



HAL
open science

Poorly soluble drugs

Juergen Siepmann, Thomas Rades, Anette Muellertz, Thorsteinn Loftsson

► **To cite this version:**

Juergen Siepmann, Thomas Rades, Anette Muellertz, Thorsteinn Loftsson. Poorly soluble drugs. International Journal of Pharmaceutics, 2020, International Journal of Pharmaceutics, 577, pp.119055. 10.1016/j.ijpharm.2020.119055 . hal-04457762

HAL Id: hal-04457762

<https://hal.univ-lille.fr/hal-04457762>

Submitted on 29 Apr 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Editorial

Poorly soluble drugs

Seven years ago, in 2013 we published one of the (by far) most downloaded and most cited special issues in the history of the *International Journal of Pharmaceutics*, which was dedicated to the formulation of poorly water-soluble drugs. This clearly indicates the outstanding importance of this topic in our field. Even today the articles of this 2013 special issue are still very frequently downloaded and referred to: For example, 3 of these papers are among the “top 4 most cited articles” of the journal, when considering the time period “2013-today”. And also in the last 7 years, numerous research and review articles have been dedicated to the challenges raised by drugs and drug candidates exhibiting poor solubility in water. This is why we, again, devote a special issue of this journal to this “continuously hot topic”.

If a drug cannot dissolve to a sufficient extent in the aqueous body fluids, it is generally not able to reach its target site. This is because (in most cases) the drug must be *dissolved* (be in the form of *individual* molecules, ions or atoms) to have a chance to cross key barriers in the living organism, such as the mucosa in the gastro intestinal tract. Thus, even if a drug molecule has an “ideal” chemical structure to interact with its target in the body (e.g. with a specific receptor) to cure the patient, *in vivo* the treatment will fail if the solubility of the drug in water is too low: The active agent will never “have the opportunity” to induce the desired therapeutic effect. The use of high-throughput screening techniques, which offer an interesting potential in the drug discovery process, is in great part responsible for the fact that formulation scientists are nowadays very frequently confronted with this fundamental challenge during product development. The ability of numerous potential drug candidates to interact with a target is rapidly evaluated using automated tests, while the substances are artificially dissolved in organic solvents (e.g., dimethyl sulfoxide). However, in the human body, they must dissolve in aqueous fluids. Since many years the large majority of the drug candidates in the pipelines of the pharmaceutical companies world-wide suffers from poor aqueous solubility.

For these reasons tremendous efforts have been undertaken to offer formulation strategies allowing to overcome this fundamental physical hurdle. There is no universal approach, which can be applied to all types of drugs and drug candidates. Each chemical entity has its unique structure and specific “needs”. In this special issue, world-wide leading experts in the field of poorly soluble drugs report on their most recent research findings and give comprehensive overviews on a large variety of techniques and strategies which can be applied. Also the underlying physico-chemical phenomena are addressed, since often a better understanding of the mechanisms that are involved in drug dissolution and re-precipitation can help facilitating product optimization. Special attention is placed on potential changes occurring within the dosage forms during storage to assure long term stability. To illustrate the considerable diversity of the topics that are addressed in this special issue, here are some

examples: amorphous solid dispersions, co-amorphous systems, complexing agents (including cyclodextrins), mesoporous systems, recrystallization phenomena, supersaturation effects, spray drying, melt extrusion, electrospinning, supercritical antisolvent (SAS) process, nanofibers, liposomes, nanocrystals, self-nanoemulsifying drug delivery systems, salt formation, biopolymers, drug absorption and the solubility-permeability interplay, Raman mapping as well as theoretical (including thermodynamic) considerations.

We would like to cordially thank all the authors of the articles of this special issue for their time and efforts as well as the reviewers for their highly valuable help. Please enjoy reading, we hope you will be able to benefit from the provided information.

Juergen Siepmann*

Univ. Lille, Inserm, CHU Lille, U1008, F-59000 Lille, France

Thomas Rades, Anette Muellertz

*Department of Pharmacy, University of Copenhagen, Universitetsparken 2,
2100 København Ø, Denmark*

Thorsteinn Loftsson

*Faculty of Pharmaceutical Sciences, University of Iceland, Hofsvallagata 53,
IS-107 Reykjavik, Iceland*

E-mail addresses: juergen.siepmann@univ-lille.fr (J. Siepmann),

thomas.rades@sund.ku.dk (T. Rades),

anette.muellertz@sund.ku.dk (A. Muellertz),

thorstlo@hi.is (T. Loftsson),