



# Drug-Release Mechanisms Elucidated by Imaging Techniques: Visualizing the Invisible!

Susanne Florin Muschert

## ► To cite this version:

Susanne Florin Muschert. Drug-Release Mechanisms Elucidated by Imaging Techniques: Visualizing the Invisible!. Pharmaceutics, 2022, Pharmaceutics, 14 (6), pp.1165. 10.3390/pharmaceutics14061165 . hal-04008636

**HAL Id: hal-04008636**

**<https://hal.univ-lille.fr/hal-04008636>**

Submitted on 28 Feb 2023

**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.



Distributed under a Creative Commons Attribution 4.0 International License

## Editorial

# Drug-Release Mechanisms Elucidated by Imaging Techniques: Visualizing the Invisible!

Susanne Florin-Muschert 

Univ. Lille, Inserm, CHU Lille, U1008, F-59000 Lille, France; susanne.muschert@univ-lille.fr

Imaging techniques such as Raman spectroscopy, electron microscopy, laser scanning confocal microscopy, atomic force microscopy, tomography, magnetic resonance imaging, and terahertz are powerful tools to elucidate drug-release mechanisms from different types of delivery devices.

Drug penetration, as well as mass transport mechanisms, can be highly complex, and applying theoretical approaches to interpret underlying mass transport mechanisms might cause misguidance, especially if one of the conditions (of the prediction model) involuntary changes during the dissolution test [1].

Images offer the advantage of picturing the fate of the active molecule within the dosage form or at the site of action and give highly useful supplementary information during dissolution tests.

This Special Issue collected high-standard original research articles on the application of imaging techniques to explain drug delivery (Figure 1). There were seven papers submitted, and five of them have been published.

Kaushik et al. reported very interesting findings on the penetration mechanisms of a dye from Vaseline-based ointment [2]. Thanks to inverted epifluorescence microscopy, the authors showed that there are three mechanisms of penetration of the active ingredient into the skin, (i) by convection or solvent-dragged penetration, (ii) via passive diffusion of the active ingredient, and (iii) local penetration phenomena (for example, liquid menisci due to massage).

A capsule-in-capsule drug delivery device was analyzed in terms of the disintegration time and location as a function of the capsule material [3]. The MRI images of black iron oxide (in the inner capsule) revealed capsule disintegration in different regions of the gastrointestinal (GI) tract and have been compared to the established method of tracing salivary caffeine (radio-labeled in the inner capsule and natural caffeine in the outer capsule). Unfortunately, hibiscus tea powder also placed in the outer capsules could not be visualized upon capsule disintegration via the MRI method. Rump et al. showed the reliability of the two analyzing techniques to monitor the fast disintegration time for single capsules and the delayed disintegration time for the capsule combinations. Here, inter-subject GI variability caused variance in the disintegration time, which was higher with delayed liberation of capsule content.

Dong and co-workers investigated water transport into immediate-release tablets of varying formulations and microstructures [4]. With these types of tablets, water transport is of utmost importance to control drug release and tablet disintegration. Terahertz pulsed imaging allows monitoring the advancement of the waterfront within the tablet upon contact with the dissolution medium. Interestingly, tablet porosity predominantly impacted tablet dissolution.

Fahier et al. used Raman spectroscopy to monitor changes in core and film coating composition of pellets loaded with the weakly basic drug verapamil HCl and coated with a polymer blend [5]. The confocal Raman microscopic images allowed for non-invasive monitoring of pore creation within the film coating due to leaching of the water-soluble



**Citation:** Florin-Muschert, S. Drug-Release Mechanisms Elucidated by Imaging Techniques: Visualizing the Invisible! *Pharmaceutics* **2022**, *14*, 1165. <https://doi.org/10.3390/pharmaceutics14061165>

Received: 20 May 2022

Accepted: 24 May 2022

Published: 30 May 2022

**Publisher's Note:** MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

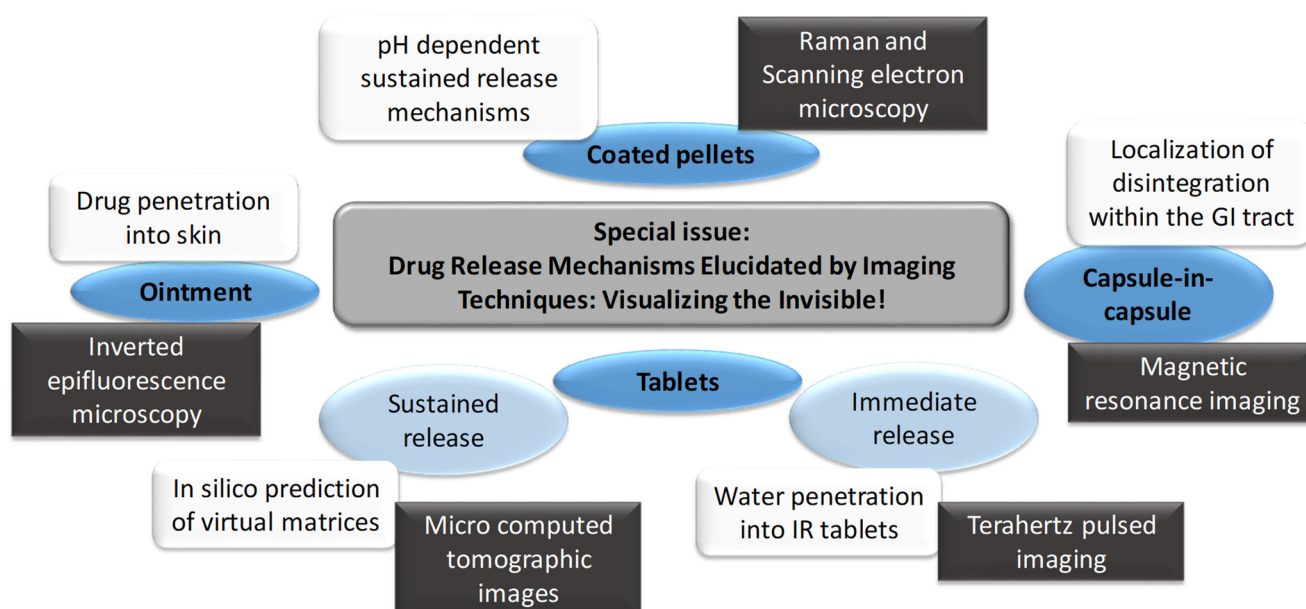


**Copyright:** © 2022 by the author. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

polymer. Fluorescence spectroscopy was also used to trace changes in the pH within the coated single pellets non-invasively.

Bollmann and Kleinebudde used X-Ray micro-computed tomography images of real pharmaceutical tablets to design virtual matrices (such as cylindrical tablets) and predicted the dissolution of the latter [6]. Thus, the ratio of active ingredient (API) and polymer in the binary mixtures, as well as the porosity of the matrix, could be virtually varied, and the dissolution profile could be calculated. The drug-release mechanism was either purely diffusion-controlled for lower API contents, or erosion of the matrices occurred with higher API contents. Thus, in silico predictions were based on the Higuchi and Korsmeyer-Peppas plot. However, with pharmaceutical systems with diffusion-based drug-release mechanisms, the dissolution could not be predicted in silico. This work adds important considerations to the long journey of in silico formulation development.

This Special Issue offers a selection of possibilities to employ imaging techniques to explain drug mobility and the disintegration of pharmaceutical dosage forms. This collection of high-quality scientific articles shows the diversity of application areas and the multitude of information that can be drawn from this type of analytical tool.



**Figure 1.** Schematic presentation of the Special Issue's contents.

**Funding:** This research received no external funding.

**Acknowledgments:** I would like to deeply acknowledge all authors that contributed to this Special Issue with their very interesting and groundbreaking research. Regardless of the final decision made, I want to express my gratitude to all authors who had submitted manuscripts and all feedback, comments, and exchanges that helped improve the work. I express my gratitude to the rigorous and professional reviewers as well as the very reactive editorial team of Pharmaceutics. I especially want to address the supplementary academic editors for kind support.

**Conflicts of Interest:** The author declares no conflict of interest.

## References

1. Siepmann, J.; Peppas, N.A. Higuchi equation: Derivation, applications, use and misuse. *Int. J. Pharm.* **2011**, *418*, 6–12. [[CrossRef](#)] [[PubMed](#)]
2. Kaushik, V.; Ganashalingam, Y.; Schesny, R.; Raab, C.; Sengupta, S.; Keck, C.M. Influence of Massage and Skin Hydration on Dermal Penetration Efficacy of Nile Red from Petroleum Jelly—An Unexpected Outcome. *Pharmaceutics* **2021**, *13*, 2190. [[CrossRef](#)] [[PubMed](#)]

3. Rump, A.; Weiss, F.N.; Schulz, L.; Kromrey, M.-L.; Scheuch, E.; Tzvetkov, M.V.; White, T.; Durkee, S.; Judge, K.W.; Jannin, V.; et al. The Effect of Capsule-in-Capsule Combinations on In Vivo Disintegration in Human Volunteers: A Combined Imaging and Salivary Tracer Study. *Pharmaceutics* **2021**, *13*, 2002. [[CrossRef](#)] [[PubMed](#)]
4. Dong, R.; DiNunzio, J.C.; Regler, B.P.; Wasylaschuk, W.; Socia, A.; Zeitler, J.A. Insights into the Control of Drug Release from Complex Immediate Release Formulations. *Pharmaceutics* **2021**, *13*, 933. [[CrossRef](#)] [[PubMed](#)]
5. Fahier, J.; Vukosavljevic, B.; De Kinder, L.; Florin, H.; Goossens, J.-F.; Windbergs, M.; Siepmann, F.; Siepmann, J.; Muschert, S. Towards a Better Understanding of Verapamil Release from Kollicoat SR:IR Coated Pellets Using Non-Invasive Analytical Tools. *Pharmaceutics* **2021**, *13*, 1723. [[CrossRef](#)] [[PubMed](#)]
6. Bollmann, S.; Kleinebudde, P. A New Validation Methodology for In Silico Tools Based on X-ray Computed Tomography Images of Tablets and a Performance Analysis of One Tool. *Pharmaceutics* **2021**, *13*, 1488. [[CrossRef](#)]