PHARMACY

The researchers are sorted into research areas. In pharmacy we distinguish between Drug Transport and Delivery, Drug Formulation and Drug Transporters in ADME. Researchers from chemistry and physics also offer projects within pharmacy.

Drug Transport & Delivery

Drug Formulation

Drug Transporters in ADME

Supervisors from other research areas

You can find a description of these researchers in the designated catalogue.

Adam Cohen Simonsen ..... Physics

Christine McKenzie ..... Chemistry

Erik Donovan Hedegård ..... Chemistry

Francesca Serra..... Physics

Himanshu Khandelia ..... Chemistry

Jacob Kongsted ..... Chemistry

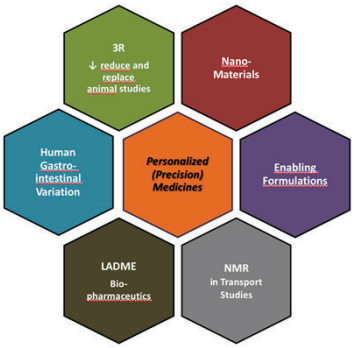
Poul Nielsen ..... Chemistry

Stefan Vogel ..... Chemistry

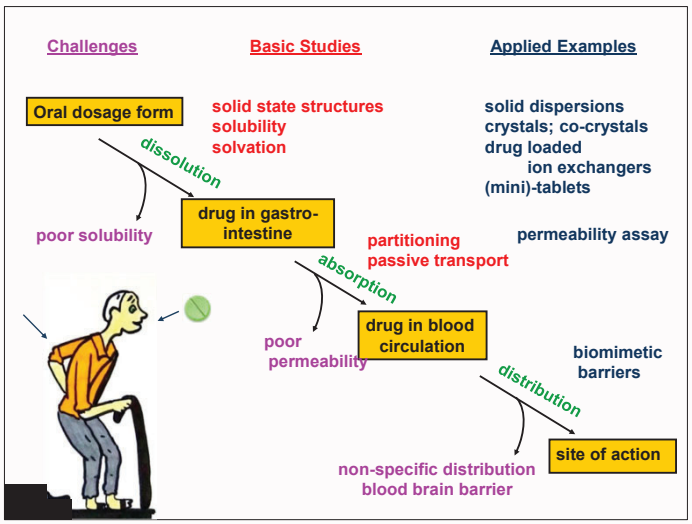
SDU

Professor Annette Bauer-Brandl

Research Group:
- Drug Transport & Delivery -
Formulations and Biopharmaceutics



Oral Drug Transport & Delivery



Oral Drug Dosage Forms (e.g. tablets, and capsules) are the most used drug formulations. However, there are a number of challenges for the drug substance to reach the target site (e.g. receptor).
We address these challenges through basic physico-chemical experiments to characterize both the drug substances themselves and selected (model) drug formulations. Moreover, in order to confirm our understanding and to apply the knowledge, we use in vitro-models to avoid animal tests.

Taken from SDU homepage at:: https://www.sdu.dk/en/om_sdu/fakulteterne/naturvidenskab/nyheder-2020/ny-medicin-uden-dyreforsoeg

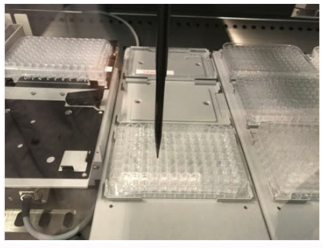
We want to save the lives of animals by studying drugs and formulations in detail using artificial experimental methods and data modelling.
Our novel artificial barrier Permeapd ® mimics the permeability of different biological barriers. We develop models for biopharmaceutical property characterization of drugs and drug formulations to select the most promising ones without the use of animals.

High Throughput Sceening

Based on our novel artificial barrier Permeapd ® that mimics different biological barriers we have developed a microtiterplate system fir for automated handling.

Advantages:
cost-effective; easy to use; reproducible results; functional stability in presence of "aggressive" excipients

Uses:
- *in vitro* measurement of permeability
- Automated High throughput Screening of drug permeability; data mining



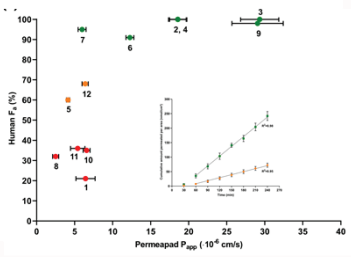


Figure 1: Principle of the PermeaPad™ assay and examples of results; Jacobsen et al., 2020

Enabling Formulations: *Development; Preparation; understanding of in vivo performance*

Example: Solid Phospholipid Nanoparticles
Formulation of Nanoparticles for better uptake and better bioavailability of poorly available drug substances:
Manufacture of Nanoparticles by Spray Drying
In vitro characterization of their properties:
- Solid state structure
- Solubility
- Dissolution Rate
- Permeability

In vivo bioavailability; IVIVC

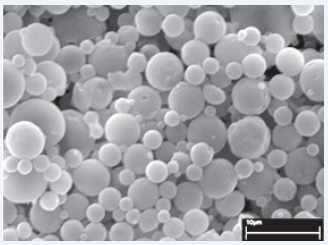


Figure 2: SEM micrograph of the SPLN Nanoparticles

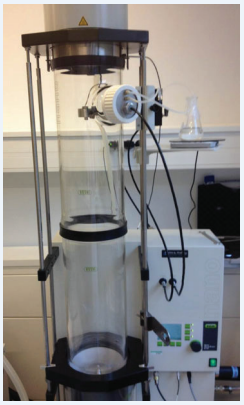


Figure 3: Nano Spray Dryer

ABB, 2015

https://www.sdu.dk/en/forskning/drug-transport-delivery

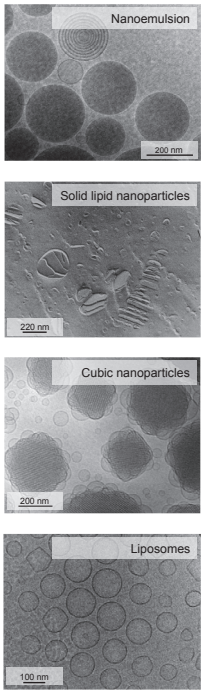
email: annette.bauer@sdu.dk

Associate Professor Judith Kuntsche

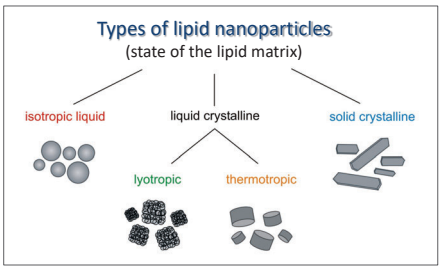
Topic: Pharmaceutical Technology

SDU UNIVERSITY OF SOUTHERN DENMARK

Lipid nanoparticles and liposomes

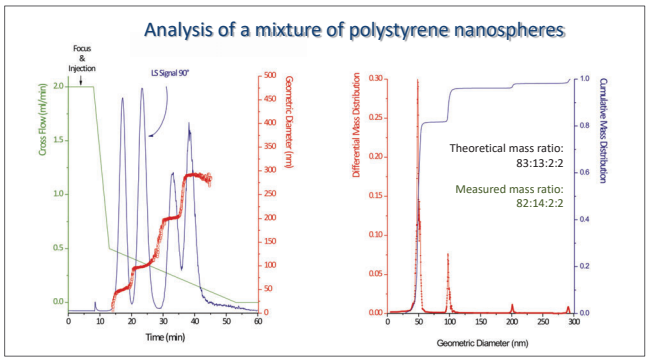


- Can be prepared from physiological compounds (e.g. glycerides, cholesterol esters, phospholipids).
- Particle size in the nm-size range facilitates intravenous administration.
- **Purposes:**
  - solubilization of poorly water-soluble drugs,
  - drug targeting (e.g. tumor targeting),
  - enhancement of drug absorption.
- **Liposomes** can encapsulate both lipophilic (membrane) and hydrophilic (aqueous core) drugs.
- **Lipid nanoparticles** have a lipid matrix.



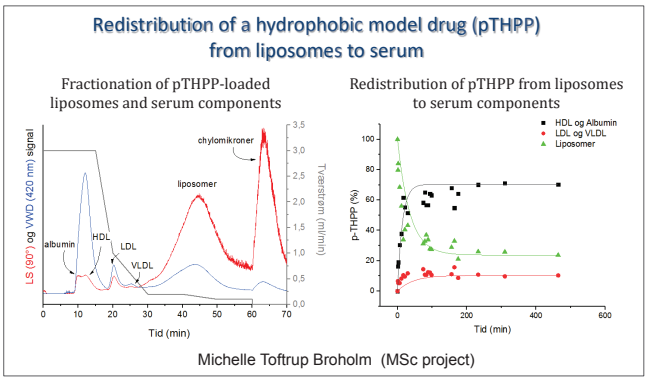
Flow field-flow fractionation

- Separation of molecules and particles in dependence on size by applying a cross flow in a thin separation channel.
- Broad size range of about 5 kDa – 1 µm and versatile separation conditions, no stationary phase.
- Connection with different detectors for comprehensive characterization (MALLS, dRI, UV/Vis).
- Focus of research on
  - **size** determinations (also **stability** in e.g. serum),
  - quantification of **co-existing colloidal structures** (e.g. micelles, nanoparticles, vesicles),
  - **drug release** and transfer studies.



Parenteral drug delivery

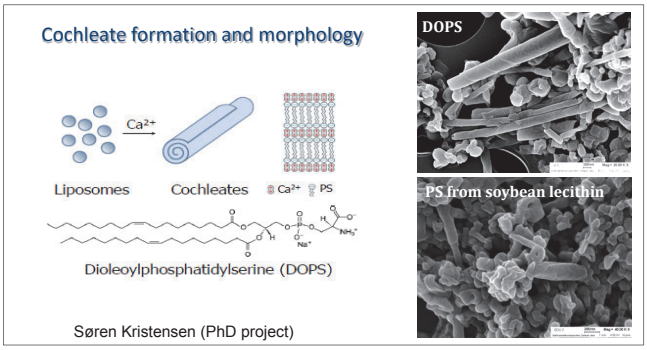
- **Drug solubilization** to facilitate intravenous administration (nanoemulsions in clinical use for, e.g. diazepam, propofol and etomidate) -> rapid drug release and no distinct alteration of drugs pharmacokinetic profile.
- **Drug targeting** due to passive accumulation of nanoparticles in tissues with disturbed endothelia (e.g. solid tumors).
- Focus of research on
  - comprehensive physicochemical **characterization** (colloidal structures, morphology, size and size distribution),
  - stability in **physiological media** (e.g. serum),
  - understanding of the mechanism of **drug release** and redistribution at the molecular level.



Michelle Toftrup Broholm (MSc project)

Cochleates

- Cochleates are cylindrical particles composed of tightly packed phospholipid membranes.
- They are formed by the addition of calcium ions to negatively charges liposomes, e.g. phosphatidylserine vesicles.
- Due to the tightly packed lipid structure, cochleate cylinders possess a considerably high physical stability which makes them very interesting for drug delivery.
- Focus of research on
  - preparation of cochleates and similar lipid particles from **naturally derived lipids** (e.g. lower purity),
  - **optimization** of composition and production parameters including scaling up, lyophilization and sterilization and
  - **drug incorporation** and **release**.



Søren Kristensen (PhD project)

web: http://findresearcher.sdu.dk/portal/da/person/kuntsche E-mail: kuntsche@sdu.dk

Professor René Holm

Topics: Physical pharmacy and advantaged drug delivery

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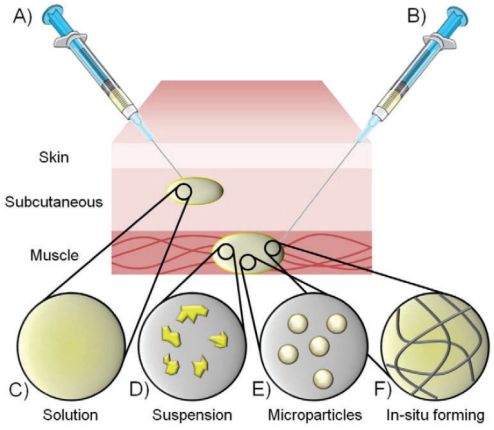
Long acting injectables

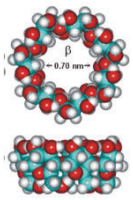
Long acting injectables provide patients with a more effective treatment when compared to daily oral administration. Depending on the molecule a number of different formulation strategies can be applied – we conduct active research in all of them, including formulation evaluation, in vitro dissolution method development and manufacturing.

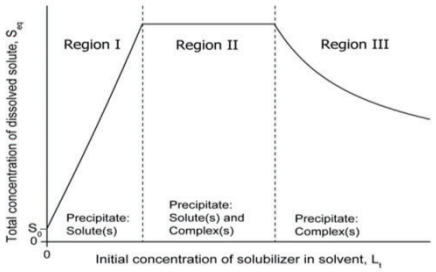


Preformulation

Understanding the formulation system through well designed characterisation is the best way to make a robust formulation.

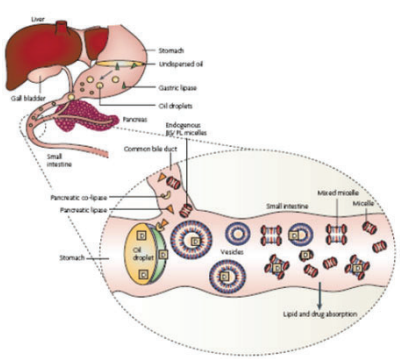
We look into a number of important formulation fundaments, e.g. characterisation of cyclodextrin complexation, stability of suspensions or emulsions as a function of stabiliser, solubility enhancement, measurement of solid solubilities, biophysical investigations on biomolecules in formulation relevant buffers etc. all linking towards novel and innovative formulations where we develop a deep scientific insight.

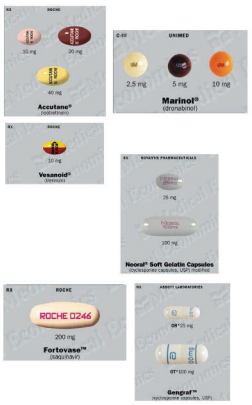




Lipid based formulations

Lipid based formulations have been applied commercially in a number of products – using the lipids solubilizing power and the body's physiology to make a robust formulation. We conduct research in lipid based formulations with focus on hard to formulate compounds and combination of approaches, i.e. lipid suspensions, lipid formulations with crystallization enhancers, use of liquid crystals to enable oral absorption of biomolecules.





The world is our lab

Bachelor and master could be linked up to ongoing research projects, where examples are provided above.

Master thesis can also be conducted in cooperation with another university, e.g. in Belgium, US, UK, Ireland, Switzerland, where you will be a part of the research conducted at that institution.

Industrial projects, can be set up in both Danish and international companies, e.g.

- Pharmaceutical engineering and modelling
- Formulation design
- Biopharmaceutics
- Pharmaceutical processes

Specific project to be defined in cooperation with the company

web: https://portal.findresearcher.sdu.dk/da/persons/ren%C3%A9-holm

email: reho@sdu.dk

Drug transporters in ADME Group

Professor Carsten Uhd Nielsen
Maria Pedersen, Sebastian Jakobsen, Bala Krishna Prabhala,
Mohsin Ali Reza, Ahmed Al-Ali,

SDU
Syddansk Universitet

Solute carriers and efflux transporters affect permeability, ADME and bioavailability

We change absorption – ADME:

The movement of drug substances in the body may be described by a number of different processes:

Absorption (A), e.g. from the intestine
Distribution (D), e.g. into the brain
Metabolism (M), e.g. in the liver
Excretion (E), e.g. via the kidney
Together these processes define the exposure of the body to a drug substance, often expressed as the plasma-concentration-time profile:

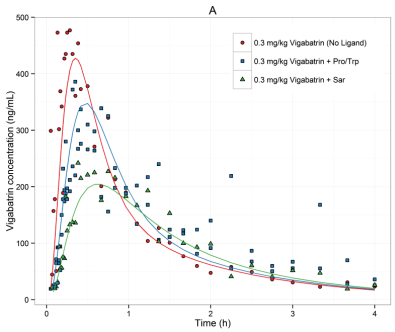


Figure 1: Vigabatrin plasma concentration in rats after oral administration (Nøhr *et al.* EJPS, 2015)

We use or modulate drug transporters:

Solute Carriers (SLCs) and ATP-binding cassette (ABC) transporters affect the ADME properties of many drug substances, and could also be drug targets:

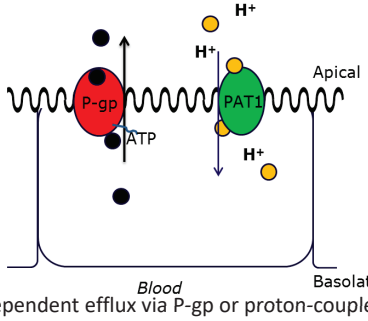


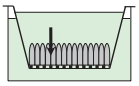
Figure 2: ATP-dependent efflux via P-gp or proton-coupled influx of substrates via PAT1 in an epithelial cell.

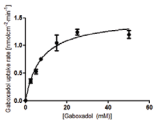
Drug transporters may facilitate or limit drug absorption, may facilitate or limit drug distribution, metabolism or excretion, and may transport drug metabolites. Thus, cause dose-dependent drug absorption and drug-drug interactions (DDIs) due to effects on ADME properties.

We use in vitro models:

Our research use cell cultures cultured at the FKF cell culture facility by Maria Pedersen:

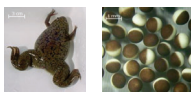
Epithelial cell cultures
- Intestinal Caco-2 cells
- Renal MDCK cells
- Prostate cancers PC-3 cell



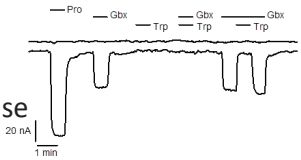


Modified cell cultures
- MDCK MRP2 cells
- MDCK MDR1 cells

Expression systems for transporters



To quantify drug substance transport we need
- Assay development
- Specific inhibitors



To quantify transporters, we use
- PCR,
- Western Blotting

To Knock-down transporters we use siRNA approaches

We run research project:

Currently, Bachelor or Master Thesis projects could relate to:

- Modulation of efflux transporter activity in cell cultures using pharmaceutical excipients or new potential inhibitors.
- Transport via the amino acid transporter SNAT2 and identification of inhibitors hereof.
- Drug transport in cell cultures and other non-cell based models.
- Nutrient transporters in prostate cancer cells – impact osmolarity on transporter expression
- Models to study P-gp mediated transport.
- Novel materials for formulation of drug delivery systems

Want to see the world?: It is possible to make Master Thesis projects at pharmaceutical companies in Denmark or abroad or at universities abroad. Such projects are not necessarily transporter-related research.

http://www.sdu.dk/ansat/cun

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