PENSATECH PHARMA

Your Partner for Innovative Drug Delivery Solutions

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.

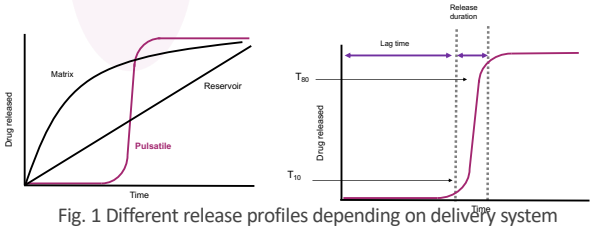

Fig. 1 Different release profiles depending on delivery system

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.

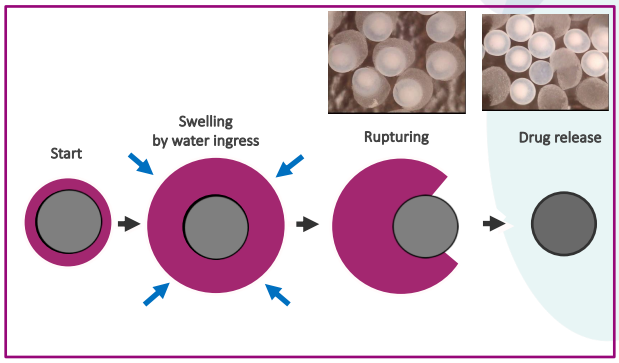

Fig. 2 Release mechanism for rupturable systems

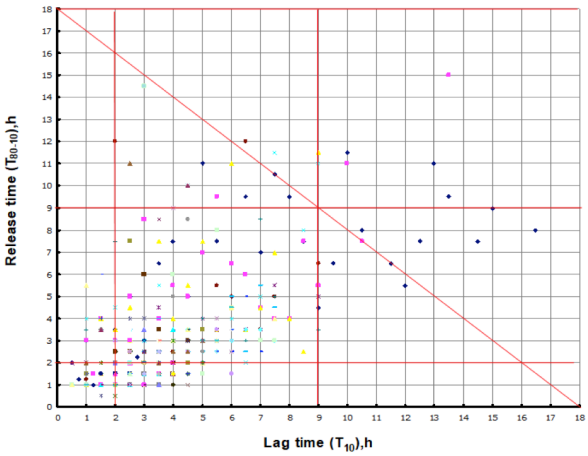

Fig. 3 Release duration (T80-10) vs. lag time (T10)

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.

Pensatech Pharma GmbH • Kelchstr. 31 D-12169 Berlin • Germany
+49 30 224 64 666 • info@pensatechpharma.com • www.pensatechpharma.com