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VISUALIZATION AND CHARACTERIZATION OF THE DYNAMIC STRUCTURE OF SOLID DOSAGE FORMS DURING THE DISSOLUTION PROCESS USING HIGH-RESOLUTION X-RAY TOMOGRAPHY

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1. Introduction

To identify the release mechanism of pharmaceutical dosage forms and to understand the effect of processing conditions on the behavior of the product, detailed information about the internal structure of the sample is necessary (e.g., porosity, tortuosity of the pores, density of the ingredients). In this regard, visualization of solid dosage forms structure at microscale will provide essential information to design samples of optimal properties via adapting the processing techniques.

This project aims to develop a method to monitor and characterize both the inner and outer structure of pharmaceutical tablets during the dissolution process using high-resolution dynamic x-ray tomography (4D-µCT). A flow-through cell dissolution method was designed and developed capable of providing reliable in vitro dissolution process. It can be easily positioned at an x-ray µCT setup and allows to image the microstructure of the investigated sample during the drug release process. To increase the contrast between sample and the dissolution medium, suitable contrast agents were used.

2. Materials and Methods

A dissolution apparatus consisting of a flow cell, peristaltic pump, and hot plate with stirrer was developed (Figure 1). The flow cell was designed and manufactured on Polymethyl methacrylate (PMMA), due to its relatively low x-ray attenuation. Two different kinds of formulation were studied, one made of an inert polymer (Polycaprolactone (PCL)) and the other consist of hydrophilic polymer (Hydroxypropyl Cellulose (HPC)). Cesium chloride and $BaSO_4$ were used as the contrast agent for tablets made of PCL and HPC respectively.

Dynamic high-resolution imaging was performed at the Environmental Micro-CT (EMCT) scanner of the Ghent University Center for X-Ray [1]. In this system, the sample remains fixed while the x-ray tube and detector are rotating around the sample during the acquisition. All scans were reconstructed using Octopus reconstruction. Image analysis and visualization were done using Octopus Analysis [2], a custom-developed python script, and VGSTUDIO (Volume Graphics). For the sample made of HPC, a Digital Volume Correlation approach is employed to track the deformation in the sample due to the swelling and erosion of the polymer.

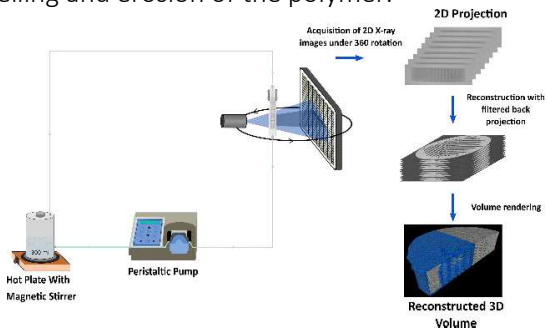

Figure 1. Graphical abstract of the research work.

3. Results and Conclusion

The introduced method provides us detailed information about the dynamic behavior of the studied samples (e.g., penetration of dissolution medium, porosity, swelling, and erosion of the sample) during the dissolution process. The contrast agents enabled us to discriminate between the sample and the dissolution medium, therefore, track the structural changes in the samples during the dissolution process, while it was impossible with a system without a contrast agent.

4. Acknowledgments

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5. References

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