

**Lipocine's Lip'ral™-SSR  
Technology Platform for  
Superior Controlled Absorption  
of Poorly Water Soluble Drugs**

# **Limitations of Conventional Controlled Release Technologies for Poorly Soluble Drugs**

**Conventional controlled release technologies do not adequately address**

- precipitation/ solubility/dissolution aspects of the problem with poorly water soluble drugs**
- transport challenges across the aqueous barrier layer**
- effect of physiological factors such as food, pH etc. on drug absorption**

# **Lip'ral™-SSR Technology Platform**

- **Controlled Synchronized Release of Poorly Soluble Drug and Solubilizers**
- **Release Profile can be Customized for Delayed, Pulsatile or Extended Release**
- **Uses Bioacceptable Excipients**
- **Conventional Scale-up and Manufacturing Processes**
- **Protected by several issued and pending patents, world-wide**

# CASE STUDY 1

## Model Compound **LPCN 1010**

- **High solubility in gastric pH, very low solubility in intestinal pH**
- **Need for delayed absorption to minimize side effect associated with rapid initial absorption**

**Marketed product must be taken with food to delay absorption and minimize side effect**

# Lip'ral™ SSR Objectives

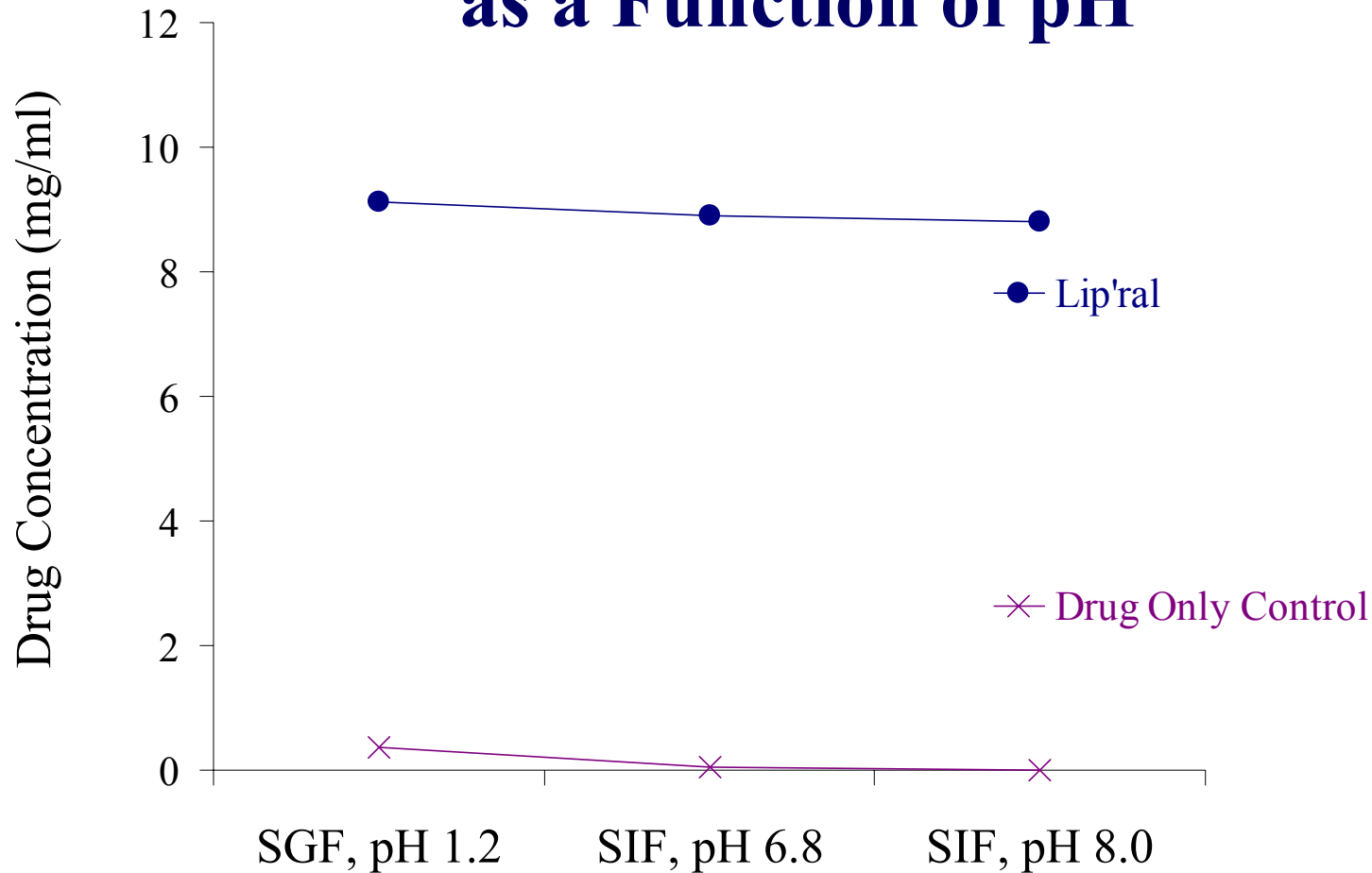
- **pH independent solubilization of LPCN 1010**
- **delayed release of LPCN 1010**

**leading to**

**→Improved bioavailability**

**→Delayed release leading to potentially reduced side effect profile**

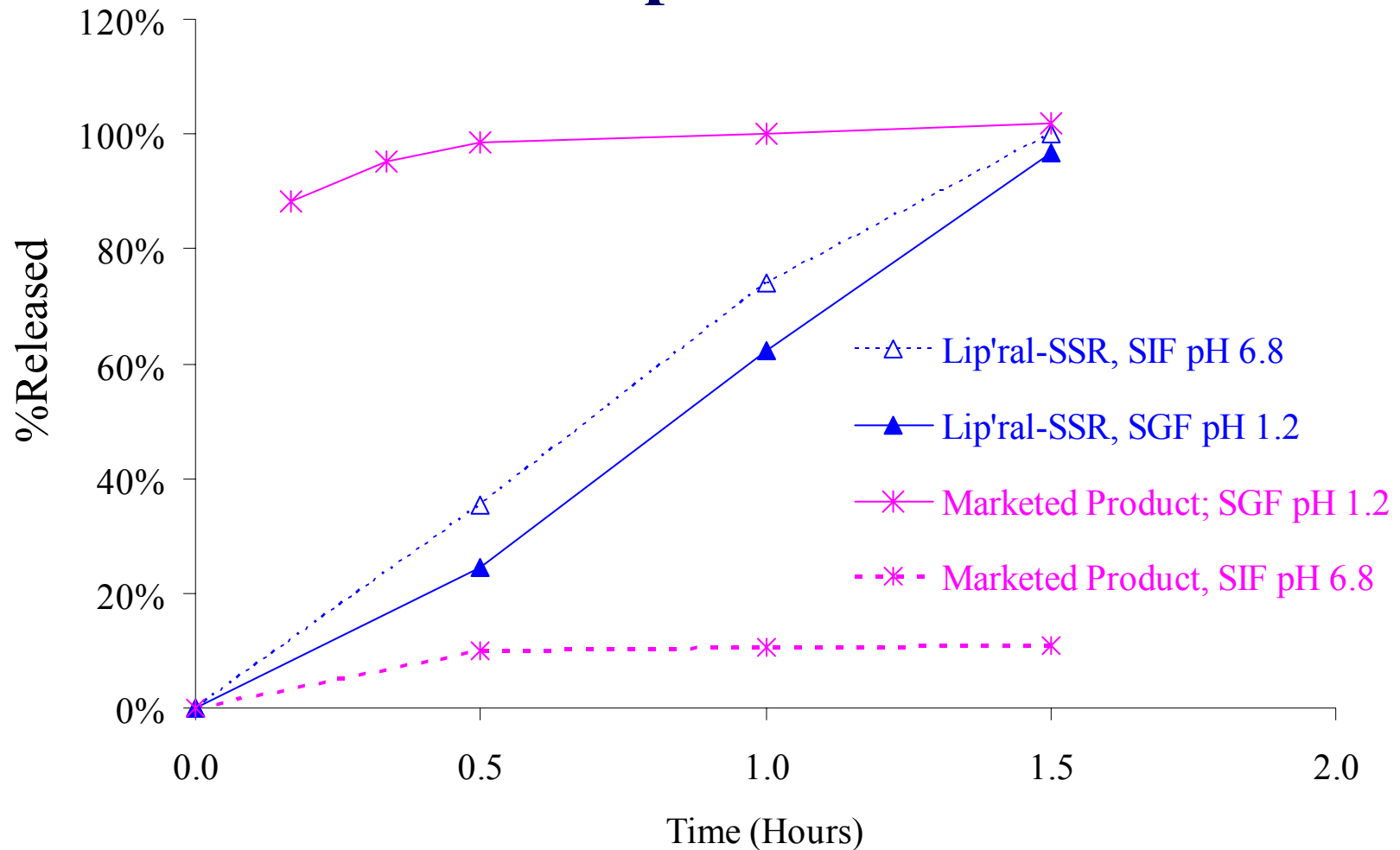
# LPCN 1010 Solubilization as a Function of pH



*Dramatic solubility increase with  
Lip'ral™*



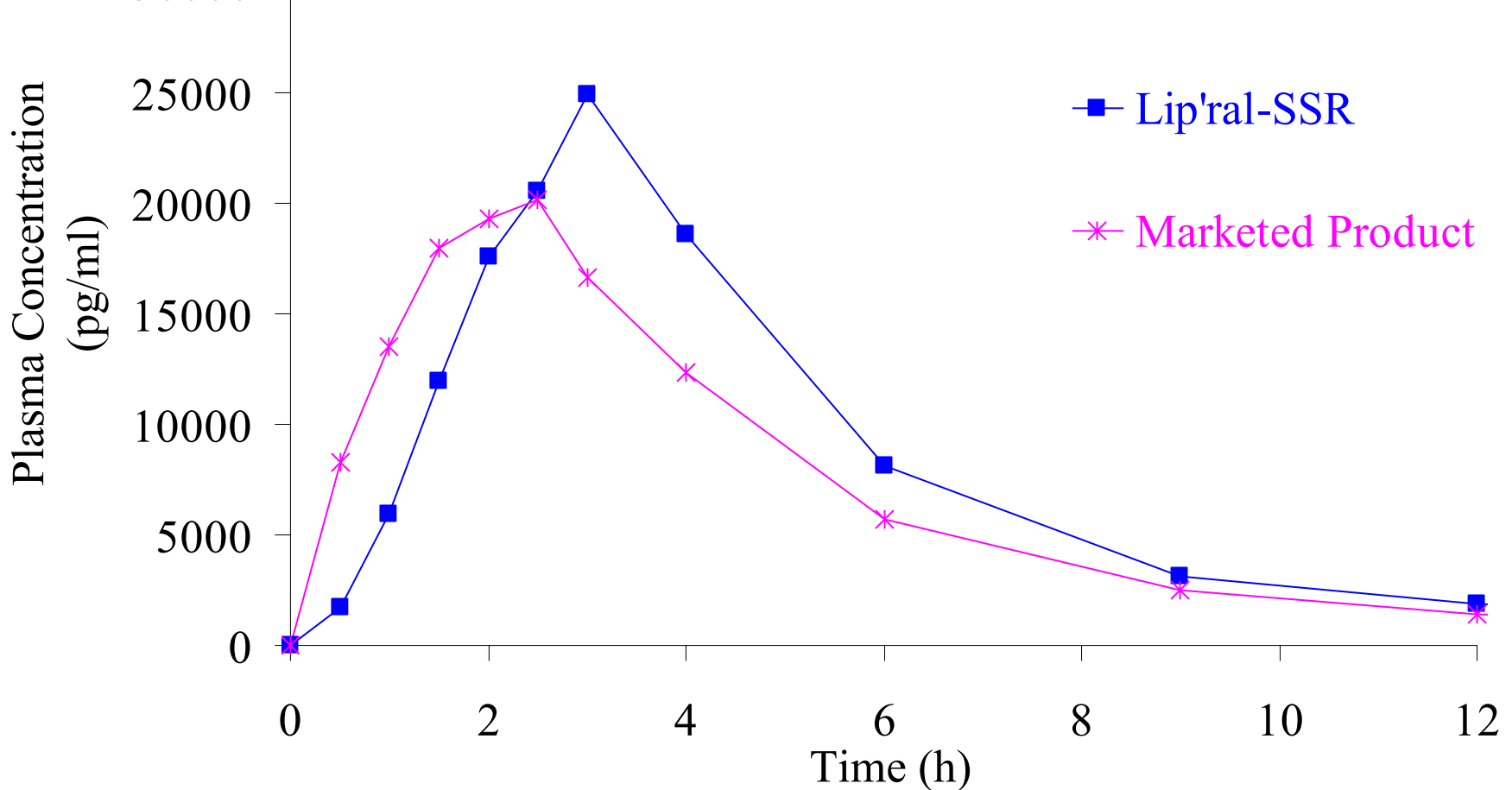
# pH Independent LPCN 1010 Release from Lip'ral™-SSR



*pH independent release with  
Lip'ral™-SSR*

# Plasma Concentration Profile for Lip'ral™-SSR and Marketed Product

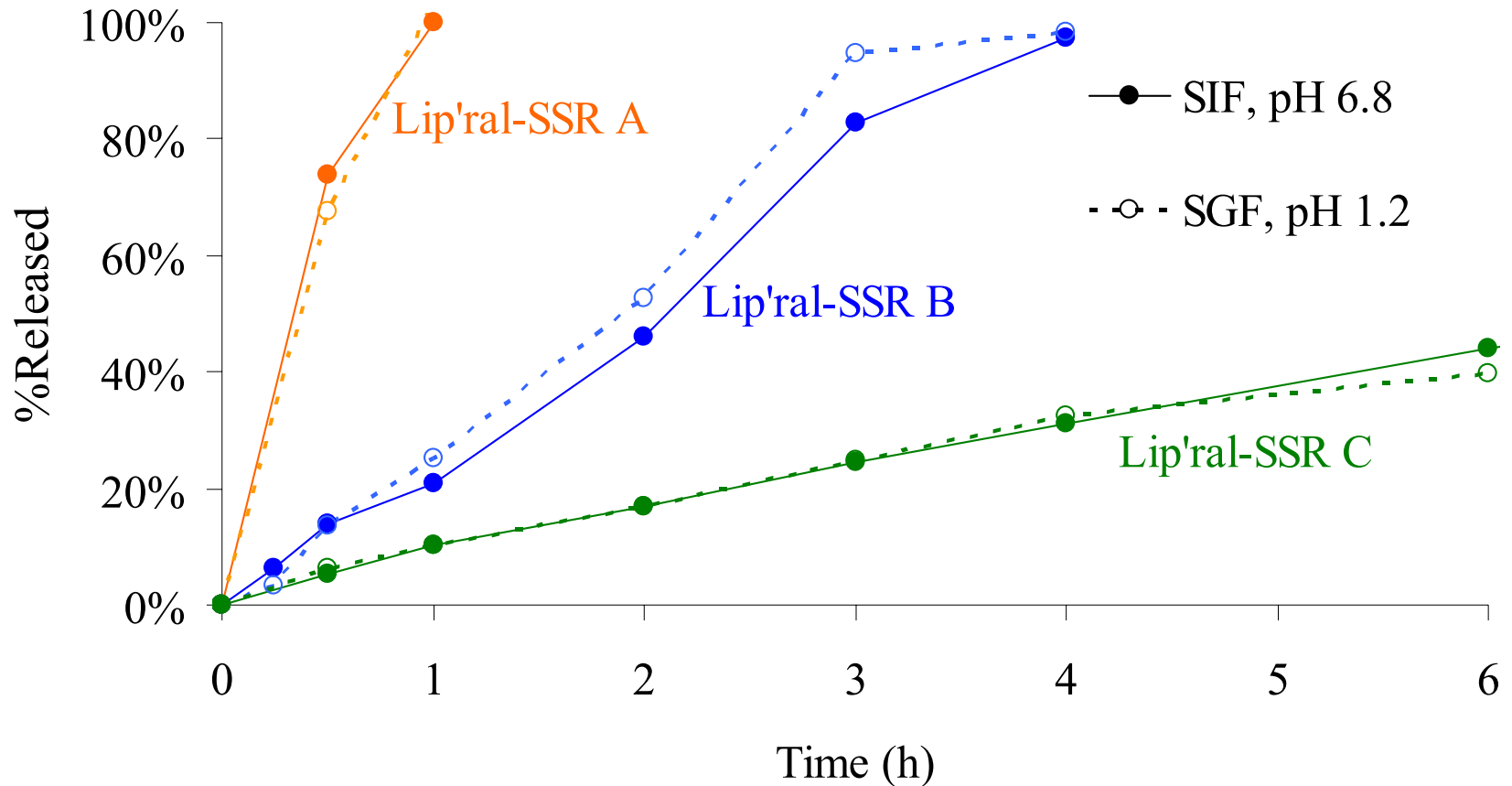
Protocol 1010-02-001, n=9 healthy volunteers



*Absorption rate delayed relative to marketed product with Lip'ral™-SSR*



# Release Profile of LPCN 1010 as a Function of Lip'ral™-SSR Formulation Composition

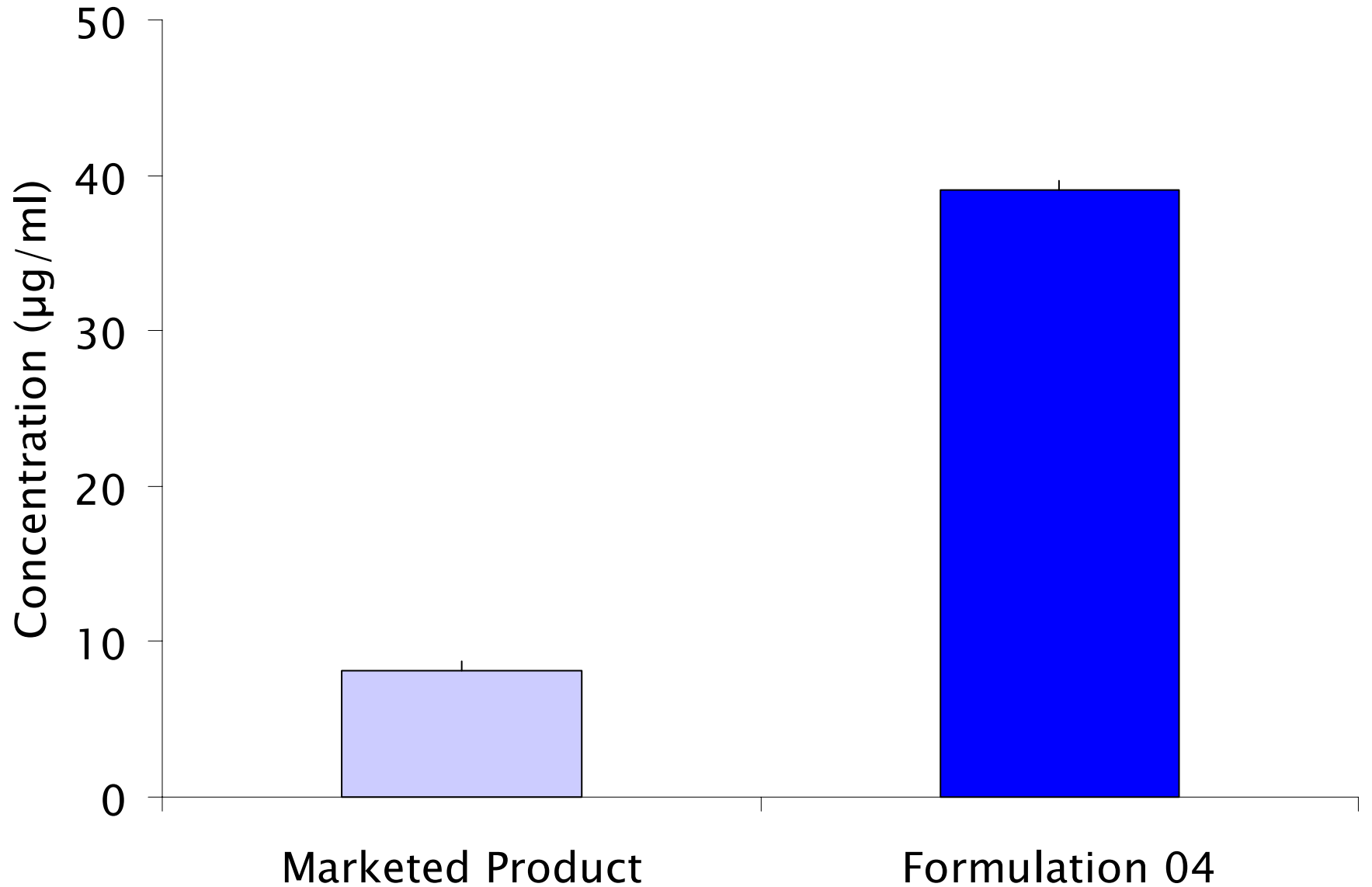


# CASE STUDY 2

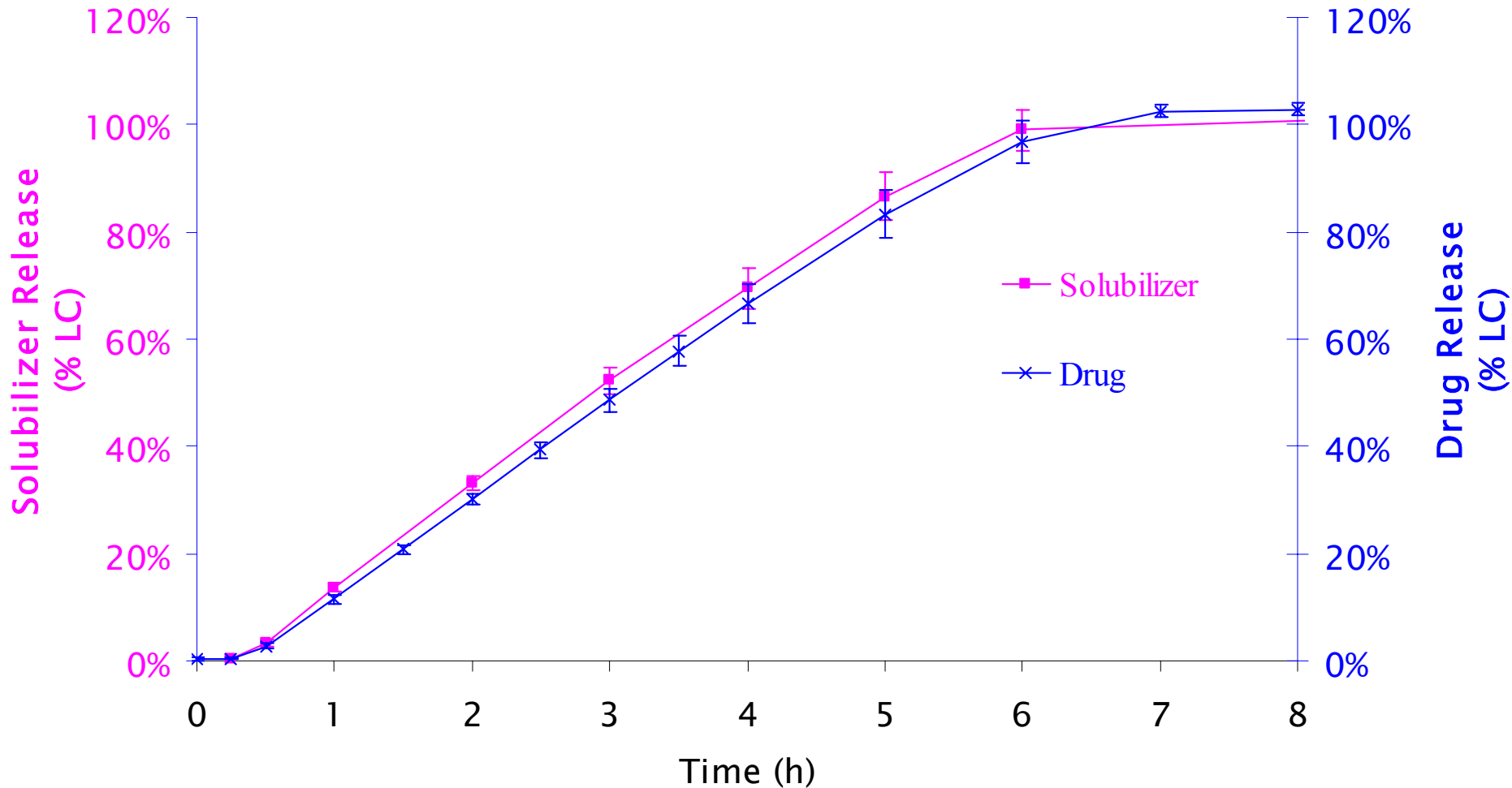
## Model Compound LPCN 1012

- **Improved solubilization of model compound**
- **Sustained synchronized release of drug and solubilizer leading to**
  - **Improved bioavailability**
  - **Once-a-day dosing**

# In Vitro Solubilization

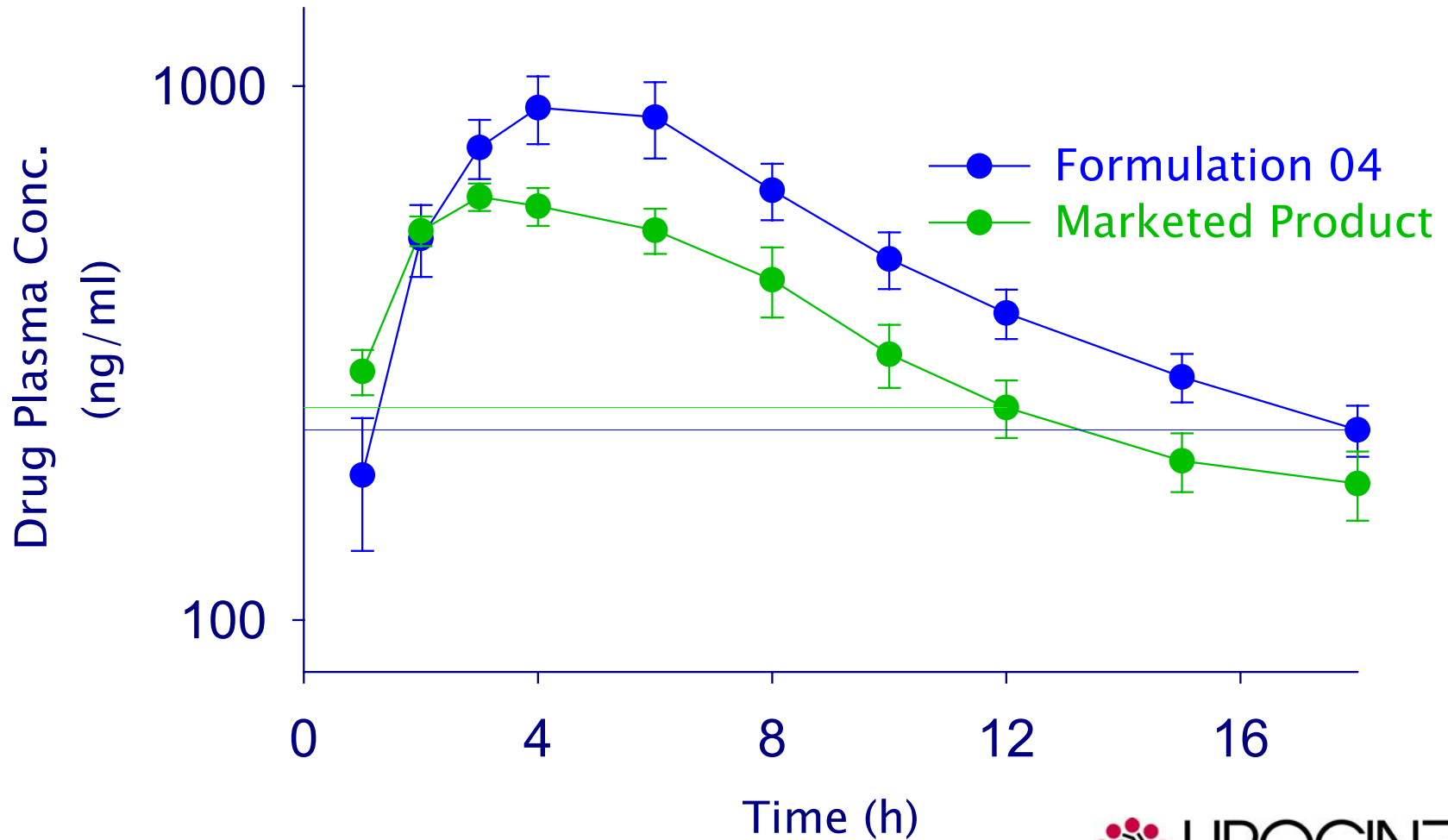


# Synchronized Solubilizer and Drug Release with Formulation 04

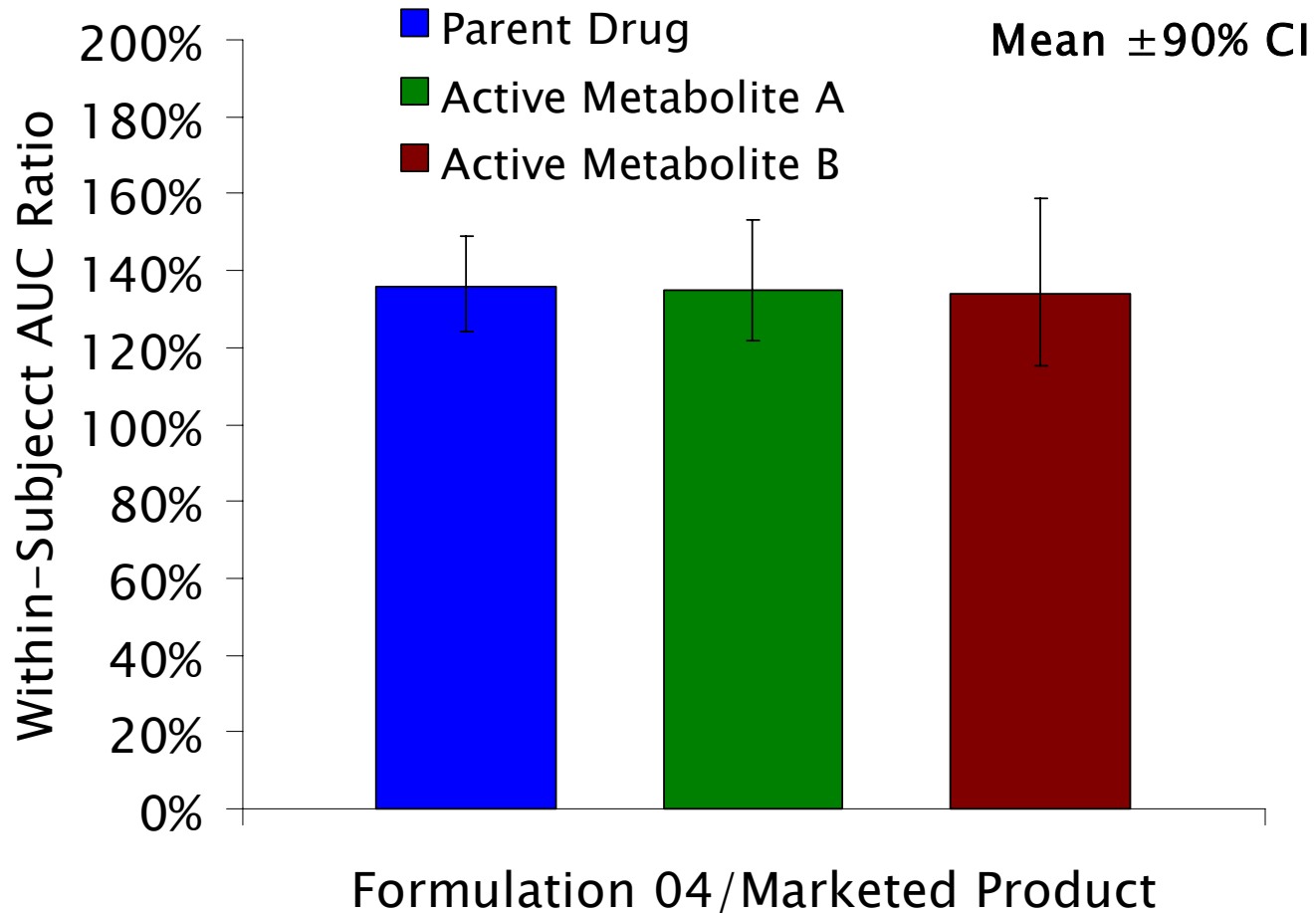


# Improved in Bioavailability with Sustained Release

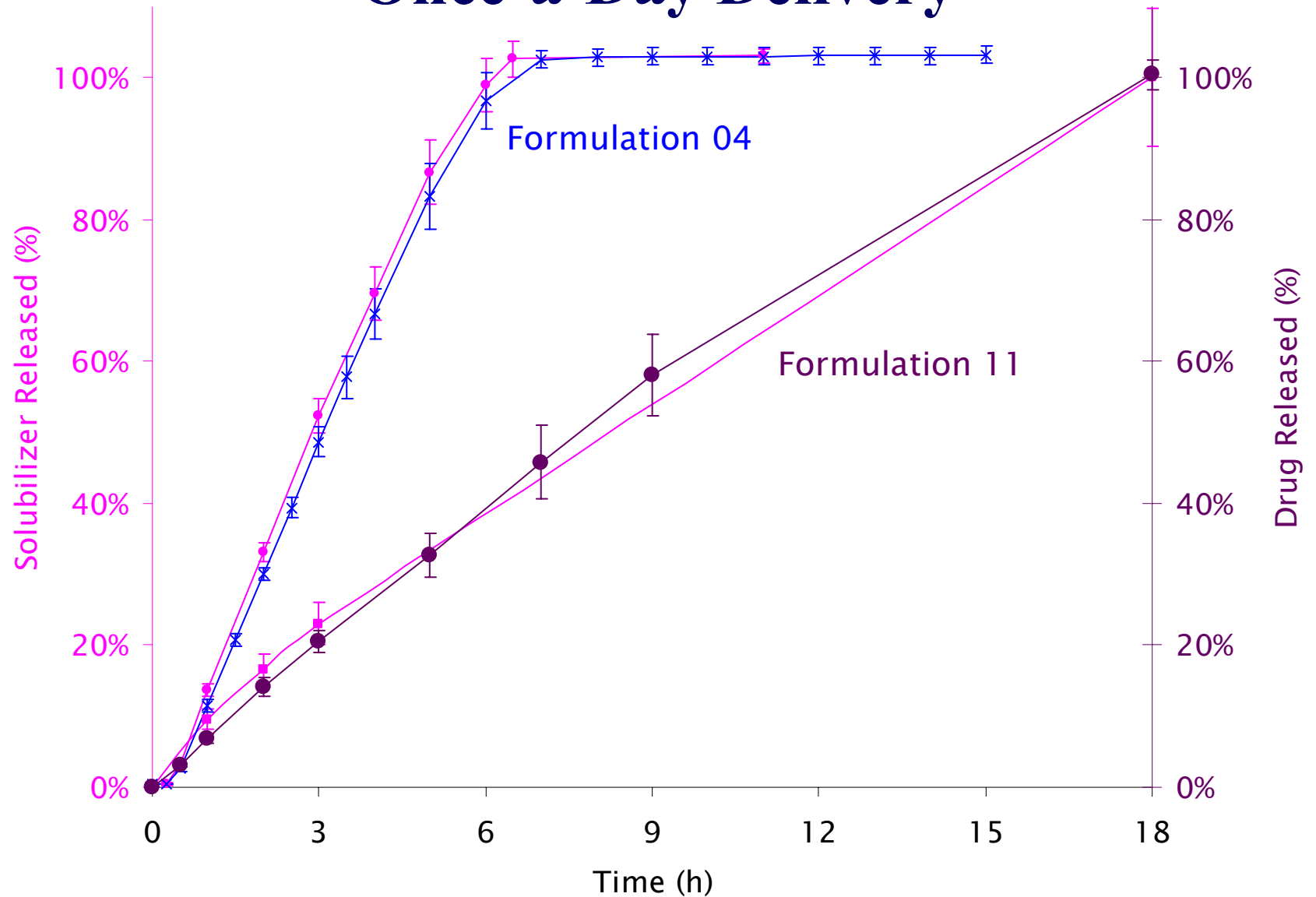
Protocol 1012-03-001, n=11 healthy volunteers



# Improved Bioavailability without Affecting Metabolism

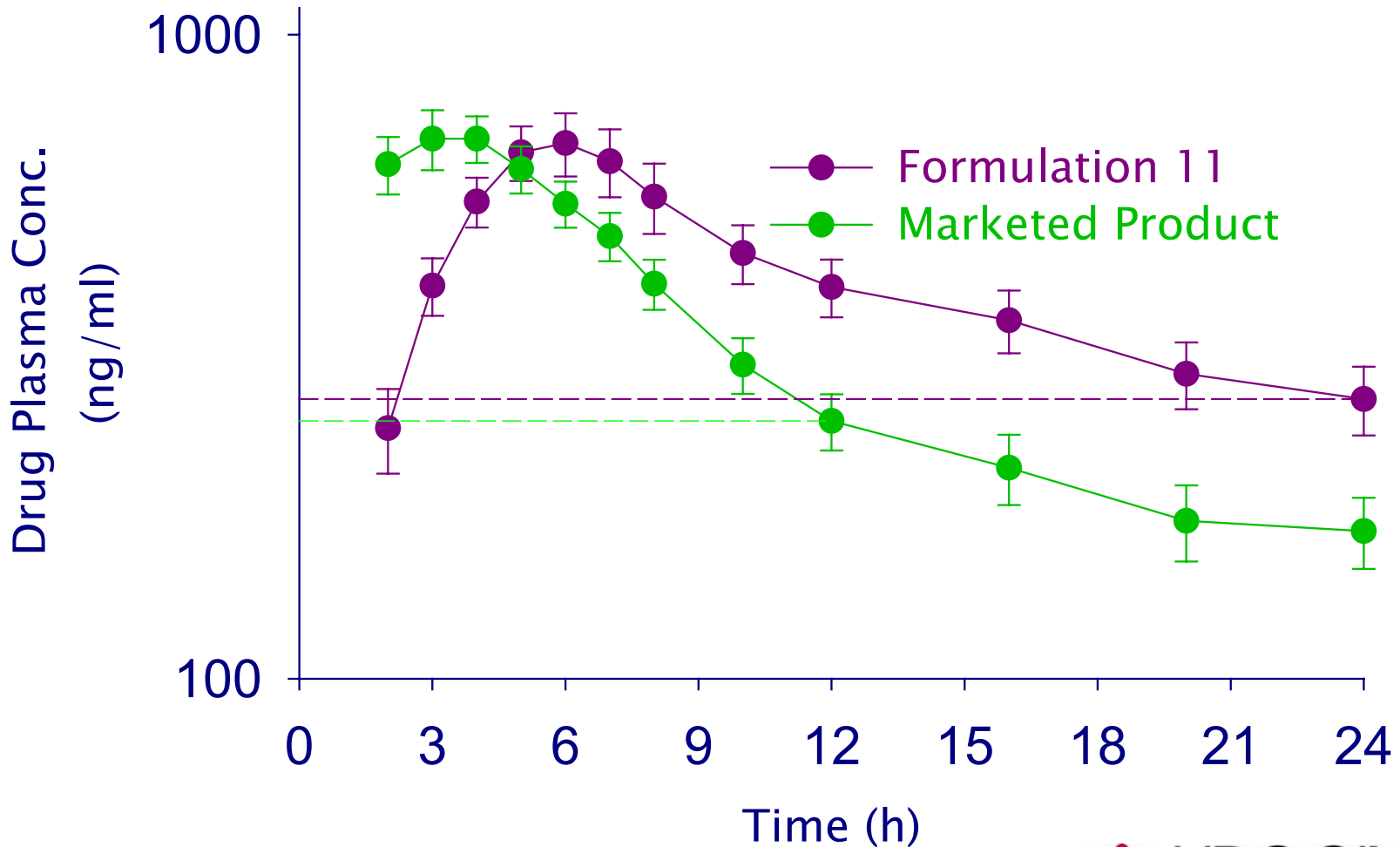


# Lip'ral™-SSR Release Profile Modified for Once-a-Day Delivery

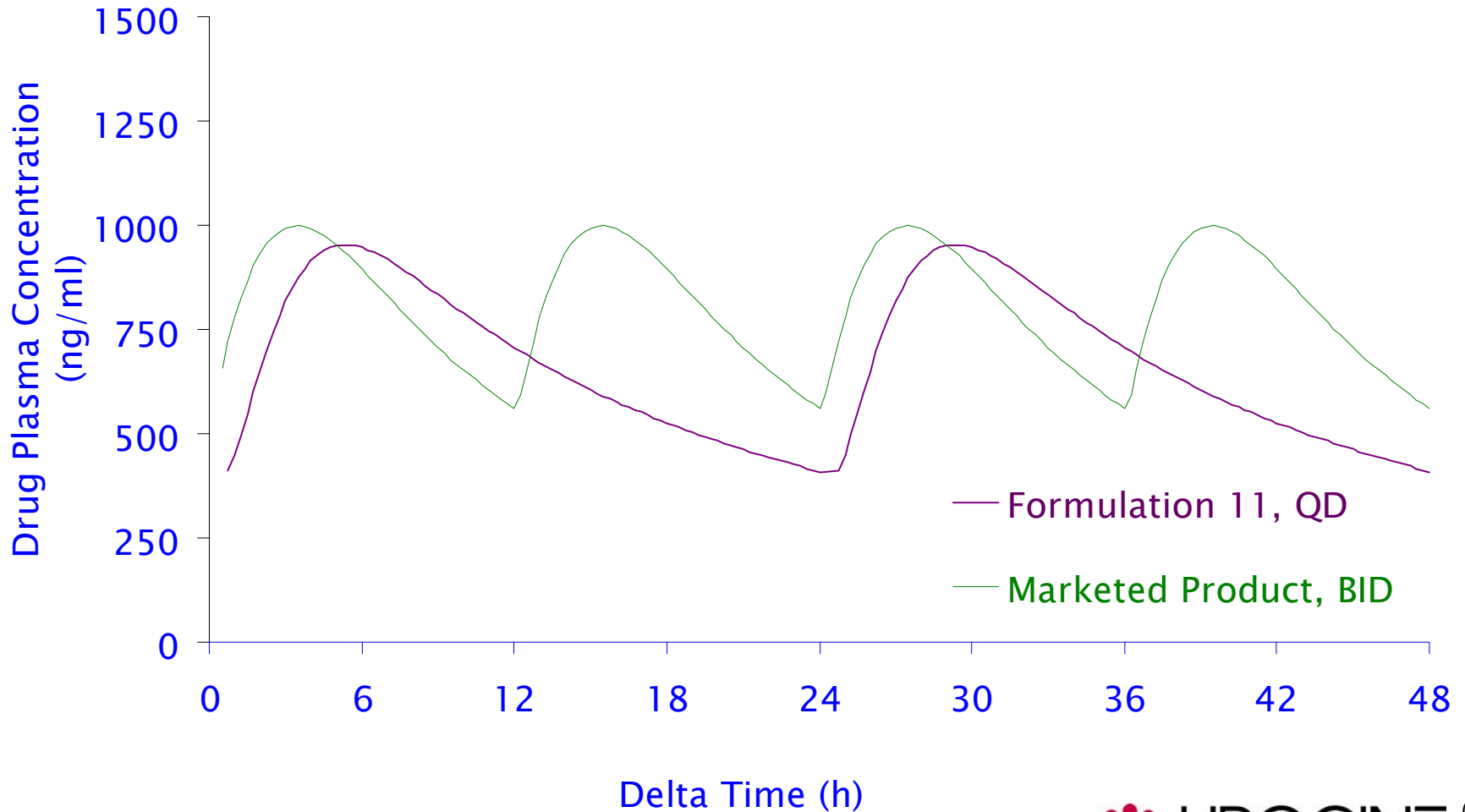


# Once-a-Day Dosing with Lip'ral™-SSR

Protocol 1012-05-001, n=15 healthy volunteers



# Projected Steady State Plasma Concentrations



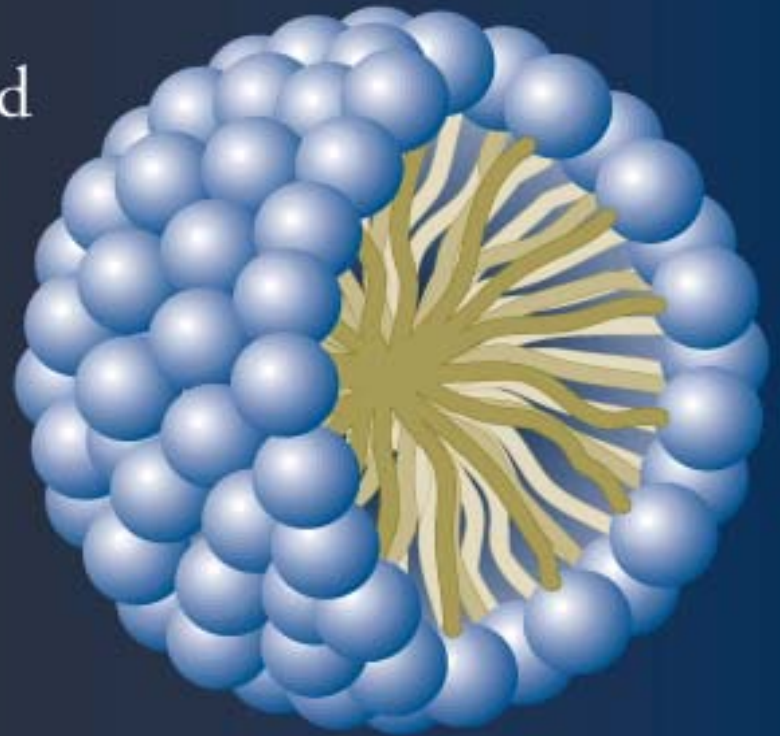
# Lip'ral™-SSR Uniqueness

- **Improved bioavailability with sustained absorption for poorly water soluble drugs**
- **Versatility – ability to readily modulate release profiles**
- **Particularly suited for drugs with poor solubility at intestinal pH**

# Lip'ral™ SSR Technology Benefits

---

- Increased Bioavailability
- Adaptable for Faster Onset and Extended or Pulsatile Release
- Refractory To Food Effects
- pH Independent Drug Solubilization
- More Consistent Product Performance



# Uniqueness of Lipocine Technology

- **Very Strong Proprietary Position**
  - **Technology Platform Patents**
  - **Product Specific Patents**
  - **Additional Firewall Patents**
- **Breakthrough Technologies**
  - **Clinically Validated**
  - **Superior to Competing Technologies**
  - **Conventional Manufacturing Techniques**
  - **“Bioacceptable” Excipients**

# What Lipocine Can Do For You

- **Develop Proprietary Products with Improved Safety/Efficacy/Compliance**
- **Enable Product/Brand Life Cycle Management Beyond Compound Patent**
- **Discovery/Development Support for NCE –Identify “Winners” and Shelve “Losers”**