

A High-Throughput Workflow for API Solubility in Complex Biorelevant Media

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The solubility of orally administered drugs is highly influenced by the composition of the intestinal fluids, the presence of fatty acids and cholesterol, and the pH. All these factors can be affected by the individual's diet (food effect) [1, 2]. Typical biorelevant studies, however, fail to capture food effects as the experiments are commonly performed on fixed simulated intestinal fluid (SIF) compositions.

Here, we propose a new high-throughput workflow for the study of API solubility in complex biorelevant media. The media are prepared ad hoc to simulate food effects, varying the content of lecithine, cholesterol, fatty acid and the bile salts composition. This automated workflow allows to screen a number of parameters (e.g., SIF composition, pH, influence of excipients) in shorter time (70 % time saving), using less material, and capturing more parameters (e.g., pH monitoring) compared to the manual process.

The study shows the marked impact of pH and phospholipids on the solubility of the API. These findings could not be seen in the classical approach, performing biorelevant solubility screens at fixed pH and SIF composition. The study demonstrates how the HT approach can be applied to obtain large data sets to better inform the PBPK model.

- [1] Madsen, C. M.; Feng, K.-I.; Leithead, A.; Canfield, N.; Jørgensen, S. A.; Müllertz, A.; Rades, T., *European Journal of Pharmaceutical Sciences* **2018**, *111*, 311-319.
- [2] Pentafragka, C.; Symillides, M.; McAllister, M.; Dressman, J.; Vertzoni, M.; Reppas, C., *Journal of Pharmacy and Pharmacology* **2018**, *71* (4), 557-580