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Dr. Torsten Hoppe-Tichy

Printing Drugs

The „Why“ and „How“ from the perspective of a hospital pharmacist

UK HD

Conflict of Interest

THT works in a project around 2D/3D-Printing together with

➜ Department of Clinical Pharmacology and Pharmacoepidemiology, Heidelberg University Hospital, Germany

➜ DiHeSys - Digital Health Systems GmbH, Munich, Germany

➜ Gen-Plus GmbH, Munich, Germany

without any financial funding or support

Questions

After attending this seminar participants should be able to answer the following questions

Q1: What are the advantages of „Printing Medicines“?

Q2: What is one of the biggest challenge of printing on orodispersible films?

Q3: What are the patient populations with a possible unmet need regarding printed medicines?

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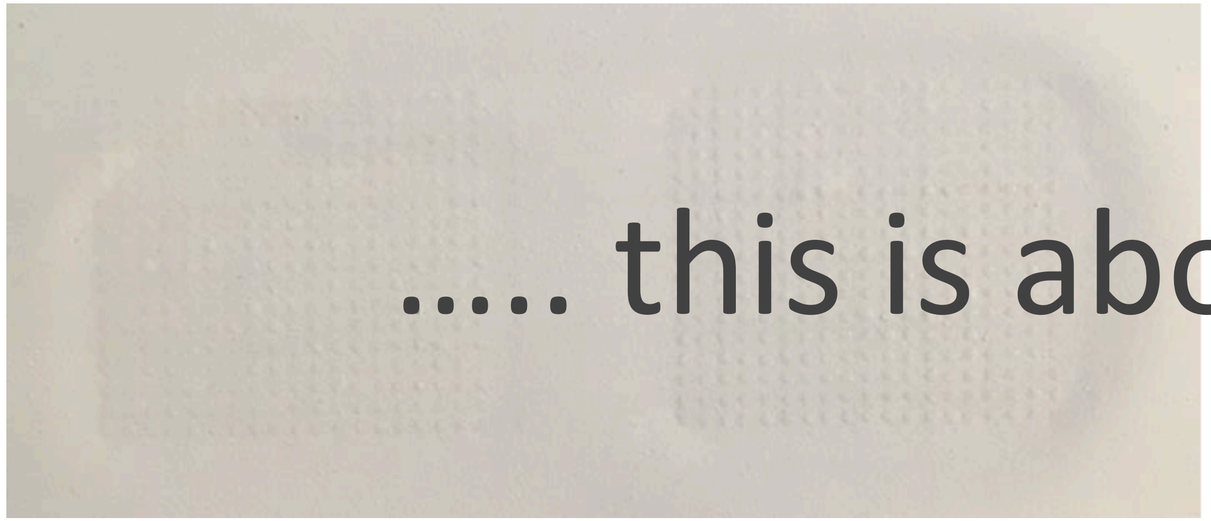
First at all …



….. this is about 2D-printing!

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But, for heavens sake, why shall we print drugs?

Some thoughts on automating

Why is there a need to print drugs?

- Is this unmet need the same in any patient group?

The local level approach, perspective Heidelberg University Hospital (UKHD)

How?

- Project planing at UKHD

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1st Problem[DE (only???)]

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Small Scale Production in Hospitals[DE]

drug production in German hospital pharmacies

because

no drug in the market (wrong dose, route of application)

e.g. child care, „ready-to-administer“ syringes

produced from licensed proprietary medicinal products available in the market (➜ reworking)

drug too expensive or drug shortages

e.g. rare diseases

produced from „cheap“ raw substances if available in the market

Small-Scale Production in Hospitals[DE]

„extemporaneous formulation“

individual production for a single patient

e.g. special dose for children ➜ capsules, solutions

„real“ small-scale production

batch production for a patient group

e.g. drug not available or not „ready-to-administer“

Why is this a problem?

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The biggest challenges for health systems in the near future

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➜ financing

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☞ *Automating should take place wherever possible!*

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cytotoxic reconstitution, TPN (compounding robots), logistics (unit-dose, picking robots), extemporaneous formulations (2D/3D-printing), … … …

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2nd Problem

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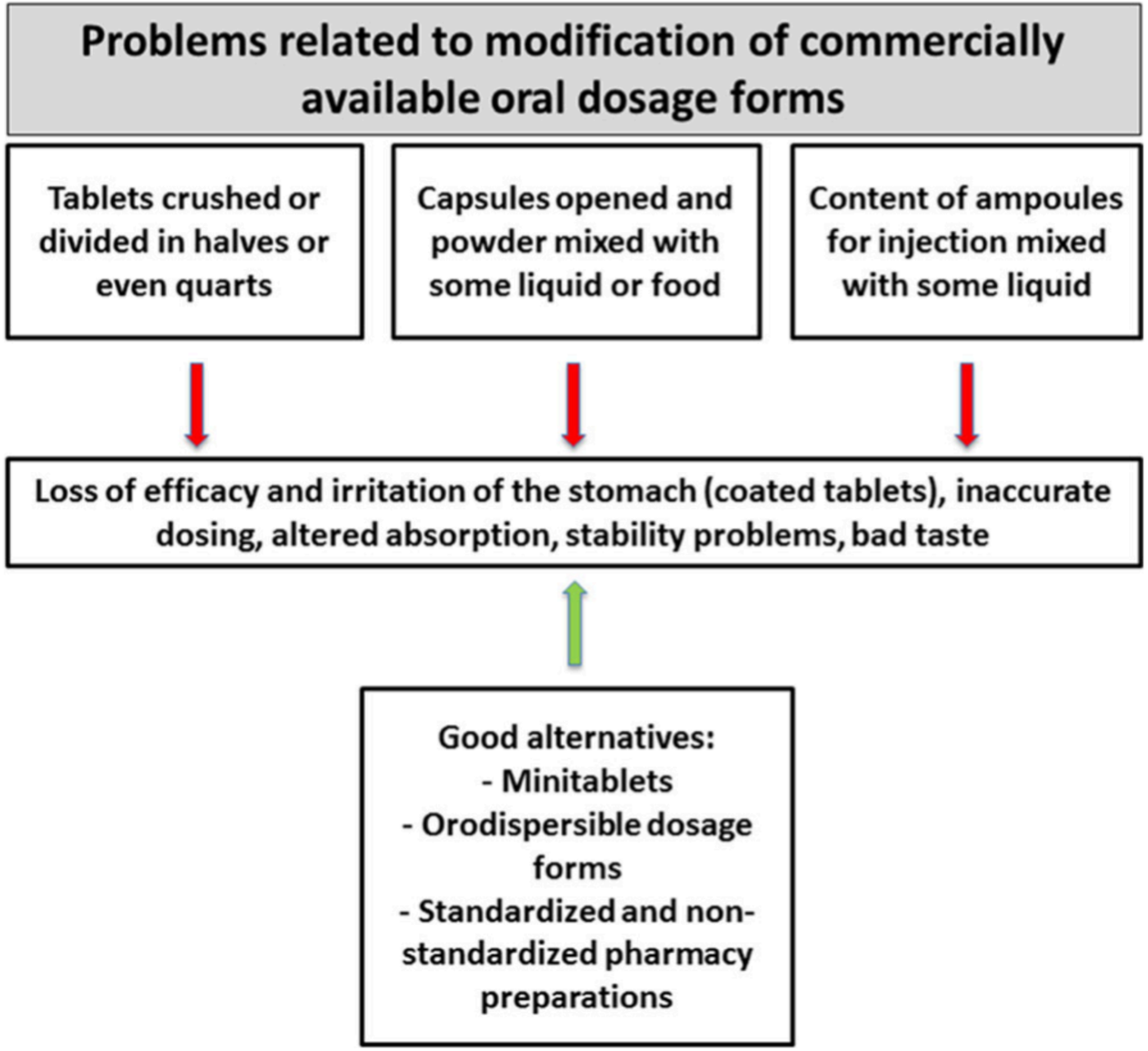
Problems in Special Patient Groups

Children

- dose of commercial available drugs often has to be adapted
- problems with swallowing tablets or capsules
- problems with taste of solutions
- no data on stability when mixed with food (baby food/mash)



Visser JC, Woerdenbag HJ, Hanff LM, Frijlink HW.· Personalized Medicine in Pediatrics: The Clinical Potential of Orodispersible Films. AAPS Pharm Sci Tech 2017;18(2):267

Special Doses for Children ➜ Capsules, Solutions

ADKA's Special Interest Group on Pediatrics names 51 active ingredients which are used in extemporaneous formulations

Wishlists exist in different settings

Reasons are not only „wrong dose" but also

„bad taste"

„problems with swallowing of tablets and capsules"

➜ 11.000 capsules/y

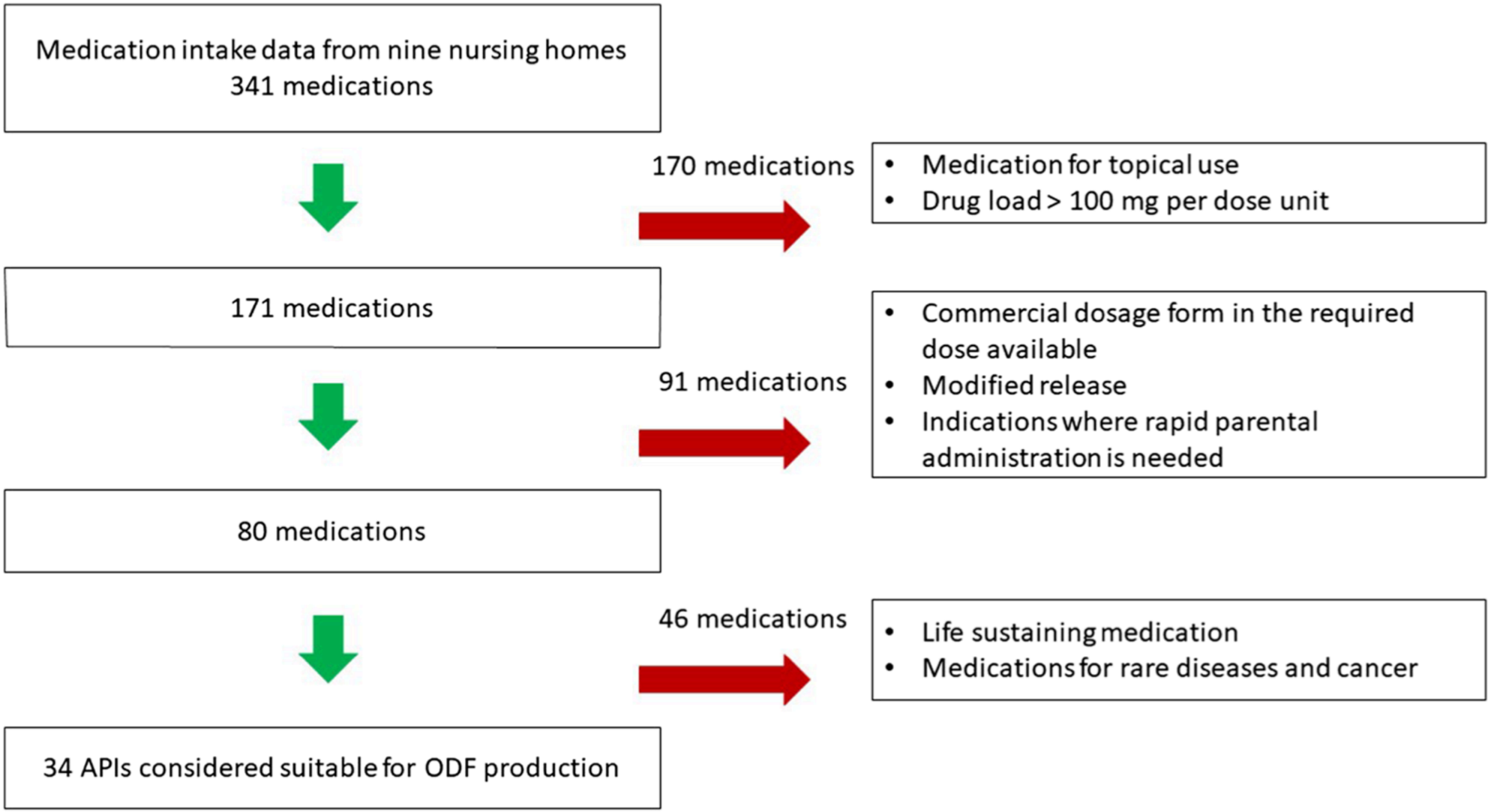
➜ 1.500 bottles with liquid formulations/y

UKHD

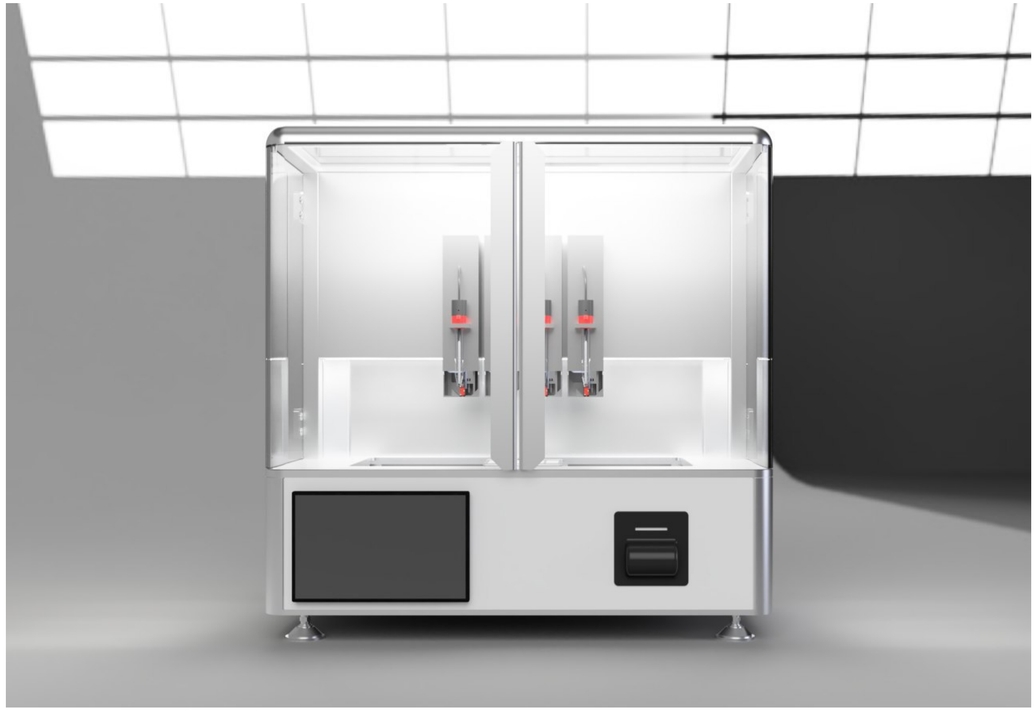
Nr.	Wirkstoff
1	Spironolacton
2	Sildenafil
3	Propranolol(hydrochlorid)
4	Captopril
5	Coffein(citrat)
6	Chloralhydrat
7	Hydrochlorothiazid
8	Clonidin(hydrochlorid)
9	Metoprolol(tartrat)
10	Melatonin
11	Enalapril(maleat)
12	Natriumbenzoat
13	Lisinopril
14	Amlodipin(besilat)
15	Omeprazol
16	Carvedilol
17	Tacrolimus
18	Hydrocortison
19	Levothyroxin(natrium)
20	Flecainid(acetat)
21	Midazolam(hydrochlorid)
22	Morphin(hydrochlorid)
23	Sotalol
24	Metronidazol
25	Phenobarbital
26	Theophyllin
27	Valganciclovir
28	Acetazolamid
29	Azathioprin
30	Colecaciferol
31	Clenbuterol
32	Clopidogrel
33	Colistin

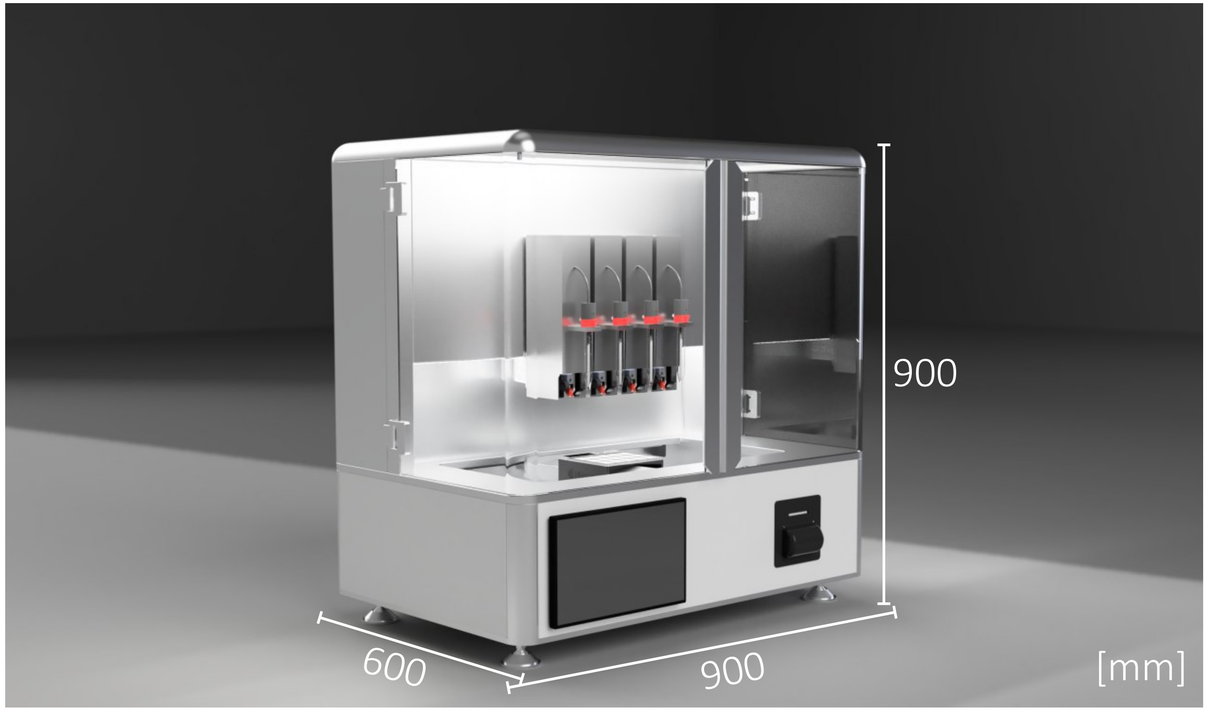
Temozolomid	PaedOnko
Trametinib	PaedOnko
Dabrafenib	PaedOnko
Risperidon	Psych
Quetiapin	Psych
Haloperidol	Psych
„Tinibe"	Thorax
ASS	Paed allgemein
Clopidogrel	Paed allgemein
Ramipril	Paed allgemein
Penicillin	
Corticosteroide	Paed allgemein

Environment: Nursing Home



Visser JC, Wibier L, Mekhaeil M, Woerdenbag HJ, Taxis K. Orodispersible films as a personalized dosage form for nursing home residents, an exploratory study. Int J Clin Pharm 2020 Feb 13. doi: 10.1007/s11096-020-00990-w. [Epub ahead of print]





possible problem-solving model

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What does it mean to implement such a system in hospital pharmacy?

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„What does it mean to implement such a system in hospital pharmacy?“

➜ you need partners

development, implementation, research, clinical study, … …

➜ you should have an innovation-friendly environment

➜ you need the money

➜ you have to find enthusiastic pharmacists in your department

➜ your team should have enough knowledge around drug production issues

Implementation/Research

Decision ➜ Which drug should be studied?

Analytics ➜ HPLC method

Production of ink

- Solvent?
- Stability testing for selected ink (➜ stress tests)

Substrate development (➜ Which kind of orodispersible film[1]?)

Compatibility/Stability testing of ink/solvent on ODF

Adaption ➜ ink, thickness of ODF, printing process, temperature … …

[1]Orodispersible Film: ODF

Questions before you start

Solubility

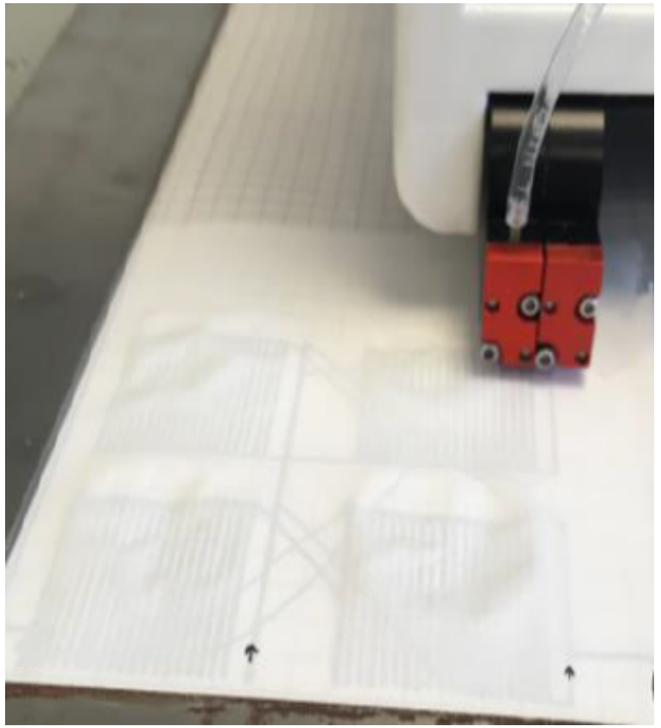
Is the drug soluble in an „printing-appropriate“ solvent?

Is the drug stable in the ink (solvent)?

Is the ink printable?

Will the concentration of the ink be high enough to get a dose printed?

Is the ink (solvent) compatible with the ODF chosen?



Questions before you start

Orodispersible films (ODF)

which is the right formulation of the ODF

(physical) stability

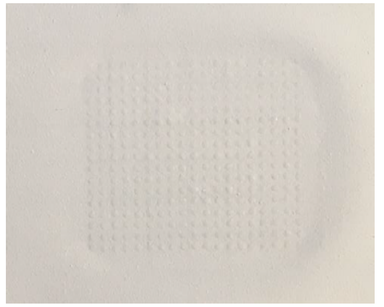
disintegration time

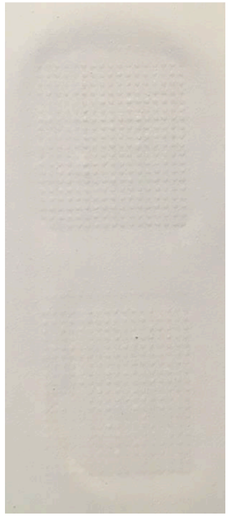
release of drug

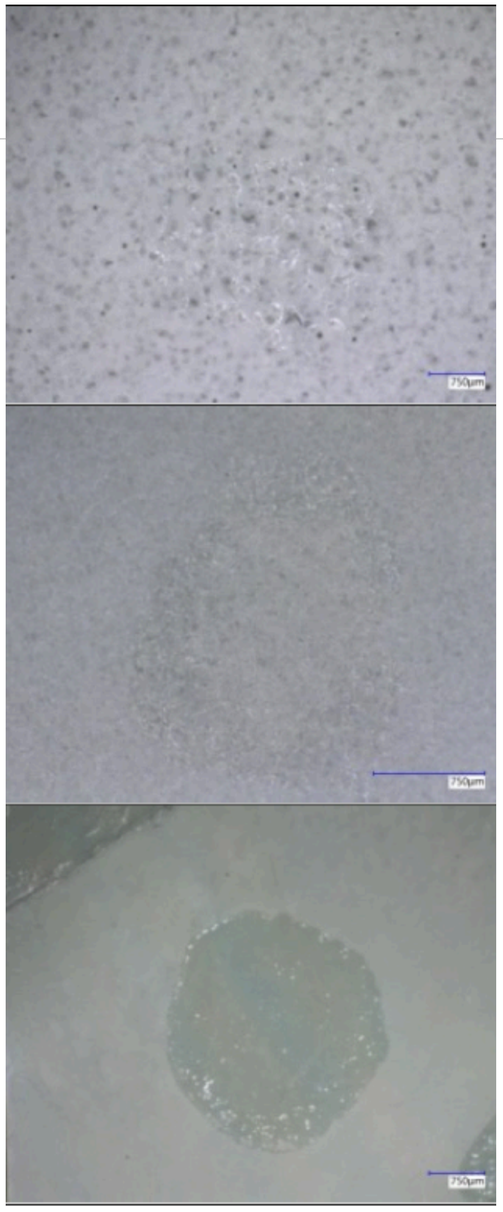
carrying capacity („ink“)

storage conditions

compatibility with ink







Our Wishlist

extemporaneous production of ink should be possible in hospital pharmacy

changing ink should be easy

- easy cleaning procedure of printhead is a prerequisite
  - ➜ cross contamination protocols

different ODFs should be easily available (like empty capsules)

easy and cost-effective packaging of printed ODFs should be developed

Conclusion

In our center children with the need for individualized oral dosages are the target population

Geriatric patients with polypharmacy[1] might be another patient population

2D-Printing on ODF is the preferred method at UKHD

[1]Polypharmacy is defined by the World Health Organisation as "the administration of many drugs at the same time or the administration of an excessive number of drugs"