PENSATECH PHARMA

Your Partner for Innovative Drug Delivery Solutions

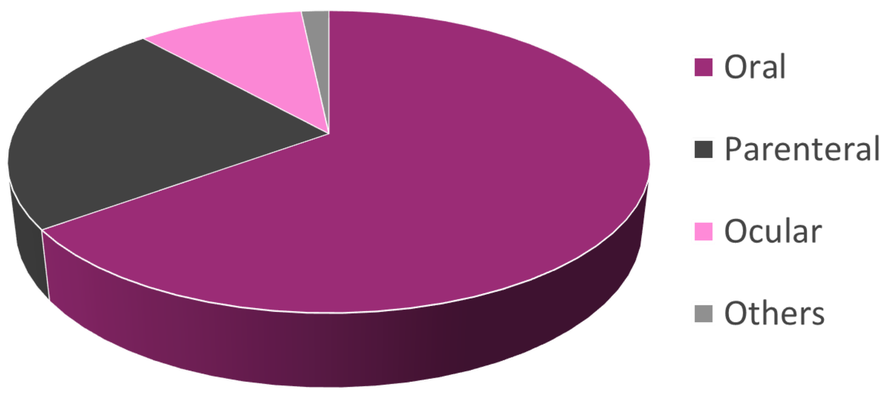
Pensatech Pharma is a specialized contract R&D partner for advanced drug delivery solutions. Based on a comprehensive suite of classical and innovative drug delivery systems technologies and our unique, science- and data-based expertise, we are designing and developing innovative dosage forms for new and existing APIs.

By addressing the most difficult development issues and specific product requirements through commercially viable advanced drug delivery and dosage form technologies, we add unique value to the product portfolio of our customers.

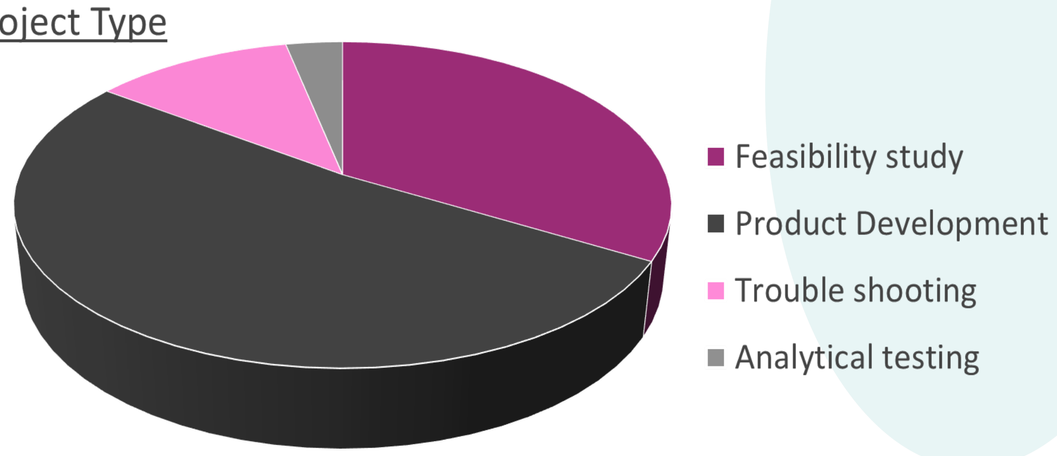
Pensatech Pharma offers a wide range of drug delivery technologies especially for difficult-to-formulate drug molecules, covering all administration routes at any development stage.

The figures show our successful drug delivery projects 2012-2021

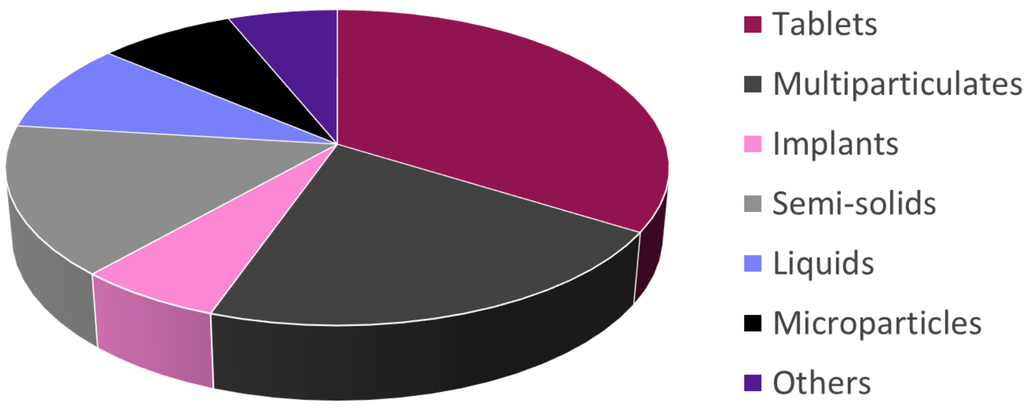
Route of administration



Project Type

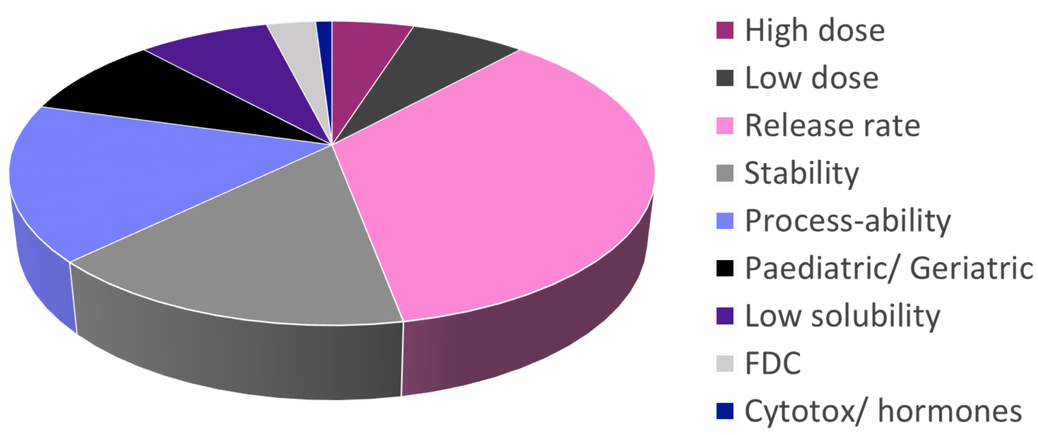


Dosage Form Technology



Tablets: IR, MR, bi-layer
Multiparticulates: pellets, mini-tablets
Semi-solids: gels, emulsions, ointments
Liquids: solutions for ophthalmic use and freeze-dried formulations
Microparticles: parenteral biodegradable formulations

Challenges



Our successful drug delivery technologies and partnerships cover:

- ✓ Parenteral IR and depot DDS: biodegradable PLGA micro-/nanoparticles and implants, aqueous and oily solutions, micro- and nano- drug suspensions, polymeric and lipidic nanocarriers, liposomes, lyophilized forms
- ✓ Bioavailability enhancement: micro- and nano drug suspensions, solid solutions and dispersions (HME, spray drying, fluidized bed)
- ✓ Oral modified release drug DDS: granules, pellets, minitablets, osmotic tablets, matrix and coated systems, high dose, fixed dose combination
- ✓ Local DDS: e.g., ophthalmic and dermal
- ✓ Patient centric forms (paediatric and geriatric): multiparticulates, minitablets, taste masking, fixed dose combinations, fast disintegrating oral drug delivery systems (ODT), swallowability enhancement
- ✓ Viable formulation and processing for very high/low dosed drugs
- ✓ Improved product stability

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Our partnership supports every requirement like:

- ✓ Preformulation
- ✓ Formulation and Process development:
  - ✓ Formulation and technology assessment and selection
  - ✓ Feasibility studies
  - ✓ Development of enabling formulations for rapid evaluation in the clinic
  - ✓ Full development of a wide range of pharmaceutical dosage forms
- ✓ Analytical method development, optimization, transfer, validation and stability studies
- ✓ Quality control testing (physicochemical and pharmaceutical analysis) as well as batch certification of finished products and investigational medicinal products in our GMP-certified laboratories
- ✓ Regulatory, IP and exclusivity assessment and guidance
- ✓ Formulation development of highly potent APIs and cytotoxics
- ✓ Formulation development of controlled substances (narcotics)

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Application laboratory for advanced drug delivery

- Formulation and dosage form development for challenging new chemical entities (NCE`s) or existing drugs e.g., 505(b)(2), drug repurposing

Pre-formulation Services	Formulation & Process Dev. Services	Analytical Development Services
Stability Studies	GMP QC & Batch Certification Services	Partnering opportunities

Innovation laboratory for advanced drug delivery

- Idea generation and feasibility for innovative product development
- Concept and technical product development for out-licensing or partnering

- ✓ We believe that any innovation starts with a challenge or unusual idea, however each challenge or idea is worth while to be explored
- ✓ We believe in utilizing our expertise, breath of technologies and capabilities we will be able to find the right answer for your challenges and ideas
- ✓ We believe in data driven science and creative solutions to truly add the value your challenging and ambitious projects deserve

Please contact us at info@pensatechpharma.com to discuss how we could assist you during the development of your product.

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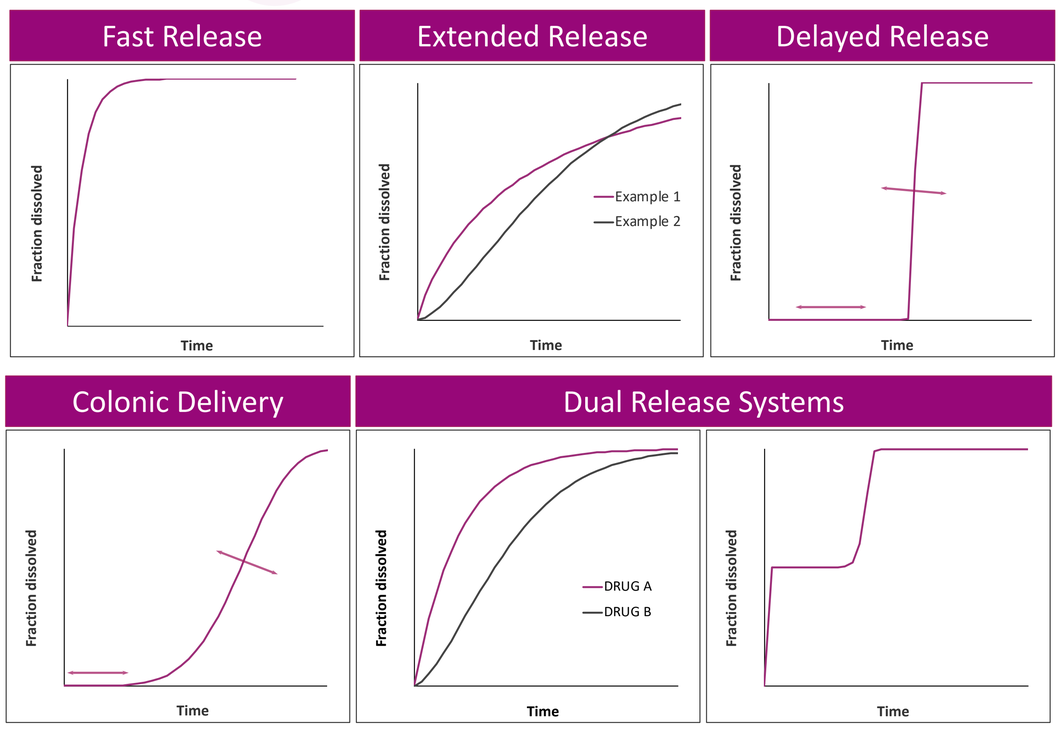
Oral Modified Release Drug Delivery

Introduction

Oral dosage forms are the predominant delivery system due to ease of use and patient acceptability. Modified release systems are being used to circumvent gastric degradation, improve pharmacokinetics, reduce dosing frequency or adverse drug reactions as well as to enable oral dosing for drugs with a very short biologic half-life or achieve additional clinical benefits e.g., new indications.

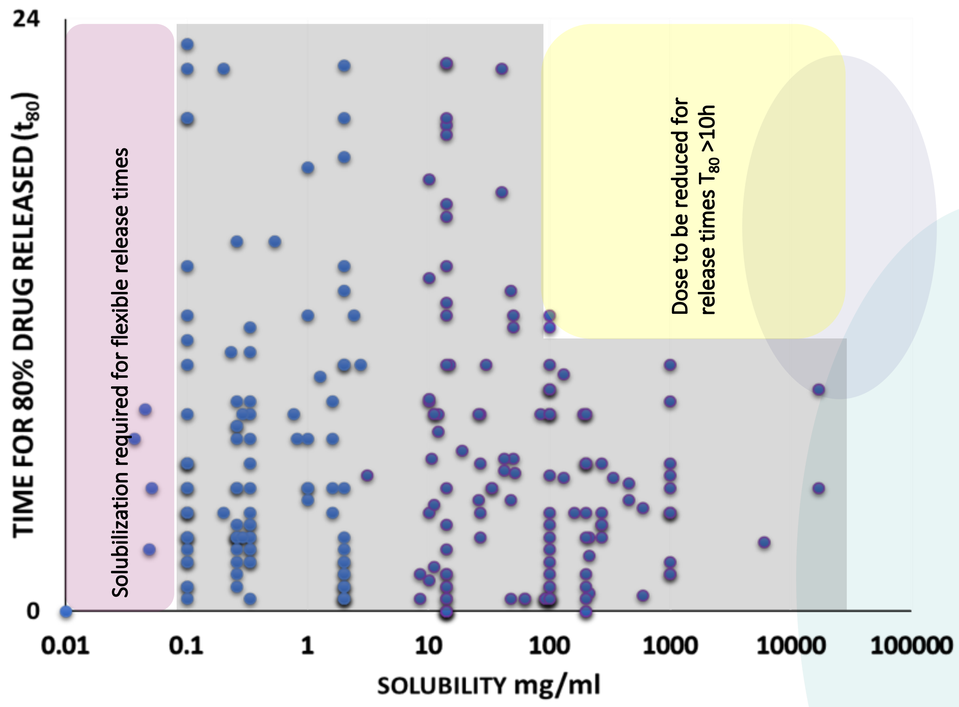


Our approach:

Based on physicochemical and biopharmaceutical characteristics of a drug, we use our expertise in modified release technologies to develop commercially viable products to our customer needs. These include:

- ✓ Modified release dosage forms
  - Multiparticulates (granules, pellets, minitablets)
  - Single unit tablets
  - Osmotic tablets
  - Matrix and coated systems
  - Hydrophilic and lipophilic polymeric matrix and coating materials
- ✓ High dose modified release DDS
- ✓ Fixed dose combinations with independent release adjustment for each API
- ✓ Reduced food or alcohol effect (robustness against intestinal forces, fluids and food/food degradation products)
- ✓ Enteric / colonic delivery dosage forms
- ✓ Pulsatile drug delivery

Technology applicability map - Example: Single units



Knowledge-based formulation: Discriminat. dissolution

- ✓ Rationale selection of dosage form, formulation and processes based on expertise in drug delivery and biopharmaceutics
- ✓ Defining target release profile based on PK analysis
- ✓ Risk-based approach to decision making within a Quality-by-Design framework

Single units | Coated multiparticulates

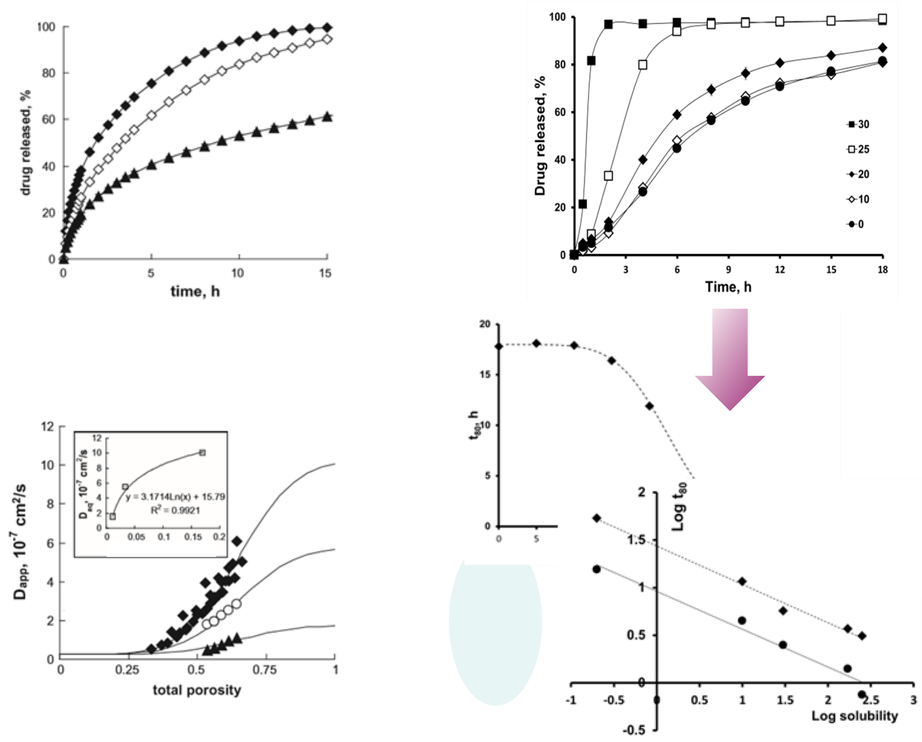


Figure: Drug release data sets (above) and their mechanistic evaluation (below) of oral DDS

Summary

- ✓ Formulation selection and development starts with an in-depth analysis of the characteristics of the API.
- ✓ The Target Product Profile is defined, and formulation approaches are selected based on science and data.
- ✓ Formulation options are evaluated, and the most suited dosage form is developed by QbD principles.

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Pulsatile Drug Delivery

Introduction

A pulsatile drug release is characterized by a lag phase with no release followed by a period of drug release. Such sigmoidal drug release patterns enable release of drugs to address chronopharmaceutical delivery or release of two drugs requiring time dependent sequential delivery or therapeutic plasma profiles.

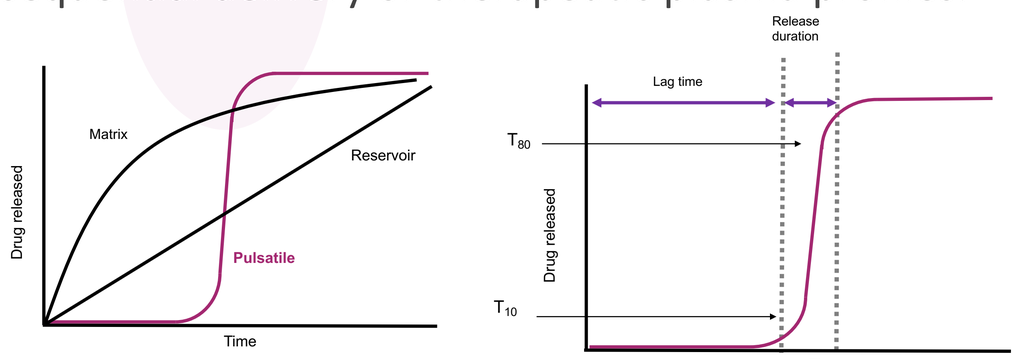

Fig. 1 Different release profiles depending on delivery system

Applications of pulsatile drug delivery:

1. Chronotherapy – Enabling new treatments

- ✓ Drug release at a rhythm that ideally matches the biological requirement of a given disease therapy
- ✓ Eliminate midnight or early morning dosing

Disease	Chronological behaviour	Drugs
Hypertension	BP is at lowest during the sleep cycle and rises steeply during the early morning awakening period	ACE inhibitors, Calcium Channel Blockers
Arthritis	Pain in the morning	NSAID's, Glucocorticoids
Asthma	Precipitation of attacks during night or morning	β_2 agonists

2. Target the release in a specific section of the GI tract e.g., colon targeting

- ✓ Drugs with short half-life (multiple pulses)
- ✓ Reduce "first pass effect"
- ✓ Time-dependent release

Our approach:

Pensatech Pharma offers a formulation development framework for erodible and swelling-induced (rupturable) pulsatile drug delivery systems.

Mechanism	Advantages	Challenges
Erodible coatings	• Simpler design • Flexible lag times	• Premature, non-pulsatile release • Suitability for pellets?
Rupturable coatings	• Good reproducibility • Flexible lag times • Environment-independent	• Multiple coating layers

Case study: Rupturable Coatings

The drug release is swelling-induced. Medium ingress leads to expansion of the swelling layer which builds pressure towards a semi-permeable outer membrane and ruptures it at pre-determined time points (lag time). Lag time and release duration is controlled by the composition-derived properties of the outer layer.

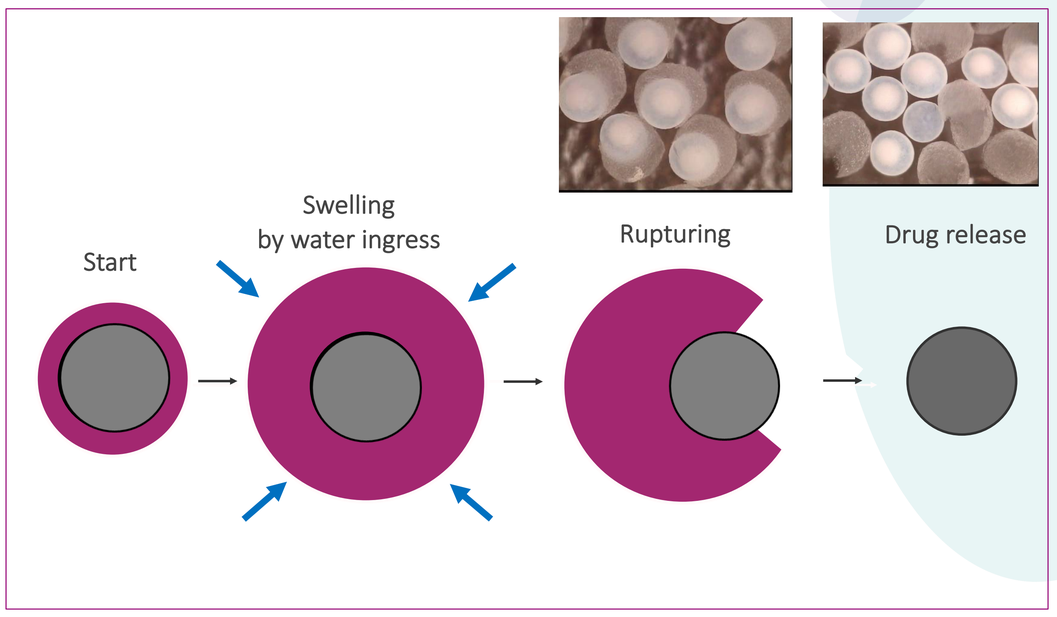

Fig. 2 Release mechanism for rupturable systems

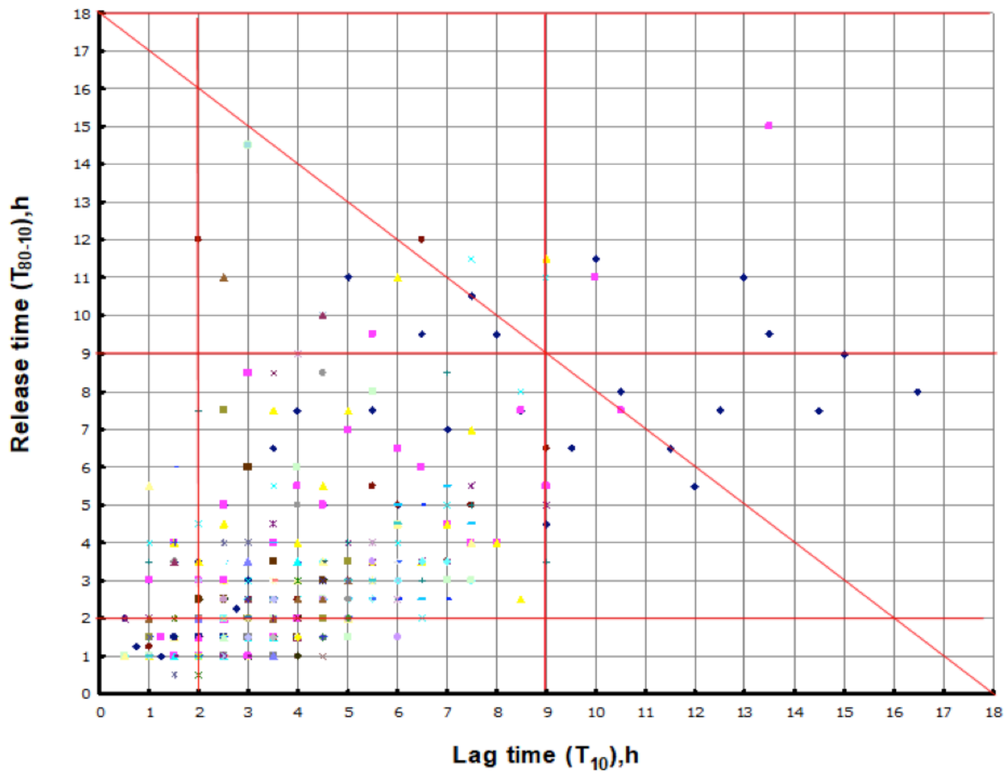

Fig. 3 Release duration (T80-10) vs. lag time (T10)

Pensatech Pharma has developed a technology applicability map with short/ long lag and release durations with rupturable and erodible pulsatile drug delivery system along with discriminatory dissolution tests predictive for the in-vivo performance.

Summary

- ✓ The pulsatile drug delivery formulation is selected based on the drug characteristics and the desired plasma profiles.
- ✓ Development is based on a mechanistic, data-driven approach and commercial manufacturability.

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Parenteral Drug Delivery Systems

Introduction

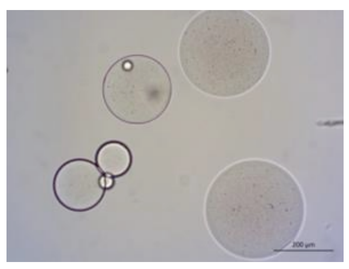
Small molecules with poor or variable oral bioavailability or biologics are delivered via parenteral routes. To avoid frequent injections due to short half-life, compliance issue or a narrow therapeutic window, controlled release parenteral systems play an important role. To deliver the drug in a predictable manner at a controlled rate, different approaches are being used at Pensatech Pharma.

Our approach:

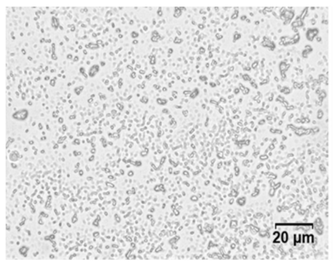
Every product with its characteristics and desired performance profile requires the development of a specific formulation and process. Defining a target product profile, appropriate scientific approaches are evaluated from different technologies:

- ✓ Depot formulations (aqueous and oily solutions and micro- and nano-suspensions)
- ✓ Biodegradable nano-/ microparticles (various encapsulation methods and carriers)
- ✓ Implants (HME, in situ forming implants)
- ✓ Multivesicular and conventional liposomes

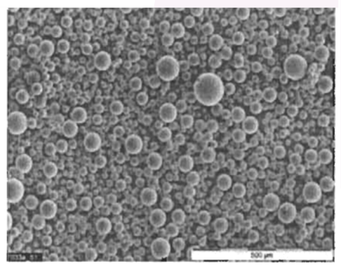
The selection for the lead formulation technology is based on our prior experience, a mechanistic model and data generated. The formulation and processing is developed on a series of performance testing including suitable in-vitro dissolution testing.



Nanoemulsions

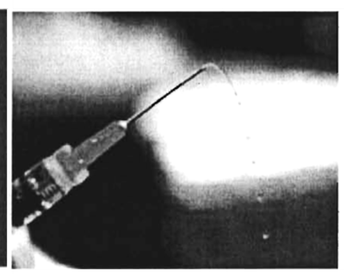


Nanosuspensions

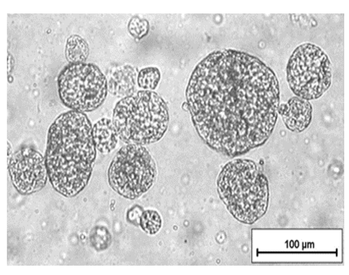


Microparticles

Solid implants



In situ forming implants



Multivesicular liposomes

Application examples of PLGA DDS with long and flexible delivery periods

Implants | In-situ implants | Microparticles

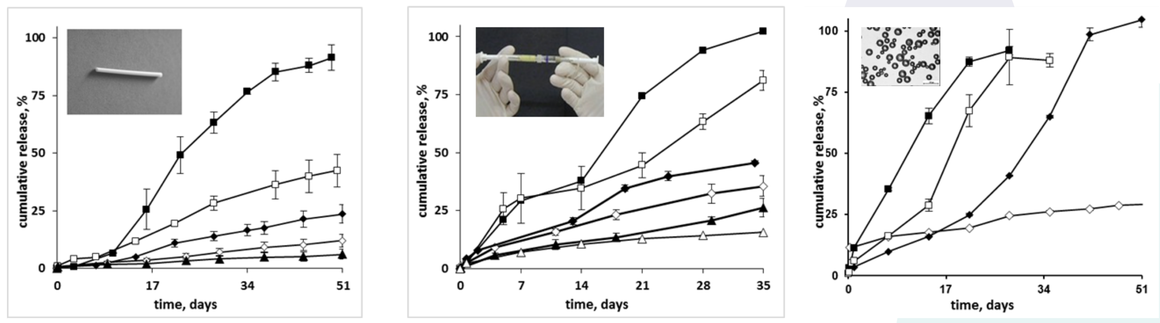


Fig. 1 In vitro drug release from different PLGA DDS

- ✓ Broad experience with various APIs (small molecules, peptides, proteins) and PLGA grades including a mechanistic understanding of the drug release characteristics (→ Hydrolysis → Erosion → Drug release)

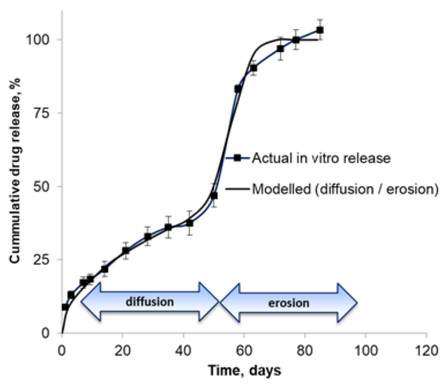


Fig. 2 Example of an actual and modelled release profile from PLGA DDS

Case reports of successful partnerships:

- ✓ Prototype development for toxicology studies (hormone biodegradable implants and microparticles, lipid microparticles for veterinary use)
- ✓ Formulation, process and analytical development of a freeze-dried powder of cytotoxic drug
- ✓ Formulation development/ feasibility studies for liposome formulations and depot aqueous suspension.
- ✓ Process understanding and scale-up of biodegradable implants

Summary

- ✓ Development of a long-acting parenteral formulation requires an in-depth analysis of the API and a tailored formulation technology.
- ✓ The technology selected is based on a mechanistic model of the drug release.
- ✓ Understanding the critical material attributes and critical process parameter is key during the development of a commercial product.

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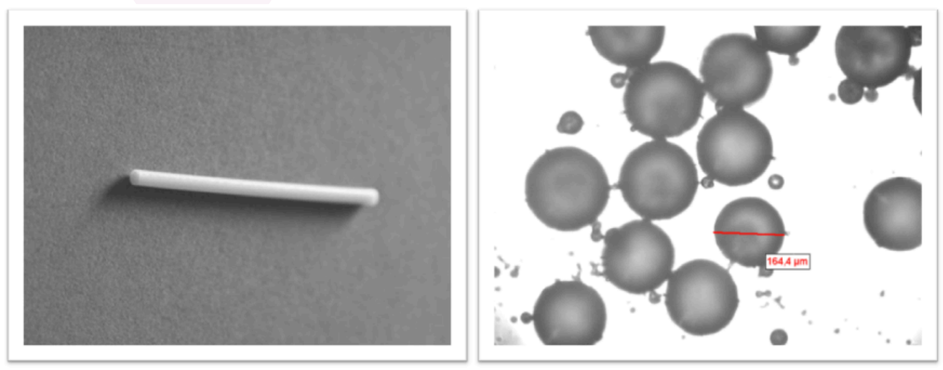
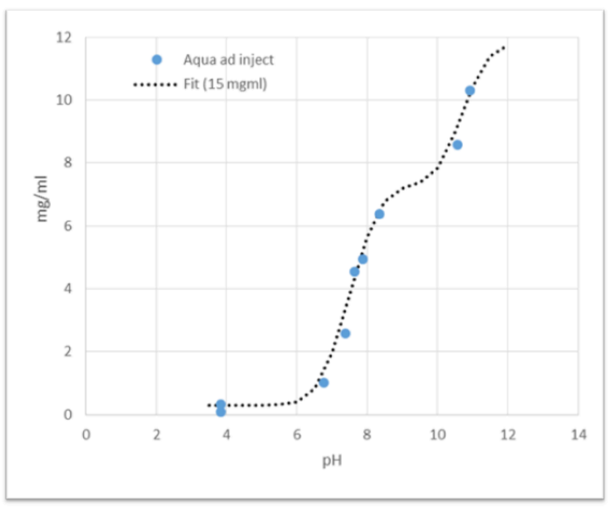
Specialized Drug Delivery

Poorly bioavailable drugs

- ✓ Solid solutions/ (amorphous) dispersions
- ✓ Lipidic systems, nanocrystals
- ✓ Hot melt extrusion/ granulation
- ✓ Spray drying/ congealing
- ✓ Milling / nano-sizing



Hot melt extrudate and spray congealed particles



pH / solubility profile of API (Sirius inForm)

Unstable drugs

- ✓ Various stabilization techniques (O_2, RH, light)

Highly potent and CMR drugs

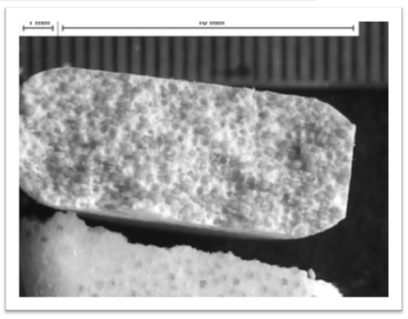
- ✓ Hormones
- ✓ Anti-cancer drugs

Controlled substances

- ✓ Narcotics

Fast disintegrating oral DDS (IR / MR)

- ✓ Tablets (ODT)
- ✓ Lyophilized DDS



Pediatric dosage forms

- ✓ Liquids, reconstitutable dosage forms
- ✓ Multiparticulates (e.g., pellets, minitablets)
- ✓ ODTs

Microencapsulated peroral products

- ✓ Antibiotics
- ✓ Drugs and nutraceuticals

Taste masking

- ✓ Solids (swallowable, chewable, ODTs)
- ✓ Liquids (flavoring, ion-exchange resins)
- ✓ Tablet coating
- ✓ Microencapsulation

Lyophilization

- ✓ Aqueous and organic
- ✓ Optimization of freeze-drying cycles

Services

- ✓ Preformulation, Formulation development
- ✓ QbD approach
- ✓ Life cycle management
- ✓ Trouble shooting
- ✓ Analytical (selection below)
  - Solid state: PXRD, DSC, TGA, DVS
  - Powder properties
  - Particle size: Laser diffractometry (liquid and powder), photon correlation spectroscopy
  - Chromatography: HPLC (UV, RI, ELSD), GPC / SEC (RLS, RI, Viscosity), GC
  - Release testing: Compendial / non-compendial, real time / accelerated
  - Rheology / torque rheology
  - Stability and stress testing

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