CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187

Available online at: http://www.iajps.com *Review Article*

A REVIEW ON PULSATILE DRUG DELIVERY SYSTEM

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Abstract:
In recent times the concept of Pulsatile Drug Delivery systems has been gaining a lot of attention and importance this is due to the fact that they can release and deliver the medication "At the right place at the right time". They release a rapid dose of medication after a lag period on the basis of a pre-determined pulse. The most significant application of PDDS is where consistent dosing is not required. They are an innovative system of chronopharmacological conduct that work on the circadian rhythm of the body. This article focuses on the study of Pulsatile Drug Delivery Systems their classification, types, advantages, and disadvantages.

Keywords: - Chronobiology, chronopharmacolgy, stimulus, circadian rhythm, pre-determined lag period.

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Please cite this article in press Chandrasekhara Rao Baru et al ***A Review On Pulsatile Drug Delivery System****, Indo Am. J. P. Sci, 2024; 11 (02).*

INTRODUCTION:

The rapid and brief release of a certain dosage of drug molecule in a brief length of time following a predefined off-release interval, or lag time, is what defines a PDDS. There are several situations in which the prescription ought to have been filled following a lag period at the specific location. Therefore, in these circumstances, force the creation of a pulsatile delayed quick release system. systems of release.[1] It is necessary to generate a pulse such that a full and rapid drug release is achieved following the opportunity for lag time in accordance with the circadian rhythm of the body. There are two release phases that define these systems. There is a first phase in which the medication is released in little amounts, and a second phase in which the medication is released fully in a brief amount of time following a lag time.[2] These innovative drug delivery systems aim to release the medicament on a programmed pattern. They are called the "Intelligent Drug Delivery Systems" that can modify medication release frequency in response to the body's physiological requirements.

Drugs can be delivered using time-delayed dose forms after a predetermined lag period, which might be significant in clinical settings wherein a medical condition has demonstrated a reliance on the circadian rhythm. For instance, patients with coronary heart disease may have morning peaks in the start of a myocardial infarction, cardiac arrest, and stable angina. These situations may be mitigated by timely administration of an appropriate medicine, for instance verapamil, if given to the patient. [3,4,5]

Similar to other circadian rhythm-based bodily functions, such as chemical emission (follicle-stimulating hormone, luteinizing hormone [LH], LH-releasing hormone, oestrogen, and progesterone), corrosion-prone emission in the stomach, gastric exhaustion, and gastrointestinal (GI) blood bonding, a variety of conditions call for pulsatile discharge. Natural resilience-producing medications need a system that prevents them from continuously existing at the BioPhase, since such action will generally lessen their beneficial effects. For medications that undergo degradation in an acidic stomach environment (peptide medicines, for example) and irritate the stomach mucosa or cause nausea and regurgitation, the interim period is critical. [6,7,8]

TYPES OF PULSATILE DRUG DELIVERY SYSTEMS

PDDS can be broadly classified into three types,

1) Time controlled
2) Stimuli induced
3) Externally regulated

A) Time Controlled

To resemble the circadian rhythm, time-controlled medication delivery systems produce pulsatile release following a predetermined interval of time. Two parts make up this kind of PDDS: an instant release component and a pulsed release component. Numerous techniques that are available for time-controlled.

1) Delivery systems with rupturable coating layer

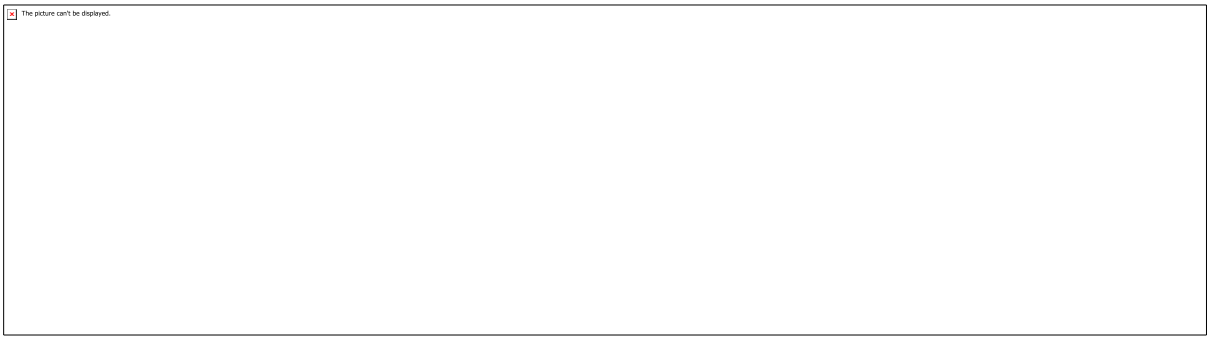
These systems comprise of a porous coating that is water insoluble and subject to a mechanically triggered rupture phenomenon, controlled by an outside trigger.

By adding swellable, osmotic, or effervescent agents to the reservoir, the film rupture can be achieved. Release of medications can be achieved at a predetermined time interval by adjusting the mechanism.

2) Delivery systems provided with erodible coating layers

In these systems, the outer layer that is employed on the drug-containing core dissolves or erodes, controlling the release of the drug. This idea led to the development of an oral dosage form that releases pharmaceuticals after a predetermined amount of time has elapsed, allowing for time-dependent circulation of the drug's active ingredient through optimal outer coat thickness. The system consists of a drug-containing core and a hydrophilic layer that slowly interacts with aqueous fluids to postpone the release of the drug. These are of two types-

a) Bulk eroding system
b) Surface eroding system



3)Capsule shaped system provided with release controlling plug

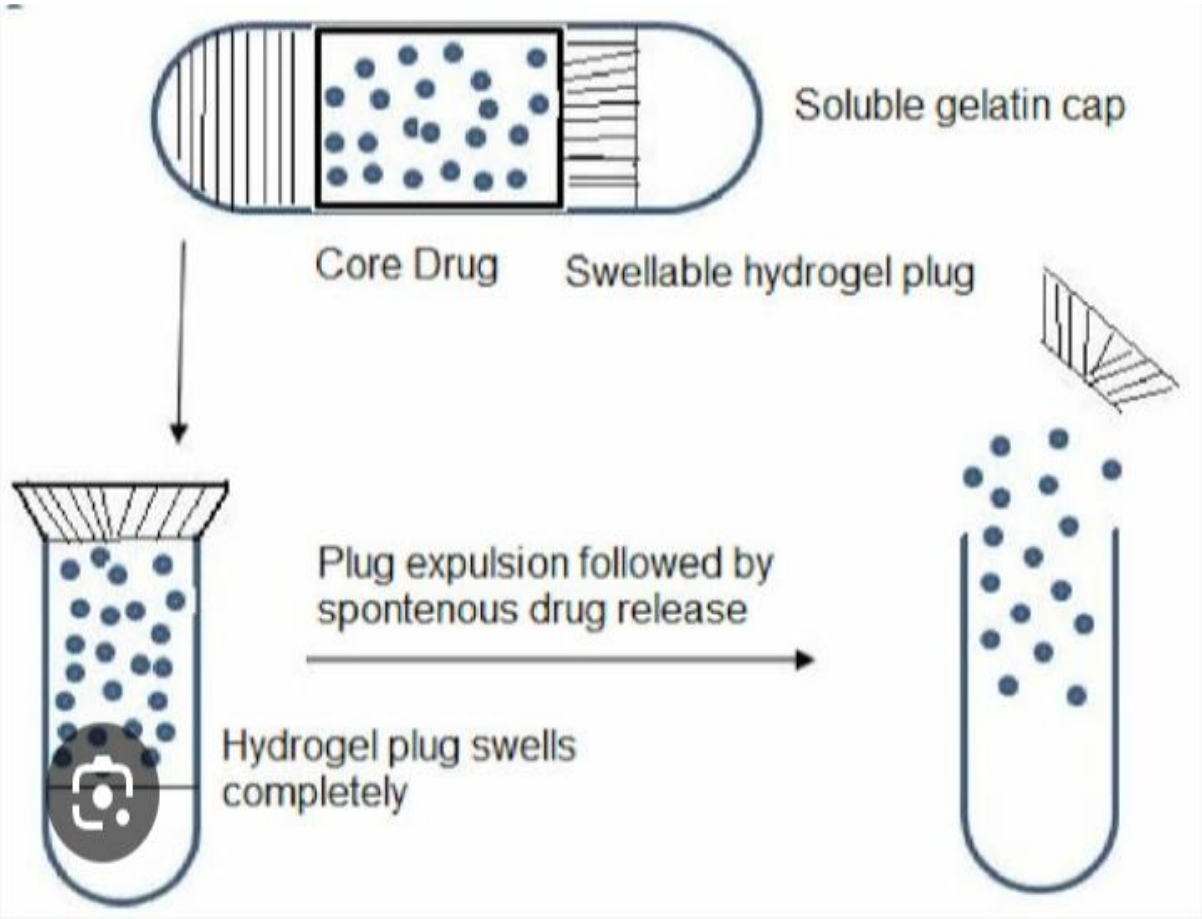
Between the instant release compartment and the pulsed release compartment, these systems have a release regulating plug. When the cap comes into contact with water, it dissolves quickly, delivering the instant release component first, then the pulsed release component. The plug that is put into the body provides the lag time.

B) Stimuli induced pulsatile drug delivery systems

In these approaches, the medicine is released in response to any biological stimulus, such as temperature, or chemical stimulus. They can further be classified as-

1) Thermo –responsive hydrogel systems

This technology makes use of hydrogels that can vary their volume reversibly in response to temperature variations. These gels shrink at an intermediate temperature that is associated with the linear polymer's lower critical solution temperature (LCST). A particular attraction for water causes thermosensitive hydrogels to expand at temperatures lower than the point of transition temperature, while exhaling water causes them to shrink at temperatures over the transition temperature.



2) Glucose-responsive insulin release devices

When a person has diabetes mellitus, their blood glucose levels rise rhythmically, necessitating timely insulin injections. glucose oxidase that has been fixed in a pH-sensitive hydrogel. Glucose oxidase transforms glucose into gluconic acid when blood glucose content rises, altering the pH of the system. Insulin is released as a result of the polymer swelling caused by this pH shift. Insulin lowers blood glucose levels by nature. As a result, gluconic acid levels also drop and the system enters a deswelling phase, which inhibits insulin release.

3) pH sensitive drug delivery system

Two components make up this kind of pulsatile drug delivery system: an instant release component and a pulsed release component that releases the drug in response to a pH shift. The fact that distinct pH environments exist in different regions of the GIT has been leveraged in the case of pH-dependent systems. It is possible to obtain medication release at a specific place by choosing pH-dependent polymers.

Example- cellulose acetate phthalate, polyacrylates, sodium carboxymethylcellulose.

C) **Externally regulated systems**

Another method for pulsatile drug release is through externally regulated systems, wherein external stimuli such as magnetic, ultrasound, electrical effect, and radiation are used to program drug release. The implant has magnetic beads that are part of a magnetically regulated system. When using ultrasonically modulated devices, the drug release is modified by the degeneration of the matrix of polymers brought on by ultrasonic waves.

MARKETED PRODUCTS:

Table 1: Marketed technologies of Pulsatile drug delivery [11, 12-14]

Technology	Mechanism	Proprietary name and dosage form	Active pharmaceutical ingredients	Disease
PULSYS ™	Rupturable system	Pulsincap™	Dofetilide	Antiarrhythmic
Physicochemical modification of API	Tablet	Pepcid®	Famotidine	Ulcer
OROS	Osmotic mechanism	Covera-H5 XL tablet	Verapamil HCl	Hypertension
Three-dimensional printing	External regulated systems	Their form	Diclofenac sodium	Inflammation
DIFFUCAPS*	Multiparticulate system	Innopran XL, tablet	Verapamil HCl	Hypertension
Pulsincap™	Rupturable system	Pulsincap™	Dofetilide	Hypertension
CODAS®	Extended-release capsule	Verelan®PM	Verapamil HCl	Hypertension
TIMERx®	Erodible/ER Tablets	OPANA®S	Oxymorphone	Pain management

CONCLUSION:

The concept of Chronobiology and Chrono pharmacology is a new and innovative concept that is gaining popularity of scientists and health care professionals worldwide. There is always a necessity for the development of new and improved drug delivery systems to provide patients with improved health care and better therapeutic benefits. PDDS is one such type of innovation that delivers the drug to right place at the right time and in right dose and is extremely promising for patients who are suffering from Chronic diseases and ailments.

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