

# Lipid-Based Formulation in Customized Enteric Capsule for Oral GLP-1 Receptor Agonist Peptide Delivery\*

(Dumont C, Gonzalez V, Picco S, et al. Eur Conf Pharmacol 2025:Abstract [poster])

\*Dr Vincent Jannin, Director of R&D and Head of Innovaform® Accelerator at Colmar, France, is a co-author of this briefing paper



# Objectives of this study

Multiple factors affect oral delivery of therapeutic peptides such as acidic and enzymatic degradation in the upper gastrointestinal tract and poor intestinal permeability.

Several studies report the benefit of lipid-based formulations (LBF) combined with the formation of hydrophobic ion pairs (HIP) to enhance oral bioavailability of peptides. Therefore, the objectives of this study were to:

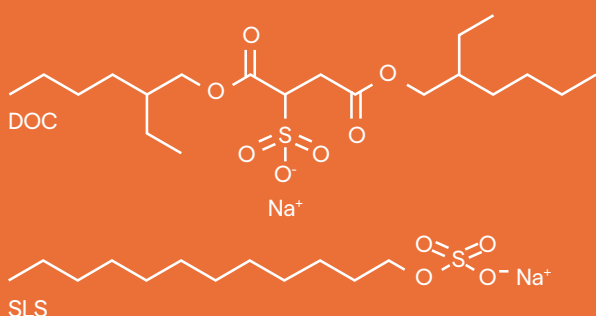
- Develop an LBF of glucagon-like peptide-1 (GLP-1) receptor agonist, exenatide (EXE)
- Manufacture an enteric capsule compatible with EXE formulation
- Demonstrate innovative capacities of formulation and customized functional capsules

## Methodology of the study

### EXE HIP formation and characterization

#### EXE HIP formation & characterization

Ability of sodium lauryl sulfate (SLS) and sodium docusate (DOC) to form HIPs with EXE was evaluated by measuring unprecipitated EXE using HPLC.



#### Customized enteric capsule manufacturing and characterization

Customized size #0 gelatin/HPMC-AS double layer capsules were manufactured using patent pending technology.

The ability of the capsule to protect sensitive APIs from gastric acid and protease degradation were evaluated by:

- **dissolution** using uncoated, acid-sensitive esomeprazole pellets in unsealed capsules
- **disintegration** with lactose-filled capsules using the Ph. Eur. method for gastro-resistant capsules

#### Formulation development

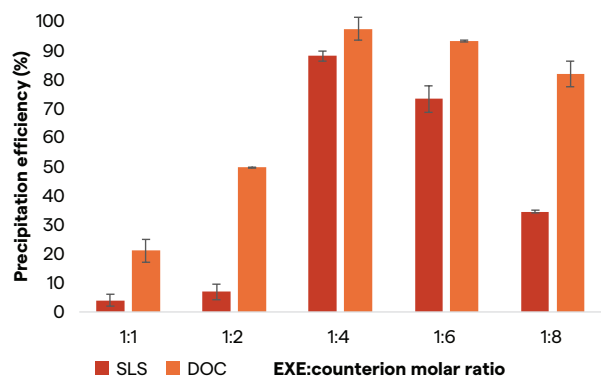
Solubility of EXE and EXE:DOC HIP in several lipid excipients, including oils, surfactants and solvents, was measured by HPLC. The best solvents for native EXE and HIP were selected after ensuring homogeneity at room temperature and upon dispersion in purified water at 37°C. LBF was selected to protect from protease-induced degradation, and permeation enhancer (sodium caprate) was included to boost absorption.

#### Filled capsule enteric properties

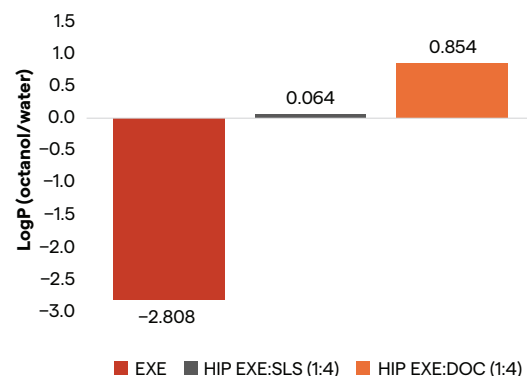
Retention of enteric properties of size #0 gelatin/HPMC-AS capsules filled with EXE-loaded LBFs was evaluated using Apparatus B disintegration test: filled capsules placed in 0.1N HCl for 1 hour, followed by 1 hour in buffer pH 6.8.

# Results

## EXE HIP formation and characterization



Precipitation efficiency of EXE:counterion molar ratio



LogP measurements

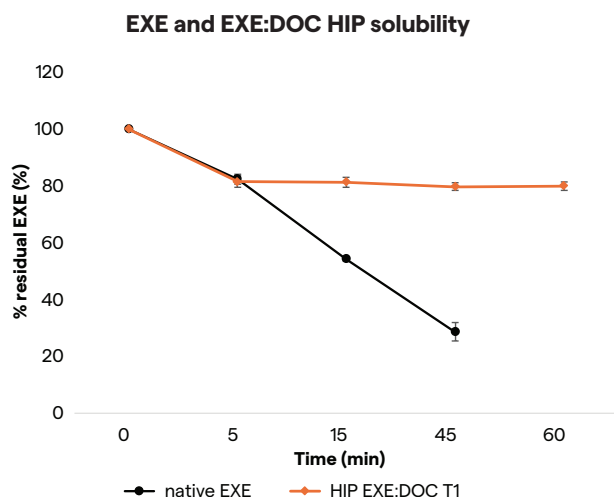
- The highest measured precipitation efficiency was for the molar ratio 1:4 (EXE:DOC)—an expected result, given that EXE exhibits 4 cationic function in an acid medium, and each pairing with one anionic function of the selected counter ion
- This ratio was selected for assessing LBF development
- LogP measurement show higher lipophilicity increase with DOC as counter ion

| Type        | Commercial name   | Solubility (mg/g) |          |
|-------------|-------------------|-------------------|----------|
|             |                   | EXE.              | DOC. HIP |
| Oils        | Maisine® CC       | <LOQ              | 0.03     |
|             | Soybean oil       | <LOD              | <LOD     |
| Surfactants | Capryol® 90       | <LOD              | 0.02     |
|             | Labrafac™ MC60    | <LOQ              | 9.54     |
|             | Lauroglycol™ 90   | <LOD              | <LOD     |
|             | Labrafil® M1944CS | 0.7               | <LOD     |
|             | Labrasol®         | <LOD              | 5.47     |
|             | Kolliphor® ELP    | <LOD              | <LOD     |
|             | Tween® 20         | <LOD              | 0.06     |
|             | Tween® 80         | <LOD              | <LOD     |
| Solvents    | PEG 400           | <LOD              | 2.28     |
|             | Propylene glycol  | 9.9               | 9.04     |
|             | Glycerin          | 5.2               | 0.89     |

LOD: limit of detection; LOQ: limit of quantification.

- Labrafac®MC60 and propylene glycol were selected as the best solvents
- A homogeneous formulation with small particle size upon dispersion was selected to favor intestinal absorption

| Formulation prototype (T1)                |                |
|-------------------------------------------|----------------|
| Labrafac® MC60                            | 85%            |
| Kolliphor® RH40                           | 10%            |
| Propylene glycol                          | 5%             |
| Particle size measurements in water, 37°C |                |
| Dilution                                  | Z-average (nm) |
| 1:1000                                    | 104            |
| Solubility evaluation                     |                |
| EXE                                       | 0.3 mg/g       |
| HIP EXE:DOC (1:4)                         | 7.8 mg/g       |
| Sodium caprate                            | 20 mg/mL       |



EXE degradation profile

### Formulation characteristics

The LBF prototype was defined as:

- 85% Labrafac®MC60 (glycerol monocaprylocaprate)
- 10% Kolliphor®RH40 (Polyoxyl 40 castor oil)
- 5% propylene glycol
- 6 mg/mL EXE (in native form or HIP)
- 20 mg/mL sodium caprate

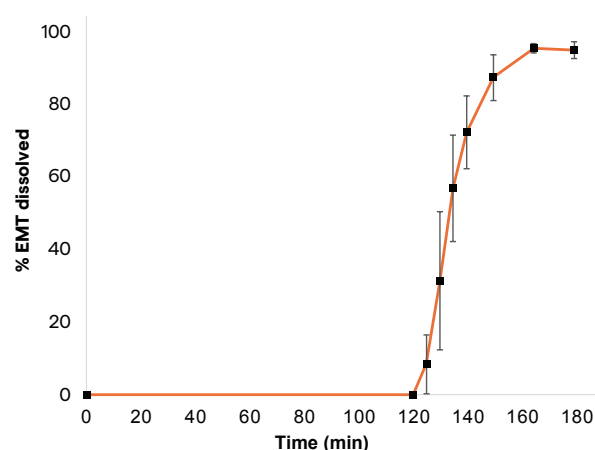
The presence of LBF protected EXE from  $\alpha$ -chymotrypsin-induced proteolysis

- There was rapid degradation of EXE in the presence of chymotrypsin
- The designed LBF provided a protective effect

# Customized enteric capsule manufacturing and characterization



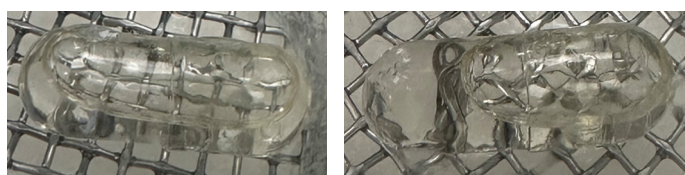
Customized size #0 capsule



EMT release profile (2 hrs in HCl 0.1N + 1 hr pH 6.8, N=6)

- The EMT dissolution test confirmed the capsule's enteric properties
- No release of encapsulated EMT in acid milieu, followed by rapid and complete EMT release at pH 6.8

## Filled capsule enteric properties



Customized size #0 gelatin/HPMC-AS double-dipped capsules filled with EXE:DOC HIP showed:

- No dissolution and retention of enteric properties after 1 hour in HCl 0.1N
- Disintegration within 5 minutes at pH 6.8

## Conclusion

This study proposes an innovative and scalable solution to increase oral bioavailability of therapeutic peptides using a combination of lipid-based formulations, hydrophobic ion pairing, permeation enhancer and customized enteric capsules.

The results highlight the capacity to support formulation development, and manufacture a functional capsule that is compatible with fill formulation.

This offers biopharmaceutical companies a novel way to maximize the effectiveness of their therapeutic peptide. If you would like to discuss how we can support you with your drug development journey, please speak with our scientists at Innovaform® Accelerator.



**To learn more,  
scan the QR code  
to see the full  
scientific poster**

### Abbreviations:

**DOC:** docusate; **EMT:** esomeprazole magnesium trihydrate; **EXE:** exenatide; **GLP-1:** glucagon-like peptide-1;  
**HCl:** hydrochloric acid; **HIP:** hydrophobic ion pairs;  
**HPLC:** high-performance liquid chromatography;  
**HPMC-AS:** hydroxypropyl methylcellulose ("hypromellose") acetate succinate; **LBF:** lipid-based formulation;  
**LOD:** limit of detection; **LOQ:** limit of quantification;  
**PDI:** polydispersity index; **SLS:** sodium lauryl sulfate.

The information contained herein is intended for general marketing purposes only. While Capsugel makes efforts to include accurate and up-to-date information, it makes no representations or warranties, expressed or implied, as to the accuracy or completeness of the information provided herein and disclaims any liability for the use of this publication. All access to and use of the information contained herein are at the user's own risk. Capsugel may change the content of this publication at any time without notice but does not assume any responsibility to update it. All trademarks belong to Capsugel and are registered in Switzerland, the EU and/or the USA, or belong to their respective third-party owners and are used for informational purposes only.

© 2026 Capsugel. All rights reserved. Capsugel Edition No. 08-2026.

CHI-M26-028-A