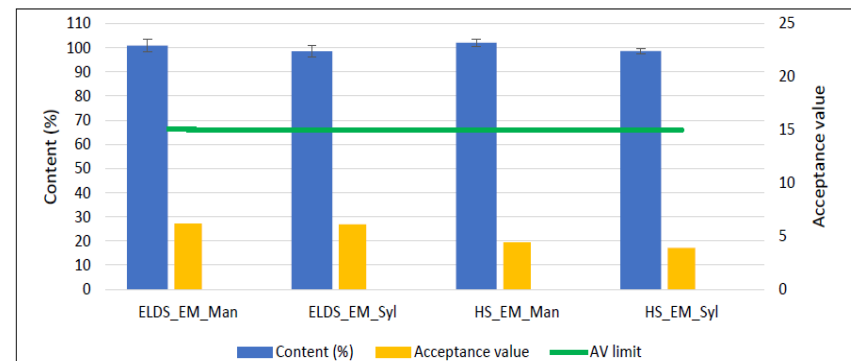
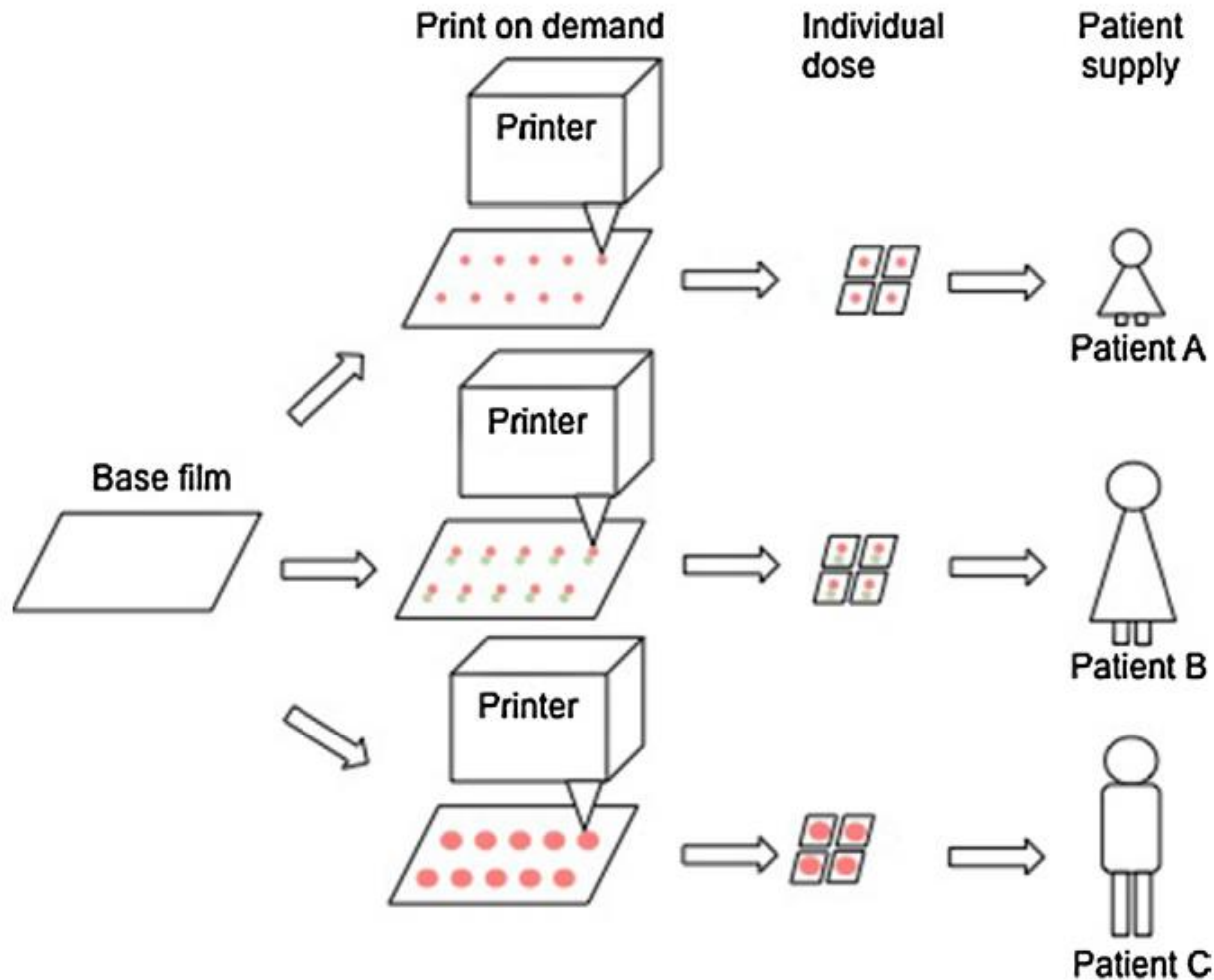


Figure 28: Comparison of mean content recovery (%), acceptance value and SD for Enalapril maleate capsules containing Mannitol and Syloid® XDP 3150 dosed with different liquid dosing device ($\bar{X} \pm sd$, n= 10)

Naming of labelling in Figure 28: Dosing device_API_excipient where ELDS=Electronic liquid dosing system, HS=Hamilton syringe, EM= Enalapril maleate, Man= Mannitol and Syl= Syloid® XDP 3150

R. Tasnim, MSc thesis HHU Düsseldorf (2021)

2. Printing onto ODFs



M. Preis, J. Breitkreutz, N. Sandler, Int. J. Pharm. 494: 578-584 (2015)

2. Printing onto ODFs

Printing concepts:

Complete surface



Central



Point by point



Lines



symmetric

Fixed dose combinations



asymmetric

Anti-counterfeiting and identification



Serialization



Barcode

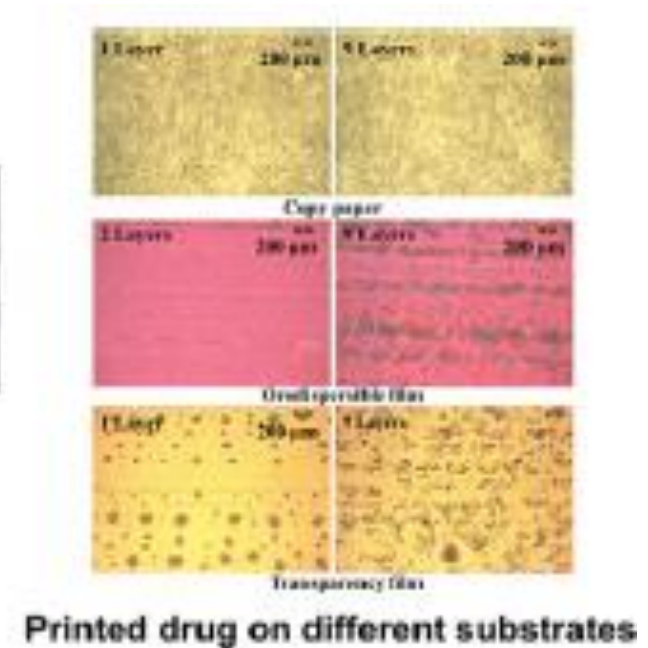
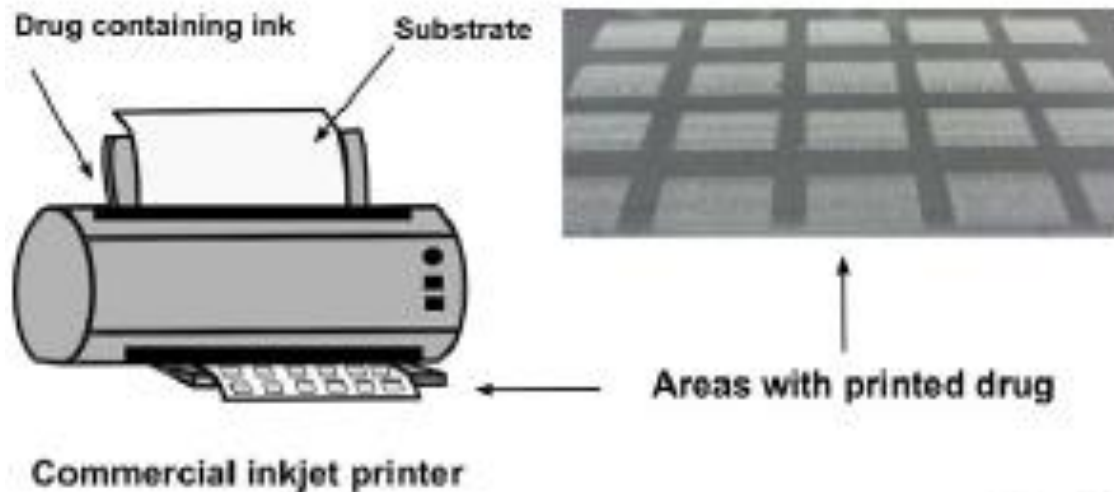


Identification

M. Preis, J. Breitzkreutz, N. Sandler, Int. J. Pharm. 494: 578-584 (2015)

2. Printing onto ODFs

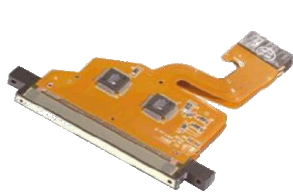
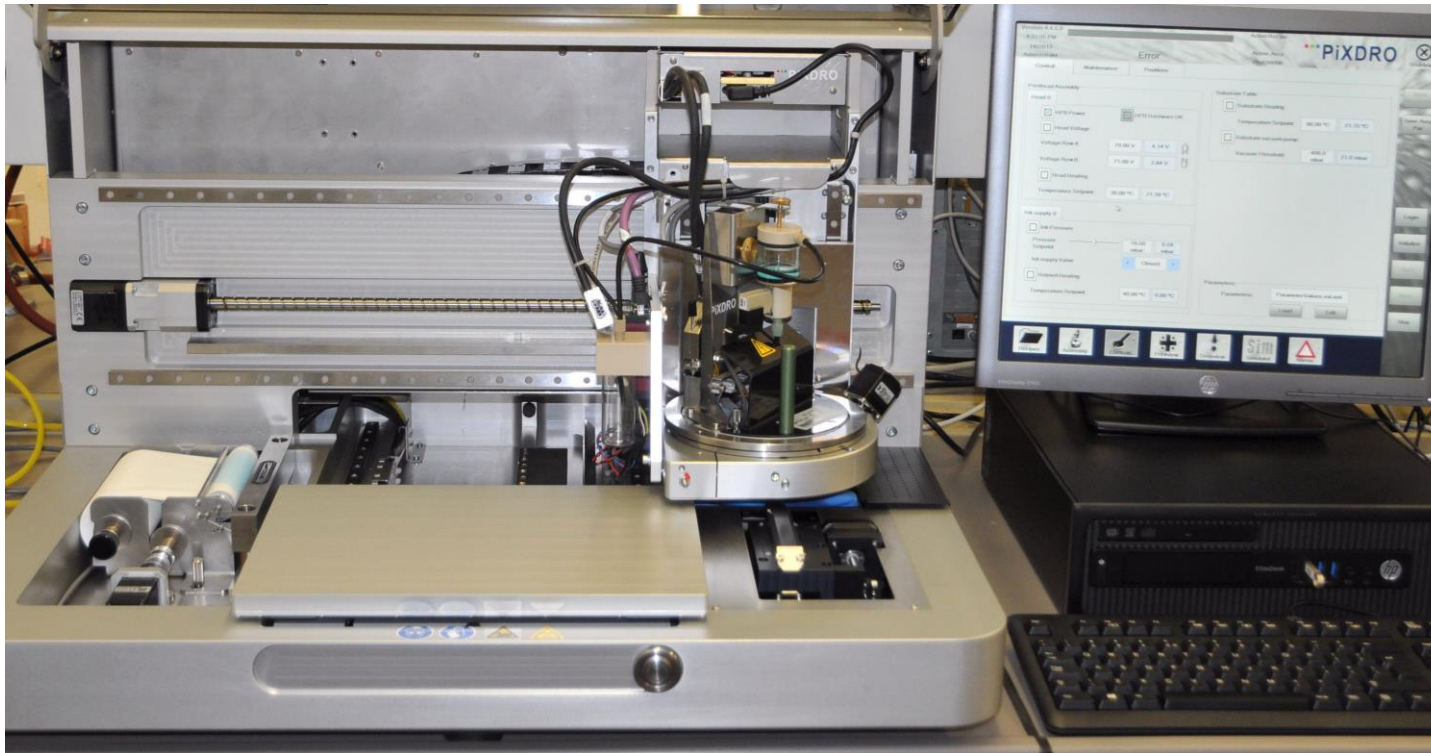
Stand-alone Inkjet Printing



N. Genina, E.M. Janssen, A. Breitenbach, J. Breitzkreutz, N. Sandler
Eur. J. Pharm. Biopharm. 85: 1075-1083 (2013)

2. Printing onto ODFs

PixDro LP50 high-resolution Inkjet-Printer (Meyer Burger)



Spectra



Konica Minolta



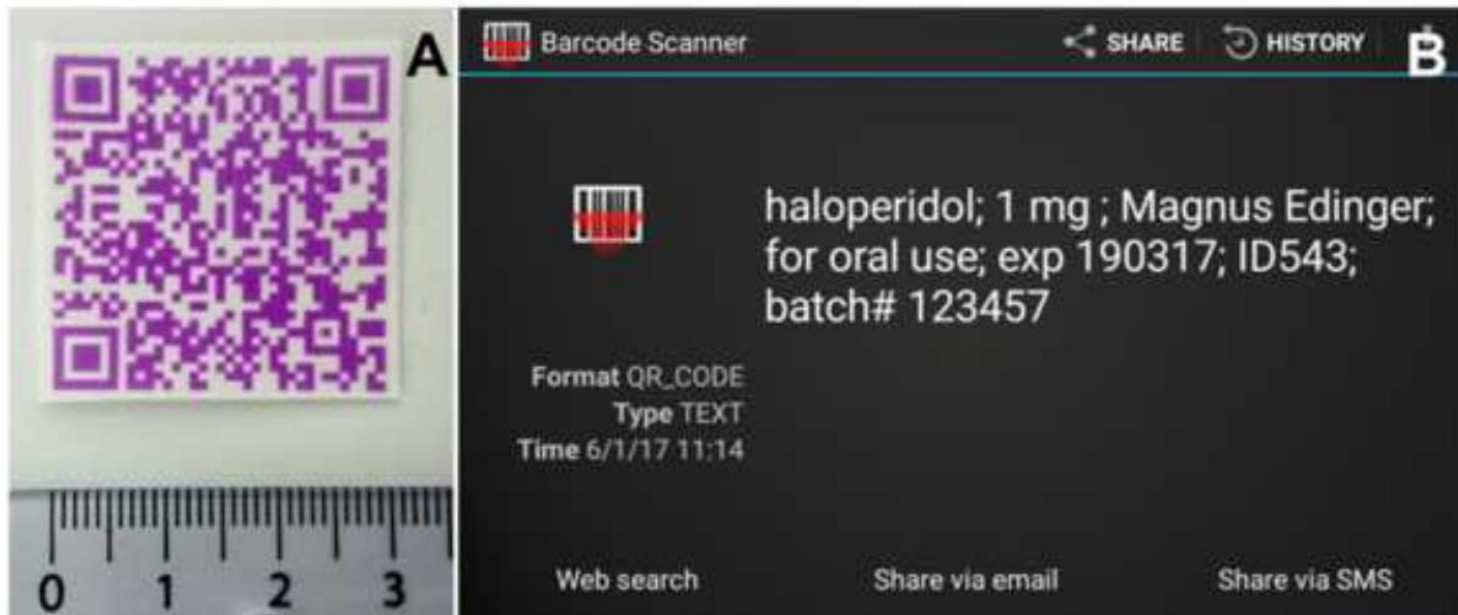
Trident



XAAR

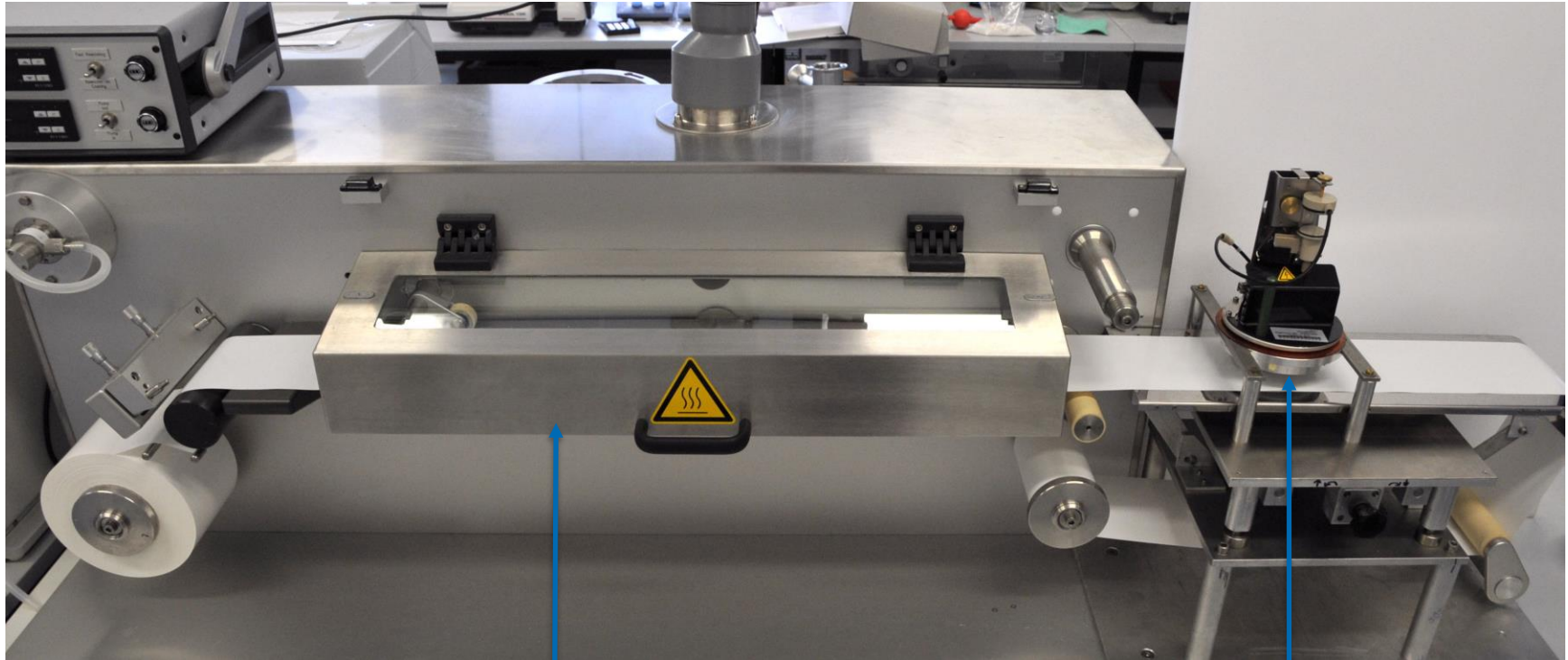
K. Knop / N. Sandler

QR-encoding



*M. Edinger, D. Bar-Shalom, N. Sandler, J. Rantanen, N. Genina
Int. J. Pharm. 536: 138-145 (2018)*

3. Continuous ODF printing

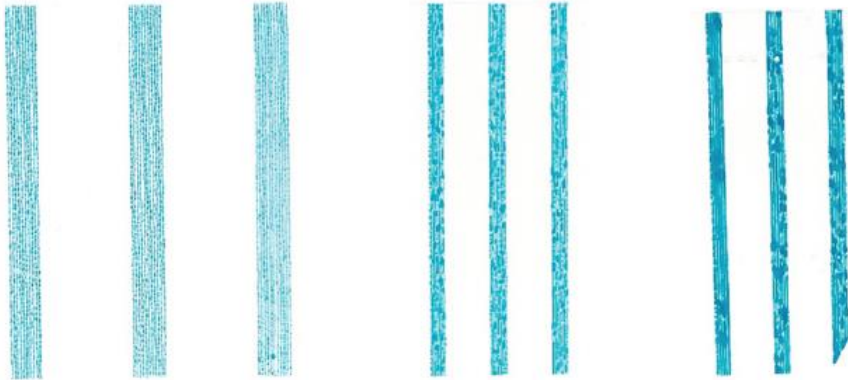


Continuous casting machine
(Optimags Coatmaster,
Dr. Zimmermann, Karlsruhe)

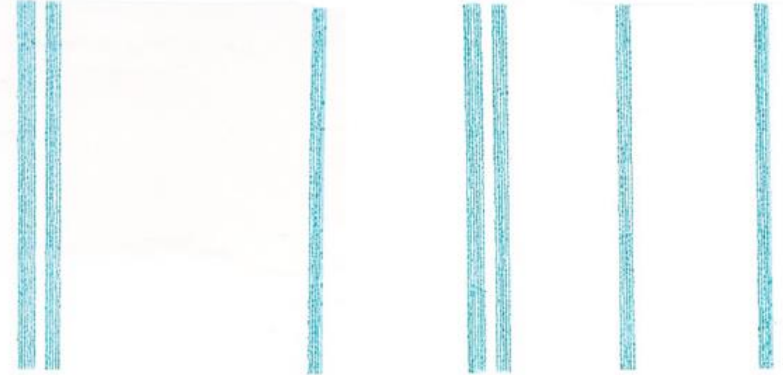
High-resolution ink-jet printer
(Pixdro LP50, Roth-Rau, Eindhoven
equipped with Spectra print head)

3. Continuous ODF printing

Symmetric lines



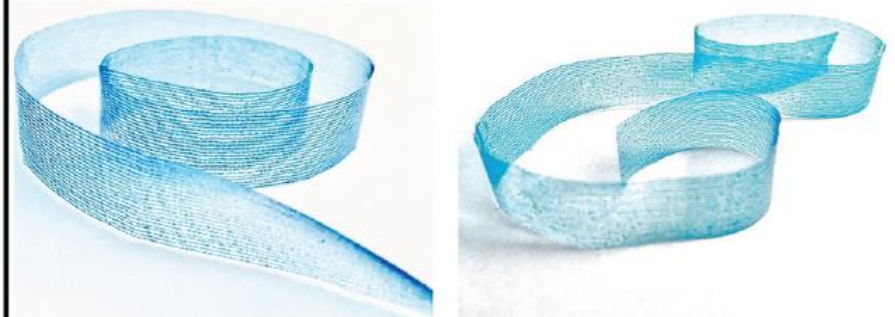
Asymmetric lines



central printing, dots



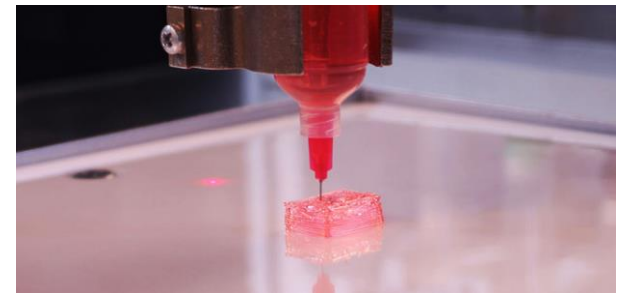
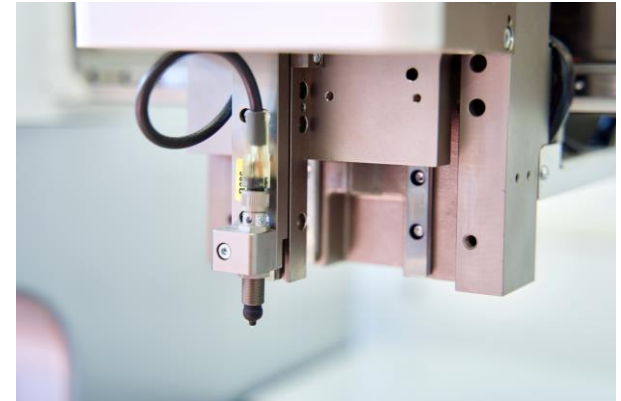
complete imprinting



Y. Thabet, R. Sibanc, J. Breitreutz, J. Manuf. Process. 35: 205–215 (2018)

3. Extrusion-based gel printing

Pressure-assisted Microsyringe (PAM)



U. Oberländer, HHU

Developer Series (Envisiontec, Gladbeck)

Printing of gels, pastes and suspensions at room temperature

3. Extrusion-based gel printing

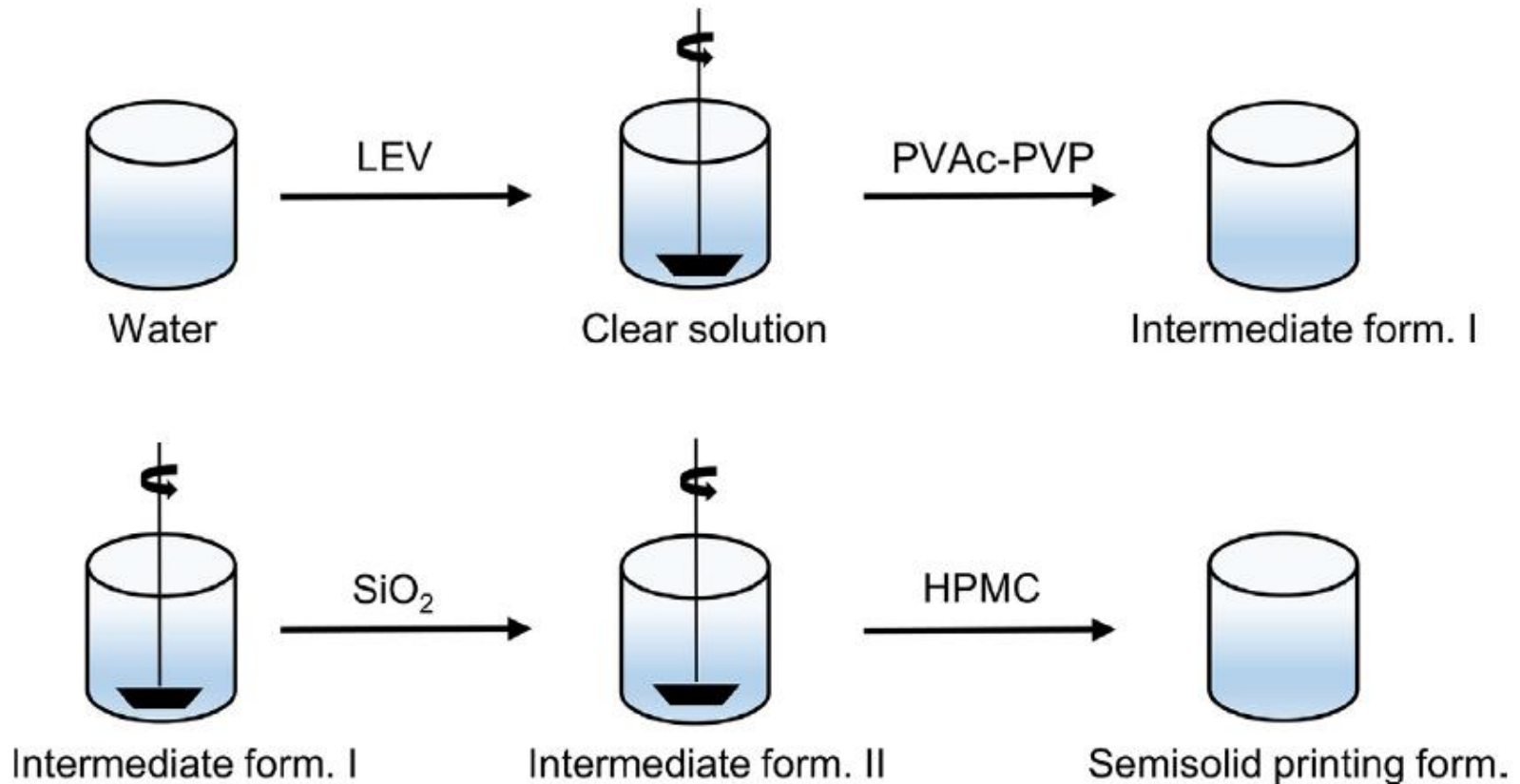


Fig. 1. Preparation of the semi-solid printing formulations.

I. El-Aita, J. Breitreutz, J. Quodbach, Eur. J. Pharm. Sci. 146, 105266 (2020)

3. Extrusion-based gel printing

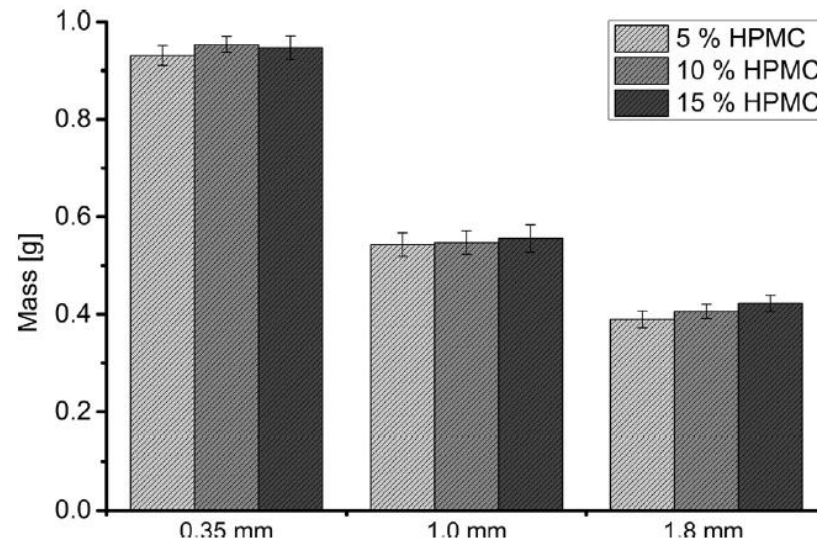
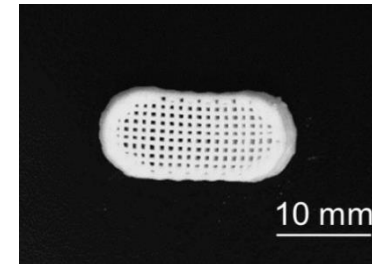


Fig. 7. Mass variation of printed tablets; $n = 20$; mean $\pm$ SD.

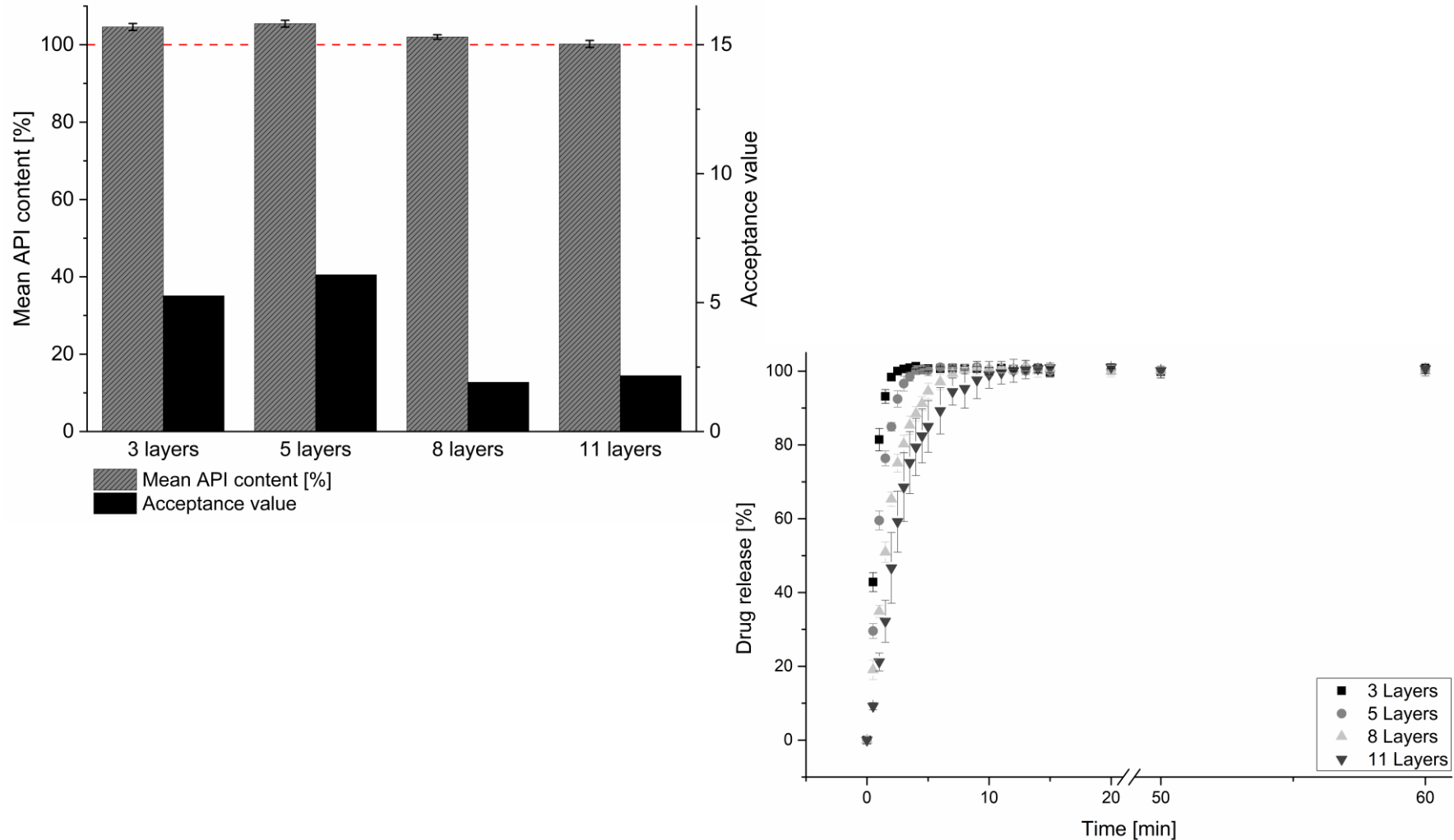


API content of printed tablets; $n = 10$, mean $\pm$ standard deviation (SD) and coefficient of variation (CoV).

API Content [mg]			
	0.35 mm	1.0 mm	1.8 mm
5% HPMC	334.63 $\pm$ 7.07	195.11 $\pm$ 8.48	139.95 $\pm$ 6.17
CoV [%]	2.11	4.35	4.41
10% HPMC	342.72 $\pm$ 5.66	196.93 $\pm$ 8.38	145.85 $\pm$ 5.03
CoV [%]	1.65	4.26	3.45
15% HPMC	340.25 $\pm$ 8.54	199.64 $\pm$ 9.73	141.71 $\pm$ 5.91
CoV [%]	2.51	4.88	3.90

I. El-Aita, J. Breitzkreutz, J. Quodbach, Eur. J. Pharm. Sci. 146, 105266 (2020)

3. Extrusion-based gel printing



I. El-Aita, J. Rahman, J. Breitkreutz, J. Quodbach, Eur. J. Pharm. Biopharm. 157: 59-65 (2020)

3. Extrusion-based gel printing

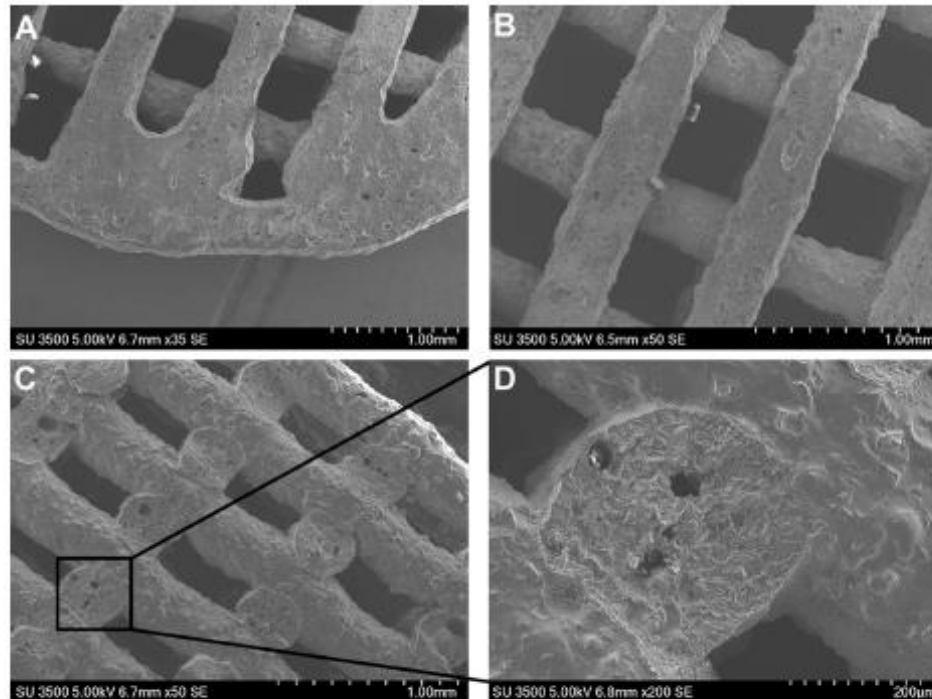


Fig. 5. SEM images; A. Edge of the bottom of a printed tablet, B. Surface of a printed tablet, C. Cross section of a printed tablet and D. Close-up view of the cross cut.

I. El-Aita, J. Breitkreutz, J. Quodbach,
Eur. J. Pharm. Biopharm. 134, 29-34 (2019)

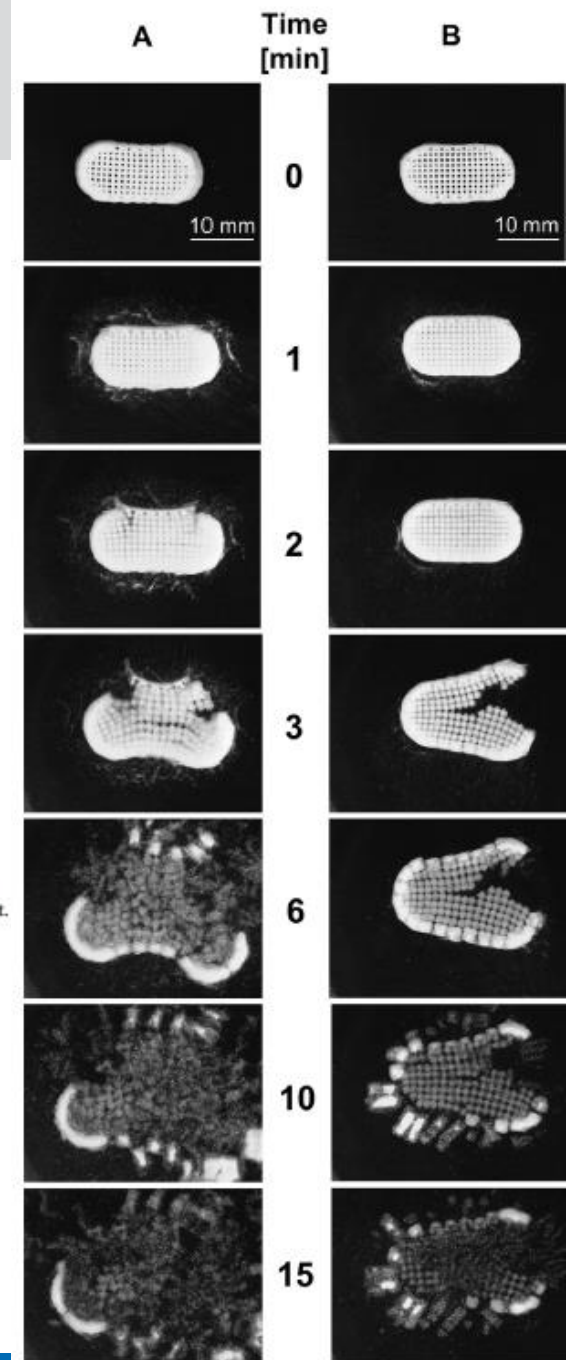
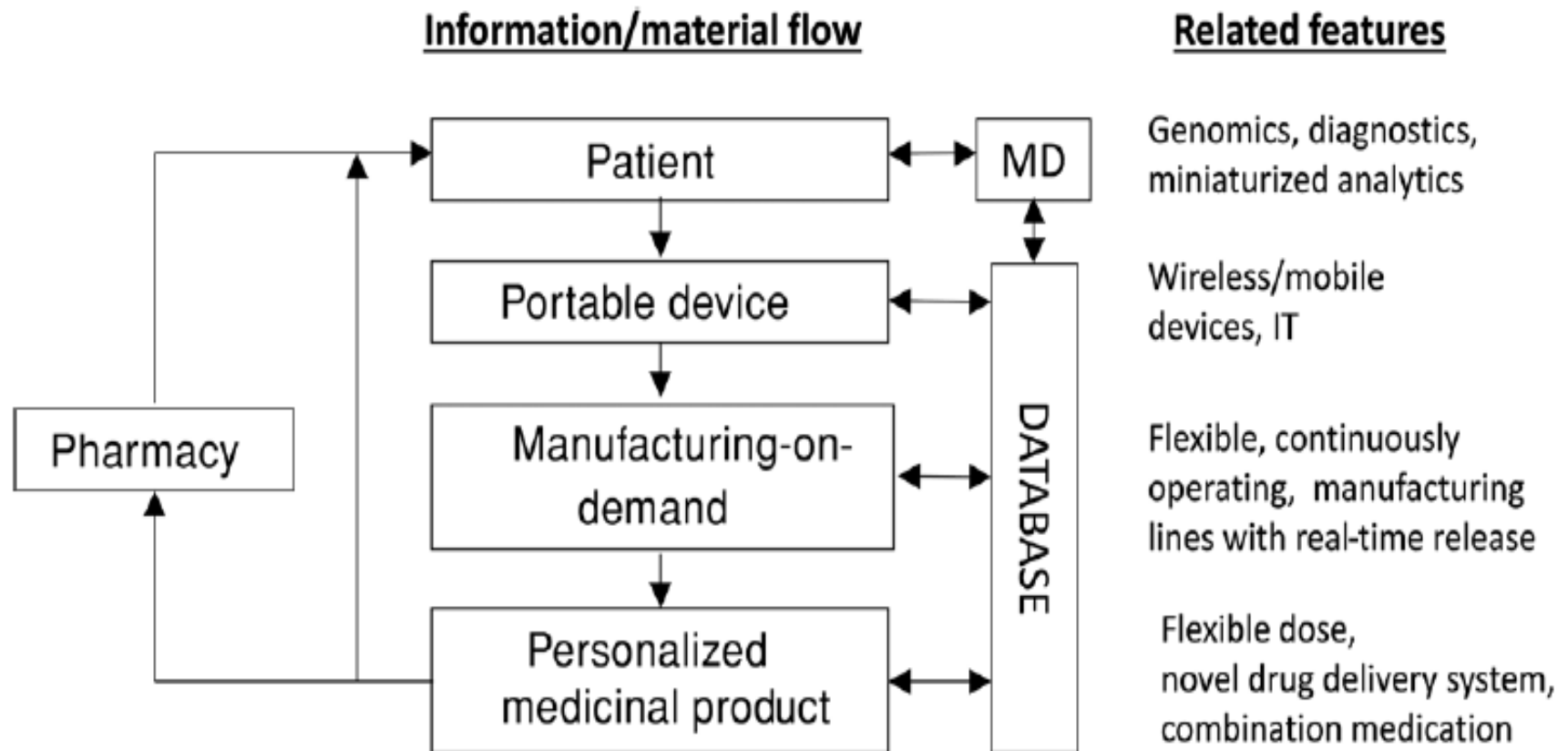
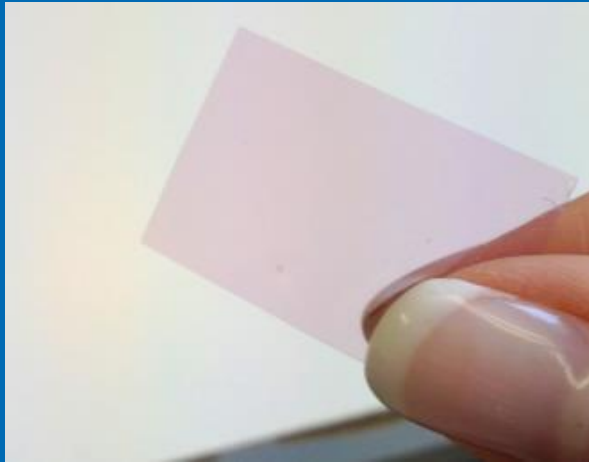


Fig. 6 Disintegration behavior of printed tablets in water without stirring 25 °C, A: formulation A, B: formulation B.



J. Breitzkreutz, J. Rantanen „Drivers for a change - manufacturing of future medicines for personalized drug therapies “, In: P. Kleinebudde, J. Khinast „Continuous Manufacturing“, Wiley (2017)

Thank you for your kind attention!



My personal thanks go to all collaborators
and funding organisations.

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