# OLEOGEL MATRICES FOR CONTROLLED DRUG RELEASE USING IBUPROFEN AS A MODEL COMPOUND

Becca Putans, Kevin O'Donnell, Tanner Southern, Tom Watson,
Anette Müllertz, Matthias Knopp - Pharma Solutions, IFF

Where science & creativity meet

## The Background

Poorly soluble active pharmaceutical ingredients (APIs) are often formulated into a liquid filled hard or soft capsule. The API can be solubilized or dispersed into the lipophilic carrier vehicle to help increase bioavailability. One limitation to this approach is that upon dissolution of the capsule, the drug-infused oil will immediately deliver its content, making controlled release difficult to achieve. Oleogels are a way to make a solid structure from a liquid oil, allowing for new dosage forms that can modify the release rate of the API.

## The Study

Researchers at IFF investigated the potential for modifying the release properties of a model API from an oleogel, or structured oil carrier. They synthesized gels with varying physical properties, using different concentrations and viscosity grades of ethylcellulose to understand the impact on drug release. To characterize the release rate, researchers used standard USP II dissolution methods and an in-vitro lipolysis model.

## The Method

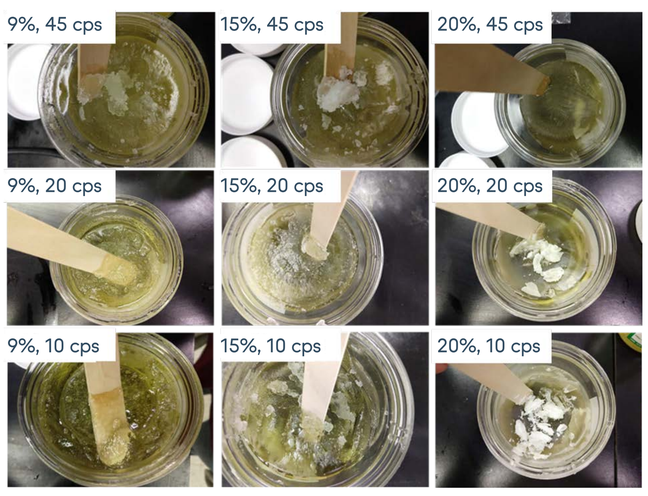
Researchers prepared structured gel samples by heating an oil and polymer mixture in a jacketed reactor vessel equipped with an overhead stirrer at 400 rpm. After all material was added, they then applied a nitrogen blanket to reduce oxidation of the oil; the mixture was heated to 160 °C. After 35-40 minutes, the powder was dissolved, and the oleogel was allowed to cool in ambient conditions. A pre-cooled gel was re-melted, between 70 °C to 130 °C, depending on gel properties, in a glass jar using an oil bath – the API (ibuprofen) was incorporated via overhead stirring. The mixture was mixed for 45-120 minutes to ensure all the API was dispersed. The molten oleogel was then pipetted into a mold or a two-piece hard-shell capsule and stored until tested.

Researchers conducted standard USP II dissolution testing in pH 7.4 potassium phosphate buffer with a paddle speed of 100 rpm. The solution was sampled through 1.0 mm cuvettes and 222 nm wavelength was monitored for the API. It was then pumped back into the vessel to maintain constant volume. The in-vitro lipolysis took place as previously described by Larsen et al. , using simulated intestinal media and porcine pancreatic lipase.

## The Results

Nine gels were synthesized with either 9%, 15%, or 20% of one of three viscosity grades of ethylcellulose; 10 cps, 20 cps, or 45 cps. The physical texture ranged from a flowable liquid at low polymer loading and low viscosity grade, to a stiff candle-like consistency at high polymer loading and high viscosity grade, (Fig.1).

**Figure 1: Gel consistency**




Polymer percentage had the biggest impact on release rate, with more polymer, or more viscous oleogels, leading to slower release (Fig.2). The higher polymer loading (dark blue traces)had a denser matrix  Which slowed down diffusion and therefore slowed drug release.

**Figure 2: Effect of polymer concentration on ibuprofen release**

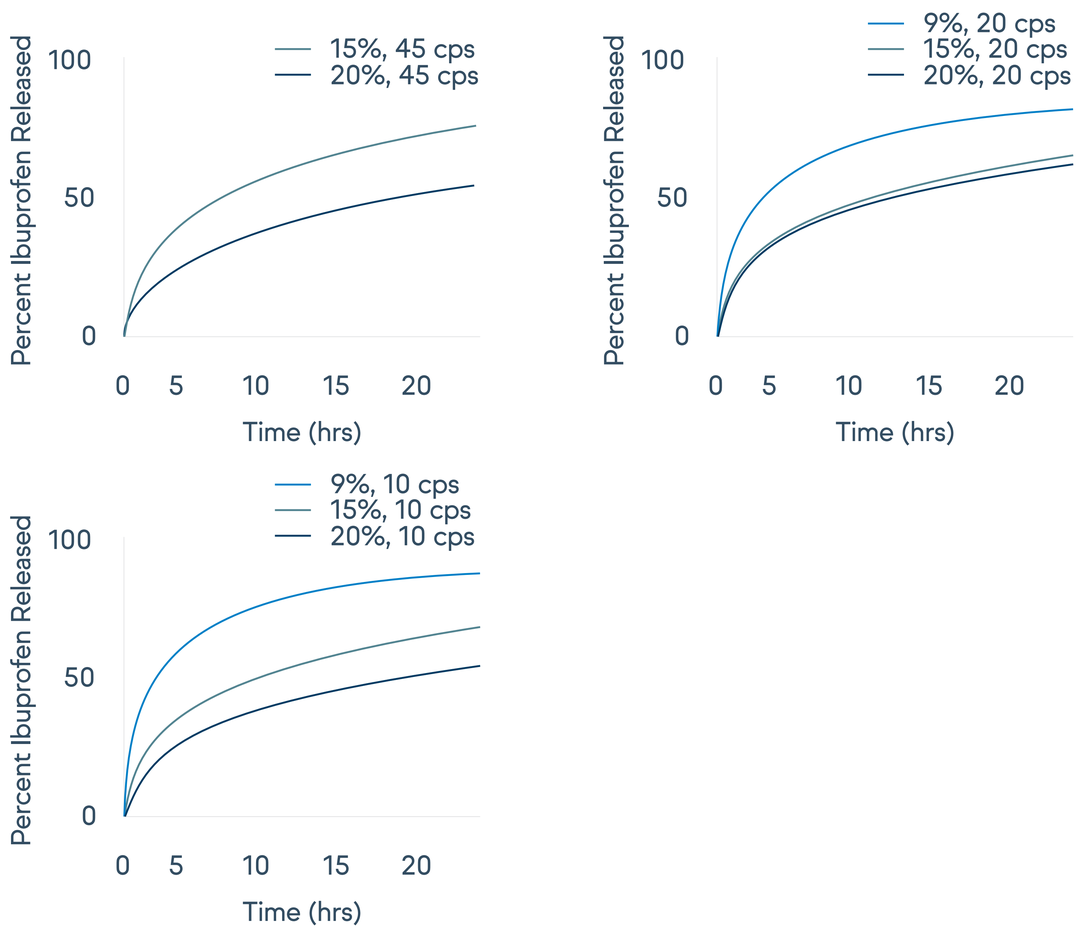
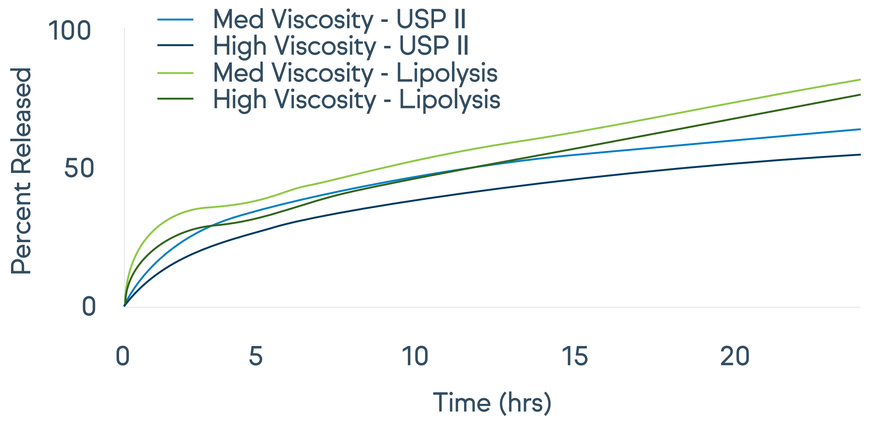



Figure 3 shows the in-vitro lipolysis and standard USP II dissolution data for a medium and high viscosity oleogel. While the in-vitro lipolysis did result in more of a burst effect in the first hour, likely due to surface oil on the oleogel immediately dispersing into the media, the remaining drug was slowly released over the next 23 hours. The gel viscosity was directly correlated to the rate of release in both a standard USP II type apparatus and in an in-vitro lipolysis model.

**Figure 3: Drug dissolution USP II vs. digestive**




## The Conclusion

This work investigated the potential for tuning release properties of a model API from a structured oil carrier. Throughout the study, researchers demonstrated a formulation technique for delivering controlled release of active ingredients that are soluble or dispersible in an oil. By modulating the physical properties of structured oil gels, researchers were able to modify the release of a model API. This gives formulators the opportunity to create novel dosage forms for APIs that are oil soluble or dispersible.

To learn more about IFF's innovation in drug delivery, visit **www.iff.com/portfolio/markets/pharmaceutical**.

References:
1. Larsen, Anne & Sassene, Philip & Müllertz, Anette. (2011). In vitro lipolysis models as a tool for the characterization of oral lipid and surfactant based drug delivery systems. International journal of pharmaceutics. 417. 245-55. 10.1016/j.ijpharm.2011.03.002