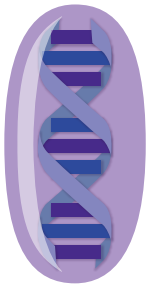
Catalent
rp scherer softgel



CASE STUDY
OptiGel Bio™ Technology Enables IV to Oral Therapy Conversion

Executive Summary

An early-stage biotechnology company had developed a novel macromolecular intravenous (IV) therapy for an anti-thrombolytic post-surgical indication. While the therapy had shown complete absorption via IV, the dose form was not ideal due to a number of factors including manufacturing costs, compliance, and ease of use, as well as as well as the long term treatment requirements. This case study demonstrates how Catalent OptiGel Bio™ technology can provide a pathway for an IV to oral delivery conversion, resulting in enhanced therapies for patients.

The Challenges

Though soluble, the macromolecule presented a number of permeability challenges, which hindered delivery of an active therapeutic dose across the lumen of the small intestine to achieve the desired therapeutic effect.

PHYSIOCHEMICAL PROPERTIES	High molecular weight (>2500 Da) Strong negative charge* Rigid, inflexible geometry*
TARGETED DELIVERY	Functional API must be delivered to the small intestine in order to achieve bioavailability
PERMEABILITY	Mucus layer physical barrier Random and limited transcellular pathways "Fence and gate" function of tight junctions
PHARMACOKINETIC PROFILE	Oral delivery must reach exposure within therapeutic range

*Salamat-Miller N et al. , Pharmaceutical Research, 2005, 22(2):245-254

By incorporating OptiGel Bio™ technology and our formulation expertise, an optimized oral therapy was developed combining permeation enhancement and targeted delivery.

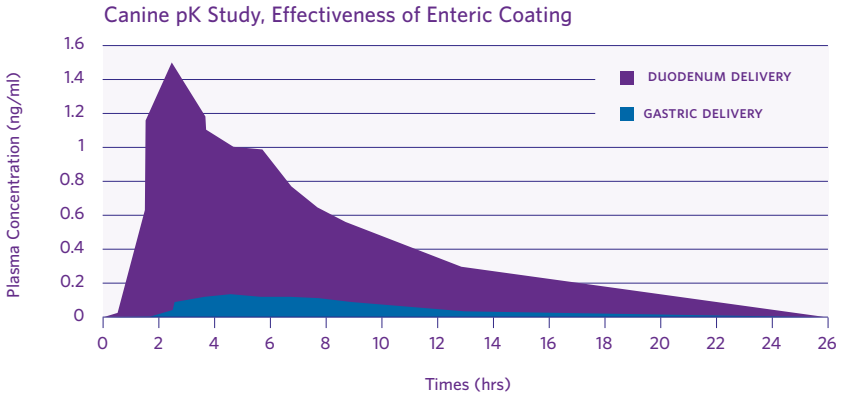
The Catalent Solution

ENHANCED PERMEABILITY The first challenge to overcome in development was enhancing the permeability of the macromolecule. A stepwise screening approach utilizing both *in vitro* and *in vivo* models yielded lead formulation candidates for further evaluation.

Stage	Process	Results
Digestion	In vitro screen in simulated digestion media	Formulations varied in concentration of solvents, surfactants lipids, etc.
Bioavailability / Permeability	Intra duodenum rodent screen at absorption site	Formulations with higher levels of lipid digestion products showed enhanced permeability
Pharmacokinetics	Lead candidates evaluated in oral canine pK study	Lead candidates showed high, but variable, bioavailability

TARGETED DELIVERY Despite the improvements in bioavailability, the pharmacokinetic variability highlighted the need for a targeted delivery utlizing an enteric coating.

Stage	Process	Results
Enteric Coating	Screening of capsules and coating formulation, varying the percentage of coating, plasticizer and solvent	Lead formulation chosen; coated softgel and confirmed homogeneity with scanning electron microscope (SEM)
Disintegration Test	Followed European Pharmacopoeia	Formulations met EP specifications
Imaging / Pharmacokinetic Profile	Iodine tagged capsules orally dosed and imaged with pK samples (canine model)	Enteric coated capsule batches delivered active to small intestine; reduced variability and enhanced bioavailability



Conclusion

Using OptiGel Bio™ technology, we overcame the challenges traditionally associated with the oral delivery of macromolecules and enabled conversion from an IV to a more efficient, more convenient and less invasive oral dose form while maintaining an effective pK profile. Through a multi-step drug delivery screening process and our OptiGel Bio™ technology, we can enable enhanced therapies—resulting in better treatments and more value for innovators, healthcare professionals and patients.

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