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Review Article

# Advances in Pulsatile Drug Delivery System: A Promising Strategy for Tailored Therapeutics in Modern Medicine- Review

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## ABSTRACT

The pulsatile drug delivery system is based on a reservoir system consisting of a drug-containing effervescent core and which are coated with a swelling membrane and a polymeric coating which is insoluble but water permeable outer membrane. The swellable polymer in swelling layers induces the rupturing of outerpolymer coating. An apparatus was designed to measure simultaneously the swelling energy/force and water uptake of discs, made of polymers. It is an advanced therapeutic technique designed to optimize the drug release patterns to accompany with the body's circadian rhythm. PDDS is distinct from the conventional drug delivery system, which typically facilitate continuous and sustained release of the Drug. While PDDS are engineered to deliver drugs in a time-controlled or stimulus-induced manner, thereby matching the chronopharmacological needs of the patient. PDDS are beneficial in the management of chronic diseases that exhibits predictable patterns viz. cardiovascular diseases, asthma, arthritis, and peptic ulcers in which the symptoms are time-dependent. By releasing the drug at a precise time, it ensures that the drug's therapeutic effect aligns with the disease's activity cycle, enhancing efficacy while decreasing the side effects and the potential for drug tolerance. PDDS are of two types: Time-controlled systems and stimuli-induced systems. The time-controlled system depends on pre-programmed mechanisms like capsular, osmotic, and reservoir devices to release the drug after a specific lag time. Whereas a stimuli-induced system releases the drug in response to specific physiological or external stimuli, such as pH, temperature, enzymes, or external triggers like light. The polymers used in PDDS are Hydroxypropyl Methylcellulose (HPMC) Polyvinyl Alcohol (PVA), Sodium alginate, Poly (Lactic-co-Glycolic Acid) (PLGA), Polylactic Acid (PLA) Polyglycolic Acid (PGA). The present work is focused on the requirements, advantages, disadvantages and a review on various drugs and polymers used in the development of PDDS.

**Keywords:** Pulsatile drug delivery system, Swelling Membrane, Polymers, Chrono pharmacology, Circadian rhythm.

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## INTRODUCTION

In the modern pharmaceutical environment, traditional drug delivery methods have primarily focused on providing a continuous and constant release of drugs to maintain consistent therapeutic levels in the bloodstream (Ahmed *et al.*, 2020). Designed to balance efficacy with the lowest adverse effects, this steady-state strategy guarantees that medications stay within a designated therapeutic window. Although this approach is successful for many stable diseases and chronic disorders, it usually ignores the demands of diseases marked by changing symptoms or biological rhythms (Al-Zoubi and Al-Jallad, 2019). Pulsatile Drug Delivery Systems (PDDS) present a breakthrough alternative by delivering drugs in a regulated, pulsatile fashion that more closely resembles the body's normal physiological cycles. This new approach was inspired by chrono pharmacology, which combines chronobiology and pharmacology (Andrade *et al.*, 2018). We made it by examining biological rhythms such as circadian rhythms (24-hr cycles), ultradian rhythms (less than 24 hr), and infradian rhythms (more than 24 hr) (Basak *et al.*, 2021). These rhythms are crucial for controlling many physiological processes, including hormone production, metabolism, and drug absorption. By synchronizing drug delivery with these natural cycles, PDDS has the potential to maximize treatment results, increase drug efficacy, and improve patient compliance (Beg *et al.*, 2020).

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Circadian rhythms profoundly affect medication action and metabolism. The body's internal clock coordinates immunological responses, hormonal changes, and sleep-wake cycles, all of which affect medication processing (Bhandari *et al.*, 2019). Cholesterol production in the liver follows a circadian cycle, rising in early morning. Giving PDDS cholesterol-lowering drugs in the evening could coincide with the body's natural rhythms and enable more efficient decrease of cholesterol levels. For patients with disorders like asthma, which typically aggravates at night, we can design a PDDS delivering medication in the evening to assist control symptoms and improve their quality of life. This synchronization with circadian rhythms allows for a more customized approach to drug distribution, thereby improving the efficacy and acceptability of therapies (Chawla and Gupta, 2018).

Complicated and chronic conditions like cancer, where the timing of medicine delivery can significantly impact therapy outcomes, also benefit PDDS. Tumor cells, which often show different cycles of activity, can be modified to release chemotherapeutic medications in line with their cell cycle, thereby improving therapeutic efficacy and reducing adverse effects. For instance, some cancer cells may proliferate rapidly during specific phases of their cycle; consequently, it is advisable to administer drugs at these periods to maximize their effects. This approach not only reduces systematic toxicity but also targets tumor cells more specifically, therefore enhancing the general patient outcomes. Moreover, since the timing of some chemotherapeutic treatments can change their effects, we can customize PDDS to the circadian rhythms of cancer patients. By customizing treatment plans based on circadian cycles, we can lower side effects and increase therapy efficacy, so improving patient well-being and quality of life (Chen *et al.*, 2022). Although PDDS presents a spectrum of technological and developmental possibilities, its progress and application come with a set of difficulties. Timing the drug release presents one of the toughest difficulties. Thorough knowledge of physiological elements such as gastrointestinal transit times and individual patient parameters is necessary for both building PDDS and ensuring medicine distribution at the prescribed timings. Maximizing therapeutic effects depends solely on giving drugs exactly as required. Still another important difficulty is keeping drugs stable within the delivery mechanism. We have to create pulsating release mechanisms to stop deterioration and guarantee their efficacy (Choudhary and Raval, 2021).

Right up until the planned release date. Formulating and packaging determine significantly whether the medicine stays stable and whether it stays strong and safe for use (Cuenca and Cañadas, 2019). Changing PDDS to fit the particular needs of the patient requires adaptability considering elements such the kind of disease, symptom trends, and personal preferences of the patient. Although this degree of customizing affects design and manufacturing processes, PDDS is an interesting field of research and development. Some potential benefits include reduced side effects, increased patient compliance, and improved treatment outcomes (Dadwal *et al.*, 2020).

The majority of studies on PDDS focus on overcoming obstacles and exploring new approaches to this technology. PDDS innovations resulting from advances in materials science and drug delivery technologies create ever more intricate and robust systems. Sensitive materials, nanocarriers, and smart polymers are under investigation to raise the precision and reliability of pulse drug delivery (Das and Chaudhuri, 2018). These advances aim to raise PDDS performance and expand their applications in a more widely therapeutic domain. Future studies should concentrate on creating new forms of different medications, enhancing PDDS technology to maximize release mechanisms, and evaluating these systems in clinical settings to ensure they run well and are safe for a spectrum of patient groups. Cooperative research and development using multidisciplinary approaches combining pharmacology, chronobiology, and biomedical engineering will be very important for the advancement of PDDS technology (Dehghan and Shohrati, 2021).

Pulsed drug delivery devices represent a major advancement over traditional continuous-release methods in the field of pharmacology. Matching drug release with the body's natural cycles and the timing of disease symptoms helps PDDS to offer a more tailored and efficient method of treatment (Dhar and Khatri, 2022). This strategy presents new opportunities for improving patient care through customized therapeutic approaches, addressing some of the constraints associated with the distribution of traditional medications. Reduced side effects, more therapy efficiency, better control of illness symptoms, and more patient adherence to medicine define the expected benefits of PDDS. By means of ongoing research and development, PDDS could revolutionize drug distribution and improve patient quality of life. More precise, efficient, and patient-centered treatments are made possible by a fresh approach in pharmacology combining chronobiology with drug delivery devices (Dey and Dubey, 2019).

Taking all factors into account, pulsed medication delivery systems offer an innovative and promising solution to address the limitations associated with traditional continuous-release methods (Farag *et al.*, 2020). Matching disease symptoms with the natural rhythms of the body and drug delivery improves patient care and increases the effectiveness of treatments. While present deployment and improvement of these systems present difficulties, continuous study and technical development will surely help to overcome these limitations and maximize the use of PDDS (Garg *et al.*, 2018). By allowing drug customizing, lower side effects, and improved therapy efficacy, these technologies should transform pharmaceutical research. Growing this sector creates new opportunities for creating more effective and patient-oriented therapy plans. Thus, the future of customized medicine may rely much on improved drug delivery systems (PDDS).

## METHODOLOGIES FOR PDDS

### Time controlled pulsatile release

A. Single unit system.

B. Multi-particulate system.

### Stimuli induced

A. Thermo-Responsive Pulsatile release.

B. Chemical stimuli induced Pulsatile systems.

### External stimuli pulsatile release

A. Electro responsive pulsatile release.

B. Magnetically induced pulsatile release.

### Pulsatile drug release systems for vaccine and hormonal products

#### *Time Controlled Pulsatile Release*

According to circadian rythms the drug release occurs at certain specific time intervals in our body. This type of delivery system consists of two components.

1) Immediate release 2) pulsed release

Circadian rhythms (Figure 1) regulate various physiological processes including sleep-wake cycles, hormone release, and metabolism illustrates the core molecular components of the circadian clock. Circadian rhythms are natural, internal processes that regulate the sleep-wake cycle and repeat roughly every 24 hr. They are influenced by environmental cues like light and darkness, helping to synchronize bodily functions with day and night. The brain's master clock, located in the Suprachiasmatic Nucleus (SCN) of the hypothalamus, controls these rhythms. Circadian rhythms affect various physiological processes, including hormone release, body temperature, digestion, and alertness. Disruptions to these rhythms-such as through shift work, jet lag, or irregular sleep schedules-can negatively impact health and well-being. Maintaining consistent sleep patterns and exposure to natural light can help keep circadian rhythms aligned (Godara and Sinha, 2021).

### Single unit systems

#### *Capsular Systems*

A basic -design of capsular systems consists of insoluble capsule body and it contains a drug and a plug. The plug is detached after a certain time lag because of swelling, erosion, or dissolution. Pulsin cap system -water-insoluble capsule: open end will be closed with a swellable hydrogel plug, this hydrogel comes in contact with the dissolution medium or GI fluids and the plug itself will be pushed out, finally drug will be released spontaneously after a lag time (Gowda and Kumar, 2022). The time lag can be controlled by adjusting the dimension and position of the plug.

The drug release process typically includes an initial burst phase, a sustained release phase, and a final depletion phase illustrates these phases in a typical release profile (Guo and Song, 2020). plug material: insoluble but permeable and swellable polymers (e.g.: polymethacrylates), erodible compressed polymers (E.g: hydroxyl propyl methyl cellulose, polyvinyl alcohol, polyethylene oxide), congealed melted polymers (E.g: saturated polyglycolated glycerides, glycerylmonolate and enzymatically controlled erodible polymer (e.g: pectin). no irritations (gi) are occurred. Pulsatile drug delivery systems are designed to release drugs in a controlled manner after a specific lag time (Figure 2). The release typically occurs in three phases: lag phase (no drug release), burst phase (rapid drug release), and sometimes a sustained release phase. In the lag phase, the drug is protected by a coating or barrier that prevents immediate release. Once the barrier is breached by time, pH, enzymes, or other triggers the burst phase and rapidly delivering the drug. This system is especially useful for conditions that follow a biological rhythm, such as asthma or arthritis, where timed drug delivery improves therapeutic effectiveness (Gupta and Kesarwani, 2019; Gupta and Mishra, 2021).

### Port systems

The Port System: This consists of a gelatin capsule coated with semipermeable emembrane (cellulose Acetate) encloses insoluble plug and osmolytically active agent with drug formulation (Han and Yang, 2018). The drug will come in contact with the aqueous medium and the water diffuses into the capsule across semi permeable membrane and the plug will be ejected due to inner pressure after a lag time. Based on thickness of the semi permeable membrane time lag can be controlled. If the drug should be in a liquid form the drug will be delivered by osmotic capsular system (He *et al.*, 2022). The liquid drug will be absorbed by large sized particles and it will release into semipermeable membrane after barrier layer is dissolved which consists of expanding osmotic layer (Huang and Feng, 2020). The moisture in our body enters the osmotic layer of the capsule and this system is based on this principle. The capsule wall consists of an orifice and the material used for the capsule wall preparation is elastic material. As the osmosis continues the pressure inside the capsule increases and reaches to a point where orifice stops the release of the drug after certain period of time it allows the drug release as the wall attains beyond threshold limit (Jain and Sharma, 2019). Elastomers, like styrene-butadiene copolymer are used.

### Delivery by a series of stops

Implantable capsule system, this contains a series of compartments contains drug and an osmatic engine and separated by a movable separation. The pulsatile delivery is achieved by a series of stops along the inner wall of the capsule. The number of stops and the gap in between the capsule decides the frequency and intensity of the drug release. It was used to deliver porcine somatotropin (Jhaveri and Dubey, 2021).

## Delivery by solubility modulation

This system contains solubility modulator and it depends upon solubility. The agents used for the modulator are solid organic acid, inorganic salt, or organic salt (Kale and Swaminathan, 2018).

## Delivery through reservoir systems having erodible or soluble barrier coatings

This is a reservoir device coated with a barrier layer. This layer dissolves or erodes after a certain lag time. The time lag depends on the thickness of the coating layer. The Time Clock system consists of acoated solid dosage form with lipid barriers made up of carnauba wax and bees wax along with surfactants. The Chronotropic system consists of a drug core coated by lipophobic swellable Hydroxypropyl Metylcellulose (HPMC), which is responsible for a time lag in the onset of drug release (Kang and Lee, 2022).

## Systems with rupturable coating

In this system the release of drug controlled by disintegration of coating for the rupture of the coating the pressure will be occurred by disintegrants, effervesent excipients, osmotic pressure. The tablet core contains effervescent mixture of citric acid and sodium bicarbonate, the carbon dioxide causes the coating to rupture after it comes into contact with dissolution fluid. Super disintigrents goes on principle of swelling the tablet contains a swellable layer, and a rupturable layer examples: cross carmellose sodium, sodium starch glycolate, L-HPC. The release of drug depends upon the coating layers and its thickness (Ke *et al.*, 2019).

## Multiparticulate Systems

This system are mainly oral dosage forms consisting of a many small discrete units, in which the active substance is present as a number of small independent subunits.

Pulsatile drug delivery systems are often composed of multiple layers, each designed to control the timing and rate of drug release illustrates the typical structural layers involved in such systems. Pulsatile drug delivery systems consist of multiple layers that control the timing of drug release. The innermost core layer contains the active pharmaceutical ingredient. Surrounding it is a barrier or lag-time controlling layer, which delays the release until the desired time or trigger is reached (Figure 3). An optional outer protective layer may be included to shield the system from environmental conditions like stomach acid or moisture (Khan and Sahni, 2020).

## Pulsatile System with Rupturable Coating

This is a multiparticulate system in which drug is coated on non-pareil sugar seeds followed by a swellable layer and an insoluble top layer resulting in rupture of film with subsequent rapid drug release (Lee and Park, 2019). Environmental factors like pH and drug solubility does not affects the release of drug. The lag time can be increased with coating thickness or by adding

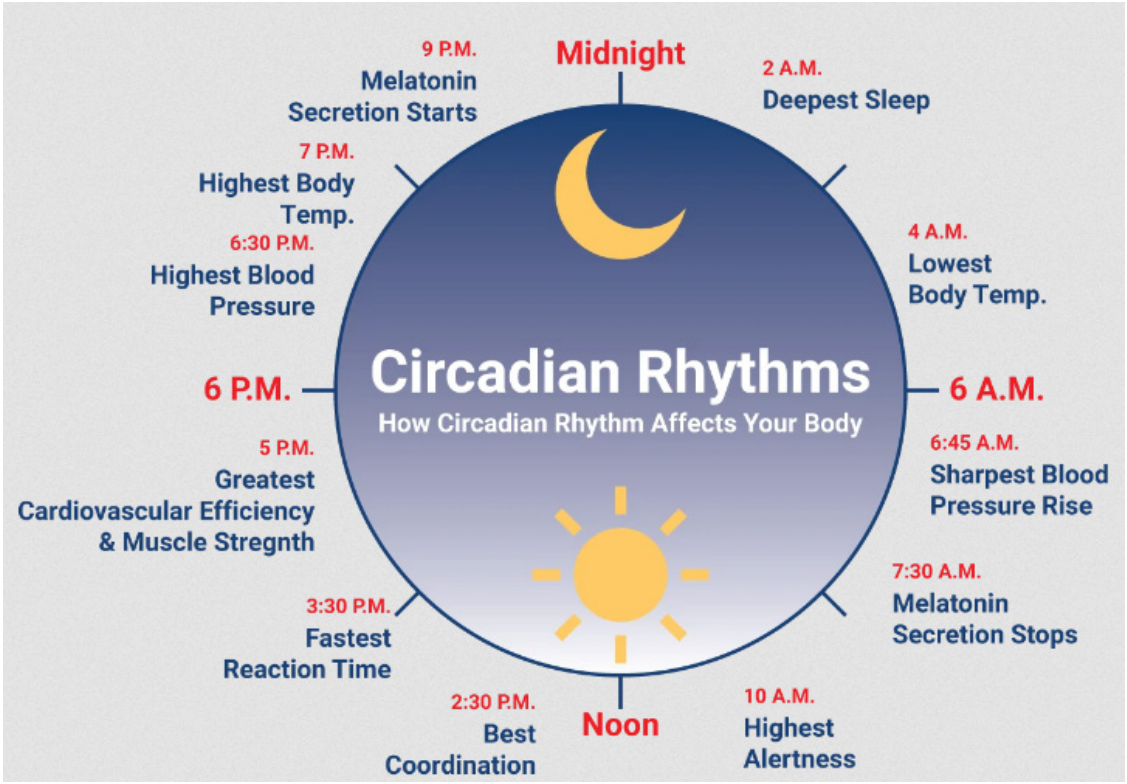


**Figure 1:** Circadian Rhythms

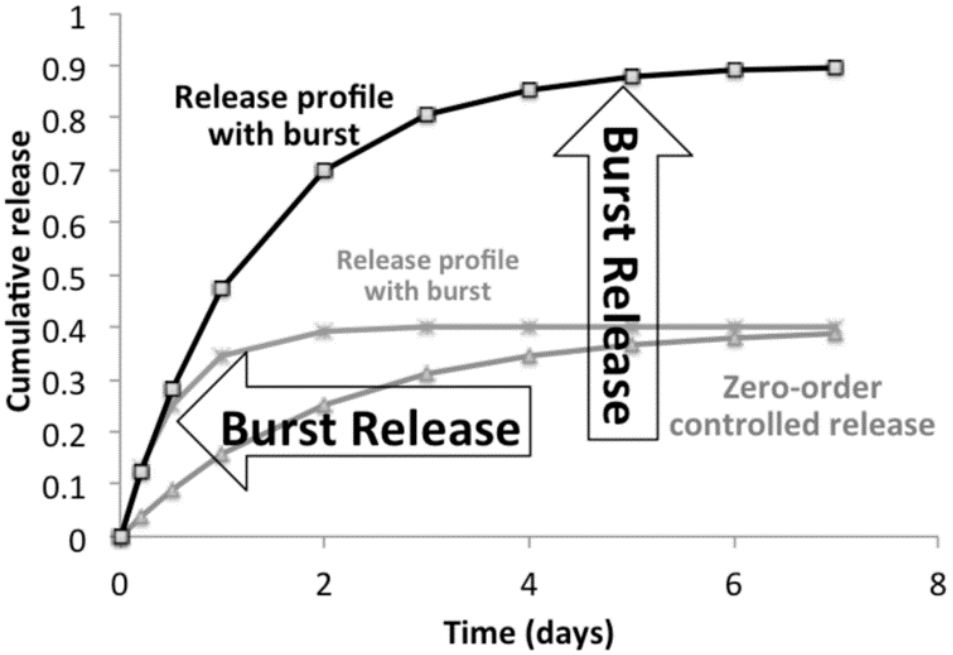


**Figure 2:** phases of drug release

large amounts of hydrophobic plasticizer in the outermost layer (Kumar and Sharma, 2018).

### Time controlled expulsion system

It contains core, swelling agent and osmotic effects due to depletion of internal layer, internal stress increases and the capsule explodes and the release of drug occurs (Lee and Park, 2019).

### Pulsatile drug Delivery by Change in the membrane permeability

Acrylic polymers are used and it is based on ion exchange followed by change in permeability (Li and Liu, 2020).

### Low density multiparticulate pulsatile systems

In low density floating multiparticulate pulsatile dosage forms reside only in stomach and not affected by variability of pH, local environment or gastric emptying rate. Local delivery in stomach and drugs which are absorbed in the stomach can be done by this type of dosage form (Liu and Jiang, 2021).

## STIMULI INDUCED PULSATILE SYSTEM

In this system the release of the drug will be done after stimulation by any biological factor like temperature, and other chemical stimuli. These systems are further classified as:

1. Thermo-Responsive Pulsatile release, 2. Chemical stimuli induced pulsatile system

Pulsatile drug delivery systems are designed to release drugs after a predetermined lag time, followed by rapid or multiple release phases graphically represent this relationship between drug releases and lag time in pulsatile drug delivery systems, the graph of drug release versus time shows a distinct lag phase with no drug release, represented by a flat line along the x-axis. After the lag time, the graph exhibits a sudden, steep rise, indicating a rapid or burst release of the drug (Figure 4). This sharp increase reflects the pulsatile nature of the system, delivering the drug at a specific time rather than continuously. Depending on the design, the graph may show multiple pulses or plateau after the burst, indicating complete or stage-wise drug release (Liu *et al.*, 2022).

### Thermo-Responsive Pulsatile release

Thermo-responsive hydrogel systems are developed for pulsatile release. In these systems the polymer undergoes swelling or deswelling phase in response to the temperature which modulates drug release in swollen state. In development of temperature induced system indomethacin was released in pulsatile release pattern and the temperature ranges between 20°C & 30°C was developed by using reversible swellable properties of copolymers of N-isopropylacrylamide and butyrylacrylamide (Majumder and De, 2018).

### Chemical stimuli induced Pulsatile system

#### *Glucose-responsive insulin release device*

The drug releases as the glucose concentration alters in the body, pH sensitive hydrogel contains glucose oxidase stabled in the hydrogel. The release of drug will be done by change in pH which occurs due to gluconic acid this whole process will be happened due to high glucose concentrations. The change in PH induces swelling of the polymer which results in insulin

release. Insulin by virtue of its action reduces blood glucose level and consequently gluconic acid level also decreases causing the system to enter deswelling mode thereby decreasing the insulin release (Manchanda and Bhardwaj, 2021). Ex: chitosan, polyol etc.

### Inflammation-induced pulsatile release

On acquiring any physical or chemical stress, such asinjury, fracture etc., inflammation take place at the injured sites. As we know hyluronic acid degrades hydroxyl radicals which are produced from inflammatory cells So hyluronic acid gel injection produce a synergistic action with anti-inflammatory drug and release drug in a pulsatile pattern and helps in treating inflammatory diseases like rheumatoid arthritis (Martins and Miguel, 2020).

### Drug release from gels responding to antibody concentration

There are many kinds of bioactive compounds exists in the body the swelling and deswelling properties of capsule changes by bioactive compounds. The antigen-antibody complex forms cross-linking units in the gel, such interaction is very specific. Using the difference in between polymerized antibodies and naturally derived antibodies towards specific antigens, reversible gel swelling or deswelling and drug permeation changes occurs (Mishra and Swain, 2019).

### pH sensitive drug delivery system

This type of PDDS contains two components. The first one is fast release type while the other is pulsed release which releases the drug in response to change in pH by selecting the pH dependent polymers drug release at specific location can be obtained (Morsi and El-Kamel, 2022).

Examples: celluloseacetate phthalate, polyacrylates, and sodium carboxymethylcellulose. These polymers are used as enteric coating materials to provide release of drug in the small intestine (Nissa and Rao, 2020).

## EXTERNAL STIMULI INDUCED

### Electro responsive pulsatile release

Electrically responsive delivery systems are prepared from polyelectrolytes (polymers contains high ionisable groups) and they are both pHresponsive as well as electro-responsive. Examples of naturally derived polymers include hyaluronic acid, chondroitin sulphate, agarose gel (Prasad and Singh, 2021).

### Micro Electro Mechanical Systems (MEMS)

Polymer-based systems and microchip, the microchip consists of an array of reservoirs that extend through an electrolyte-impermeable substrate. Microchip controls both release time and rate (Raza and Ansari, 2022).

### Magnetically induced pulsatile release

One of the old methodologies was oscillating magnetic field which modulates the rates of drug release from polymer matrix (Sharma and Chouhan, 2020).

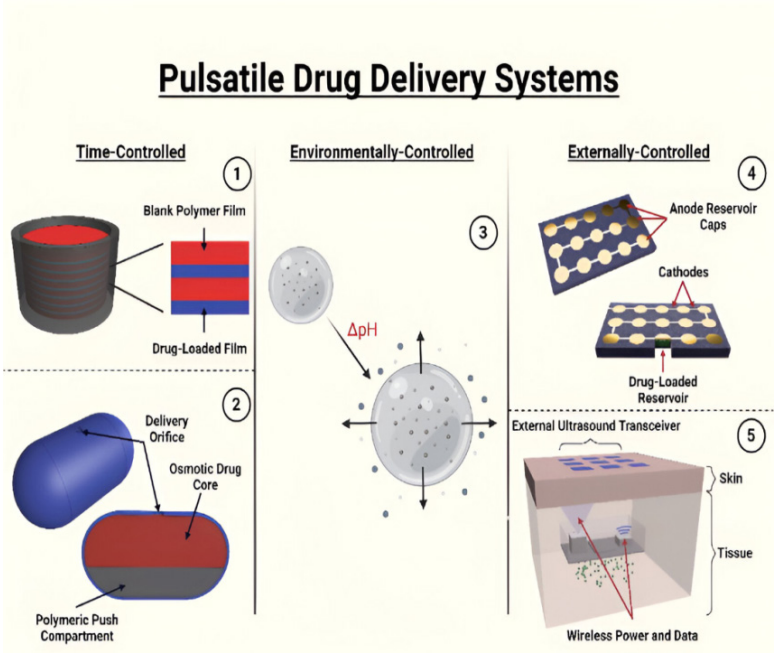


**Figure 3:** Layers of pulsatile drug release

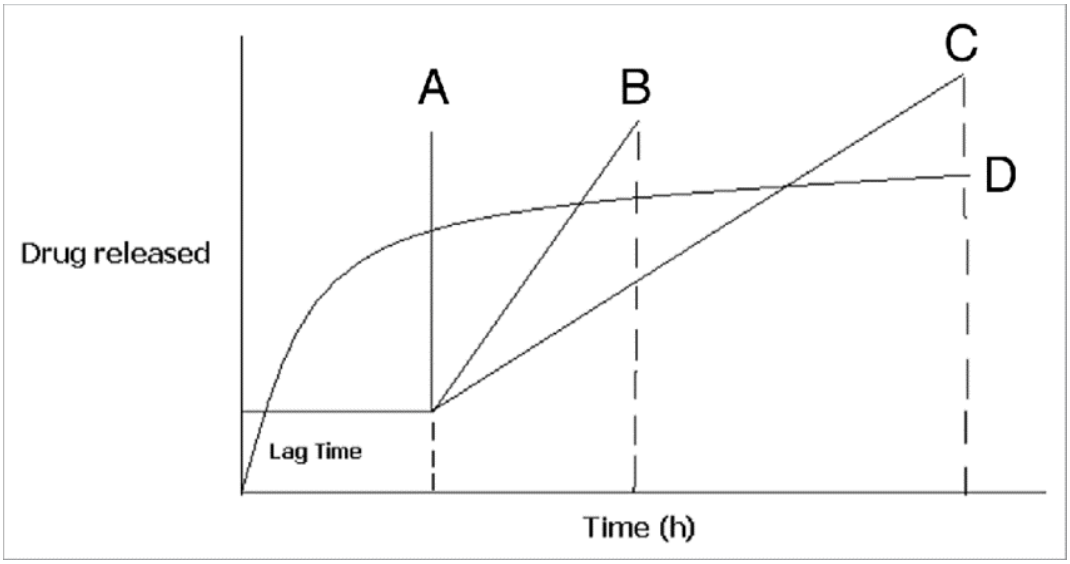


**Figure 4:** Graphical representation of drug release vs lag time

## PULSATILE RELEASE SYSTEM FOR VACCINES AND HORMONAL PRODUCTS

Vaccines are traditionally administered as an initial shot of an antigen followed by repeated booster shots to produce protective immunity. In PDDS system the vaccine of both initial and booster dose can be given in a single shot as the booster dose is release is controlled Pulsatile drug release can occur in time-controlled, stimuli-induced, or externally triggered forms. In time-controlled systems, drug release happens after a predetermined lag time, often using erodible or swellable coatings. Stimuli-induced systems respond to internal triggers like pH, enzymes, or temperature changes at the target site (Figure 5). Externally triggered systems release the drug in response to external cues such as light, ultrasound, or magnetic fields (Sharma *et al.*, 2024).

Pulsatile drug delivery systems can be tailored to various diseases by aligning drug release with biological rhythms or symptoms peaks, as outlined in table. The drug release mechanism in a Pulsatile Drug Delivery System (PDDS) is designed to release the drug after a specific lag time, matching the body's biological rhythms. This is achieved using coatings or barriers that delay release until they are eroded, ruptured, or dissolved by physiological conditions such as pH or enzymes (Figure 6). Once the barrier is breached, the core drug is rapidly released in a burst. This mechanism ensures targeted, time-specific delivery, improving therapeutic outcomes for chronobiological diseases (Singh and Bajpai, 2021).

## SUMMARY

Pulsatile Drug Delivery Systems (PDDS) represent a significant advancement in modern pharmacotherapy, designed to release drugs in a controlled, time-dependent manner that mimics the body's natural rhythms. Traditional drug delivery methods often lead to suboptimal therapeutic outcomes due to constant release rates, which can result in fluctuating drug levels and adverse side effects. In contrast, PDDS aim to deliver drugs in a manner that aligns more closely with the circadian patterns of biological processes, optimizing therapeutic efficacy and minimizing side effects. The fundamental principles of PDDS will lie on their ability to release therapeutic agents at predetermined times, thus enabling synchronization with the body's biological cycles. This approach is particularly beneficial for treating diseases that exhibit diurnal variations, such as asthma, hypertension, and certain types of cancer. By tailoring the release profile, PDDS can enhance the pharmacological response, improve patient compliance, and reduce the frequency of dosing. Various technologies have been developed to facilitate pulsatile release, including swellable systems, osmotic systems, and capsule-based approaches. Swellable systems, for instance, utilize hydrophilic polymers that expand in response to aqueous environments, creating a delay in drug release until a specific time point is reached. Osmotic systems, on the other hand, employ osmotic pressure to control the release rate, allowing for a rapid release of the drug after an initial lag phase. The formulation of PDDS requires careful consideration of several factors, including the choice of polymers, the nature of the drug, and the intended release profile. Biodegradable polymers are often favored for their compatibility with biological systems and their ability to minimize side effects. Additionally, the incorporation of triggers such as pH, temperature, or specific enzymes-can enhance the responsiveness of the delivery system, ensuring that the drug is released at the right moment.

Clinical applications of PDDS are expanding, with significant implications for chronic disease management. For instance, in the treatment of diabetes, PDDS can be designed to release insulin in response to postprandial blood glucose levels, thus closely mimicking natural insulin secretion. Similarly, in the management of hypertension, drugs can be released during the early morning

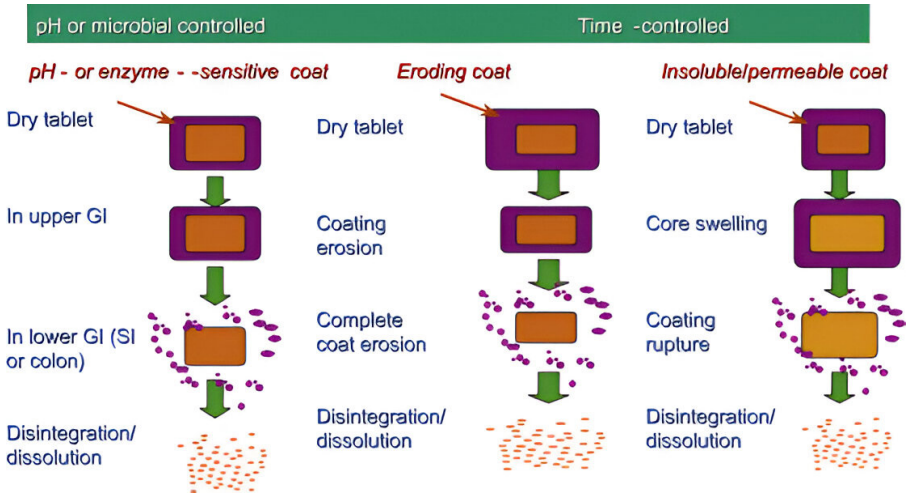


**Figure 5:** Different forms of pulsatile drug release.

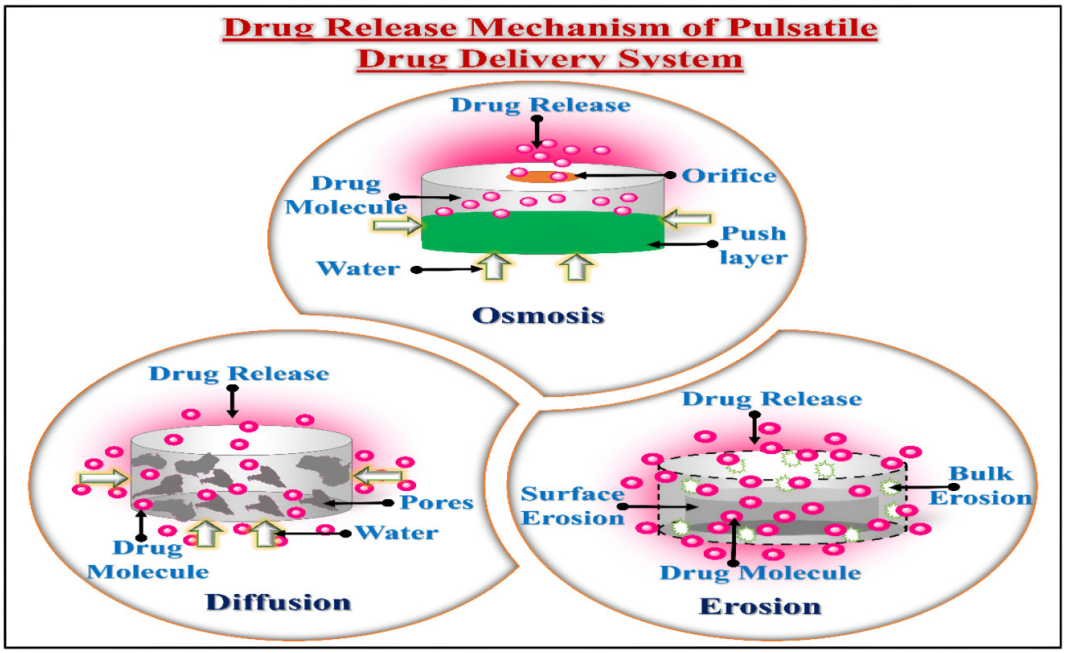


**Figure 6:** Drug release mechanism of Pulsatile Drug Delivery System.

hours when blood pressure tends to peak, improving control over cardiovascular events. Despite their promising advantages, the development of PDDS is not without challenges. Formulation complexities, potential manufacturing issues, and the need for extensive regulatory approval can hinder their widespread adoption. Additionally, the stability of the formulations and the reproducibility of the release profiles are critical factors that must be addressed to ensure therapeutic effectiveness.

In summary, pulsatile drug delivery systems represent a transformative approach in drug delivery, offering tailored therapeutic interventions that align with the body's natural rhythms. By improving the pharmacokinetic and pharmacodynamic profiles of medications, PDDS hold great promise in enhancing treatment efficacy and patient compliance. As research advances and technology evolves, the potential for PDDS to revolutionize modern medicine becomes increasingly apparent, paving the way for more effective and personalized therapeutic strategies. The integration of these systems into clinical practice could mark a significant leap forward in the management of various chronic diseases, ultimately leading to better health outcomes.

## CONCLUSION

Pulsatile Drug Delivery Systems (PDDS) represent a significant advancement in the field of modern drug delivery, offering a targeted and time-controlled release of therapeutics that aligns closely with the body's natural biological rhythms. The traditional drug delivery methods often suffer from limitations such as uncontrolled release rates, leading to suboptimal therapeutic outcomes and increased side effects. In contrast, PDDS aims

to mimic the body's physiological needs, providing medication at specific intervals to enhance efficacy and minimize toxicity. One of the key advantages of PDDS is its ability to overcome the limitations associated with chronic diseases that require timely administration of drugs. For conditions such as hypertension, asthma, and inflammatory diseases, PDDS can deliver medications in a manner that synchronizes with the pathophysiology of the disease, thereby improving patient compliance and therapeutic outcomes. By enabling a pulsatile release, these systems can help in managing diseases where drug action is required only at certain times of the day, thereby enhancing the overall treatment experience. The design of PDDS is diverse, utilizing various technologies such as multi-layered tablets, microencapsulation, and smart polymer systems that respond to specific stimuli. These innovative approaches not only enhance the precision of drug delivery but also allow for customization based on the pharmacokinetic and pharmacodynamic profiles of the drugs involved. Advances in materials science and biotechnology have further propelled the development of PDDS, enabling the use of biocompatible and biodegradable materials that align with regulatory standards for safety and efficacy. Despite these advancements, there are challenges that need to be addressed for the widespread adoption of PDDS in clinical settings. Manufacturing complexities, stability issues, and the need for extensive *in vitro* and *in vivo* studies to ascertain the performance of these systems pose significant hurdles. Moreover, the regulatory landscape for novel drug delivery systems can be stringent, requiring comprehensive documentation and evidence of safety and efficacy, which can be a barrier for developers. Future research should focus on optimizing the design and functionality of PDDS, particularly in the context of personalized medicine. Tailoring drug delivery to the individual's needs based on genetic, metabolic, and environmental factors can significantly enhance therapeutic outcomes. Additionally, integrating PDDS with smart technology-such as wearable devices or mobile health applications—could further revolutionize drug delivery by providing real-time monitoring and control over drug release profiles. In summary, pulsatile drug delivery systems offer a promising and innovative approach to modern pharmacotherapy. Their ability to provide controlled, targeted, and timed release of drugs aligns well with the dynamic nature of human physiology and disease. As technology continues to evolve, PDDS holds the potential to significantly improve treatment regimens across a variety of medical conditions, ultimately leading to enhanced patient outcomes and quality of life. Continued collaboration between researchers, clinicians, and regulatory bodies will be essential to navigate the challenges and fully realize the potential of pulsatile drug delivery in clinical practice.

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## CONFLICT OF INTEREST

There are no conflicts of interest among authors.

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