A Review Article On Controlled and sustained release drug technologies

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ABSTRACT

Controlled and sustained drug release technologies are important in modern pharmaceutical science. This systems are designed to deliver medicines to the body in a slow, and continuous manner over an extended period of time. Controlled and sustained release systems maintain a steady amount of drug in the body. This helps improve treatment effectiveness while reducing unwanted side effects. The main goal of sustained drug release is to extend the duration of drug action by releasing the drug gradually, these systems reduce the need for frequent dosing. This is especially useful for patients who require long-term treatment, such as those suffering from chronic illnesses. Fewer doses improve patient convenience and increase adherence to therapy. Controlled drug release systems further enhance this concept by regulating the rate, timing, and sometimes the location of drug release. These systems can be designed to respond to specific conditions within the body, such as changes in pH, temperature, or biological signals.Various technologies are used to achieve controlled and sustained drug release.

Key Words: Polymer, Mechanism, Matrix System, Sustained Release.

INTRODUCTION [1.2.3]

Drug is a substance which is used in a diagnosis, cure, mitigation, treatment or prevention of a disease in a patient.

Control drug delivery system is a system in which drug is deliver in a predetermine and specified rate for a specific period of time by delivering the drug by local or systemic route of administration.

Sustained drug delivery system is a system in which release of drug at a predetermined rate by maintaining a constant drug level in a body for specific period of time with minimum side effect.

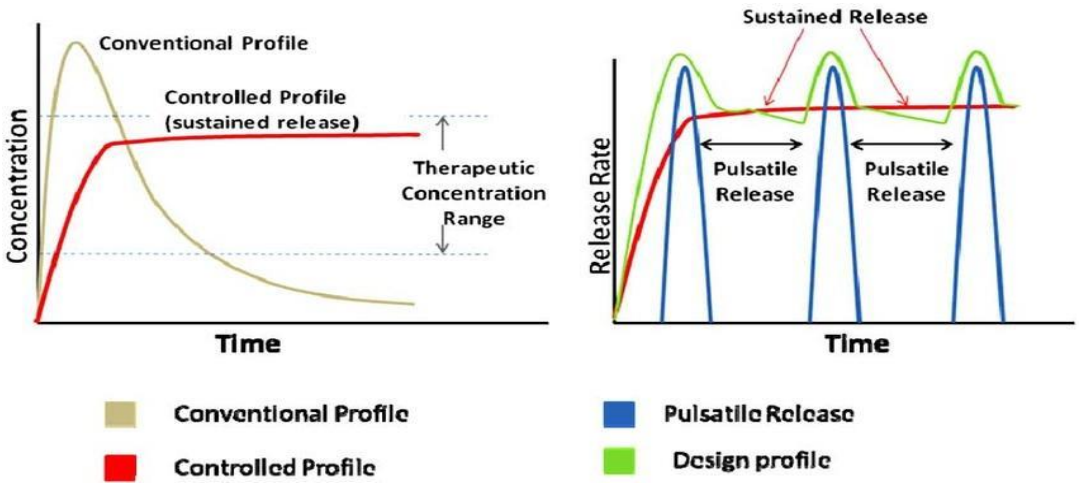


Figure 1- controlled and sustained release system

Advantages of controlled and sustained drug release [3,6]

1. Reduce dosing frequency
2. Improve patient complaints
3. Enhanced therapeutic efficacy
4. Reduced side effects and toxicity
5. Better utilization of drug with narrow therapeutic index

Disadvantages of controlled and sustained drug release [3,6]

1. **Dose dumping risk-** Failure of the polymer Matrix or coating may lead to rapid release of the entire drug dose, causing toxicity.
2. **High cost of formulation and production-** These system require specialized polymers, equipments and processing techniques making them more expensive than conventional dosage form.
3. **Limited drug loading capacity-** Only drugs with suitable dose size, solubility, and half life can be formulated into controlled and sustained release system.
4. **Risk of polymer-drug interaction-** Incompatibility between drug and polymer may affect drug stability, released profile and therapeutic efficacy.
5. **Patient related risk-** crushing or chewing sustained release tablet candysttroy the release mechanism, leading to dose dumping.

POLYMER [1,3,9,11]

A polymer is a high molecular weight macromolecule composed of a large number of repeating structural units known as monuments, se which are covently bonded to each other in a regular and irregular arrangement to form long chains,branched chained or three dimensional network.

These repeating monomer units are derived from simple low molecular weighted molecules that undergo chemical reaction such as polymerization or polycondensation resulting in materials with distinct physical, chemical, mechanical and biological properties.

Example- gelatin, methyl cellulose, hydroxy propyl methyl cellulose, poly vinyl alcohol etc.

General formula representation

If M represents a monomer unit then a polymer can be represented as

$$(M)_n$$

When n= degree of polymerization (number of repeating unit)

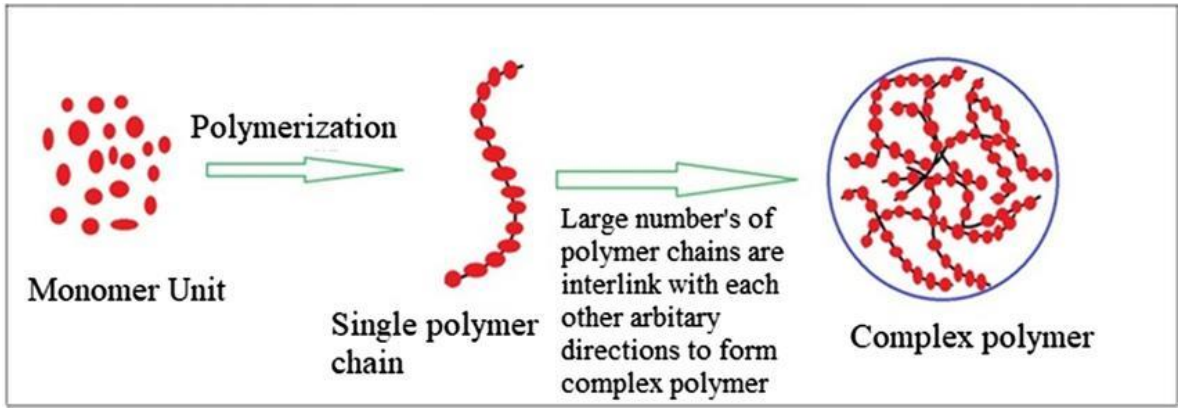


Figure 2- monomers to polymer

Role of polymer in controlled and sustained drug release system [3,9]

- Polymers are used in formation of microcapsule system and matrix system in controlled release Drug delivery system.
- Polymers are also used as binder in tablet formation and in formation of capsule shell, they are also used as thickening agent and disintegrating agent.
- Polymers are used as coating material in implantable device, they are also enhance the solubility and bioavailability of poorly soluble drugs.
- Polymers are used to improve drug stability by protecting them from the degradation.

Classifications of polymers [2,3,9,11]

1) On the basis of source
2) On the basis of structure
3) On the basis of function
4) On the basis on degradability

1) On the basis of source-

a) Natural polymer- these polymer are obtained from natural source such as animal, plant, microorganisms are used to control drug release due to their biocompatibility and biodegradability.
Example – Gelatin, alginate, chitosan,, starch etc.

b) Semi synthetic polymer- These polymers are chemically modified natural polymers designed to improve stability, mechanical strength, and drug release properties.
Example- Hydroxypropyl methylcellulose, carboxymethyl cellulose,ethyl cellulose etc.

c) Synthetic polymer- These are chemically synthesized polymers with well defined and reproducible properties that allow precise control over drug release.
Example-Polylactic acid, poly co-glycolic acid, polyethylene glycol etc.

2) On the basis of structure- on the basis of structure polymers are divided into three types:

a) Linear polymers- In this polymers monomers are connected to each other in a straight line.
Example- nylons, polyethene, polyvinyl chloride etc

b) Branched chain polymers- These polymers contain side chain which is attached with straight chain.
Example- glycogen, amylopectin, polypropylene etc

c) Cross linked polymers- In this polymers two linear chains are connected with each other with the help of covalent bonds.
Example- Bakelite,melamine, formaldehyde resins etc.

3) On the basis of function

a) Film farming polymers- These polymers are used in coating of tablets and capsule shell to protect drug and control release.
Example- hydroxy propyl methyl cellulose, eudragit, cellulose acetate etc.

b) Matrix farming polymers- These type of polymers are used in sustained and control release formulation to regulate release of drug.
Example- ethyl cellulose, hydroxy propyl methyl cellulose, carbopol etc.

c) Bioadhesive/ mucoadhesive polymer- These type of polymers are used in adherence of drug on the surface of mucosal to release the drug in controlled manner.
Example- chitosan, carbopol etc.

d) Enteric polymers- These type of polymers are used to protect the drug from the stomach acid and release them in the intestine.
Example- cellulose acetate pathalate, eudragit etc.

e) **Osmotic polymers-** These type of polymers are used in osmotic systems to release drug at the controlled rate.
Example- cellulose acetate, polyethylene glycol etc.

4) **On the basis of degradability-** These type of polymers are classified on the basis of degradability and capability of the drug.

a) **Biodegradeble polymer-** These polymer are degrade in the body into non toxic by product through enzymatic or hydrolic processes, releasing the drug over time.
Example- Polylactic acid, chitosan, gelatin, etc

b) **Non biodegradable-** These polymers are not degrade in the body and control drug release mainly by diffuse through the polymer matrix or membrane.
Example- Ethyl cellulose, eudragit,etc.

Mechanism of controlled and sustained drug release [1,2,3,9,11]

Controlled and sustained drug-release technologies are designed to deliver a drug at a predetermined rate for a prolonged period**.**

There are various mechanism for controlled and sustained drug release,

1. **Physicochemical method-** Physicochemical method are those methods in which drug release is controlled by the physical or chemical properties of the drug or doses form without relaying on biological factors.

A. **Dissolution controlled system-**In this method drug release depends on the rate at which the drug or its coating dissolves in gastro intestinal fluid. This method is suitable for the drug which are highly soluble in stomach fluids.
These are two types:

I. **Matrix type-** In this method drug is uniformly dispersed in a polymer Matrix and release gradually as polymer dissolve.
Example- Aspirin sustained release tablet (HPMC, carbopol, bees wax, castor oil)

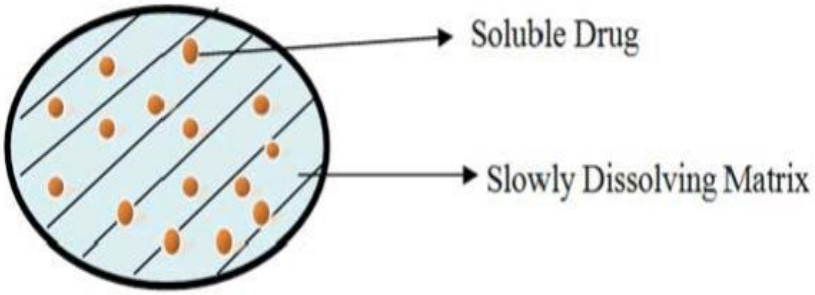
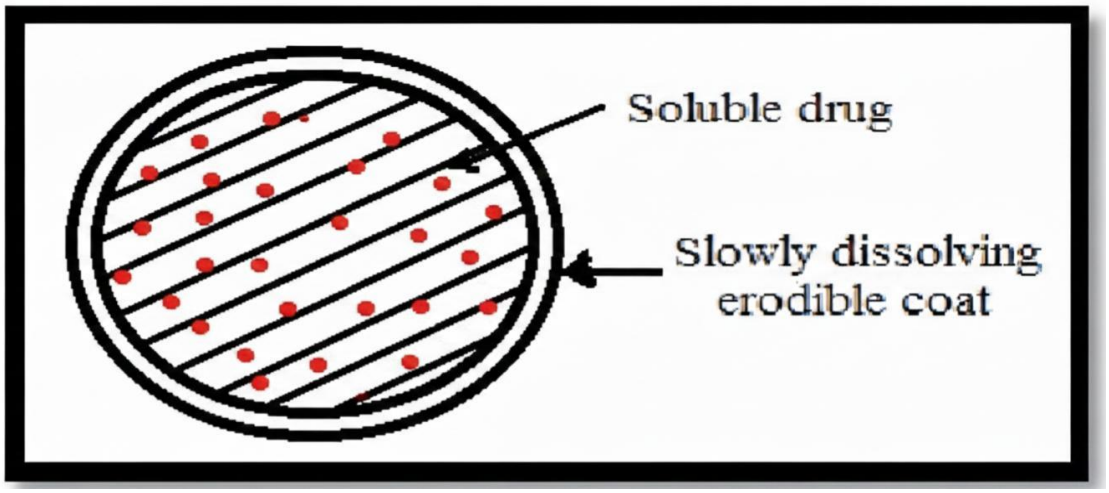


Figure 3- matrix type

II. **Reservoir type-** In this method drug particles are coated or encapsulated with slowly dissolving polymer. Drug is released gradually layer by layer.

Example- Theophylline coated sustained release tablets(ethyl cellulose, cellulose acetate, bees wax, carnauba wax).



. **Figure 4- reservoir type system**

B. **Diffusion controlled system-** In this method drug release occurs as the drug passes through a polymeric or wax barrier by diffusion. Drug release rate depend on the thickness and type of polymer or wax.

These are two types:

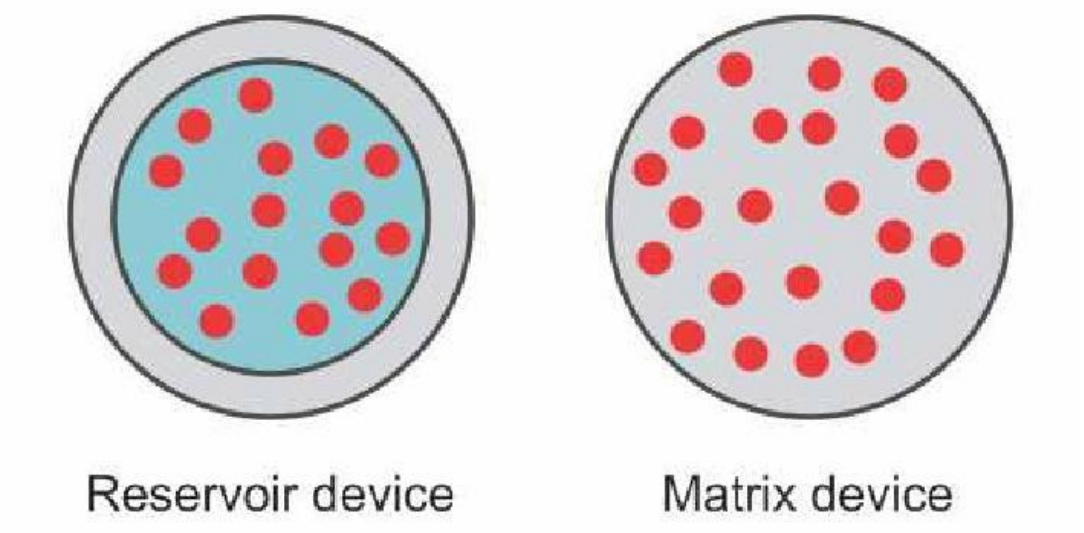


Figure 5- diffusion controlled system-

I. **Matrix type-** Drug uniformly dispersed in a polymer or wax matrix release gradually as its diffuse through the matrix.
   Example- Verapamil sustained release tablet.
II. **Reservoir type-** drug core coated with a polymer or membrane drug diffises gradually through the coating.

Example- propranolol controlled release tablet, nitro glycerine transdermal patch (ethylene cellulose cellulose acetate, bees wax, carnauba wax).

C. **Ion exchange resin system-** This system is designed to control the release of ionic and ionizable drugs.In this method, the drug is bound to a resin and released slowly by exchanging its ions with ions present in gastrointestinal fluids.
   Example- Theophylline sustained release tablet (cation exchange resin), diclofenac sustained release tablets (anion exchange resin).

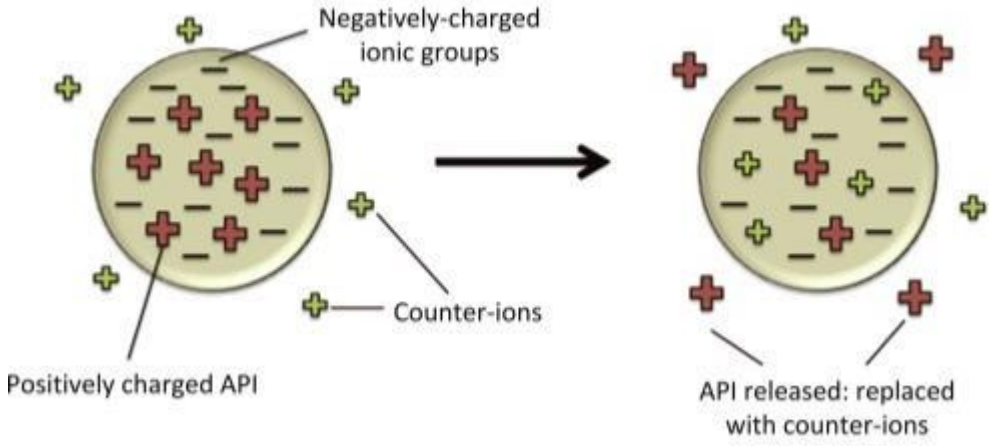


Figure 6- ion exchange resin system

D. Osmotic pressure control system- In this method drug release is controlled by osmotic pressure through a semi-permeable membrane. Water enters the core, build osmotic pressure and pushes the drug out at a controlled rate, allowing zero order release over time.
Example- Nifedipine controlled release tablet, glipizide osmotic tablet, verapamil sustained release tablets.

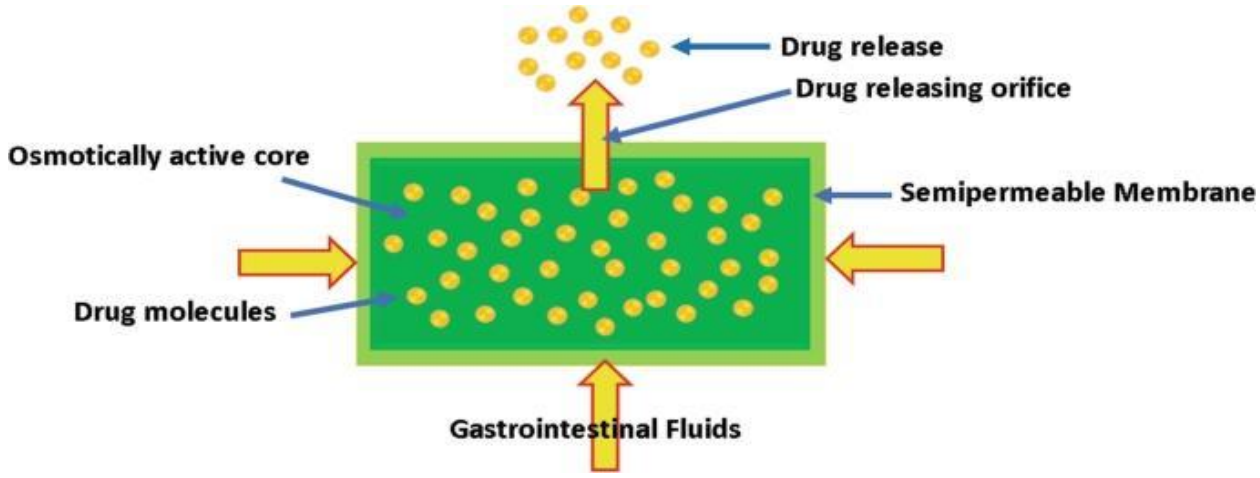


Figure 7- osmotic pump

E. pH dependent system-In this method drug release is controlled by dissolution of a polymer at a specific pH, allowing site- specific or delayed release in the gastro intestinal tract.

Example- Aspirin enteric-coated tablet, omeprazole enteric-coated capsules, diclofenac sodium enteric coated tablets.

2. **Biological method-** In these methods drug release is controlled by biological or physiological factors in the body such as enzyme GI transit time or recephtor interactions.

There are following methods:

A. **Prodrug approach-** Drug is chemically modified to an inactive or less active form and become active in the body by enzyme or chemical reaction.

Example- enalapril , as a prodrug Enalaprilat.

B. **Bio adhesive/ bioerodible systems-** Drug is mixed with bio adhesive polymers that stick to mucosal surface giving prolonged release.
Example- buccal nitroglycerine tablets.
C. **Exploting GI transit time-** Drug release is designed to match stomach or intestinal transit time for longer absorption.
Example- metformin sustain release floating tablets.
D. **Enzyme activated system-** Drug is released or activated by specific enzymes at the target site. **Example-** sulfasalazine.
E. **Receptor mediated targeting system-** Drug is attached to ligands that bind to specific receptors giving site specific release.
Example-anti cancer drug linked with antibodies.

Marketed formulation [4,5,7,8,10]

Controlled release formulation- A control release formulation is a doses form that designed to release the drug at a predetermine rate,duration and sometime at specific site, maintaining a constant therapeutic plasma concentration to improve effectiveness and reduce side effects.

Example- sodium vaporate and valporic acid controlled release tablet (anti-epileptic).

Figure 8- controlled release tablet

Sustained release formulation- Sustained release formulation is a doses formed that design to release the drug gradually to maintain therapeutic concentration over and extended period, reducing dosing frequency.

Example- nifedipine sustained release tablets (anti hypertensive), metformin sustained release tablets (Anti diabetic).

Figure 9- sustained release tablets

i. **Wellbutrin XL –** Bupropion extended-release

Uses a diffusion controlled system, where the drug diffuses out through a polymer matrix at a predictable rate. Used for depression and smoking cessation.

ii. **Ambien CR-** Zolpidem tartrate extended release.

The drug is embedded in a polymer Matrix that releases slowly over time. Prescribed for insomnia to improve sleep continuity.

iii. **Tussionex Pennkinetic ER-** Hydrocodone Polistirex+ chlorphenoramine Polistirex.

Uses ion exchange rate in technology drug is bound to resin and released when exchanged with ions in the GI tract. Provides relief for cough and cold symptoms.

iv. **Glucotrol XL-** Glipizide extended release

Based on osmotic pump technology which uses osmotic pressure to push the drug out through a tiny orifice at a constant rate. Used for type 2 diabetes to control blood glucose level.

v. **Procardia XL-** Nifedipine extended release

Also based on osmotic pump technology delivers Nifedipine slowly over 24 hours to control blood pressure in the condition of angina.

vi. **Carbidopa CR-** used in Parkinson's disease.

vii. **Omeprazole SR capsule -** contain enteric coated palettes to protect drug from gastric degradation and provide prolonged release.

viii. **Theophylline sustained release capsules-** pallets coated with polymers to wearing thickness to control release.

ix. **Glucophage XR-** hydrophilic Matrix sustain release system which is used in type two diabetes.

x. **Inderal LA(propranolol)-** used in cardiovascular disorder.

Conclusion

Sustained and controlled drug release technology has immersed as a vital advancement in modern pharmaceutical science, offering significant improvement over conventional dosage forms. By maintaining drug concentrations within therapeutic window for extended periods, the systems enhance treatment efficacy, reduce dosing frequency, and improve patient compliance. Polymers play a central role in the design of such delivery systems, as there physical,chemical properties govern key release mechanism including diffusion, erosion, swelling, and osmosis. The careful selection and modification of natural, semi synthetic, aur synthetic polymers allow precise control overdrug release profile to specific therapeutic needs. The successful translation of the technology is into marketed formulations highlights their practical relevance and clinical

value. Overall, sustained and control drug delivery systems represent a advanced pharmaceutical development and will continue to play a crucial role in optimising drug therapy in the future.

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