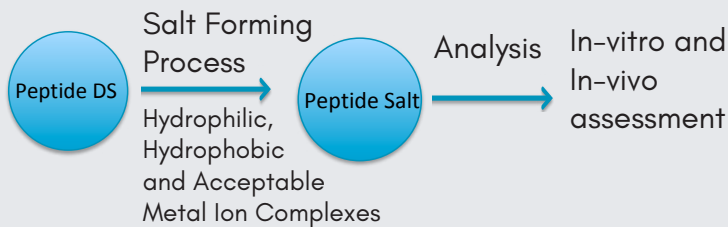


# PEPTIDE SALT SCREENING: Characterization and Selection

## Peptide Salt Selection:

*Rational and Case Study*

- Peptide salts were selected to alter the dissolution profile of the target molecule
- Salts improve bioavailability, stability, manufacturability, and patient compliance
- Peptide counter ions significantly affect the pharmaceutical properties of a drug for small molecules, peptides and proteins



PEPTIDE 1	PEPTIDE 2	PEPTIDE 3
Cyclic Structure	Cyclic Structure	Linear Structure
12 Amino Acids (MW~3k)	8 Amino Acids (MW~1k)	10 Amino Acids (MW~1k)
5 Acidic Residues 1 Basic Residue	1 Basic Residue Unnatural Linkers	1 Basic Residue Unnatural Amino Acids
High Aq. Solubility	Low Aq. Solubility	Low Aq. Solubility

## Salt Screening and Selection

*Partial list of acceptable counter ions used in salt selection*

CHARGED AND HYDROPHILIC COUNTERIONS	HYDROPHOBIC COUNTERIONS	SALTS OF ACIDIC DRUGS	OTHERS
Glutamic acid	Deoxycholic acid	Mono and di-valent metal ions	Chloride
Glycine	Oleic acid		Bromide
Lysine	Stearic acid	Tromethamine	Sulphate
Citric acid	Nicotinic acid		Carbonate
Succinic acid	Palmitic acid		Mesylate
Tartaric acid	Octanoic acid		Phosphate
Maleic acid	Caproic acid		

## Salt Selection Flow Chart:

*Salt Suspension Formulation Development*

### Salt Synthesis

- Feasibility Synthesis
- Analytical
- RP-HPLC, SEC, DLS, Particle Size, In-Vitro Dissolution



### Salt Process

- Optimize Process
- Control Particle Size
- Solubility Screening



### Suspension Formulation Vehicle Selection

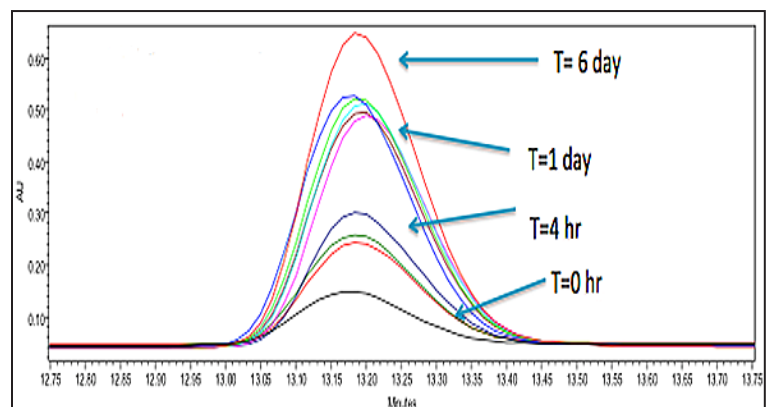
- Buffer, pH Selection
- Excipients: Tonicity, Suspending Agents, Aggregation Suppressors, Salt Solubility Screening
- Salt Suspension Stability Screening
- Device, Needle Size Control



### Animal Study

- Injection Site Reaction Study
- PK
- PD (efficacy)

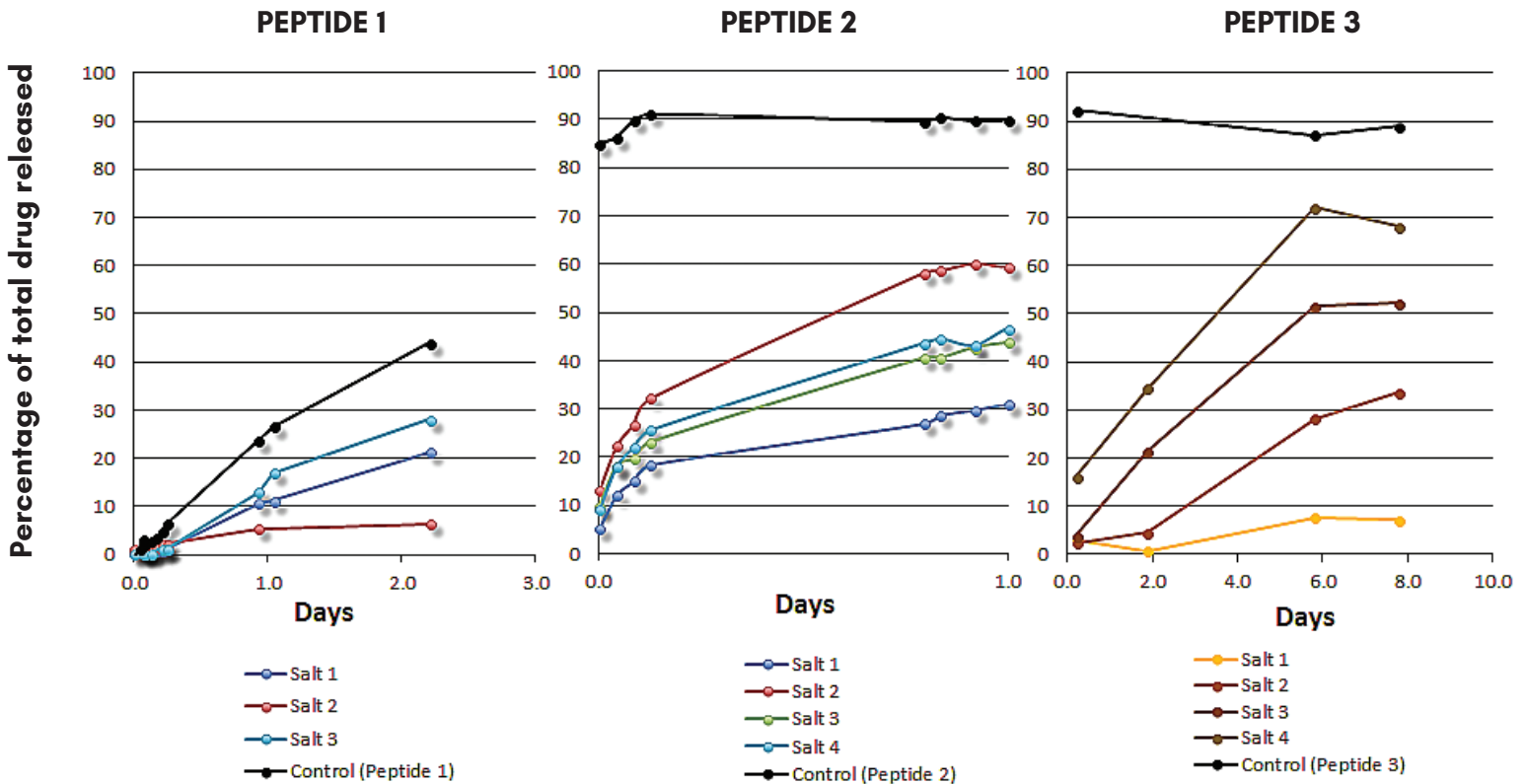
## Peptide 2 In-Vitro Dissolution Kinetics by RP-HPLC at Day 6



# PEPTIDE SALT SCREENING: Characterization and Selection

## In-Vitro Assessment: Dissolution Testing

Peptide salt is released into the dissolution media over time under sink conditions.



## In-Vivo PK Study:

Peptide 3 Salt Showing Sustained Release at Day 60 (tested)

