SUSTAINED AND CONTROLLED DRUG DELIVERY SYSTEM - AS A PART OF MODIFIED RELEASE DOSAGE FORM

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ABSTRACT

In order to overcome the drawbacks of conventional drug delivery systems, several technical advancements have led to the development of controlled drug delivery systems that could revolutionize method of medication and provide a number of therapeutic benefits like multiple dosing and single doses of sustained and controlled delivery formulations. Oral controlled release drug delivery is a drug delivery system that provides the continuous oral delivery of drugs at predictable and reproducible kinetics for a predetermined period throughout the course of GI transit and also the system that target the delivery of a drug to a specific region within the GI tract for either a local or systemic action. Over the past decades an entirely new technique for the delivery of a drug and other biologically active agents has been developed this technique for the drug administration is termed Sustained release or controlled release. Sustained release tablet owing a twofold or greater reduction in frequency of administration of a drug in comparison with the frequency required by a conventional dosage form. It is designed to maintain constant levels of a drug in the patient's bloodstream by releasing the drug over an extended period. Maintaining constant blood levels of the drug in the bloodstream increases the therapeutic effectiveness of the drug. All the pharmaceutical products formulated for systemic delivery via the oral route of administration, irrespective of the mode of delivery (immediate, sustained or controlled release) and the design of dosage form (either solid dispersion or liquid), must be developed within the intrinsic characteristics of GI physiology.

KEYWORDS

Novel Drug Delivery System, Sustained release drug delivery system (SRDDS), Classification of SRDDS, Methods for SRDDS and Polymers use for SRDDS and Drug properties SRDDS.

INTRODUCTION

Pharmaceutical products designed for oral delivery are mainly immediate release type conventional drug delivery systems, which are designed for immediate release of drug for rapid absorption. These immediate release dosage forms have some limitations such as: Drugs with short half-life require frequent administration, which increases chances of missing dose of drug leading to poor...
patient compliance. A typical peak-valley plasma concentration-time profile is obtained which makes attainment of steady state condition difficult. The unavoidable fluctuations in the drug concentration may lead to under medication or overmedication as the CSS therapeutic range. Values fall or rise beyond the therapeutic range. The fluctuating drug levels may lead to precipitation of adverse effects especially of a drug with small therapeutic index, whenever over medication occurs. In order to overcome the drawbacks of conventional drug delivery systems, several technical advancements have led to the development of controlled drug delivery system that could revolutionize method of medication and provide a number of therapeutic benefits like multiple dosing and single doses of sustained and controlled delivery formulations. In the field of pharmaceuticals, sustained release systems have been widely used in oral medication, since early 1950s. The first Sustained release tablets were made by Howard Press, in Hoboken, NJ in the early 50's and the first tablets released under his process patent were called "Nitroglyn" and made under license by Key Corp., in Florida. Today most are formulated so that the active ingredient is embedded in a matrix of insoluble substance (various: some acrylics, even chitin, these are often patented) so that the dissolving drug has to find its way out through the holes in the matrix. In some SR formulations the matrix physically swells up to form a gel, so that the drug has first to dissolve in matrix, and then exit through the outer surface.

DIFFERENT TERMINOLOGY USED

Repeat action
A dose of the drug is initially is released immediately after administration, which is usually equivalent to a single dose of conventional drug product. After a certain period a second single dose is released (Scientific and Regulatory Issues.1997).

Sustained release
This is a specific type of modified release dosage form that allows at least a two-fold reduction in the dosage frequency compared to conventional drug delivery system (Aulton et al., 2002).

Controlled release
The dosage form in which the drug is released in a planned, predictable and slower than conventional dosage form (Marroum et al., 1997, Gohel et al., 2007).

Delayed release dosage form
This is a specific type of modified release dosage form that releases the drug at a particular time. E.g. Enteric coated tablet (Lee et al., 2000).

Extended release
Pharmaceutical dosage forms that release the drug slower than normal manner at predetermined rate and necessarily reduce the dosage frequency by two folds (Kumar et al., 2012).

Prolonged release system
They are designed to release the drug slowly and to provide a continuous supply of drug over an extended period. They prevent very rapid absorption of the drug, which could result in extremely high peak plasma drug concentration (Banker et al., 2002).

Timed release drug delivery system
Timed release drug delivery system are used to obtain the drug release after a lag time of about 4-5 hrs. Enteric coated dosage forms of cellulose acetate phthalate are designed to provide protection in the stomach. Application of a thick coat causes a delay in the drug release in small intestine and delays the drug release. This time controlled drug release may be retarded up to 5 hrs this targets the drug to the colon (Leon et al., 2004).

Site-specific and receptor release
They are designed to target the drug directly to a certain biological location. In the case of site specific release, the drug directly target to a certain organ or tissue, while in receptor release, the target on the particular receptor within an organ or tissue.

NOVEL DRUG DELIVERY SYSTEM
NDDSs evolved over a period of time to improve patient compliance and optimize the dosage regimen without compromising the therapeutic efficacy (Omathanu pillai et al., 1989). The foundation was laid in 1952, with the introduction of first sustained release capsule of Dexedrine. Subsequently several
novel drug delivery systems can be classified on bases of their sophistication and mechanism of drug release as shown below.

**Sustained Release Drug Delivery System**
Sustained release, sustained action, prolonged action, controlled release, extended action, timed release and repository dosage form are terms used to identify drug delivery, which are designed to achieve a prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration single dose. In the case of injectable dosage forms this period may vary from days to months. In case of orally administrated forms this period measured in hours and critically depends on the residence time of dosage form in gastrointestinal tract. (Leon lachman, Herbert A., 2007).

**Delayed release systems**
The drug is released at later time after administration e.g. enteric coating.

**Repeat action systems**
A dose of drug is initially released immediately after administration which is usually equivalent to single dose of conventional drug formulation. After certain period of time a second single dose is released.

**Timed release systems**
The units are enteric coated to prevent release in stomach and the release process is triggered by change in pH of intestinal fluid upon gastric emptying.

**Controlled release systems**
Although this term has been interchanged with sustained release preparation in past, the term controlled release dosage forms, usually applies to preparation that are designed for all routes of administration and where the mechanism of prolonged action is inherent and determined totally by the delivery system.

**Advantages of Sustained Release Formulations**

- Enhance patient compliance and convenience.
- Reduction in dosing frequency.
- Reduced fluctuations in circulating drug levels.
- More uniform effect.
- Employ less total drug that will:
  - Minimize or eliminates local side effects.
  - Minimize or eliminates systemic side effects.
  - Minimize drug accumulation with chronic dosing.
  - Obtains less potentiating or reduction in drug activity on chronic use.

The Main Areas of Potential Challenge in the Development of Oral Sustained and Controlled Drug Delivery Systems Are

**Development of a drug delivery system**
To develop a viable oral controlled release drug delivery system capable of delivering a drug at a therapeutically effective rate to a desirable site for duration required for optimal treatment.

**Modulation of gastrointestinal transit time**
To modulate the GI transit time so that the drug delivery system developed can be transported to a target site or to the vicinity of an absorption site and reside there for a prolonged period of time to maximize the delivery of a drug dose.

**Minimization of hepatic first pass elimination**
If the drug to be delivered is subjected to extensive hepatic first-pass elimination, preventive measures should be devised to either bypass or minimize the extent of hepatic metabolic effect.

SUSTAINED RELEASE DRUG DELIVERY SYSTEM
Sustained release tablet owing a twofold or greater reduction in frequency of administration of a drug in comparison with the frequency required by a conventional dosage form. It is designed to maintain constant levels of a drug in the patient's bloodstream by releasing the drug over an extended period. Maintaining constant blood levels of the drug in the bloodstream increases the therapeutic effectiveness of the drug (Figure No.1).

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• Safety margin of potent drug is increased by technically excellent designing of formulation.

Improve efficiency in treatment which is achieved by:

• Cure or control of condition.
• Improve or control condition.
• Make use of specific effect.
  Eg. SR Aspirin for morning relief of arthritis.
• Improve bioavailability of some drugs.
• Patient care time is reduced.
• Night time dosing can be avoided for patient convenience

• Product life time is increased in sustained release formulations. Particles of drug are coated with matrix or entire product is matrix coated which along with its main function of sustained action, avoid exposure of unstable drug to the environment and render it stable.

Disadvantages of Sustained Release Drug Delivery System

• If there requires immediate change during the therapy or if any significant adverse effect is noted and prompt termination of therapy is needed, Sustained release does not permit immediate termination of therapy.
• More costly process and equipment are needed in manufacturing of SRDDS.
• Physician has less flexibility in adjusting dosage regimen as this is fixed by design of dosage form. Risk of dose dumping, usually SRDDS contain drug amount that is 3-4 times more than conventional formulations. Sometimes this large quantity of drug may get rapidly released leading to toxicity.
• Reduced drug absorption may delay onset of action. The effect of food on drug absorption.
• Kinetics may differ markedly from one SR formulations to another.
• Drug absorbed at specific time in GIT cannot be formulated in SRDDS.
• Increased potential for first pass clearance.

• For oral SRDDDS effective drug release is influenced and limited by GI residence time.
• SRDDS are designed for normal population that is on the basis of the biological half-lives. Since disease state that alters drug dispositions as well as interpatient variability in pharmacokinetics parameters are not accommodated.
• Drugs which are acted upon by enzymes in intestine undergo significant enzymatic breakdown as drug remains in body for longer time.
• In case of accidental failure of the product effective antidote may be difficult to employ.

Classification of Sustained Release Drug Delivery System

Considering the mechanism of controlling the drug release the system is classified as follows:

• Chemically controlled systems
• Biodegradable system
• Drug polymer conjugates
• Diffusion controlled systems
• Matrix diffusion
• Polymer erosion
• Polymer swelling
• Geometry

Classification Based on Drug Release from the SRDF is as follows:

Continuous release systems

These systems release the drug continuously for prolonged period of time along the entire length of GIT with normal transit time. Different systems under this class are

• Dissolution controlled release systems
• Diffusion controlled release systems
• Dissolution and diffusion controlled release systems
• Ion exchange resin drug complex
• Slow dissolving salts and complexes
• pH dependent formulations
• Osmotic pressure controlled systems
• Hydrodynamic pressure controlled systems
Delayed transit and continuous release systems
These systems are designed to prolong release of drug with increased residence time in GIT. Such dosage forms are designed to remain in the stomach. Therefore the drug presented in such systems should be stable at gastric pH. This class includes following systems
- Altered density systems
- Mucoadhesive systems
- Size based systems

Delayed release systems
These systems are fabricated to release the drug only at specific site in the GIT. The drugs those are
- Destroyed in stomach or by intestinal enzymes.
- Known to cause gastric irritation
- Absorbed from specific site in intestine, or exert local effect at specific GI site are formulated in such systems.
The two types of delayed release systems are
- Intestinal release systems
- Colonic release systems.

METHODS USED TO ACHIEVE CONTROLLED RELEASE OF ORALLY ADMINISTERED DRUGS
Diffusion Controlled System
Basically diffusion process shows the movement of drug molecules from a region of a higher concentration to one of lower concentration. This system is of two types:

Reservoir type
A core of drug surrounded by polymer membrane, which controls the release rate, characterizes reservoir devices.

Advantages
Zero order delivery is possible; release rate varies with polymer type.

Disadvantages
- System must be physically removed from implant sites.
- Difficult to deliver high molecular weight compounds.
- Increased cost per dosage unit, potential toxicity if system fails. Ficks first law of diffusion describes the diffusion process.

Matrix type
Matrix system is characterized by a homogenous dispersion of solid drug in a polymer mixture.

Advantages
Easier to produce than reservoir or encapsulated devices, can deliver high molecular weight compounds.

Disadvantages
Cannot provide zero order release, removal of remaining matrix is necessary for implanted system. System, Higuchi has derived the appropriate equation for drug release from this
\[ M = K \sqrt{t} \]
where
- \( M \) = amount of drug released per unit area,
- \( K \) = Constant

Dissolution Controlled Systems
Reservoir type
Drug is coated with a given thickness coating, which is slowly dissolved in the contents of gastrointestinal tract. By alternating layers of drug within the rate controlling coats as shown in Figure No.2, a pulsed delivery can be achieved. If the outer layer is quickly releasing bolus dose of the drug, initial levels of the drug in the body can be quickly established with pulsed intervals.

Matrix type
The most common type of dissolution controlled dosage form is shown in Figure No.3. It can be either a drug impregnated sphere or a drug impregnated tablet, which will be subjected to slow erosion.

Bioerodible and Combination of Diffusion and Dissolution Systems (Figure No.4)

Advantages
- It is characterized by a homogeneous dispersion of drug in an erodible matrix.
- It is characterized by a homogenous dispersion of drug in an erodible matrix.

Disadvantages
- Potential toxicity of degraded polymer must be considered.
- Cannot obtain zero order release.
- Removal of remaining matrix is necessary for implanted systems.
- Release Kinetics is often hard to control.
Drug release from a matrix tablet (Figure No.5)

**Advantages**
- All the advantages of matrix dissolution system.
- Removal from implant site is not necessary.

**Disadvantages**
- Difficulty to control kinetics owing to multiple processes of release.
- Potential toxicity of degraded polymer must be considered.

**Drug Examinees for Extended-Release Products**
- A successful extended-release product, the drug must be released from the dosage form at a predetermined rate, dissolved in the gastrointestinal fluids, maintained at sufficient gastrointestinal residence time, and be absorbed at a rate that will replace the amount of drug being metabolized and excreted.
- These are exhibit neither very slow nor very fast rates of absorption and excretion.
- These are uniformly absorbed from the gastrointestinal tract.
- These are administered in relatively small doses.
- A good margin of safety.

**Methods using Ion Exchange**
It is based on the drug resin complex formation when an ionic solution is kept in contact with ionic resins. The drug from these complexes gets exchanged in gastrointestinal tract and released with excess of Na+ and Cl- gastrointestinal tract.

**E. Methods using osmotic pressure**
It is characterized by drug surrounded by semi permeable membrane and release governed by osmotic pressure.

**Advantages**
- Zero order release rates are obtainable.
- Preformulation is not required for different drugs.
- Release of drug is independent of the environment of the system.

**Disadvantages**
- System can be much more expensive than conventional counterparts.

**Quality control is more extensive than most conventional tablets.**

**pH– Independent formulations**
A buffered controlled release formulation is prepared by mixing a basic or acidic drug with one or more buffering agents, granulating with appropriate pharmaceutical excipients and coating with GI fluid permeable film forming polymer (Figure No.6).

When GI fluid permeates through the membrane the buffering agent adjusts the fluid inside to suitable constant pH thereby rendering a constant rate of drug release.

**Altered density formulations**
Several approaches have been developed to prolong the residence time of drug delivery system in the gastrointestinal tract.

**Fabrication of oral controlled release delivery employs various methods**
- Hydrophilic matrix
- Plastic matrix
- Barrier resin beads
- Fat embedment
- Repeat action
- Ion exchange resin
- Soft gelatin depot capsules
- Drug complex

**Hydrophilic Matrix System**
Drug delivery technologists usually tend to consider all hydrophilic delivery systems as hydrogels. Hydrogels are hydrophilic macromolecular networks that after swelling maintain their shape due to permanent links. The very high water content and special surface properties of swollen form give them the ability to simulate natural tissues. They have been used in controlled drug delivery because of their good tissue compatibility and easy manipulation of swelling level and there by solute permeability. The most widely used polymers for drug delivery control; particularly in oral applications are swellable polymers.

**Hydrogel based Drug Delivery Systems are classified as**
- Diffusion Controlled Release System
- Reservoir System
It consists of polymeric membrane surrounding a core containing the drug. The rate-limiting step for drug release is diffusion through the outer membrane of the device (Figure No.7).
Matrix System
The drug is dispersed throughout the three dimensional structure of the hydrogel. Release occurs due to diffusion of the drug throughout the water filled pores (Figure No.8).

Release of Drug from matrix tablet (Figure No.9).
Initial wetting
The tablet surface wets as it becomes immersed in aqueous media. The polymer then begins to hydrate forming a gel layer. Drug near the surface of the tablet is released.

Matrix expansion
As water permeates into the tablet, the polymer swells causing an increase in size (Figure No.10).

Drug diffusion
The soluble drug diffuses through the gel layer. The dry core also contributes to the swelling

Matrix erosion
Outer layer becomes fully hydrated which eventually dissolves into the gastric fluids. Water continues to permeate through the tablet core.

Effect of Release Limiting Factor on Drug Release Polymers used in the matrix (Aulton et al., 2005) (Table No.1 and Figure No.11)
The parameters such as partition coefficient diffusion path thickness and other systems play various rate determining roles in controlled release of the drugs from matrix systems.

Polymer Hydration
To determine the number of polymers and different polymeric combination it is important to study polymer hydration or swelling process. The important step include adsorption/absorption of water, rupture of polymer- polymer linking, formation of water-polymer linking , separation of polymeric chains, swelling and then dispersion.

Drug Solubility
Molecular size and water solubility of the drug are two important determinants in the release of drug from swelling and erosion. For drugs with good aqueous solubility the release occur by dissolution in filtrating membrane. For drugs with poor aqueous solubility release occur by both dissolution of drug and dissolution of drug through erosion of matrix tablet.

Solution Solubility
It is important to maintain in vivo (Biological) sink condition to study the release of drug in controlled manner solely by delivery system and is not affected by solubility factor.

Polymer Diffusivity
The diffusion of small molecules in polymer structure is an energy activated process and the diffused particles move to a series of equilibrium position. The energy of activation Ed depends upon the length of polymer chain segment, cross linking and crystallinity of polymer. The release of drug may be attributed to three factors:
- Polymer particle size
- Polymer viscosity
- Polymer concentration

Thickness of Polymer Diffusional Path
The controlled release of the drug from matrix tablet is governed by Fick’s law of diffusion
\[ J_D = D \frac{dC}{dx} \]
Where
JD: diffusion flux, D: diffusivity of drug molecule, Dc/dx: concentration gradient.

Thickness of Hydrodynamic Diffusion Layer
It is observed that the drug release is the function of thickness of diffusion layer. The magnitude of drug release is decreased when the thickness of diffusion layer is increased.
During the release life of swellable matrix system, three fronts are generally expected.
The swelling front, the boundary between the still glassy polymer and its rubbery state.
The diffusion front, the boundary in the gel layer between the solid as yet undissolved, drug and the dissolved drug.
The erosion front, the boundary between the matrix and the dissolution medium. The measurement of front positions gives the possibility to determine three important parameters related to the behavior of the matrix i.e. the rate of water uptake, the rate of drug dissolution and the rate of matrix erosion associated with the movements of the swelling front, diffusion front and erosion front respectively.
These parameters are strictly linked to the drug release kinetics from matrix
Ds: Solvent diffusion co-efficient in the drug/polymer matrix
Dd: Drug diffusion co-efficient in the swollen polymers
Cs: Drug solubility at the drug core interface (R)
C: Drug volume fraction at the gel/solution interface
Cd: Polymer volume fraction at R
Cc: Polymer volume fraction at S
Ccp: Polymer volume fractioning in the glassy core
Ccd: Drug volume fraction in the glassy core.

Non-swell able controlled release systems
These systems are hollow containing an inner core of drug surrounded in a water insoluble polymer membrane. The polymer can be applied by coating or by wet granulation technique. The drug release mechanism across the membrane involves its partitioning into the membrane with subsequent release into the surrounding fluid by diffusion. The polymers commonly used in such devices are Hydroxy Propyl Cellulose, Ethyl Cellulose and Polyvinyl Acetate. A disadvantage of all such release system is a chance of sudden drug dumping which is not common with matrix devices.

Role of polymers in controlled drug delivery systems
Various synthetic and natural polymers have been examined in drug delivery applications. The three key advantages that polymeric drug delivery products can offer are:

Localized delivery of drug
The delivery system can be implanted directly at the site where drug action is needed and hence systemic exposure of the drug can be reduced. This becomes especially important for toxic drugs, which produce various systemic side effects (such as the chemotherapeutic drugs).

Sustained delivery of drug
The drug encapsulated is released over extended periods and hence eliminates the need for multiple doses. This feature can improve patient compliance especially for drugs meant for chronic indications which requires frequent administrations.

Stabilization of the drug
The incorporated polymer can protect the drug from the physiological environment of GIT and hence improve its stability in-vivo. This particular feature makes this technology attractive for the delivery of labile drugs such as proteins.

Drug properties influencing the design of sustained release drug delivery system
The performance of a drug in its release pattern from the dosage form as well as in body proper is a function of its properties (Shiraishi. S et al., 1993). The drug properties not only decide the suitability to sustained / controlled release dosage form and but also route of administration. Especially with the oral route, apart from the release the absorption phenomenon of drug is also one of functional drug properties.

Physicochemical properties of drug influencing drug product design and Performance
Dose size
Practical problem in construction of a sustained action dosage form is the volume of drug that must be administered (Robinson J.R et al., 1978.) Drugs with single oral dose larger than 0.5g are poor candidates for oral sustained release products

Aqueous solubility
The aqueous solubility of drug is an extremely important consideration in its biological performance as well as in its incorporation into controlled drug delivery system. Aqueous solubility of drug exercises its control on the absorption process in two ways i) By influence on the dissolution rate of compound, ii) By its effect on the ability of the drug to penetrate tissues. Finally drugs which are having low aqueous solubility generally suffer from low oral bioavailability. Compounds with very high aqueous solubility are sometime difficult to convert slow release dosage forms.

Partition coefficient
In the time span between drug administration and its elimination from body, the drug must cross a variety of membranes (Robinson J.R. et al., 1978). Drugs with low partition coefficient easily permeate through biological membrane however for further functions aqueous solubility is required. Drugs with
extremely high partition coefficient will either readily penetrate into membrane producing an accumulation in body tissue with subsequent slow elimination.

**Drug stability**

Drugs that are unstable in gastric pH can be developed as slow release dosage form and drug release can be delayed till the dosage form reaches the intestine. Drugs that undergo gut wall metabolism and show instability in small intestine are not suitable for oral controlled drug delivery system. In such cases drug can be modified chemically to form prodrug, which may possess different physicochemical properties (Robinson J.R. et al., 1978).

**Protein binding**

Many drugs bind to plasma proteins with a concomitant influence on the duration of drug action. Since blood proteins are recirculated and not eliminated, drug protein binding can serve as a depot for drug producing a prolonged release, provided a high degree of drug protein binding occurs. The duration of drug action is a function of protein binding. Quaternary ammonium compounds may bind to protein present in Gastro intestinal tract (G.I.T) wall (Robinson J.R. et al., 1978).

**Pka**

The pH partition hypothesis simply states that uncharged form of a drug species will be preferentially absorbed through many body tissues:

**Factors affecting drug release rate**

Factors affecting drug release rate revolve around the structure of matrix where drug is contained and the chemical properties associated with both the polymer and drug (Xiao Huang., Brazel et al., 2001).

**Polymer molecular weight**

Degradation of polymer microspheres shows a clear dependence on the molecular weight of polymer. Varying degradation profiles occur due to difference in glass transition temperature. At lower molecular weight, a relatively constant release profile was obtained, but at high molecular weight, release rate profile was initially high followed by decrease which was then followed again by an increase.

**Blends of structurally different polymers**

Physical blending of two polymers can effect the release profile of polymer sphere. (Mi et al, 2002) blended hydrophobic polylactic co-glycolic acid (PLGA) with hydrophilic chitin and examined hydration in these systems. It was found in first part of sphere degradation fast release occurred due to the readily degradable chitin polymer which was followed by a slower release from the PLGA section (Freiberg, S et al., 2004).

**Crystallinity**

Crystallinity in Microspheres has been usually investigated by differential scanning calorimeter or X-ray diffraction Release profiles suggest that amorphous spheres release the drug less rapidly than crystalline spheres. In some cases the drug employed can induce polymer chain scission through nucleophilic degradation in case of medication possessing amine groups. In case of less active, sterically hindered tertiary amine, polymer degradation was neither significant nor drug release profiles.

**Porosity**

The porosity is the character of sphere which is determined during microsphere hardening as the organic solvent evaporates during preparation. It was noticeable where a highly porous matrix released a drug at a considerably higher rate than its nonporous counterpart. Initial burst effect, is another factor related to sphere porosity.

**Size distribution**

The release profiles are also dependent on size of microspheres. Rate of drug release was found to decrease with increasing sphere size.

**Release from core shell microspheres**

Employment of shell is usually meant to enhance controlled release and possibly reduce the effect of initial burst.

**pH controlled release**

Added control over drug delivery can be achieved by employing pH triggered release. Therefore by the incorporation of pH sensitive groups microspheres can be targeted to various biological environments or to specific organs.
### Table No.1: Polymers for Sustained drug delivery system

<table>
<thead>
<tr>
<th>S.No</th>
<th>Polymers</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hydrophilic Polymers</td>
<td>Hydroxyl propyl methyl cellulose (HPMC), hydroxyl propyl cellulose(HPC), hydroxyl ethyl cellulose (HEC), Xanthan gum, Sodium alginate, poly(ethylene oxide), and cross linked homopolymers and co-polymers of acrylic acid.</td>
</tr>
<tr>
<td>2</td>
<td>Hydrophobic Polymers</td>
<td>Includes waxes and water insoluble polymers in their formulation</td>
</tr>
<tr>
<td>3</td>
<td>Waxes</td>
<td>Carnauba wax, bees wax, candelilla wax, micro crystalline wax, ozokerite wax, paraffin waxes and low molecular weight polyethylene.</td>
</tr>
<tr>
<td>4</td>
<td>Insoluble polymers</td>
<td>Ammoniomethacrylate co-polymers (Eudragit RL100, PO, RS100, PO), ethyl cellulose, cellulose acetate butyrate, cellulose acetate propionate and latex dispersion of meth acrylic ester copolymers.</td>
</tr>
</tbody>
</table>

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**Figure No.1:** A hypothetical plasma concentration-time profile from conventional multiple dosing and single doses of sustained and controlled delivery formulations

**Figure No.2:** Schematic representation of diffusion controlled drug release reservoir system
Figure No.3: Schematic representation of diffusion controlled drug release matrix system

Figure No.4: Drug delivery from (a) bulk-eroding and (b) surface-eroding Bio-erodible systems
These are used in the treatment of chronic rather than acute conditions.

Figure No.5: Drug release from a matrix tablet (The Dow Chemical Company 2000)

Figure No.6: Drug delivery from environmentally pH sensitive release systems
Figure No.7: Hydrogel formation in Reservoir Systems

Figure No.8: Hydrogel formation in Matrix System

Figure No.9: Drug release from a matrix tablet
CONCLUSION
Conventional drug delivery systems have little control over their drug release and almost no control over the effective concentration at the target site. This kind of dosing pattern may result in constantly changing, unpredictable plasma concentrations. Drugs can be delivered in a controlled pattern over a long period of time. In recent years, novel drug delivery system (NDDS) has been recognized as an attractive niche for the pharmaceutical and health industry. Among various NDDS, Sustained drug delivery systems have matured from their use with laboratory animals to the most reliable controlled release systems for human. Sustained drug delivery system uses various methods for controlled delivery of active agents. Because of their unique advantages over other types of dosage forms, Sustained drug delivery from a class of their own among the various drug delivery technologies, and a variety of products based on this technology are available on the market.

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CONFLICT OF INTEREST
We declare that we have no conflict of interest.

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