Review Article

Oral Controlled Release Drug Delivery System: An Overview

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ABSTRACT

Oral drug delivery is the most preferred and convenient option as the oral route provides maximum active surface area among all drug delivery system for administration of various drugs. The attractiveness of these dosage forms is due to awareness to toxicity and ineffectiveness of drugs when administered by oral conventional method in the form of tablets and capsules. Usually conventional dosage form produces wide range of fluctuation in drug concentration in the bloodstream and tissues with consequent undesirable toxicity and poor efficiency. The maintenance of concentration of drug in plasma within therapeutic index is very critical for effective treatment. These factors as well as factors such as repetitive dosing and unpredictable absorption lead to the concept of oral controlled release drug delivery systems. Controlled release drug delivery system works on many different mechanisms to control the release rate of drugs. Various mechanisms like osmotic pressure, matrix system, reservoir system, altered density system etc. have been utilized as formulation approaches. The present article contains brief review on various formulation approaches for controlled release drug delivery system.

Keywords: Controlled release drug delivery system, matrix type system, reservoir system.

INTRODUCTION

Sustained release (S.R)/ Controlled release (C.R) pharmaceutical products have gradually gained medical acceptance and popularity. Regulatory approval for marketing and their pharmaceutics superiority and clinical benefits over immediate release pharmaceutical products have been increasingly recognized. Modified release oral dosage forms have brought new lease of life into drugs that have lost market potential due to requirement of frequent dosing, dose related toxic effects and gastrointestinal disturbances.

The term *modified-release drug product* is used to describe products that alter the timing and/or the rate of release of the drug substance. A modified-release dosage form is defined "as one for which the drug-release characteristics of time course and/or location are chosen to accomplish therapeutic or convenience objectives not offered by conventional dosage forms such as solutions, ointments, or promptly dissolving dosage forms as presently recognized". Several types of modified-release drug products are recognized

Extended-release drug products: A dosage form that allows at least a two fold reduction in dosage frequency as compared to that drug presented as an immediate-release (conventional) dosage form. Examples of extended-release dosage forms include controlled-release, sustained-release, and long-acting drug products.

Delayed-release drug products: A dosage form that releases a discrete portion or portions of drug at a time or at times other than promptly after administration, although one portion may be released promptly after administration. Enteric-coated dosage forms are the most common delayed-release products.

Targeted-release drug products: A dosage form that releases drug at or near the intended physiologic site of action. Targeted-release dosage forms may have either immediate or extended-release characteristics.

The term controlled-release drug product was previously used to describe various types of oral extended-release dosage forms, including sustained-release, sustained-action, prolonged-action, long-action, slow-release, and programmed drug delivery.

Conventional Drug Delivery System

Pharmaceutical products designed for oral delivery are mainly conventional drug delivery systems, which are designed for immediate release of drug for rapid/immediate absorption. As can be seen in the graph (Figure 1), administration of the conventional dosage form by extravascular route does not maintain the drug level in blood for an extended period of

time. The short duration of action is due to the inability of conventional dosage form to control temporal delivery.

The conventional dosage forms like solution, suspension, capsule, tablets and suppository etc. have some limitations such as

1) Drugs with short half-life require frequent administration, which increases chances of missing the dose of drug leading to poor patient compliance.
2) 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 over medication as the steady state concentration values fall or rise beyond the therapeutic range.
3) The fluctuating drug levels may lead to precipitation of adverse effects especially of a drug with small therapeutic index, whenever overdosing 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 (Chien, 1992).

1.2 Controlled Release Drug Delivery Systems (CRDDS)

More precisely, controlled delivery can be defined as

- Sustained drug action at a predetermined rate by maintaining a relatively constant, effective drug level in the body with concomitant minimization of undesirable side effects.
- Localized drug action by spatial placement of a controlled release system adjacent to or in the diseased tissue.
- Targeted drug action by using carriers or chemical derivatives to deliver drug to a particular target cell type.
- Provide a physiologically / therapeutically based drug release system. In other words, the amount and the rate of drug release are determined by the physiological or therapeutic needs of the body. A controlled drug delivery system is usually designed to deliver the drug at particular rate. Safe and effective blood levels are maintained for a period as long as the system continues to deliver the drug. This predetermined rate of drug release is based on the desired therapeutic concentration and the drug's pharmacokinetics.

Potential Advantages of Controlled Drug Therapy

- Patient compliance due to reduction in the frequency of designing.
- Employ minimum drug.
- Minimize or eliminates local and systemic side effects.
- Obtain less protentiation or deduction in drug activity with chronic use.
- Minimize drug accumulation with chronic dosing.
- Improves efficacy in treatment.
- Cure or control confirm more promptly.
- Improve control of condition i.e. reduce fluctuation in drug level.
- Improve bioavailability of same drugs.
- Make use of special effects, e.g. sustained release aspect for morning relief of arthritis by dosing before bedtime.(Vyas and Khar, 2002)

Disadvantages of Controlled Drug Therapy

- They are costly.
- Unpredictable and often poor in-vitro in-vivo correlations, dose dumping, reduced potential for dosage adjustment and increased potential first pass clearance.
- Poor systemic availability in general.
- Effective drug release period is influenced and limited by GI residence time. (Hoffman, 1998).

Rationale of Controlled Drug Delivery

The basic rationale for controlled drug delivery is to alter the pharmacokinetic and pharmacodynamics of pharmacologically active moieties by using novel drug delivery systems or by modifying the molecular structure and/or physiological parameters inherent in a selected route of administration. It is desirable that the duration of drug action become more to design properly. Rate controlled dosage form, and less, or not at all, a property of the drug molecules inherent kinetic properties. As mentioned earlier, primary objectives of controlled drug delivery are to ensure safety and to improve efficiency of drugs as well as patient compliance. This achieved by better control of plasma drug

levels and frequent dosing. For conventional dosage forms, only the dose (D) and dosing interval (C) can vary and, for each drug, there exists a therapeutic window of plasma concentration, below which therapeutic effect is insufficient, and above which toxic side effects are elicited. This is often defined as the ratio of median lethal dose (LD 50) to median effective dose (ED50). (Chein et al., 1982)

1.3 Oral Controlled Drug Delivery Systems

Oral controlled release drug delivery is a system that provides 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 (Vora et al., 1996).

Classification of Oral Controlled Release System

A) Diffusion Controlled Systems
   I. Reservoir Devices
   II. Matrix Devices
B) Dissolution controlled system
   I. Matrix Dissolution Controlled System
   II. Encapsulation Dissolution Controlled system
C) Diffusion and Dissolution Controlled System.

A) Diffusion Controlled Systems

I. Reservoir Devices

A core of drug (the reservoir) surrounded by a polymeric membrane characterizes them. The nature of the membrane determines the rate of drug release.

The characteristics of reservoir diffusion systems are

1. Zero order drug release is possible.
2. The drug release rate is dependent on the type of polymer.
3. High molecular weight compounds are difficult to deliver through the device. Coating and microencapsulation technique can be used to prepare sub devices.

II. Matrix Devices.

It consists of drug dispersed homogeneously in a matrix. The characteristics of the matrix diffusion system are

1. Zero order release cannot be obtained.
2. Easy to produce than reservoir devices.
3. High molecule weight compounds are delivered through the devices.

B) Dissolution controlled systems

I. Matrix Dissolution Controlled System

Aqueous dispersions, congealing, spherical agglomeration etc. can be used.

II. Encapsulation Dissolution Control

Particles, seeds or granules can be coated by technique such as microencapsulation.

C) Diffusion and Dissolution Controlled System.

In a bioerodible matrix, the drug is homogenously dispersed in a matrix and it is released either by swelling controlled mechanism or by hydrolysis or by enzymatic attack.

1.4. Types of Extended-Release Products

General approaches to manufacturing an extended-release drug product include the use of a matrix structure in which the drug is suspended or dissolved, the use of a rate controlling membrane through which the drug diffuses, or a combination of both. Among the many types of commercial preparations available, none works by a single drug-release mechanism. Most extended-release products release drug by a combination of processes involving dissolution, permeation, and diffusion. The single most important factor is water permeation, without which none of the product release mechanisms would operate. Controlling the rate of water influx into the product generally dictates the rate at which the drug dissolves. Once the drug is dissolved, the rate of drug diffusion may be further controlled to a desirable rate. Table 1 shows some common extended-release product examples and the mechanisms for controlling drug release, and lists the compositions for some drugs (Leon Shargel, 2004).

1.5 Factors Influencing the Design and Performance of Sustained Release Products

The type of delivery system and route of administration of the drug presented in sustained drug delivery system may depend upon two properties (Bramhankar and Jaiswal, 1995). They are

I. Physicochemical Properties of drugs
II. Biological Factors.

I. Physicochemical Properties of Drugs

1. Dose size

For orally administered systems, there is an upper limit to the bulk size of the dose to be administered. In general a single dose of 0.5 to 1gm is considered maximum (Nicholas et al., 1987).

2. Ionization, P^{Ka}& Aqueous Solubility

The pH Partition hypothesis simply states that the unchanged form of a drug species will be preferentially absorbed through many body tissues. Therefore it is important to note the relationship between theP^{Ka} of the compound and its absorptive environment. For many compounds, the site of maximum absorption will also be the area in which the drug is least soluble.

For conventional dosage forms the drug can generally fully dissolve in the stomach and then be absorbed in the alkaline pHof the intestine. For sustained release formulations much of the drug will arrive in the small intestine in solid form. This means that the solubility of the drug is likely to change several orders of magnitude during its release.

Compounds with very low solubility are inherently controlled, since their release over the time course of a dosage form in the GIT will be limited by dissolution of the drug. The lower limit for the solubility of a drug to be formulated in a sustained release system has been reported to be 0.1mg/mL (Fincher et al., 1968). Thus for slightly soluble drugs, diffusional systems will be poor choice, since the concentration in solution will be low.

For example Tetracycline has maximum solubility in the stomach and least solubility in the intestine where it is maximally absorbed. Other examples of drugs whose incorporation into sustained release systems are limited because of their poor aqueous solubility and slow dissolution rate are digoxin, warfarrin, griseofulvin and salicylamide. Very soluble drugs are also good candidates for the sustained release dosage forms.

3. Molecular size and diffusivity

The ability of drug to diffuse through membrane is called diffusivity & diffusion coefficient is function of molecular size (or molecular weight). Generally, values of diffusion coefficient for intermediate molecular weight drugs, through flexible polymer range from 10-8 to 10-9 cm^2 / sec. with values on the order of 10-8 being most common for drugs with molecular weight greater than 500, the diffusion coefficient in many polymers frequently are so small that they are difficult to quantify i.e. less than 16-12 cm^2/sec. Thus high molecular weight drugs and / or polymeric drugs should be expected to display very slow release kinetics in sustained release device using diffusion through polymer membrane.

4. Partition coefficient

The compounds with a relatively high partition coefficient are predominantly lipid soluble and easily penetrate membranes resulting high bioavailability. Compounds with very low partition coefficient will have difficulty in penetrating membranes resulting poor bioavailability. Furthermore partitioning effects apply equally to diffusion through polymer membranes.

5. Drug Stability

The drugs, which are unstable in stomach, can be placed in a slowly soluble form and their release delayed until they reach the small intestine. However, such a strategy would be detrimental for drugs that either are unstable in the small intestine (or) undergo extensive gut wall metabolism, as pointed out in the decrease bioavailability of some anticholinergic drugs from controlled /sustained release formulation. In general the drugs, which are unstable in GIT environment, are poor candidates for oral sustained release forms.

6. Protein Binding

It is well known that many drugs bind to plasma proteins with a concomitant influence on the duration of drug action. Since blood proteins are mostly recirculated and not eliminated drug protein binding can serve as depot for drug producing a prolonged release profile, especially if a high degree of drug binding occurs.

II. Biological Factors

1. Biological Half-Life

Therapeutic compounzds with half-life less than 8 hrs are excellent candidates for sustained release preparations. Drugs with very short half-life (less than 2 hrs) will require excessively large amounts of drug in each dosage unit to maintain controlled effects. Thus forcing the dosage form itself to become too large to be administered. Compounds with relatively long half-lives, generally greater than 8 hrs are not used in the sustained release dosage forms, since their effect is already sustained and also GI transit time is 8-12 hrs (Jantzen et al., 1996). So the drugs, which have long -half life and short half- life, are poor candidates for sustained release dosage forms.

Some examples of drug with half-lives of less than 2 hours are ampicillin, cephalexin, cloxacillin, furosemide, levodopa, penicillin G and propylthiouracil. Examples of those with half-lives of greater than 8 hours are dicumarol, diazepam, digitoxin, digoxin, guanethidine, phenytoin and warfarin.

2. Absorption

The characteristics of absorption of a drug can greatly affect its suitability as a sustained release product. Drugs which are absorbed by specialized transport process (carrier mediated) and drug absorption at special sites of the gastrointestinal tract (Absorption Window) are poor candidates for sustained release products.

3. Metabolism

The metabolic conversion of a drug to another chemical form usually can be considered in the design of a sustained-release system for that drug. As long as the location, rate and extent of metabolism are known and the rate constants for the processes are not too large, successful sustained-release products can be developed.

There are two factors associated with the metabolism of some drugs, however that present problems of their use in sustained-release systems. One is the ability of the drug to induce or inhibit enzyme synthesis, this may result in a fluctuating drug blood level with chronic dosing. The other is a fluctuating drug blood level due to intestinal (or other tissue) metabolism or through a hepatic first-pass effect.Examples of drugs that are subject to intestinal metabolism upon oral dosing are hydralazine, salicylamide, nitroglycerine, isoproterenol, chlorpromazine and levodopa. Examples of drugs that undergo extensive first-pass hepatic metabolism are propoxyphene, nortriptyline, phenacetine, propranolol and lidocaine.

Drugs that are significantly metabolized especially in the region of the small intestine can show decreased bioavailability from slower releasing dosage forms. This is due to saturation of intestinal wall enzyme systems. The drugs should not have intestinal first pass effect and should not induce (or) inhibit metabolism are good candidates for sustained release dosage forms. Various technologies used for controlled release drug delivery systems were given in Table 2 (Chien et al., 1990).

1.6. Monolithic Matrix System

In pharmaceutical CRDDS, matrix based systems are the most commonly used type of release controlling methodology owing to their simple manufacturing process. The preparation of a tablet with the matrix involves the direct compression of the blends of drug, release retardant and other additives, in which the drug is uniformly distribute throughout the matrix core of the release retardant. Alternatively, drug-release retardant blends may be granulated to make the mix suitable for the preparation of tablets by wet granulation or beads (Colombo et al., 1995).

To characterize and define the matrix systems the following properties of the matrix are considered.

1. Chemical nature of the support.
2. The physical state of the drug.
3. The matrix and alteration in volume as the function of the time.
4. The routes of administration.
5. The release kinetics model (in accordance with Higuchi's equation, these system considered to release the drug as a function of square root of time).

The classification of the matrix-based systems is based on the following criteria.

- Matrix structure
- Release kinetics
- Controlled release properties (diffusion, erosion and swelling).
- Chemical nature and the properties of the applied release retardant(s).

Based on the chemical nature of the release retardant(s), the matrix systems are classified as given in Table 3.

1.7. Mechanism of Drug Release from Matrix Tablets

As shown in Figure 2, in erodible matrices, polymer erosion from the surface of the matrix determines the drug release; whilst in hydrophilic matrices, formation of the gel layer and its dynamics as a function of time determines the drug release. Gel layer thickness, which determines the diffusion path length of the drug, corresponds to the distance between the diffusion and erosion fronts. As the swelling process proceeds, the gel layer gradually becomes thicker, resulting in progressively slower drug-release rates; however, due to continuous hydration, polymer disentanglement occurs from the surface of the matrix, resulting in a gradually decreasing depletion zone and an increased dissolution rate.

1.8. Drug Release Kinetics -Model Fitting of the Dissolution Data

Whenever a new solid dosage form is developed or produced, it is necessary to ensure that drug dissolution occurs in an appropriate manner. The pharmaceutical industry and the registration authorities do focus, nowadays, on drug dissolution studies. Drug dissolution from solid dosage forms has been described by kinetic models in which the dissolved amount of drug (Q) is a function of the test time, tor Q=f (t). Some analytical

definitions of the Q (t) function are commonly used, such as zero order, first order, Hixson–Crowell, Higuchi, Korsmeyer-Peppas models. (Mulye and Turco, 1995; Colombo et al., 1999; Kim et al., 1997; Manthena et al., 2004; Desai et al., 1996; Higuchi et al., 1963).Different models expressing drug release kinetics were given in Table 4

Zero Order Kinetics

Kinetic equation for Zero order release is as follows

$$Q_1 = Q_0 + K_0 t$$

Where $Q_1$is the amount of drug dissolved in time *t*, $Q_0$is the initial amount of drug in the solution (most times, Q_0=0) and $K_0$is the zero order release constant.

$$f_t = K_0 t$$

Where f_t = 1-(W_t/W_0) and f_t represents the fraction of drug dissolved in time t and K_0 the apparent dissolution rate constant or zero order release constant. In this way, a graphic of the drug-dissolved fraction versus time will be linear if the previously established conditions were fulfilled.

Use: This relation can be used to describe the drug dissolution of several types of modified release pharmaceutical dosage forms, as in the case of some transdermal systems, as well as matrix tablets with low soluble drugs, coated forms, osmotic systems, etc. The pharmaceutical dosage forms following this profile release the same amount of drug by unit of time and it is the ideal method of drug release in order to achieve a pharmacological prolonged action.

First Order Kinetics

Kinetic equation for the first order release is as follows

$$Log\ Q_t = log\ Q_0 + K_1 t/2.303$$

Where Q_t is the amount of drug released in time t, Q_0 is the initial amount of drug in the solution and K_1 is the first order release constant. In this way a graphical representation of the decimal logarithm of the released amount of drug versus time will be linear.

The pharmaceutical dosage forms following this dissolution profile, such as those containing water-soluble drugs in porous matrices, release the drug in a way that is proportional to the amount of drug remaining in its interior, in such way, that the amount of drug released by unit of time diminishes.

Higuchi Model

$$f_t = K_H t^{1/2}$$

Where K_H is the Higuchi dissolution constant treated sometimes in a different manner by different authors and theories. Higuchi describes drug release as a diffusion process based in the Fick's law, square root time dependent. This relation can be used to describe the drug dissolution from several types of modified release pharmaceutical dosage forms, as in the case of some transdermal system and matrix tablets with water-soluble drugs.

Hixson–Crowell model

Hixson and Crowell (1931) recognizing that the particle regular area is proportional to the cubic root of its volume derived an equation that can be described in the following manner

$$W_0^{1/3} - W_t^{1/3} = K_s t$$

Where W_0 is the initial amount of drug in the pharmaceutical dosage form, W_t is the remaining amount of drug in the pharmaceutical dosage form at time tand K_s is a constant incorporating the surface–volume relation. This expression applies to pharmaceutical dosage form such as tablets, where the dissolution occurs in planes that are parallel to the drug surface if the tablet dimensions diminish proportionally, in such a manner that the initial geometrical form keeps constant all the time.

A graphic of the cubic root of the unreleased fraction of drug versus time will be linear if the equilibrium conditions are not reached and if the geometrical shape of the pharmaceutical dosage form diminishes proportionally over time. This model has been used to describe the release profile keeping in mind the diminishing surface of the drug particles during the dissolution.

Mechanism of Drug Release

To find out the drug release mechanism due to swelling (upon hydration) along with gradual erosion of the matrix, first 60% drug release data can be fitted in Korsmeyer–Peppas model which is often used to describe the drug release behavior from polymeric systems when the mechanism is not well-known or when more than one type of release phenomena is involved (Korsmeyer et al., 1983).

$$Log\ (M_t / M_\infty) = Log\ K_{KP} + n\ Log\ t$$

Where $M_t$is the amount of drug release at time *t*, M_∞ is the amount of drug release after infinite time, K_{KP} is a release rate constant incorporating structural and geometrical characteristics of the tablet, and *n* is the release exponent indicative of the mechanism of drug release.

Table 1: Examples of Oral Extended-Release Products

Type	Trade Name	Rationale
Erosion tablet	Constant-T	Theophylline
	enuate Dospan	Diethylpropion HCl dispersed in hydrophilic matrix
	Tedral SA	Combination product with a slow-erosion component (theophylline, ephedrine HCl) and an initial-release component theophylline, ephedrine HCl, phenobarbital)
Waxy matrix tablet	Kaon *Cl*	Slow release of potassium chloride to reduce GI irritation
Coated pellets in capsule	Ornade spansule	Combination of phenylpropanolamine HCl and chloropheniramine with initial- and extended-release component
Pellet in tablet	Theo-Dur	Theophylline
Leaching	Ferro-Gradumet (Abbott)	Ferrous sulfate in a porous plastic matrix that is excreted in the stool; slow release of iron decreases GI irritation
	Desoxyn gradumet tablet (Abbott)	Methamphetaminemethylacrylate,methylmethacrylatecopolymer, providone, magnesium stearate, the plastic matrix is porous
Coated ion-exchange	Tussionex	Cation ion-exchange resin complex of hydrocodone and phenyltoloxamine
Flotation–diffusion	Valrelease	Diazepam
Osmotic delivery	Acutrim	Phenylpropanolamine HCl (Oros delivery system)
	Procardia-XL	GITS—gastrointestinal therapeutic system with NaCl-driven (osmotic pressure) delivery system for nifedipine
Microencapsulation	Bayer timed-release	Aspirin
	Nitrospan	Microencapsulated nitroglycerin
	Micro-K Extencaps	Potassium chloride microencapsulated particles

Table 2: Technologies used for CRDDS

S. No.	Design Or Type Of The System	Release Mechanism
1	Dissolution Controlled Systems a)Encapsulation - Barrier coating - Embedment into a matrix of fatty materials) - Repeat action coatings - Coated plastic materials or hydrophilic materials b)Matrix Dissolution Control	The dissolution of drug from System
2	Diffusion Controlled Systems a)Reservoir Devices (Fatty polymer coated systems) b)Matrix Devices (Fatty polymer dispersed systems)	The diffusion of the drug solution through a water insoluble, permeable polymeric film
3	Dissolution and Diffusion Controlled Systems a)Non disintegrating polymeric matrix b)Hydrophilic matrices	Diffusion of a drug solution through a porous matrix
4	Ion- Exchange Resin Systems	Ion- Exchange between the resin - drug complex and ions in the GI tract
5	pH - Independent formulations	Influenced by change in pH and ionic permeability of the membrane coating
6	Osmotically Controlled System	They contain the buffering agents in a system which maintains constant pH throughout the GIT, so the drug release from the device is not affected by variable pH of GIT. Water entering by Osmosis dissolves the drug, and the drug solution is forced out through a laser drilled orifice

Table 3: Classification of Matrix Systems

Type of the Matrix System	Mechanism
Hydrophilic	Unlimited swelling delivery by diffusion swelling controlled delivery eg: Hydroxyethylcellulose, Hydroxypropylmethylcellulose
Inert	Inert in nature Controlled delivery by diffusion : Ethylcellulose
Lipidic	Delivery by diffusion & erosion eg: Carnauba wax.
Biodegradable	Non lipidic nature Controlled delivery by eg surface erosion
Resin Matrices	Drug release from drug-resin complex eg: Ion exchange resins

Table 4: Drug Release Kinetics

Kinetic Model	Relation	Systems Following the Model
First order	$\ln Q_t = \ln Q_o + K_t$ (release is proportional to amount of drug remaining)	Water-soluble drugs in porous matrix
Zero order	$f_t = K_o t$ (independent of drug concentration)	Transdermal systems Osmotic systems
Higuchi	$f_t = K_H t^{1/2}$ (proportional to square root of time)	Matrix formulations
Hixson-Crowell	$W_o^{1/3} - W_t^{1/3} = K_s t$	Erodible isometric matrices
f_t= fraction of dose release at time 't'. K_H, K_o, and K_s = release rate constants characteristic to respective models. Q_o= the drug amounts remaining to be released at zero hour. Q_t= the drug amounts remaining to be released at time't'. W_o= initial amount of drug present in the matrix. W_t= amount of drug released at time't'.		

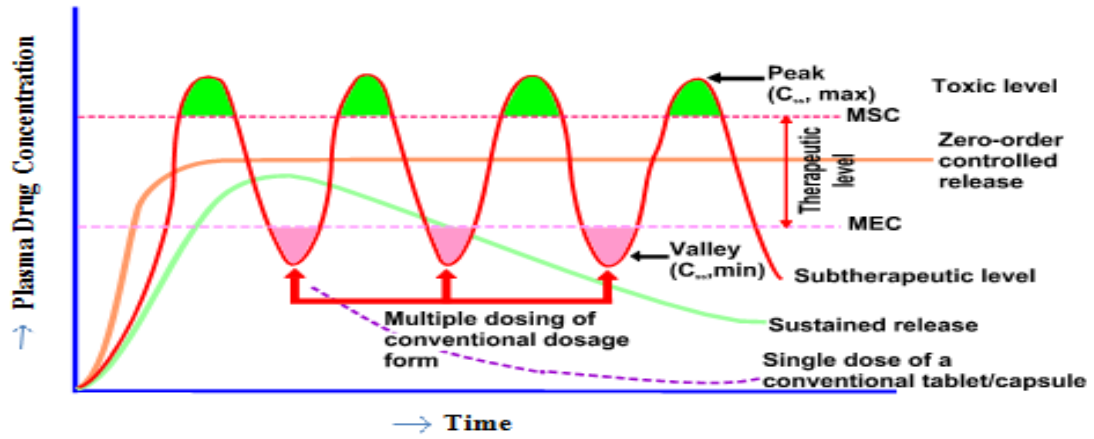

Fig. 1: A hypothetical plasma concentration-time profile from conventional multiple dosing and single doses of sustained and controlled delivery formulations. (MSC = maximum safe concentration, MEC = minimum effective concentration)

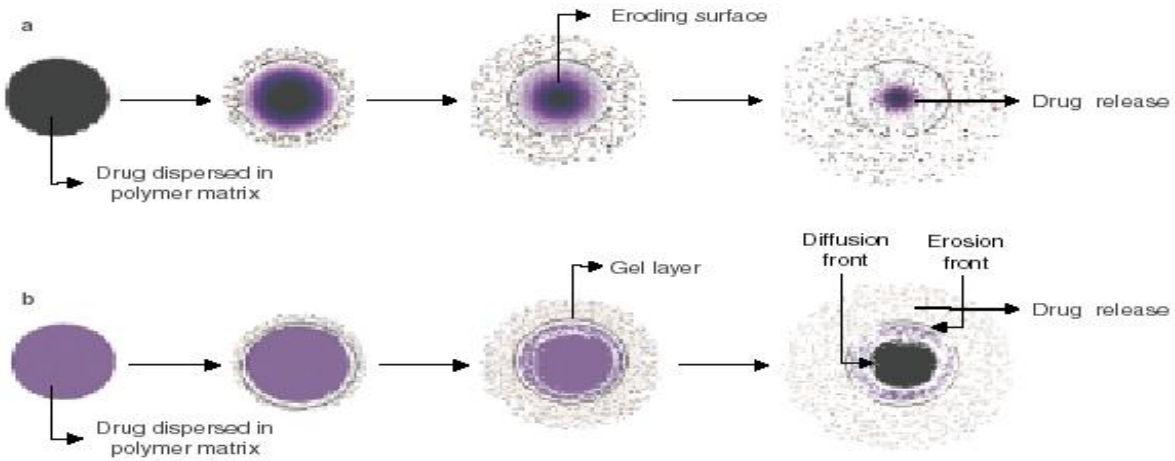

Fig. 2: Schematic drug release from matrix diffusion controlled-release drug delivery systems with the drug homogenously dispersed in: (a) an erodible polymer matrix; and (b) a hydrophilic, sellable polymer matrix

CONCLUSION

The controlled release drug delivery system aims to release the drug at the desired rate over extended period of time to maintain the therapeutic level in blood. Nowadays, the oral route of administration for controlled release drug delivery system has received more attention due to its more flexibility, reduced dosing frequency and better patient compliance. The design of oral controlled release drug delivery system depends on various factors like, physic-chemical properties of drug, type of delivery system, disease being treated,patient condition, treatment duration, presence of food, gastrointestinal motility and co-administration of other drugs. From the above discussion, we can concluded that the controlled release drug delivery system is very helpful in increasing the efficiency of the dose as well as the patient compliance. Moreover; the reasonable cost of oral controlled release drug delivery system has lead ease of market penetration as replacement of oral conventional drug delivery system.

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