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Recent Advancement in Pulsatile Drug Delivery Systems

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Abstract

Pulsatile drug delivery system is the most interesting time- and site-specific system. This system is designed for chronopharmacotherapy which is based on circadian rhythm. The principle rationale for the use of pulsatile release is for the drugs where a constant drug release, i.e., a zero-order release is not desired. A Pulsatile drug delivery program is a very interesting program - and exact time. This system is designed for the drug delivery system Pulsatile is defined as the rapid and rapid release of a certain number of molecules shortly after the prescribed release. Various systems like capsular systems, osmotic systems, pulsatile system based on the use of soluble or erodible polymer coating, use of rupturable membranes and pulsatile system based on membrane permeability are summarized in this article. These systems are beneficial for the drugs having chrono pharmacological behavior where night time dosing is required and for the drugs having high first-pass effect and having specific site of absorption in gastrointestinal tract.

Key words: Capsular system, chronopharmacotherapy, erodible and rupturable system, osmotic system, pulsatile drug delivery system

INTRODUCTION:

Drug delivery system is the rapid and temporary release of certain molecules in a short period of time immediately after the prescribed release time, lag time, or these systems have a peculiar mechanism of delivering the drug rapidly and completely after a lag time Pulsatile drug delivery systems are developed to deliver drug according to circadian behavior of diseases. This means that these systems will deliver drugs at a time when diseases show their worst and fatal condition during the circadian cycle (24 hrs.). Intensive drug delivery is timely and local drug delivery, thus providing local and temporary delivery and increasing patient compliance. The product follows the sigmoidal drug release profile indicated for the duration of withdrawal (remaining time) followed by rapid and complete drug release. Therefore a medicine can be delivered at the right time, at the right price and at the right place to work using that method. Drug delivery refers to the technology used to deliver a drug to the desired location for the drug to be released and absorbed, or the subsequent transport of active ingredients from biological components to the workplace. Drug withdrawal from: spread, decay, inflammation, and closely related processes. Some of the most common routes of administration include enteral (intestinal tract), parenteral (injection), sniffing, transmission, advanced and oral methods. The goal of a drug delivery program aimed at

stretching, positioning, directing and interacting with drug-protected interactions with diseased tissues. The most common drug delivery system is the absorption of the drug into the biological membrane, and the targeted drug delivery system releases the drug in moderation. Medications can be taken in a variety of ways - by swallowing, inhaling, inhaling the skin, or by intravenous injection. Each method has its advantages and disadvantages, and not all methods can be used for all medications.

PROMOTED DRUG PRODUCTS:

Released drug product has been replaced by those that change the time and / or rate of release of the drug substance.

The types of modified drug products are:

1. Delayed release
2. Extended release
3. Targeted discharge
4. Oral dispersed tablet

1. DIFFERENT SALE PRODUCTS: A dosage form that removes part / s of a drug from time to time without being released immediately after handling. The first part can be removed immediately after administration. e.g., Enteric dosage forms are standard products for delayed release (enteric-bound aspirin and other NSAID products).

2. PROPERTY RELEASE PRODUCTS: A dosage form that allows for at least a double dose reduction dose compared to the drug presented as an immediate (standard) dosage form. It includes controlled releases, continuous releases, and long-acting drug products.

3. PRESCRIBED DISCLOSURE PRODUCTS: A measurement form that removes a drug from or near an area of physical activity. Targeted release rate forms may have immediate or extended release marks.

4. Completely differentiating tables: ODTs are designed for rapid separation of saliva after oral administration. It can be used without the addition of water. The drug is dispersed in saliva and swallowed with little or no water.

Pulsatile Drug Delivery System

Pulsatile drug delivery system is defined as the rapid and rapid release of a certain number of drug molecules in a short period of time immediately after the prescribed release time, i.e., the remaining time. These systems are designed in such a way that there is a rapid and rapid release of a certain amount of drug molecule in a short period of time immediately after a certain period of lag. The duration of the lag is possible depending on the requirement of the disease condition .The general graph of the delivery of drugs with pulsatile differs from the controlled release.

Intensive drug delivery aims to deliver the drug in a planned pattern i.e. at the right time and in the right place to work. It is chrono pharmaco therapy designed according to the rhythm of the circulatory system. It is a type of Intelligent Drug Delivery System that can adjust drug levels to respond to the body's need.

THE NEED FOR PULSATILE DDS

1. Initial immunity: Beta blockers and salicylamide.

2. Biological tolerance: Transdermal nitroglycerin, salbutamol sulphate.

3. Special chronopharmacological needs: Asthma and angina pectoris are most common in the morning.

4. Local need for treatment: Inflammatory bowel disease.

5. Stomach upset or drug instability in the gastrointestinal tract: Environmental protection of the stomach is essential for drugs such as gastric acidic medium (eg peptide drugs), irritating the gastric mucosa (NSAIDS) or causing nausea and vomiting.

BENEFITS OF PULSATILE MEDICINAL INFECTION SYSTEM

i. It increases the absorption and availability of the finder rather than a standard discharge or a continuous discharge drug.

ii. Site administration allows for the delivery of inaccessible drugs that can be destroyed in the GI tract area. e.g., peptides and protein molecules.

iii. Reduce the dose of the drug without reducing the side effects of treatment.

iv. There is no risk of losing volume and side effects. v. Slight differences between internal and external.

v. Pulse release allows for multiple measurements in the form of a single measurement.

vi. The system can be used for many measuring forms such as granules, microspheres, microparticles, tablets, capsules and pellets.

vii. Limited risk of local irritation.

viii. Improves stability.

PDDS Limitations:

i. Multiple production steps and a large number of process flexibility.

ii. The similarity of the unity of the anointed barrier is mandatory to ensure the speculation of lag time.

iii. Cracking time cannot always be adequately controlled as it depends on the physicochemical properties of the polymer.

iv. High production costs.

v. Raw material is not readily available.

v. The design of the scale form requires highly skilled / trained professionals.

vi. The technology used and the equipment used are sophisticated.

PLANNING

PDDS classification system timely system Internal Stimulus involving an external Multi particulate System system for vaccine and hormonal products

The various methods of the pulsatile system are broadly divided into the following:

1. CONTROLLING SYSTEMS: Controlled drug delivery is the type of system that releases drugs in the dosage form at a local or fixed dosage for a specified period of time.

a) Automatic capsule drug release:

One-unit systems are mostly built in capsule form. The remaining time is controlled by a plug, which is removed by swelling or erosion, and the drug is released as a "Pulse" into the body of the insoluble capsule. This dosage form consists of a non-invasive body capsule containing a drug as well as leaky and dampened plugs made of materials such as polymer hydrophilic or lipids. The lag time can be controlled by tricking the size and shape of the plug. Polymers used to design hydro gel plug include: Immovable but flexible and swollen polymers (eg, polymethacrylate) Compressed polymers (eg, hydroxypropylmethyl cellulose, polyvinyl alcohol, Polyethylene oxide). Melted polymers (e.g., polyglycolated-filled glycerides, glyceryl monoleate) An erodible polymer administered Enzymatically (e.g., pectin).

Capsule release scheme diagram: When in contact with liquid liquid, the cap dissolves rapidly thus releasing a rapid release component followed by a pulse release component. The length of the plug determines the lag time.

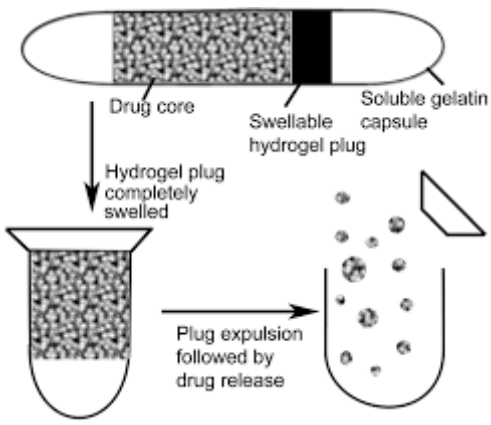

Fig. no 1 Automatic capsule drug release

b) System based on osmosis

It contains capsule coated semipermiable membrane. Inside the capsule there was an unlit plug containing an Osmotically active agent and drug formulation. Such a system has been used to deliver methylphenidate used for the treatment of attention deficit hyperactivity disorder as an intensive port system. Eg. The system of the hole.

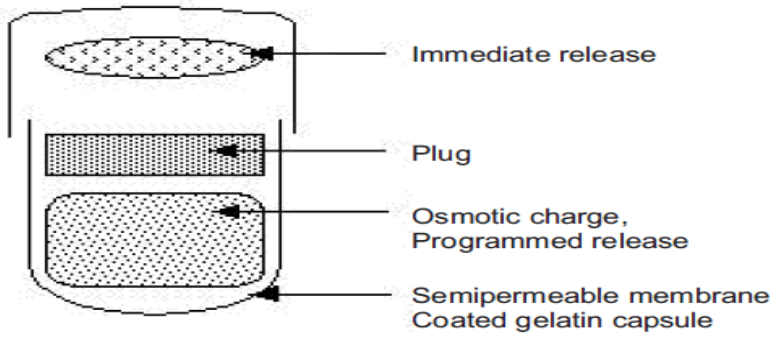

Fig. no 2 System based on osmosis

c) Solibilization or orosion systems

In such systems, the core containing drug is coated with the soluble or erodible polymer as outer coat and drug release is controlled by the dissolution or erosion of the outer coat. Time dependent release of the drug can be obtained by optimizing the thickness of the outer coat as show in fig. e.g. The Time Clock system and the chronotropic system.

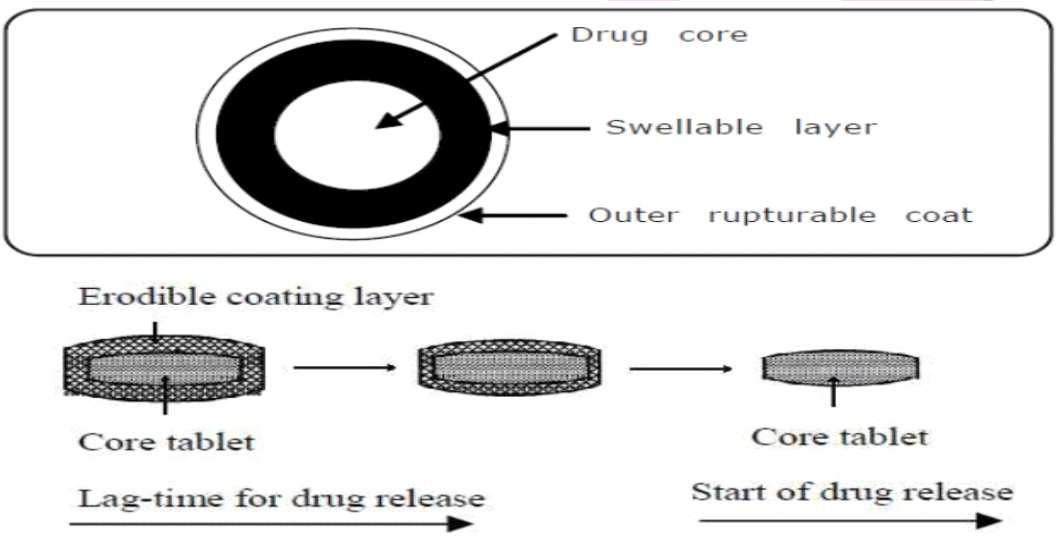

Fig.no 3 Solibilization or orosion systems

d) System with ruptureable coating membrane

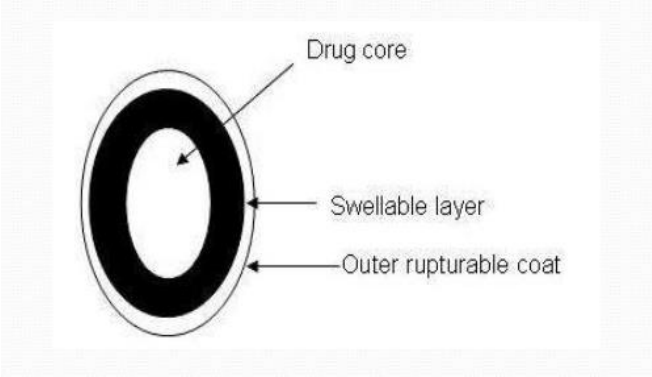

Fig.no 4 System with ruptureable coating membrane

Instead of swelling or erosion, these systems rely on the separation of the tissue to release the drug. The pressure required for the fabric to crack can be achieved by swelling, disintegration, active adhesives, or osmotic pressure. Waterlogging and mechanical resistance of the outer membrane are major factors affecting the lag period. Eg .: Buflomedil HCl is used for the treatment of vascular disease

2. Internal Stimuli Induced Systems:

a)Temperature Induced System: This deviation can sometimes serve as a catalyst for the release of therapeutic chemicals from several drug delivery systems that respond to the treatment of flu-related illnesses. The temperature at which the dynamic and dynamic drug delivery system utilizes a variety of polymer structures, including the flexible coil / globule flexible thermal coating of polymer molecules, network swelling, glass modification and

Thermo-responsive hydrogel systems

Thermo-responsive hydrogel systems use hydrogels that perform a variable volume change in response to temperature changes. These gels reduce the temperature fluctuations leading to the temperature of the low-pressure solution (LCST) of the direct polymer. Hydrosgelic hydrosensitive hydrogels have a certain chemical attraction to water, so they absorb water and swell at temperatures below the changing temperature and decrease or remain at higher temperatures by changing the water. Hydrogels and therapeutic membranes have been widely used as pulsatile drug delivery platforms.

Thermo responsive polymeric micelle systems

In this case, the gel system firmly retains the target drug in micelles and quickly removes the controlled amount of the drug by turning off external stimuli such as temperature or infrared laser beam. Eg. Y.H. Bae et al developed an indomethacin pulsatile release pattern at temperatures between 20oC and 30oC by using the flexible inflammatory properties of N-isopropylacrylamide copolymers and butyrylacrylamide.

b) Programs by Chemical Stimuli

In these systems, there is a release of the drug after reactivation by any biological factor such as an enzyme, pH or other chemical stimulant. pH Sensitive Drug Deliver System.

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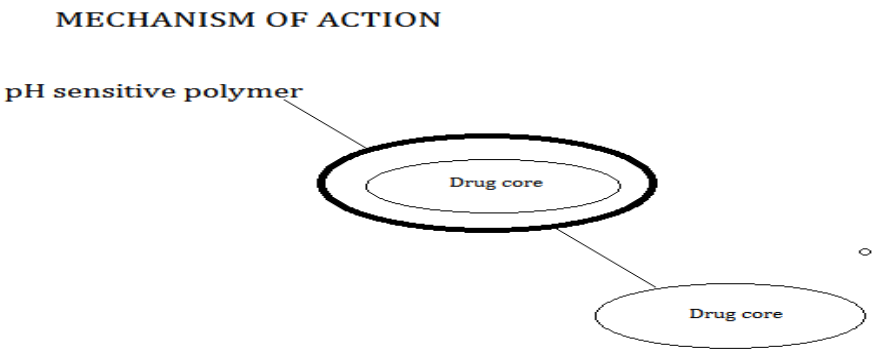

Fig.no 5 Programs by Chemical Stimuli

Glucose-insulin-releasing insulin release devices: In a glucose-rich environment, such as blood after a meal, glucose oxidation to gluconic acid promoted by glucose oxidase can lower the pH to about 5.8. This change in pH causes inflammation of the polymer leading to insulin secretion. Insulin due to its action lowers the level of glucose in the blood and as a result the level of gluconic acid also decreases and the system turns to a waste mode thus reducing insulin secretion. Examples of sensitive pH polymers include N, N-dimethylaminoethyl methacrylate, chitosan, polyol etc.

Inflammation causes pulsatile relief: When you experience any physical or chemical stress, such as injuries, fractures, etc., inflammation occurs in the injured areas. During inflammation, hydroxyl radicals are produced in these cells that respond to inflammation. Damage to hydroxyl radicals however, tends to rule out and is faster when Hyaluronic Acid gel is injected into flammable areas. Therefore, it is possible to treat patients with inflammatory diseases such as rheumatoid arthritis; using anti-inflammatory drugs including HA gels as new ways to reduce drugs.

Drug release into smart gels that respond to antibody concentrations: There are many types of interlocking elements present in the body. Recently, gel novels have been developed in response to changes in the concentration of bioactive chemicals to alter their inflammatory / disposal properties. Special attention was given to the complex structure of the antigen-antibody as gel-binding units, because such interactions are very clear. Using differences in the composition structures between polymer antibodies and antibodies that are naturally derived from certain antigens, gel changes inflammation / decomposition and drug overdose occur.

Enzymatically made liposome:

Drug-loaded liposomes were incorporated into microcapsules of alginate hydrogels. Liposomes within microcapsules are bound to phospholipase A2 to achieve the release of drug molecules. Phospholipase A2 has been shown to accumulate at the water / liposome junction and remove acyl

group from the phospholipids in the liposome. The resulting liposomes release their drug molecules, thus allowing drug release to be regulated by the level that determines the membrane of the microcapsule. Reversal: stability due to the absorption of plasma proteins in the lipid bilayer and thus reducing the utilization of these compounds.

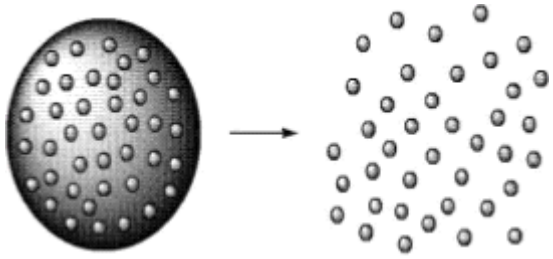

Fig.no 6 Enzymatically made liposome

3. Internal Control-Released System: This system does not use them, but instead requires external environmental changes to initiate drug delivery. These may include magnetic field, ultrasound, electric field, light and energy.

I) Magnetic fields: The use of a flexible magnetic field to measure the release rates of a drug from a polymer matrix was one of the oldest methods. Magnetic conductors derive their magnetic response from magnetic forces from composite materials such as Magnetite, Iron, Nickel, Cobalt etc. In biomedical applications, magnetic carriers must be dehydrated, regenerated, non-toxic and do not use an immunogenic mechanistic magnetic-based approach to attract the slowdown of oral drugs into the intestinal system. This can be done by filling an additional magnetic field into capsules or pills. The speed of the gastrointestinal tract may be reduced in some areas by external magnetism, thereby changing the duration and / or magnitude of drug absorption in the stomach or intestines

II) Electrical field installation system: Electrification delivery systems are prepared from polyelectrolytes (polymers that contain the highest concentration of visible groups next to the spinal cord) and as a result, pH- and electro-response. Under the influence of the electric field, excessive reacting hydrogels usually bend, depending on the shape of the electrode-shaped gel while the grounding occurs when the hydrogel sleeps differently from the electrodes. Eg. Poly (acrylamide-grafted-xanthan gum) is a hydrogel for transdermal delivery of ketoprofen.

III) Ultrasound-produced extraction system: Ultrasound is widely used as a booster to improve drug penetration through biological barriers, such as skin. Ultrasound devices are used to achieve a 27-fold increase in the extraction of 5-fluorouracil from ethylene and vinyl acetate matrix. Increased ultrasound intensity resulted in a corresponding increase in the amount of 5-fluorouracil extracted.

IV) Light-emitting system: Light-sensitive hydrogels have potential applications in creating optical switches,

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display units, and opthalmic drug delivery devices. The interaction between light and objects can be used to measure drug delivery. heat, increasing the temperature of the composite hydrogel above its LCST, the hydrogel collapses and leads to an increase in the rate of dissolution of the soluble drug stored within the matrix.

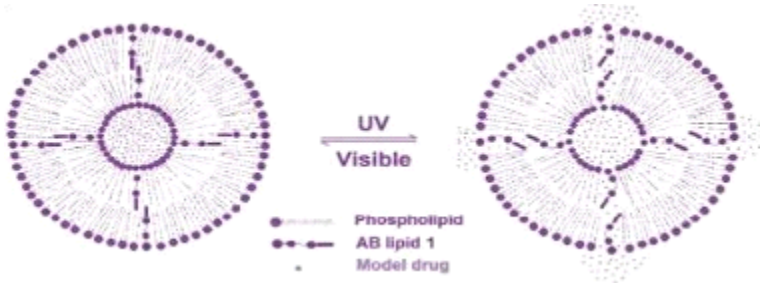

Fig. no 7 Light-emitting system

4) Multiparticulate Systems: Such systems are: Reservoir systems with rupturable polymeric Coatings. Reservoir systems with soluble or eroding polymer coatings. Floating multiparticulate pulsatile systems. The purpose of designing multiparticulate dosage form is to develop a reliable formulation that has all the advantages of a single unit formulation and yet devoid of the danger of alteration in drug release profile and formulation behaviour due to unit to unit variation. The system consists of uniform spheroidal beads of 1-2mm in diameter containing drug & excipients and is coated with product specific controlled release polymers and drug releases by erosion or diffusion.

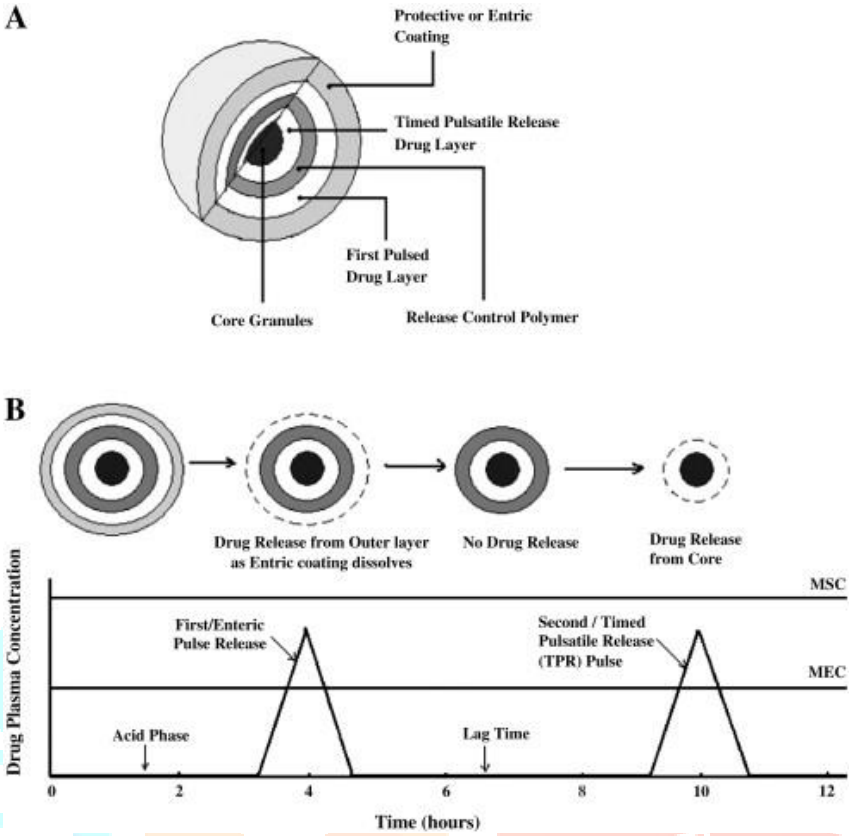

Fig.no 8 Multiparticulate Systems

5) System Products and Hormone Products: Vaccines are traditionally used as a starting point for antigen followed by repeated shooting to produce self-defense. PDDS offers the potential for a single vaccine if the initial antigen release can be detected from a single system where the booster release time is controlled. GnRH binding and secretion of luteinizing hormone to the hormone-stimulating follicle in cows.

Diseases That Required Pulsatile Drug Delivery System

DISEASE	SYMPTOMS	CHRONOLOGICAL BEHAVIOUR	DRUGS USED
Peptic ulcer	Upper abdominal pain, Nausea, Bloating, Lack of appetite, Weight loss, Heartburn	Acid secretion is high in the afternoon and at night.	H2 blocker
Asthma	Shortness of breath, Difficulty breathing, Dry cough, Chest pain, Wheezing, Night cough.	Precipitation of attacks during night or at early morning.	B2 agonist, anti-histamines.
Cardiovascular diseases	Angina, Shortness of breath, Arrhythmia, Heart attack, Heart failure	BP is at its lowest during the sleep cycle and rises steeply during the early	Nitro-glycerine, calcium channel blocker, ACE inhibitors

		morning.	
Arthritis	Chronic pain in affected area, Pain and stiffness in joints, especially those with previous injury, Pain and stiffness more noticeable after immobility, such as overnight, swelling.	Level of pain increases at night	NSAID's, Glucocorticoids
Diabetes mellitus	Frequent urination, feeling very hungry or thirsty, Extreme fatigue, Blurry vision, Dry itchy skin.	Increase in blood sugar level after meal.	Sulfonylurea, Insulin
Hypercholesterolemia	Fatty skin deposits called xanthomas over parts of the hands, elbows, knees, ankles and around the cornea of the eye, Chest pain, Coronary artery disease, cramping when walking.	Cholesterol synthesis is generally higher during night than day time	HMG CoA reductase, Inhibitors

Table no 1 Disease That Required Pulsatile Drug Delivery System

Peak time of various biological processes:

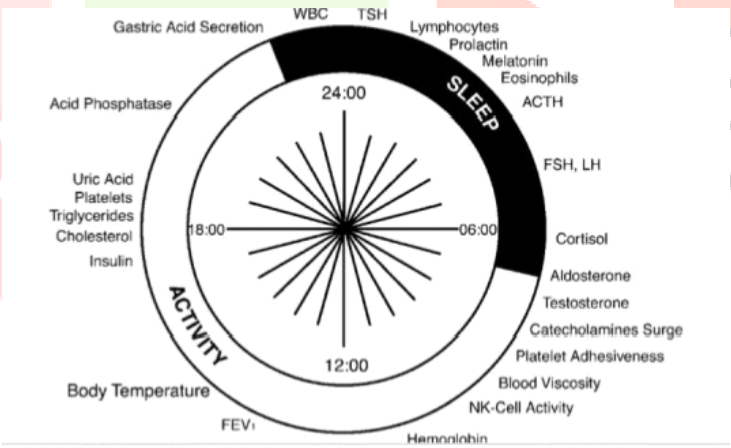

Fig. no 9 Peak time of various biological processes:

RECENT ADVANCEMENT IN PDDS

ACCU-BREAK ™ Technology

Accu-Break Pharmaceuticals, Inc. and Azopharma Product Development Group, Inc. Accu-Break tablets are manufactured on an available multilayer compression machine. Accu-Break ™ Technology is divided into two types ACCU-B ™ Technology and ACCU-T Technology.

SODAS® technology

SODAS® (Spheroidal Oral Drug Absorption System) is Elan's Multiparticulate drug system. Depending on the production of controlled bead release, SODAS ® technology is defined by its natural flexibility, which allows the production of customized dosage forms that respond directly to the needs of each drug user. Elan's SODAS® Technology is based on the production of similar circular beads 1-2 mm wide containing drugs and bonding materials and wrapped in specially formulated polymers. Recent authorization approaches to the SODAS-based system that take place through the introduction of daily oral form forms of Avinza ™, Ritalin® LA and Focalin® XR.

IPDAS® technology

The Intestinal Protector Drug Absorption System (IPDAS® Technology) is a multi-component computerized technology, designed for use with GI irritant compounds. As soon as the IPDAS ® tablet is inserted, it rapidly dissolves and disperses the beads containing the drug into the stomach, which extends to the duodenum and intestinal tract in a controlled and slow motion, independent of the digestive tract. The extraction of the active ingredient from multiparticulates occurs by a process of proliferation using a polymeric membrane. a polymer micromatrix / active ingredient built into multiple extruded / circular multiparticulates. Naprelan®, sold in the United States and Canada, uses IPDAS® technology. This is a new invention of naproxen sodium.

CODAS technology ™

Elan drug delivery technology can be configured to dispense medication after a pre-determined delay. The drug delivery system CODAS ™ triggers the onset of drug withdrawal delays, leading to a drug release profile that accurately recommends circadian patterns. - Élan's Verelan® PM represents a commercial product using CODAS ™ technology. The Verelan® PM formulation was designed to begin delivering Verapamil approximately four to five hours after posting. This delay is introduced by the polymer level that controls the extraction used in drug-laden beads.

PRODAS® technology

The Programmable Oral Drug Absorption System (PRODAS® Technology) is a multidisciplinary technology, unique in that it incorporates the benefits of tablet technology within the capsule. The PRODAS® delivery system is introduced as a number of small minutes combined with a hard gelatin capsule. Very flexible, PRODAS® technology can be used to create a drug release program in a pre-program. It is possible to add many different minerals, each of which is individually designed and programmed to extract the drug at different points within the intestinal tract. It is also possible to install minitablets of different sizes to make loading of drugs easier.

TMDS technology

TMDS (Time Multiple Action Delivery system) The technology provides a multi-ingredient control release within a single tablet in the form of a system. TMDS Technology allows more than one active ingredient in a single tablet design to provide multiple release profiles over an extended period of time.

DMDS technology

DMDS (Dividable Multiple Action Delivery System) is designed to provide greater measurement flexibility that improves product performance and minimizes adverse effects. A custom-released tablet usually loses their controlled delivery system when broken. However, DMDS technology allows the tablet to be split in half so that each component of the tablet achieves the same output profile as the overall tablet. This

allows the patient and the physician to adjust the dosage according to the needs of the outpatient clinic

PMDS technology

The PMDS technology (Programmed Multiple-action Delivery System) is designed to provide more phasic delivery of any highly controlled ingredient compared to conventional extraction technology. - to find acceptable similarities with product reproduction at different output levels. It is designed to provide greater measurement flexibility that enhances product efficiency and can reduce it

GEOCLOCK ® technology

Skye Pharma has developed a new technology for oral drug delivery, Geoclock®; allowing the preparation of chronotherapy-coated tablets based on pressure. Geoclock® tablets have an active ingredient within the outer tablet cloth containing a mixture of hydrophobic wax and material to obtain a stand-alone pH independent time before the basic drug delivery at a pre-determined release rate. This dry covering method is designed to allow for timely release of slow release and immediate release of active cores by removing the inner table first after the time when the outer outer shell is gradually dispersed. Using this latest technology, SkyePharma has been developing Lodotra ™, a rheumathoid arthritis drug, on behalf of Nitec Pharma. Lodotra ™ will deliver an effective herbal ingredient at the right time of day

GEOMATRIX Technology ™

Geomatrix ™ technology is used to achieve the prescribed levels of controlled release of certain drugs and can achieve simultaneous release of two different drugs with different values on the same tablet. Controlled extraction is achieved by building a tablet with a wide variety made from basic components; 1) hydrophilic polymers such as hydroxypropyl methycellulose (HPMC) and 2) that regulate the barrier layers. -diclofenac- the ratiopharm® uno ratiopharm and Madopar DR® for Roche.

PULSYS technology ™

MiddleBrook ™ (Formerly known as Advancis Pharmaceuticals) Pharmaceuticals developed PULSYS ™, an oral drug delivery technology that enables a single dose of pulsatile daily. The dosage form PULSYS ™ is a compressed tablet containing pills designed to dispense the drug in various regions of the intestinal tract in an alarming manner. The PULSYS ™ Technology's Moxatag ™ tablet contains Amoxicillin designed to deliver amoxicillin at a lower dose than short-term treatment in a single daily formulation. Advancis also showed that in pre-treatment studies that improved the bactericidal effect of amoxicillin when delivered in a pulsatile manner compared to conventional dosage and even drug resistance

IntelliMatrixTM technology

IntelliPharmacetical is a pharmaceutical technology development company with a suite of related tablet technology. IntelliMatrixTM drug delivery platform is a unique composition of many different „smart polymers such as hydroxy ethylcellulose and an earlier channel such as Lactose.

Eurand's pulsatile system and chrono release System

The Eurand's Time pulsatile release system is able to provide one or more instantaneous pulses at pre-set times, such as when needed for chronotherapy, and in some other areas, such as the absorption of a GI tract. - Eurand has created a circadian form of cardiac output (CRR) of the heart drug, Propranolol hydrochloride, with a four-hour delay in withdrawal after oral

administration. Administered at bedtime, Propranolol is released after the initial delay so that high plasma levels appear in the morning, when the patient is at high risk.

Banner's VersetrolTM technology

VersetrolTM Technology is a relatively new technology that provides timely release of a wide variety of medications. In this technology the drugs are injected into a lipophilic or hydrophilic matrix and that is more than just incorporated into a gelatin capsule shell. This technology has a variety of functions because depending on the chemical composition of the drug it can be an emulsion or the suspension can be improved. For lipophilic drugs the composition of the suspension is preferred while using the emulsion form of hydrophilic drugs. By using a combination of lipophilic and hydrophilic matrices the desire for a profile release can be achieved.

Magnetic Nanocomposite Hydrogel

Magnetic nanocomposite for heat-reacting hydrogel has been used as a remote controlled drug delivery. Nanocomposites are synthesized by the incorporation of superparamagnetic Fe3O4 particles into high temperature poly (N-isopropylacrylamide) hydrogels. A high frequency of magnetic power generation was used in the production of nanocomposite hydrogel. The temperature of the Nanocomposite hydrogel rises above the LCTS and therefore, leads to a rapid collapse of the gel. Nanocomposites hydrogel is therefore one type of open device where drug release can be opened using another magnetic field.

MARKETED PRODUCT

Technology	Mechanism	API	Disease
Pulsys	Timed-controlled System	Amoxicillin	Pharygitis/tonsillitis
Uniphyl	Externally Regulated system	Theophylline	Asthma
Ritalina	Osmotically Regulated	Methyl Phenidate	Attention Deficit Hyperactivity Disorder
Opana ER	Timed-Controlled System	Oxy morphine	Pain Medicine
TheirForm	Externally Regulated system	Declofenac Sodium	Inflammation

Table no. 2 Marketed Product

History and early use of chronotherapeutics: The first chronotherapy used in the clinic was introduced in the 1960s with different daily doses of common corticosteroid tablet medications. Since there are other chronotherapies used in medical treatment in the US, Europe and Asia this includes theophylline systems in the evening for chronic obstructive pulmonary disease. A common H2 receptor antagonist antagonist for peptic ulcer with standard cholesterol medications for evening hyperlipidemia. For the past 10-15 years, it has been introduced as a sleeping tablet and a capsule to lower blood pressure by releasing the drug in line with the behavior

of SBP and DBP in primary hypertension. Various limited programs are sold for Hypertension treatment.

CONCLUSIONS: Although the ongoing and controlled drug delivery programs have been very successful and effective in the medical field, these programs fail to deliver drugs in terms of disease behavior where pulsatile systems benefit. In order to successfully develop chronotherapeutic dosage form, knowledge of the cycle time cycle, rhythm in the pathophysiology of the disease or a 24-hour pattern in strengthening the symptoms of chronic conditions and chronopharmacology of medicine are required. Significant progress has been made in implementing a drug delivery system that has the potential to effectively treat diseases with a consistent treatment regimen.

Reference

1. Hermida RC, Ayala DE, Calvo C, et al. (2007) Adv. Drug Del. Rev. (In press)

2. Lemmer (1991) J. Control. Rel. 16:63-74

3. Krogel I and Bodmeier R (1999) Int. J. Pharm. 187:175-184

4. Sungthongjeen S, Puttipipatkhachorn S, Paeratakul O, et al. (2004) J. Control. Rel. 95:147-159

5. Thombre AG, Appel LE, Chidlaw MB, et al. (2004) J. Control. Rel. 94:75-89

6. Gazzaniga A, Paluga L, Foppoli A, et al. (2007) Eur. J. Pharm. and Biopharm. (In Press)

7. Sangalli ME, Maroni A, Foppoli A, et al. (2004) European Journal of Pharmaceutical Sciences 22:469-476

8. Jimoh AG, Wise DL, Gresser JD, et al. (1995) J. Control.Rel. 34:87-95

9. Kost J and Langer R (2001) Adv. Drug Del. Rev. 46:125-148

10. Kikuchi A and Okano T (2002) Adv. Drug Del. Rev. 54:53-77

11. Burns, J.S., Stevens, H.N.E., McEwen, J., Pritchard, G., Brewer, F.M., Clarke, A., Johnsons, E.S. and McMillan, I., J. Control.Release, 1996, 38, 151.

12. Stevens, H.N.E., Rashid, A. and Bakshee, M., US Patent No., US5474784, 1995.

13. Ross, A.C., Macrae, R.J., Walther, M., Stevens, H.N.E. J. Pharm.Pharmcol., 2000, 52, 903.

14. Krogel, I. and Bodmeier, R., Pharm. Res., 1998, 15, 474.

15. Stevens, H.N.E., Ross, A.C. and Johnson, J.R., J. Pharm.Pharmcol., 2000, 52, S41.

16. Soutar, S., Stevens, H.N.E., Mahony, B.O., Bakshee, M., Perkins, A.C., Grattan, T. and Wilson, C.G., Proc. Int. Symp. Control ReleaseBioact. Mater.,2001, 28, 790.

17. Dashevsky A and Mohamad A.Development of pulsatile multiparticulate drug delivery system coated with aqueous dispersion Aquacoat ® ECD. Int J Pharm. 2006; 318:124– 131.

18. Gazzaniga A, Paluga L and Foppoli A. Eur J Pharm and Biopharm. 2007. (In Press).

19. Hermida RC, Ayala DE and Calvo C. Adv Drug Del Rev. (2007). (In press).

20. Katstra WE, Palazzolo RD and Rowe CW. Journal of Control. Rel. 66:1-9.

21. Kikuchi A and Okano T ; Pulsatile drug release control using hydrogels. Advan Drug Del Reviews. 2002;54:53-77.

22. Krogel I and Bodmeier R. Floating or pulsatile drug delivery systems based on coated effervescent cores. Int J Pharm. 1999;187:175–

184.

23. Lemmer B. Circadian rhythms and drug delivery. J J Control Release. 1991;16:63-74.

24. Miyata N, Asami T, Uragami. A reversibly antigen responsive hydrogel. Nature. 1999;399:766–769. 25. Miyazaki S, Yokouchi C and Takada M. Journal Pharm Pharmacol. 1988;40:716-717.

26. Yui N, Okano T and Sakurai Y. Inflammation responsive degradation of crosslinked hyaluronic acid gels. J Control Release. 1992;22:105–116.

27. Panoz D and Geoghegan E. Elan Corporation, United States. 1989;49.

18. Percel P, Vishnupad K and Venkatesh GM. Timed pulsatile drug delivery systems. US Patent 6,627,223; 2002;236:27-34.

29. Pozzi, Furlani, Gazzaniga. Journal of Controlled Release. 1994;31:99-108.

30. Rathod Shruti. Colon Targeted Pulsatile Drug Delivery.A Review. Pharmainfo net. 2007;5(2): 1-11

31. Saslawski O, Weigarten C and Benoit JP. Magnetically responsive microspheres for pulsed delivery of insulin Life Sci. 1988;42(16):1521-1528.

32. Sharma S and Pawar A. Low density multiparticulate system for pulsatile release of meloxicam. Int J Pharm. 2006;313:150–158

33. Stevens H, Wilson C and Welling P. Evaluation of Pulsincap to provide regional delivery of dofetilide to the human GI tract. Int J.