

Most new drugs are poorly soluble in water, resulting in low bioavailability, which means that only a small portion of the active substance is absorbed into the bloodstream. To address this issue, scientists have developed special formulations known as enabling formulations. One such formulation is amorphous solid dispersions (ASDs). ASDs are advanced drug delivery systems where the drug is dissolved in a polymer matrix, designed to improve solubility and bioavailability and thus allow for oral delivery of such compounds. Understanding the dissolution process of these formulations is crucial for developing more efficient drug delivery methods. However, this is complicated due to a process known as spontaneous liquid-liquid phase separation (LLPS), leading to the formation of two distinct phases: a drug-rich colloidal phase and an aqueous phase with molecularly dissolved drug. Studies like this one aim to better understand this phenomenon and thereby improve the assessment of drug bioavailability.

The primary goal of this project is to develop in vitro tools that will allow for a deeper understanding of the dissolution and combined dissolution/permeation (D/P) processes of drugs from ASDs. The applicants aim to elucidate the complex mechanism of drug release from ASDs, which could lead to better predictions of their effectiveness without the need for animal testing.

The studies will use two advanced analytical techniques: asymmetrical flow field-flow fractionation (AF4) and microdialysis. AF4 is a technique that enables the separation of colloidal particles formed during the dissolution of the formulation, while microdialysis allows for real-time monitoring of the molecularly dissolved drug. The model drug selected for our research is itraconazole (ITZ), a triazole antifungal agent with poor water solubility but good permeability, classified in class 2 of the Biopharmaceutics Classification System (BCS). The studies will be conducted in simulated intestinal fluids to reflect the in vivo conditions of dissolution and permeation processes. This will also allow us to examine the impact of these factors on LLPS and the molecularly dissolved ITZ fraction.

This project has the potential to significantly impact the field of oral drug delivery research, improving research methodologies and understanding the mechanisms that enhance the bioavailability of poorly soluble drugs. By combining AF4 and microdialysis techniques, we hope to gain new, valuable insights into drug dissolution and release mechanisms. We anticipate that our research will lead to the development of more effective drug delivery methods, which could increase their clinical efficacy and enable the prediction of their performance without the need for animal testing.

The project focuses on developing and applying advanced analytical tools to study amorphous solid dispersions, which are key to improving the bioavailability of modern drugs. By utilizing asymmetrical flow field-flow fractionation and microdialysis, we hope to obtain new information on drug dissolution and release mechanisms. This will allow us to develop more efficient drug delivery methods and improve the clinical efficacy of poorly soluble therapeutic compounds.