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A REVIEW ON ORAL CONTROLLED DRUG DELIVERY SYSTEM

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ABSTRACT

An ideal dosage regimen in the drug therapy of any disease is the one which immediately attains the desired therapeutic concentration of drug in plasma (or at the site of action) and maintains it constant for the entire duration of treatment. This is possible through administration of a drug delivery system in a particular dose and at a particular frequency. Controlled drug delivery is the most advanced type of technique used for the optimized release of drug. This review consist all the information oral drug delivery.

KEY WORDS

Dosage regimen, Controlled drug delivery, Therapeutic and Plasma concentration.

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INTRODUCTION[1]

Pharmacotherapy cans be defined as the treatment and prevention of illness and disease by means of drugs of chemical or biological origin. It ranks among the most important methods of medical treatment, together with surgery, physical treatment, radiation and psychotherapy. There are many success stories concerning the use of drugs and vaccines in the treatment, prevention and in some cases even eradication of diseases (e.g. smallpox, which is currently the only human infectious disease completely eradicated). Although it is almost impossible to estimate the exact extent of the impact of pharmacotherapy on human health, there can be no doubt that pharmacotherapy, together with improved sanitation, better diet and better housing, has improved people's health, life expectancy and

quality of life. Unprecedented developments in genomics and molecular biology today offer a plethora of new drug targets. The use of modern chemical synthetic methods (such as combinatorial chemistry) enables the syntheses of a large number of new drug candidates in shorter times than ever before. At the same time, a better understanding of the immune system and rapid progress in molecular biology, cell biology and microbiology allow the development of modern vaccines against old and new challenges. Different types of mechanisms shown in Figure No.1.

Advantages of Controlled Drug Delivery System[1]

1. Improved patient convenience and compliance due to less frequent drug administration.
2. Reduction in fluctuation in steady-state levels (Figure No.2) and therefore:-
   Better control of disease condition, and
   Reduced intensity of local or systemic side-effects.
3. Increased safety margin of high potency drugs due to better control of plasma levels.
4. Maximum utilization of drug enabling reduction in total amount of dose administered.
5. Reduction in health care costs through:-
   Improved therapy
   Shorter treatment period
   Lower frequency of dosing, and

Disadvantages of Controlled-Release Dosage Forms[1]

1. Decreased systemic availability in comparison to immediate-release conventional dosage forms.
   This may be due to:-
   Incomplete release
   Increased first-pass metabolism
   Increased instability
   Insufficient residence time for complete release
   Site-specific absorption
   pH-dependent solubility.
   Poor *in vitro–in vivo* correlation.
2. Possibility of dose dumping due to food, physiologic or formulation variables or chewing or grinding of oral formulations by the patient and thus, increased risk of toxicity.
3. Retrieval of drug is difficult in case of toxicity, poisoning or hypersensitivity reactions.
4. Reduced potential for dosage adjustment of drugs normally administered in varying strengths.
5. Higher cost of formulation.

Design and Fabrication of Oral Delivery Systems[2-10]

Within the scope of this review, a variety of controlled-release systems are discussed. Included among these are the following:

1. Dissolution-controlled release
2. Osmotically controlled release
3. Diffusion-controlled release
4. Chemically controlled release
5. Miscellaneous controlled release.

Dissolution-controlled release Drug delivery System

These systems are those where the rate-limiting phenomenon responsible for imparting the controlled-release characteristics to the DDS is either of the two -

(a) Slow dissolution rate of the drug - the drug present in such a system may be one of the following two types:

i. Drug with inherently slow dissolution rate

ii. Drug that transforms into slow dissolving forms on contact with GI fluids.

(b) Slow dissolution rate of the reservoir membrane or matrix - the drug present in such a system may be the one having high aqueous solubility and dissolution rate. The challenge in designing such systems lies in controlling the drug dissolution rate by employing either or combination of following techniques:-

i.Embedment in slowly dissolving, degrading or erodible matrix. The matrix in addition may have low porosity or poor wet ability.

ii.Encapsulation or coating with slow-dissolving, degrading or erodible substances. In this approach, the rate of dissolution fluid penetration and/or wet ability of the reservoir system are controlled.

Slowly soluble and erodible materials commonly employed to achieve these objectives include hydrophobic substances such as ethyl cellulose

(containing an added water-soluble release modifying agent such as PVP), polymethacrylates with pH independent solubility and waxes such as glyceryl monostearate, and hydrophilic materials like sodium CMC. Figure No.2 shows the mechanism of dissolution controlled release.

Osmotically Controlled Release Drug Delivery System

In addition to the mechanism of solution diffusion, drug release from a membrane-reservoir device can also take place through a membrane via an osmotic pumping mechanism. In this case, a semipermeable membrane, such as cellulose acetate, is utilized to regulate osmotic permeation of water. With constant reservoir volume, this type of device delivers a volume of drug solution equal to the volume of osmotic water uptake within any given time interval. The rate of osmotic water influx, and therefore the rate of drug delivery by the system, will be constant as long as a constant thermodynamic activity gradient is maintained across the membrane. However, the rate declines parabolically once the reservoir concentration falls below saturation. Such an osmotic delivery system is capable of providing not only a prolonged zero-order release, but also a delivery rate much higher than that achievable by the solution-diffusion mechanism. Osmotically controlled release is also applicable to drugs with a wide range of molecular weight and chemical composition, which are normally difficult to deliver by the solution-diffusion mechanism (shown in Figure No.3).

Diffusion-Controlled Release

These systems are those where the rate-controlling step is not the dissolution rate of drug or release controlling element, but the diffusion of dissolved drug molecule through the rate-controlling element. The rate-controlling element in such a system is thus neither soluble, erodible nor degradable but is water-swellable or water-insoluble. Water-swellable materials include hydrophilic polymers and gums such as xanthan gum, guar gum, high viscosity grades of HPMC and HPC, alginates, etc. Water-insoluble polymers most commonly used in such systems are ethyl cellulose and polymethacrylates. The mechanism shown in Figure No.4.

Chemically Controlled Release Drug Delivery System

Chemically controlled systems include all polymeric formulations in which solute diffusion is controlled by a chemical reaction, such as the dissolution of the polymer matrix or cleavage of the drug from a polymer backbone. In most chemically controlled systems, solute release is controlled by the geometric shape of the device. Depending on the type of degradation reaction, these systems may be classified as chemically degradable (e.g., by hydrolysis) or biodegradable (e.g., by enzymatic reaction) controlled-release systems.

In chemically controlled drug delivery systems, the release of a pharmacologically active agent usually takes place in the aqueous environment by one or more of the following types of mechanisms:

1. Gradual biodegradation of a drug-containing polymer matrix.
2. Biodegradation of unstable bonds by which the drug is coupled to the polymer matrix.
3. Diffusion of a drug from injectable and biodegradable microbeads.

In contrast to mechanical and osmotic devices, the main advantages of such biodegradable systems are the elimination of the need for their surgical removal, their small size, and potential low cost. On the other hand, all biodegradable products, as well as their metabolites, must be nontoxic, noncarcinogenic and nonter- atogenic. These requirements are not easily met and must be subject to careful scrutiny.

Miscellaneous Forms of Controlled Release Drug Delivery System[11-15]

The miscellaneous forms of Controlled drug delivery system are

1. Ion-Exchange Resins

Resins are water-insoluble materials containing salt-forming groups in repeating positions on the resin chain. Ion-exchange resins have been used as drug carriers for preparing prolonged and sustained delivery by releasing the drug from the complex over approximately 8 to 12 h into the gi tract.

2. Altered Density: Drug-Coated Micro Pellets

Empty globular shells, which have an apparent density lower than that of gastric juice, can be used as carriers of drugs for sustained-release purposes.

3. pH-Independent Formulations

4. **Pro-Drugs**

A pro-drug is a compound resulting from chemical modification of a pharmacologically active compound, which will liberate the active compound in vivo due to enzymatic or hydrolytic cleavage. The primary purpose of employing a pro-drug is to increase intestinal absorption or to reduce local side effects.

5. Barrier coating

The barrier-coating principle can be applied to beads, granules, or a whole tablet. If barrier-coated beads or granules are used, one portion is usually left uncoated for the immediate dosage form, while others are coated differentially in order to acquire different release patterns.

6. Embedment in Slowly Eroding Matrix

In embedding, the active ingredients are dissolved or suspended in a mixture of fats and waxes, such as beeswax, carnauba wax, hydrated fats, synthetic waxes, butyl stearate, stearic acid, saccharose monostearate, sac- charose distearate, or in mixtures of glycerine monostearate, castor oil.

7. Embedment in Plastic Matrix

8. Repeat action

Repeat-action preparations contain two doses, one of which is released immediately upon administration, followed by a second dose, which is not a depot phase as discussed previously, but is a dose that is released after a certain time interval or in a certain environment. This is achieved by using enteric coating for the second dose.

9. Hydrophilic Matrix

Oral retard preparations based on the hydrophilic-matrix principle are pre- pared by mixing the active ingredients with non-digestible hydrophilic gums and compressing the mixture into tablets.

10. Polymer Resin Beads

Using epoxy resins, drugs can be incorporated into the plastic material, either by dissolving or suspending the active ingredient in the liquid plastic monomer. The solution or suspension is then dispersed in a hydrophilic or lipophilic medium, producing an emulsion.

Passage-sponge formation

1. Drug complex formation
2. Bioadhesive
3. Local, targeted systems
4. Synchron system
5. Pennkinetic and other liquid controlled-release systems
6. Controlled-release capsules
7. Controlled-release tablets
8. Hoffmann-la roche’s web delivery system
9. Hydrodynamic cushion system
10. Floating delivery system
11. Meter release system
12. Hydrodynamically balanced system
13. Other oral controlled drug delivery systems.

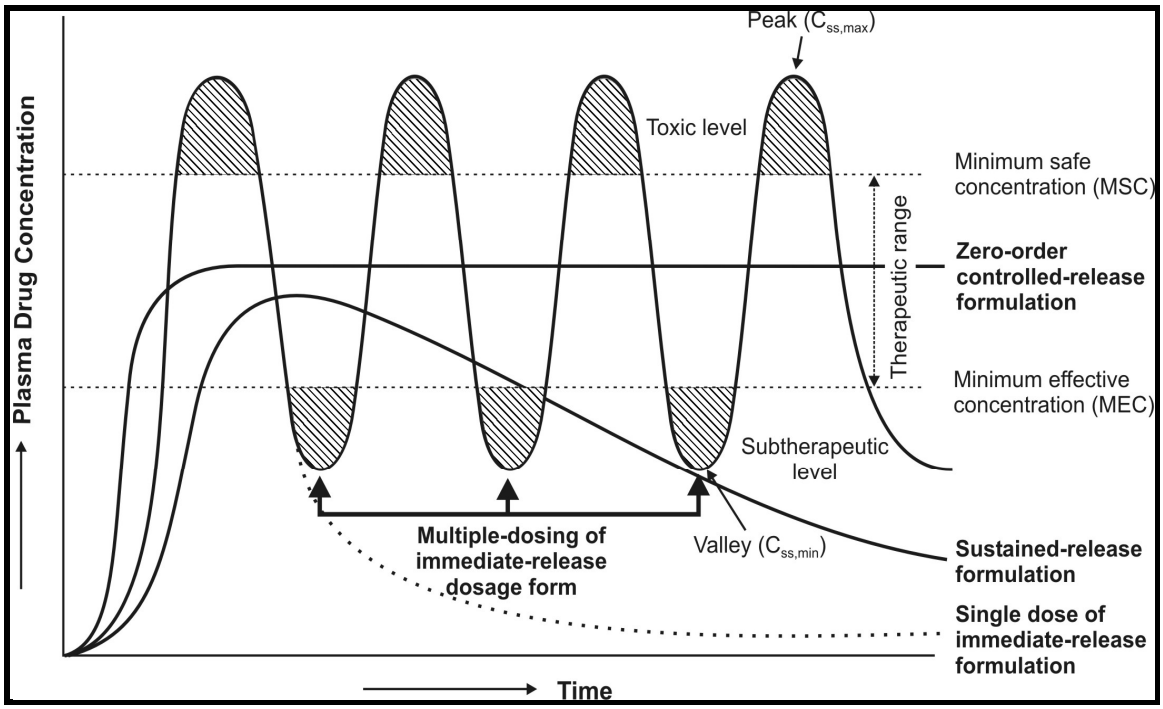

Figure No.1: Different mechanisms of Drug release

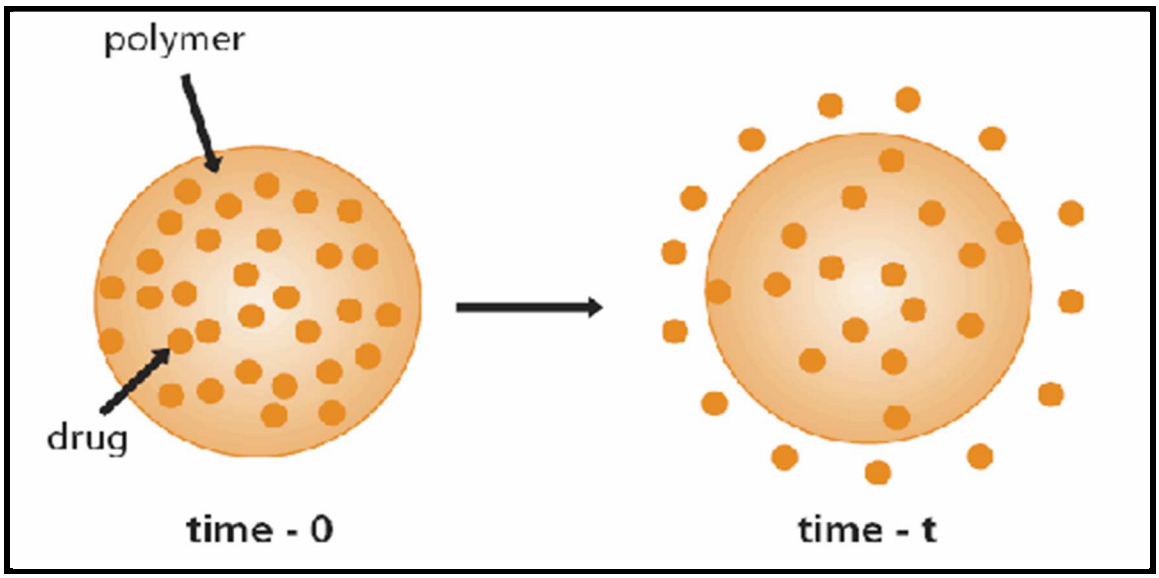

Figure No.2: Mechanism of Dissolution controlled release

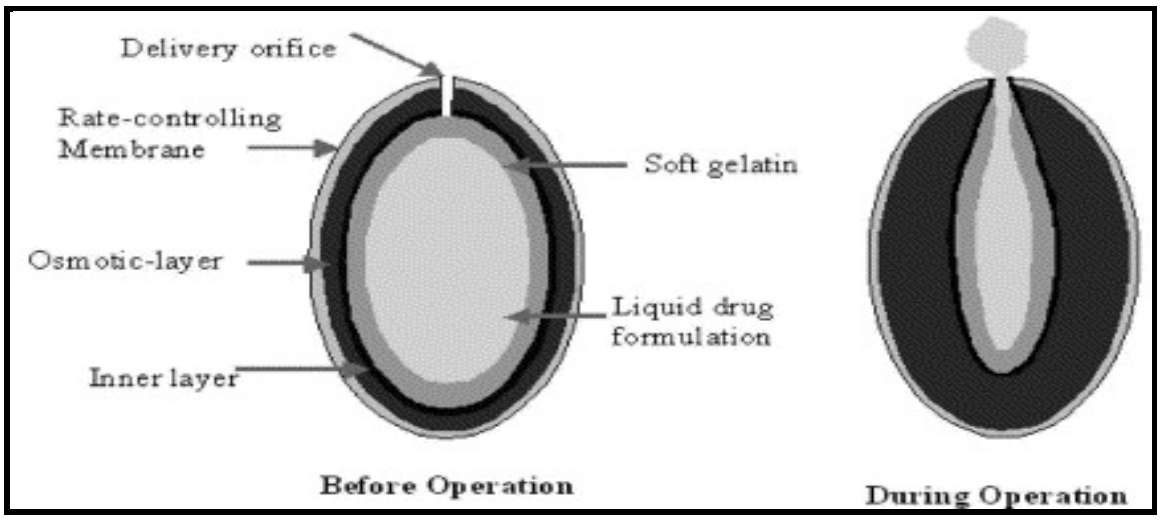

Figure No.3: Osmotic type controlled release

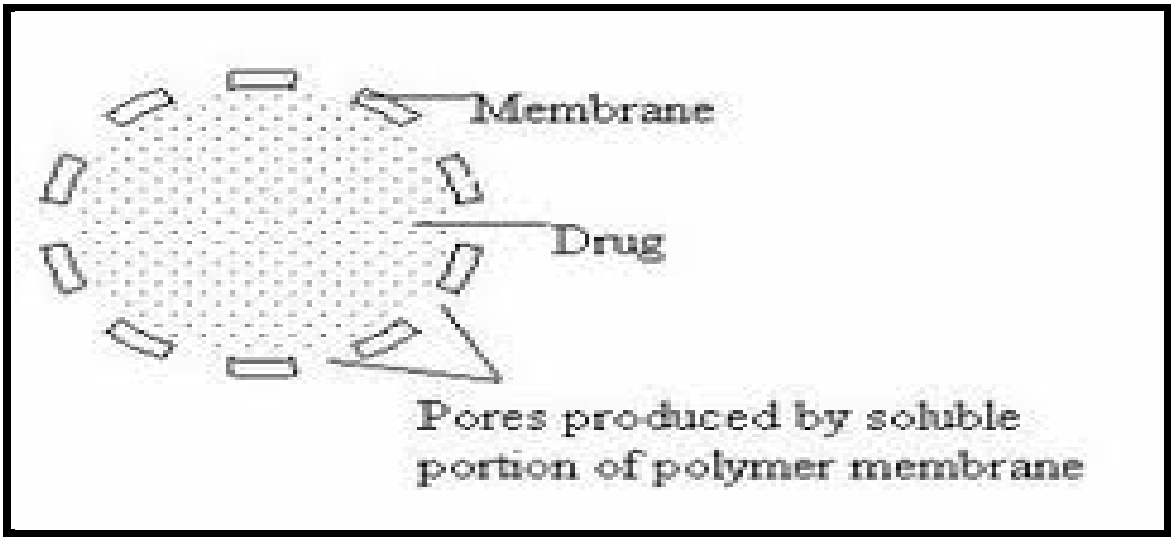

Figure No.4: Diffusion controlled release

CONCLUSION

The effective therapeutic drug delivery systems lie in the continuous drug release of the drug from the dosage form in a regular manner. Controlled drug delivery systems provide continuous drug release with a regular manner. Oral controlled-release dosage forms have been the need for strict adherence to zero-order kinetics. Given that many drugs enjoy a reasonably wide therapeutic range and that 10 to 30% differences in blood-drug levels will usually not show a change in biological response, perhaps too much has been made of this requirement. Within experimental error, a number of release-rate kinetic orders cannot be distinguished on the basis of the resulting blood levels. It is apparent that controlled drug delivery is a strategy that will remain popular for the foreseeable future and that the oral route will be a dominant approach.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

REFERENCES

1. Brahmankar M M. Biopharmaceutics and Pharmacokinetics, A treatase, 2nd edition, 2009, 235-239.
2. Banker G S. Pharmaceutical applications of controlled release: an overview of the past, present, and future. In medical application of controlled release, *CRC Press*, 2, 1984, 1-34.
3. Blythe R H, US Patent, 2, 1956, 738, 303, 1956.
4. Anon. Oral sustained products- pro's and con's, *drug and therapeutics bulletin*, 22(15), 1984, 57-60.
5. Shaw J E, Tuomisto J and Paasonen M K, Forsan Kirjapaino O Y Helsinki. Drug delivery systems, In annual reports in medicinal chemistry, *Academic press, inc., New York*, 15, 1980, 302-315.
6. Zaffaroni A. Congress of pharmacology, *Proc. Sixth int*, 5, 1975, 53-61.
7. Heilmann K. Therapeutic systems-pattern-specific drug delivery: concept and development, *G. Thieme, Stuttgart*, 1978, 154-171.
8. Urquhart J, Tuomisto J and Paasonen M K, Eds., Forsaan Kirjapaino Oy Helsinki, Proc. Sixth Int, Congress of Pharmacology, 5, 1975, 63.
9. Zaffaroni A, Di Carlo F. In Drug Metabolism Review, *Marcel Dekker, New York*, 8, 1978, 191-200.
10. Davis S S, Johnson P and Lloyd-Jones J G. Evaluation of the Gastrointestinal Transit and Release Characteristics of Drugs, *VCH Publishers, Chichester*, 28(1), 1987, 164-179.
11. Ho N F H, Merkle H P and Higuchi W I. Quantitative, mechanistic and physiological realistic approach to the biopharmaceutical design of oral drug delivery systems, *Drug Development and Industrial Pharmacy*, 9(7), 1983, 1111-1184.
12. Antonin H K H, Bieck P, Scheurlen M, Jedrychowski M and Malchow H. Oxprenolol absorption in man after single bolus dosing into two segments of the colon compared with that after oral dosing, *Br. J. Clin. Pharmac*, 19(2), 1985, 137S-142S.
13. Bruck S D. Pharmacological basis of controlled drug delivery. In Controlled Drug Delivery, *CRC Press, Inc., Boca Raton, FL*, 1(1), 1983, 1-13.
14. John V A, Shotton P A, Moppert J and Theobald W. Gastrointestinal transit of Oros drug delivery systems in healthy volunteers: a short report, *Br. J. Clin. Pharmac*, 19(2), 1985, 203S-206S.
15. Davis S S. The use of scinigraphic methods for the evaluation of novel delivery systems. In Directed Drug Delivery: A Multidisciplinery Problem, *Humana Press, Totowa, NJ*, 1(1-2), 1985, 319-340.

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