Asian Journal of Pharmaceutical Technology & Innovation
ISSN: 2347-8810

Review Article

Received on: 04-04-2016
Accepted on: 11-04-2016
Published on: 15-04-2016

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Sustained Release Drug Delivery System: A Modern Formulation Approach

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ABSTRACT

Sustained release dosage forms are designed to release a drug at a predetermined rate by maintaining a constant drug level for a specific period of time with minimum side effects. In the recent years, focus on the development of controlled release drug delivery systems has increased. The basic rationale of controlled release drug delivery system optimizes the biopharmaceutical, pharmacokinetic, and pharmacodynamic properties of a drug in such a way that its utility is maximized, side-effects are reduced and cure or control of the condition is achieved, in the shortest possible time by using smallest quantity of drug administered by the most suitable route. There are several advantages of sustained release drug delivery over conventional dosage forms like improved patient compliance due to less frequent drug administration, reduction of fluctuation in steady-state drug levels, maximum utilization of the drug, increased safety margin of potent drug, reduction in healthcare costs through improved therapy, shorter treatment period and less frequency of dosing can be achieved. This review briefly emphasizes about the sustained release drug delivery system characteristics, formulation design and drug release mechanisms.

Key-words: SRDS, controlled release, formulation approach, improved therapy.

Cite this article as:
Pooja R. Alli, Pratima B. Bargaje, Nilesh S. Mhaske, Sustained Release Drug Delivery System: A Modern Formulation Approach, Asian Journal of Pharmaceutical Technology& Innovation, 04 (17); 2016,108-118 . www.asianpharmtech.com

INTRODUCTION:-

Sustained release drug therapy:-

The basic goal of therapy is to achieve a steady state blood level that is therapeutically effective and nontoxic for an extended period of time. The design of proper dosage regimens is an important element in accomplishing this goal. Sustained release, sustained action, controlled release, extended action, timed release, depot and repository dosage forms are terms used to identify drug therapy systems that are designed to achieve a prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of single dose. In the case of injectable dosage forms, this period is measured in hours and critically depends on the residence time of the dosage form in the gastrointestinal tract. The term controlled release has become associated with those systems from which therapeutic agents maybe automatically delivered at predetermined rates over a long period of time. Products of this type have been formulated for oral, injectable and topical use and inserts for placement in body cavities. Prolonged or sustained release systems only prolong therapeutic blood or tissue levels of the drug for an extended period of time[(1)]. In some sustained-release (SR) formulations, the drug dissolves into the matrix, and the matrix physically swells to form a gel, allowing the drug to exit through the gel's outer surface. There are certain considerations for the formation of SR formulation,

i. If the active compound has a long half-life (over 6 hours), it is sustained on its own.

ii. If the pharmacological activity of the active compound is not related to its blood levels, time releasing has no purpose.

iii. If the absorption of the active compound involves an active transport, the development of a time-release product may be problematic.

iv. Finally, if the active compound has a short half-life, it would require a large amount to maintain a prolonged effective dose. In this case, a broad therapeutic window is necessary to avoid toxicity; otherwise, the risk is unwarranted and another mode of administration would be recommended[(2)].

The design of oral sustain drug delivery system(DDS) should be primarily aimed to achieve the more predictability and reproducibility to control the drug release, drug concentration in the target tissue and optimization of the therapeutic effect of a drug by controlling its release in the body with lower and less frequent dose. Conventional drug therapy typically involves the periodic dosing of a therapeutic agent that has been formulated in a manner to ensure its stability, activity and bioavailability. For most of the drugs, conventional methods of formulation are quite effective. However some drugs are unstable and toxic and have a narrow therapeutic range, exhibit extreme solubility problems, require localization to a particular site in the body or require strict compliance or long-term use. In such cases a method of continuous administration of drug is desirable to maintain fixed plasma drug levels. The goal in designing sustained or sustained delivery systems is to reduce the frequency of the dosing or to increase effectiveness of the drug by localization at the site of action, reducing the dose required or providing uniform drug delivery. So, sustained release dosage form is a dosage form that release one or more drugs continuously in a predetermined pattern for a fixed period of time, either systemically or to a specified target organ. Sustained release dosage forms provide a better control of plasma drug levels, less dosage frequency, less side effect, increased efficacy and constant delivery[(3)].

The major Drawbacks Associated with Conventional Dosage Forms are:-[(4)]

- Poor patient compliance, increased chances of missing the dose of a drug with short half-life for which frequent administration is necessary.
- The unavoidable fluctuations of drug concentration may lead to under medication or over medication.
- A typical peak-valley plasma concentration-time profile is obtained which makes attainment of steady-state condition difficult.
- The fluctuations in drug levels may lead to precipitation of adverse effects especially of a drug with small Therapeutic Index (TI) whenever over medication occur.

Potential advantages and disadvantages of sustained release dosage forms:-

Advantages:-[(1)]

1. The frequency of drug administration is reduced.
2. Patient compliance can be improved.

3. Drug administration can be made more convenient.
4. The blood level oscillation characteristics of multiple dosing of conventional dosage form is reduced, because a more even blood level can be maintained.
5. Better control of drug absorption can be attained, since the high blood level peak that may be observed after administration in an extended action form.
6. The characteristic blood level variations due to multiple dosing of conventional dosage form can be reduced.
7. The total amount of drug administration can be reduced, thus
-Maximizing availability with minimum dose.
-Minimize drug accumulation with chronic dosing.
8. Safety margin of high potency drugs can be increased and the incidence of both local and systemic adverse side effects can be reduced in sensitive patients.
9. Improve efficacy in treatment,
-Cure or control condition more promptly.
-Improve/ control i.e. reduces fluctuation in drug level.
-Improve bioavailability of some drugs.
-Make use of special effect e.g. sustained release aspirin for morning relief of arthritis by dosing before bed time.

Disadvantages:-[5]
1. Administration of sustained release medication does not permit prompt termination of therapy.
2. Flexibility in adjustment in dosage regimen is limited.
3. Controlled release forms are designed for normal population i.e., on the basis of average drug biological half-lives.
4. Economy factors may also be assessed, since most costly process and equipment are involved in manufacturing so many controlled release dosage forms.

Limitations:-[5]
1. If the active compound has a long half-life (over six hours), it is sustained on its own.
2. If the pharmacological activity of the active compound is not related to its blood levels, slow releasing then has no purpose.
3. If the absorption of the active compound involves an active transport, the development of a time-release product may be problematic.
4. Finally, if the active compound has a short half-life, it would require a large amount to maintain a prolonged effective dose. In this case, a broad therapeutic window is necessary to avoid toxicity; otherwise, the risk is unwarranted and another mode of administration would be recommended.
5. Not effectively absorbed in lower small intestine.
6. Large doses are required (more than 1 gm).
7. Drug with low therapeutic index.
8. Precise dose to individuals is required.

CHARACTERISTICS THAT MAKES DRUGS SUITABLE FOR SUSTAINED RELEASE DDS:-

PHYSICOCHEMICAL CHARACTERISTICS:-[6,7]

Some physicochemical parameters for the selecting of the drug to be formulated in sustained release dosage form which mainly includes the knowledge on the absorption mechanism of the drug form the Gastro Intestinal (G.I.) tract, its general absorbability, the drug's molecular weight, solubility at different pH and apparent partition coefficient as shown in Table 1.

Similarly there are some pharmacokinetic parameters for drug selection which includes drug's elimination half-life, total clearance, absolute bioavailability, possible first-pass effect, and the desired steady concentrations for peak and trough as shown in Table 2.

Parameter	Preferred value
Molecular weight/size	< 1000 Daltons
Solubility	> 0.1 mg/ml for pH 1 to pH 7.8
Apparent partition coefficient	High
Absorption mechanism	Diffusion
General absorbability	From all GI segments
Release	Should not be influenced by pH and enzymes

Table 1: Physicochemical parameters for drug selection.

Parameter	Comment
Elimination half-life	Preferably between 2 to 8 hrs
Total clearance	Should not be dose dependent
Elimination rate constant	Required for design
Apparent volume of distribution (V_d)	The larger V_d and MEC, the larger will be the required dose size
Absolute bioavailability	Should be 75% or more
Intrinsic absorption rate	Must be greater than release rate
Therapeutic concentration C_{ss}	The lower C_{ss} and smaller V_d, the loss among of drug required
Toxic concentration	Apart the values of MTC and MEC, safer the dosage form. Also suitable for drugs with very short half-life.

Table 2: Pharmacokinetic parameters for drug selection.

BIOLOGICAL CHARACTERISTICS:-[6,8]

1) Biological half-life:-

The simple theory of an oral SR formulation is to maintain therapeutic blood levels over an extended period of time. To achieve this, drug must enter into the blood circulation at almost the same rate at which it is eliminated. Each drug has its own characteristic related to elimination rate, which is the sum of all elimination processes, generally include metabolism, urinary excretion and all the process that permanently remove drug from the blood stream. Drugs with short half-life are best candidate for Sustain release formulation. Drugs which having shorter half life less than 2 hours such as levodopa are poor candidates for SR Formulation. Drugs which having longer half life more than 8 hours are also poor candidate in SR formulation, since their effect is already sustained. Examples: Digoxin, Phenytoin.

2) Absorption:-

The goal of forming a SR product is to control the release rate of drug is much slower than the rate of absorption. If we presume that the transit time of most drugs in the absorptive areas of the GI tract is about 8-12 hours, the extreme half-life for absorption should be in the region of 3-4 hours; otherwise, the dosage form will pass out of the probable absorptive regions before drug release is complete. Thus corresponds to a minimum apparent absorption rate constant of 0.17-0.23h-1 to give 80-95% over this time period. So, it accepts that the absorption of drug should occur at a relatively uniform rate over the entire length of small intestine. If a drug is absorbed by active transport or transport is restricted to a specific region of intestine, SR preparation may be disadvantageous to absorption.

3) Metabolism:-

Decrease bioavailability from slow releasing dosage form shown by drugs those are significantly metabolized before absorption, either in the lumen or the tissue of the intestine, can show decreased bioavailability from slow releasing dosage form. A drug which having poor water solubility can be formulated in Sustain release dosage form. For this, various techniques which are available for enhancing the solubility of the

drug after the enhancing the solubility Sustain Release formulation is possible. But during this crystallization of the drug is possible when the drug is entering into the systemic circulation, should be prevented and one should be cautious for the prevention of the same.

4) Distribution:-

The rate of elimination of drug is mainly depends upon the apparent volume of distribution. So drugs with high apparent volume of distribution, influence the rate of elimination of the drug, this drugs are consider to be a poor candidate for oral SR drug delivery system. E.g. Chloroquine.

5) Protein Binding:-

To achieve pharmacological response unbound drug concentration is important rather than bound drug concentration and all drug bound to some extent to plasma and or tissue proteins. Protein binding of drug which shows a main role in its therapeutic effect in spite of the type of dosage form as extensive binding to plasma increase biological half-life and thus sometimes SR drug delivery system is not required for this type of drug.

6) Molecular size and diffusivity:-

In several sustained release systems drug must diffuse through a rate controlling membranes or matrix. Ability of a drug to diffuse through membranes, it's so called diffusivity (diffusion coefficient), is a role of its molecular size. An important influence upon the value of the diffusivity 'D' in polymers is the molecular size for molecular weight of the diffusing species.

7) Margin of safety:-

Safety of drug generally depends upon the therapeutic index. Larger the value of therapeutic index of a drug safer is the drug. Drugs having less therapeutic index are generally poor candidates for oral SR drug delivery system.

8) Plasma concentration response relationship:-

A.P.I. having linear relationship is better candidate.

DIFFERENT POLYMERS USED IN SUSTAINED RELEASE DDS:-[9]

Hydrogels:-

- Polyhydroxy ethyl methyl acrylate (PHEMA)
- Cross-linked polyvinyl alcohol (PVA)
- Cross-linked polyvinyl pyrrolidone (PVP)
- Polyethyleneoxide (PEO)

Soluble Polymers:-

- Polyethylene glycol (PEG)
- Polyvinyl alcohol (PVA)
- Polyvinyl pyrrolidone (PVP)
- Hydroxy propyl methyl cellulose (HPMC)

Biodegradeble Polymers:-

- Polylactic acid (PLA)
- Polyglycolic acid (PGA)
- Polycaprolactone (PLA)
- Polyanhydrides

Non Biodegradeble Polymers:-

- Polyethylene vinyl acetate (PVA)
- Polydimethyl siloxane (PDS)
- Polyetherurethane (PEU)
- Polyvinyl chloride (PVC)

Mucoadhesive Polymers:-

- Polycarbophil
- Sodium carboxymethyl cellulose
- Polyacrilic acid
- Methyl cellulose

DESIGN AND FORMULATION OF ORAL SUSTAINED RELEASE DRUGDELIVERY SYSTEM AND THE FACTORS AFFECTING THERE OF:-[3,10]

The oral route of administration is the most preferred route due to flexibility in dosage form, design and patient compliance. But here one has to take into consideration, the various pH that the dosage form would encounter during its transit, the gastrointestinal motility, the enzyme system and its influence on the drug and the

dosage form. The majority of oral sustained release systems rely on dissolution, diffusion or a combination of both mechanisms, to generate slow release of drug to the gastrointestinal milieu. Theoretically and desirably a sustained release delivery device, should release the drug by a zero-order process which would result in a blood level time profile similar to that after intravenous constant rate infusion. Sustained (zero-order) drug release has been attempted to be achieved, by following classes of sustained drug delivery system.

A) Diffusion sustained system
i) Reservoir type ii) Matrix type
B) Dissolution sustained system
i) Reservoir type ii) Matrix type
C) Methods using Ion-exchange D) Methods using osmotic pressure
E) pH independent formulations F) Altered density formulations

A) Diffusion sustained system:-

Diffusion process shows the movement of drug molecules from a region of a higher concentration to one of lower concentration.

i) Diffusion reservoir system:-

In this system, a water insoluble polymeric material covers a core of drug. Drug will partition into the membrane and exchange with the fluid surrounding the particle or tablet. Additional drug will enter the polymer, diffuse to the periphery and exchange with the surrounding media. The drug release takes place by diffusion mechanism. The diffusion type reservoir system is shown in (Figure 2).

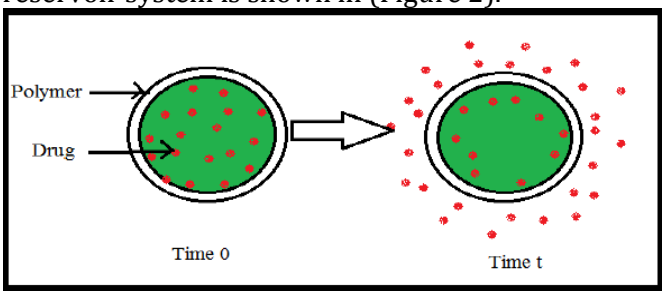

Figure 2: Schematic Representation of Diffusion Type Reservoir System.

Advantages:-

- Zero order delivery is possible.
- Release rates can be modified with polymer type & concentration.

Disadvantages:-

- Difficult to deliver high molecular weight compound.
- Generally increased cost per dosage unit.
- Potential toxicity if dose dumping occurs.

ii) Diffusion matrix system:-

The matrix system is defined as a well-mixed composite of one or more drugs with gelling agent i.e. hydrophilic polymers. Matrix systems are widely used for sustaining the release rate. It is the release system which prolongs and controls the release of the drug that is dissolved or dispersed. A solid drug is dispersed in an insoluble matrix and the rate of release of drug is dependent on the rate of drug diffusion and not on the rate of solid dissolution. The diffusion type matrix system is shown in (Figure 3).

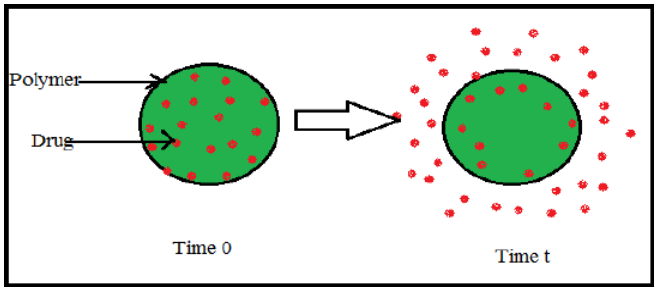

Figure 3: Schematic Representation of Diffusion Type Matrix System.

Advantages:-

- Possible to formulate high molecular weight compounds.
- Increased the stability by protecting the drug from hydrolysis or other derivative changes in gastrointestinal tract.

Disadvantages:-

- The ghost matrix must be removed after the drug has been released.
- The release rates are affected by various factors such as, food and the rate transit through the gut.
- Cannot provide pure zero order release.

Types of diffusion matrix system:-The matrix system can be divided into two categories depending on the types of retarding agents or polymeric materials.

a) Hydrophobic matrix system b) Hydrophilic matrix system c) Fat-wax matrix system

a) Hydrophobic matrix system:-

This is the only system where the use of polymer is not essential to provide Sustained drug release, although insoluble polymers can been used. As the term suggests, the primary rate controlling components of hydrophobic matrix are water insoluble in nature. These ingredients include waxes glycerides fatty acids, and polymeric materials such as ethyl cellulose, methyl cellulose and acrylate copolymer. To modulate drug release, it may be necessary to incorporate soluble ingredients such as lactose into formulation. The presence of insoluble ingredient in the formulations helps to maintain the physical dimension of hydrophobic matrix during drug release.

b) Hydrophilic matrix system:-

The primary rate limiting ingredients of hydrophilic matrix are polymers that would swell when in contact with aqueous solution and form a gel layer on the surface of the system. When the release medium is thermodynamically compatible with a polymer, the solvent penetrates into the free spaces between macromolecular chains. The polymer may undergo a relaxation process due to the stress of the penetrated solvent, so that the polymer chains become more flexible and the matrix swells. This allows the encapsulated drug to diffuse more rapidly out of the matrix. On the other hand, it would take more time for drug to diffuse out of the matrix since matrix swelling lengthens the diffusion path. For dissolvable polymer matrix, polymer dissolution is another important mechanism that can modulate the drug delivery rate. While either swelling or dissolution can be the predominant factor for a specific type of polymers, in most cases drug release kinetics is a result of a combination of these two mechanisms. The main polymers used in hydrophilic matrices are hydroxy propyl methyl cellulose (HPMC) and Hydroxy propyl cellulose (HPC), Xanthan gum, Carbopol and Alginates.

c) Fat-Wax matrix tablet:-

The drug can be incorporated into fat wax granulations by spray congealing in air, blend congealing in an aqueous media with or without the aid of surfactant and spray-drying techniques. In the bulk congealing method, a suspension of drug and melted fat-wax is allowed to solidify and is then comminuted for sustained release granulations. The mixture of active ingredients, waxy materials and fillers also can be converted into granules by compacting with roller compactor, heating in a suitable mixture such as fluidized-bed and steam jacketed blender

or granulating with a solution of waxy material or other binders. The drug embedded into a melt of fats and waxes is released by leaching and/ or hydrolysis as well as dissolution of fats under the influence of enzymes and pH change in the gastrointestinal tract. The addition of surfactants to the formulation can also influence both the drug release rate and the proportion of total drug that can be incorporated into a matrix.

B) Dissolution sustained systems:-

A drug with a slow dissolution rate is inherently sustained and for those drugs with high water solubility, one can decrease dissolution through appropriate salt or derivative formation. These systems are most commonly employed in the production of enteric coated dosage forms. This inhibits release of drug from the dosage form until it reaches the higher pH of the intestine. In most cases, enteric coated dosage forms are not truly sustaining in nature, but serve as a useful function in directing release of the drug to a special site.

i) Soluble reservoir system:-

In this system drug is coated with a given thickness coating, which is slowly dissolved in the contents of gastrointestinal tract by alternating layers of drug with the rate controlling coats as shown in (Figure 4).

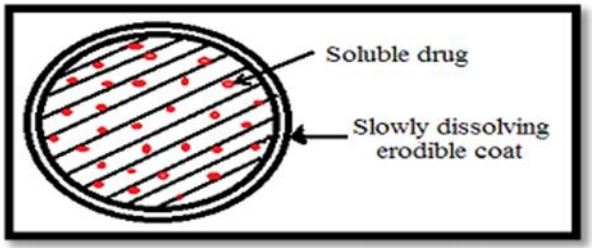

Figure 4: Schematic Representation of Dissolution of Reservoir System.

An alternative method is to administer the drug as group of beads that have coating of different thickness. Since the beads have different coating thickness, their release occurs in a progressive manner. Those with the thinnest layers will provide the initial dose. The maintenance dose of drug can be achieved by applying thicker coating.

ii) Soluble matrix system:-

It can be either a drug impregnated sphere or a drug impregnated tablet, which will be subjected to slow erosion. The more common type of dissolution sustained dosage form is shown in (Figure 6).

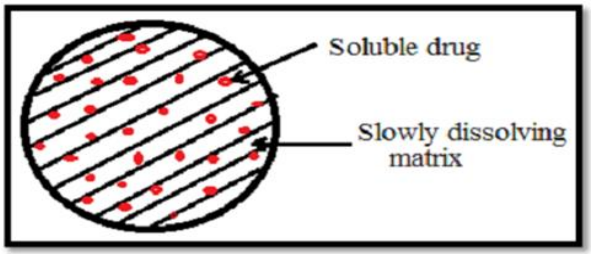

Figure 6: Schematic Representation of Dissolution Matrix System.

iii) Dissolution- sustained pulsed delivery system:-

Amongst Sustained release formulations hydrophilic matrix technology is the most widely used due to its following advantages.

- Provide desired release profile for a wide therapeutic drug category, drug and solubility.
- Ease of drug modulation through level, choice of polymeric systems & function coating.

A hydrophilic matrix tablet consists of mixture of drug, polymer & excipients (filler/diluents as well as other excipients) prepared by hydrophilic polymer in the matrix. Formulators often choose from a range of hydrophilic polymer as stand alone or in combination with different polymers for release rate control.

C) Ion exchange resins sustained release:-

Ion exchange resins are cross-linked water-insoluble polymers carrying ionisable functional groups. The resins have been used in various pharmaceutical applications, primarily for taste masking and controlled release systems. In tablet formulations, ion exchange resins have been used as disintegrant, because of their swelling ability. It forms irreversible complex with ionisable drugs upon prolonged exposure of the drug to the resin. A resin bound drug is removed when appropriate ions are in contact with ion-exchanged groups. The area and length of diffusion pathway and the amount of cross-linked polymer in the resin moiety governs the rate of drug release.

D) Methods using osmotic pressure:-

In this method, the release controlling factor that must be optimized is the osmotic pressure gradient between inside the compartment and the external environment. The simplest and most predictable way to achieve a constant osmotic pressure is to maintain a saturated solution of osmotic agent in the compartment. This technology provides zero order release used for hydrophilic drugs. Drug may be osmotically active or combine with osmotically active salt e.g. NaCl. A semi permeable membrane is placed around a tablet, particle or drug solution that allows transport of water into the tablet with eventual pumping of drug solution out of the tablet through a small delivery aperture in tablet coating. The osmotic systems are classified in major two types, i.e. type-A & type-B.

In type-A system, the core contains both, the drug and electrolytes. The electrolytes provide osmotic pressure and maintain the rate of drug release.

In type-B system, the drug solution is present in a semi permeable membrane surrounded by the electrolytes. Both the systems are shown in (Figure 7 & 8) respectively.

The ODDS can be conveniently classified in to following types:-

(A)Single chamber osmotic pump:-

i) Elementary osmotic pump (EOP)

(B) Multi chamber osmotic pump:-

i) Push pull osmotic pump. ii)Osmotic pump with non expanding second chamber.

(C) Specific types:-

i)Controlled porosity osmotic pump. ii)Monolithic osmotic systems.

iii)Osmotic bursting osmotic pump. iv)OROS – CT.

v)Multi particulate delayed release systems (MPDRS).

vi)Liquid Oral Osmotic System (L-OROS).

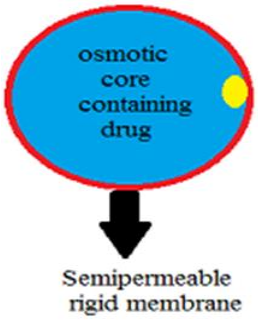

Figure 7: Type- A osmotic system

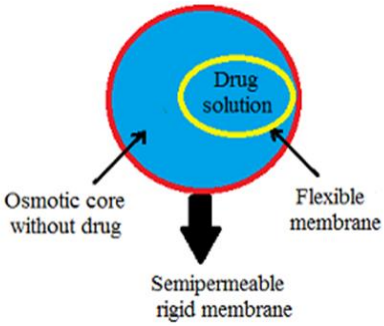

Figure 8: Type-B osmotic system

E) pH Independent formulations:-

Most drugs are either weak acids or weak bases. The release from Sustained release formulations is pH dependent. However; buffers such as salts of amino acids, citric acid, phthalic acid, phosphoric acid or tartaric acid can be added to the formulation to help to maintain a constant pH thereby rendering pH independent drug release. A buffered formulation is prepared by mixing a basic or acidic drug with one or more buffering agent, granulating with appropriate pharmaceutical excipients and coating with gastrointestinal fluid permeable film forming polymer. When gastrointestinal fluid permeates through the membrane, the buffering agents adjust the fluid inside to suitable constant pH thereby rendering a constant rate of drug release.

F) Altered density formulations:-

Several approaches have been developed to prolong the residence time of drug delivery system in the gastrointestinal tract. The delivery system remains in the vicinity of the absorption site until most, if not all of its drug contents is released. In high density approach, the density of the pellets must exceed that of normal stomach content and should therefore be at least 1-4g/cm^3. In low density approach, the globular shells which have an apparent density lower than that of gastric fluid can be used as a carrier of drug for sustained release purpose. There are several reasons for attractiveness of these dosage forms: provides increased bioavailability of drug product. This system is generally used when, the single dose for the duration of treatment whether for days or weeks as with infection, diabetes or hypertension is required.

Factors Influencing Design of sustained Release Dosage Forms:-[3]

The therapeutic efficacy of drug under clinical conditions is not simply a function of its intrinsic pharmacological activity but also depends upon the path of the drug molecule from the site of administration to the target site. Different conditions encountered by the drug molecule while traversing the path of distribution may alter either the effectiveness of the drug or affect the amount of the drug reaching the receptor site.

A) Pharmaceutics:-

This refers to the development/manufacturing of an efficient delivery system in which the drug has maximum physiological stability and optimum bioavailability.

B) Biopharmaceutics / pharmacokinetics:-

This involves the study of absorption, distribution, metabolism and excretion of the drug, before and after reaching the target site and evaluation of the relationship between delivery system and therapeutic response.

C) Pharmacodynamics/ Clinical Pharmacology:-

It is the study of the mechanism of action and clinical efficacy of a drug administered in dosage form in terms of onset, intensity and duration of pharmacological activity.

CONCLUSION:-

Wide range of drugs is formulated now in a variety of different per oral extended-release dosage forms. However, only those which result in a significant reduction in dose frequency and/or a reduction in toxicity resulting from high concentration in the blood or gastrointestinal tract are likely to improve therapeutic outcomes. To be a successful extended-release product, the drug must be released from the dosage form at a predetermined rate, dissolve in the gastrointestinal fluids, maintain sufficient gastrointestinal residence time, and may be absorbed at a rate and will replace the amount of drug being metabolized and excreted. In a nut shell, sustained-release formulations are a promising way to improve the patient's compliance by reducing dosing intervals and minimizing adverse effects. Out of many approaches to sustained drug release, matrix based approach is widely used due to its simplicity, scalability and from stability point of view.

ACKNOWLEDGEMENT:-

As a corresponding authors we are highly thankful to our Parents and Teachers for their moral support and encouragement. Last but not the least, thanks to Almighty god for showering his blessings best owned on us.

REFERENCES:-

1) N. Anuj Patnaik, T. Nagarjuna, T. V. Thulasiramaraju. Sustained release drug delivery system: A modern formulation approach. International Journal of Research in Pharmaceutical and Nano Sciences. 2(5), 2013, 586-601.

2) Dusane Abhijit Ratilal, Gaikwad Priti D., Bankar Vidyadhar H., Pawar Sunil P. A review on: Sustained released technology. International Journal of Research in Ayurveda & Pharmacy. 2011. 2 (6) 1701-1708.

3) K. P. Sampath Kumar, Debjit Bhowmik, Shweta Srivastava, Shravan Paswan, A. S. Dutta. Sustained Release Drug Delivery System Potential. The Pharma Innovation. Online Available at www.thepharmajournal.com .Vol. 1 No. 2 2012& Vol. 1 No. 1 2012. Page no. 46-56.

4) Jaimini Manish, Kothari Abhay. Sustained release matrix type drug delivery system: A review. Journal of Drug Delivery & Therapeutics. 2012, 2(6), 142-148.

5) Satinder Kumar, Shashi Kant , Bharat Prashar. Sustained release drug delivery system: A review. International Journal of Institutional Pharmacy and Life Sciences. 2(3): May-June 2012. Page no. 356-376.

6) H. D. Zalte, R. B. Saudagar. Review on sustained release matrix tablet. International Journal of Pharmacy and Biological Sciences. Volume 3, Issue 4, Oct-Dec 2013, 17-29.

7) Bhargava Ankit, Rathore R. P. S., Tanwar Y. S., Gupta S., Bhaduka G. Oral sustained release dosage form: An opportunity to prolong the release of drug. International Journal of Advanced Research in Pharmaceutical& Bio Sciences. 2013, 3(1), 7-14.

8) Khyati Patel, Dr. Upendra Patel, Bhavin Bhimani, Ghanshyam Patel, Dhiren Daslaniya. Extended release oral drug delivery system. International Journal of Pharmaceutical Research And Bio-Science. 2012: Volume1 (3): 1-26.

9) Sunil Kumar, Anil Kumar, Vaibhav Gupta, Kuldeep Malodia and Pankaj Rakha. Oral Extended Release Drug Delivery System: A Promising Approach. Asian J. Pharm. Tech. 2012; Vol. 2: Issue 2, Page no. 38-43.

10) Ratnaparkhi M. P., Gupta Jyoti P. Sustained Release Oral Drug Delivery System - An Overview. International Journal of Pharma Research & Review. Mar 2013; 2(3):11-21.