



Design For Peptide DeliverySM

Applying rational design to extend peptide release

Identify the optimal lead peptide candidate for extended release formulations while reducing development time and costs.

Lead Drug Candidate Selection ~

Lead drug candidates are conventionally selected based on bioavailability and potency. Thus, formulation options are limited and viable candidates for extended release are excluded. Design for Peptide DeliverySM addresses this limitation. By understanding the critical parameters that impact extended release, D4PD allows for the rational selection of the optimal peptide candidate.

The chemical and physical properties of the peptide, coupled with the properties of the matrix, impact the final formulation. Therefore, each of these factors must be considered when developing the dosage form.

Polymeric Delivery Systems ~

Drug parameters affecting release from a polymeric matrix (such as microparticles and implants) are described as follows:

Peptide Physical Properties:

particle size
bulk density
crystallinity

+

Peptide Chemical Properties:

salt form
conjugated ligand
amino acid modification

+

Matrix Properties:

polymer
end group
molecular weight



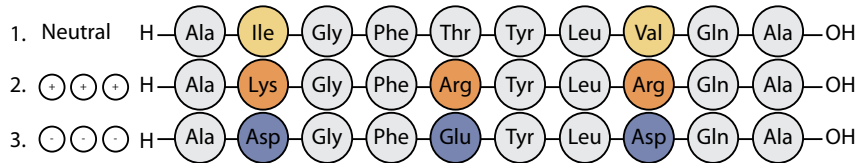
Extended Release Properties:

stability
release kinetics
loading efficiency

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Proof of Principle

Three model peptides incorporating slight modification of the amino acid sequence were synthesized as shown in the graphic below:

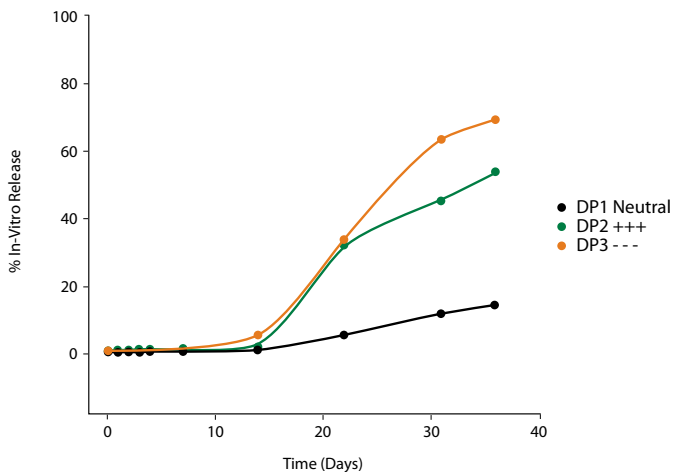


- All are acetate salts
- All peptides isolated by the same technique
- No additional additives

These peptides were subsequently formulated into extended release formulations by encapsulating them into poly(lactide-co-glycolide) microparticles using a well understood process. The resultant microparticles were analyzed to determine in vitro release and encapsulation efficiency (Case 1 & Case 2).

Case 1

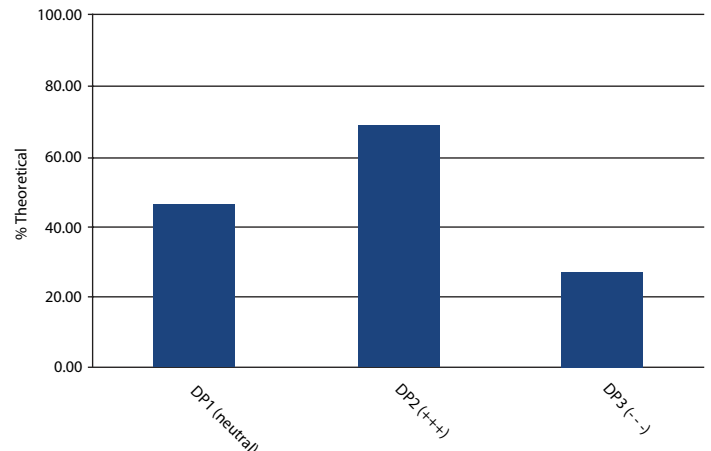
A change in the charge density has a significant effect on the release of the API from the matrix.



Conclusion: A peptide with a net charge releases faster from this polymer matrix poly(lactide-co-glycolide) than a comparable neutral peptide.

Case 2

A change in the charge density has effect on encapsulation efficiency in the matrix.



Conclusion: A peptide with a net positive charge encapsulates more easily than one with a net neutral or negative charge.