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Short review on controlled release tablet dosage form

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Abstract
The Idea Behind Oral Controlled Release Technology Is That Plasma Level Of The Drug Can Be Optimized By Controlling The Delivery Of The Drug From The Formulation In To Gastro-Intestinal Tract Control Can Be Achieved By Simple Control Release Dosage Form Which Release The Drug At Specific Rate Over Prolong Period Of Time. Controlled-Release (Cr) Formulations Were Brought Into Medication Therapy With Two Main Goals In Mind: To Minimise The Number Of Single Doses Per Day, Improving Patient Compliance, And To Limit Plasma Level Fluctuations, Resulting In Improved Therapeutic Efficacy And Reduced Toxicity. There Are A Variety Of Controlled-Release Pharmaceutical Systems Available Today, Ranging From Monolithic Matrices, Membrane Reservoirs, And Erodible Polymers To More Technologically Advanced Ph Independent Formulations, Ion Exchange Resins, And Osmotic ally And Geometrically Modified Systems. Pharmacotherapy Is The Use Of Chemical Or Biological Medications To Treat And Prevent Illness And Disease. Along With Surgery, Physical Therapy, Radiation, And Psychotherapy, It Is One Of The Most Significant Medical Treatments.

Keywords: controlled release, delivery, polymers, systems

Introduction
Regulated release systems deliver drug release in amounts sufficient to maintain therapeutic drug levels for an extended length of time, with release profiles largely controlled by the system's unique technological construction and design. As a result, the active constituent's release should ideally be unaffected by external influences. Although the release of the active ingredient in sustained release dosage forms is lower than in conventional formulations, it is nevertheless significantly influenced by the external environment into which it is discharged. Long or prolong action products are dosage forms containing chemically modified therapies compounds in order to prolong biological half-life; while extended release dosage forms are dosage forms containing chemically modified therapeutics substances in order to prolong biological half-life [1].

Terminology
Controlled drug delivery or modified release delivery systems may be defined as follows:-

Controlled Release Formulation
The controlled release system is designed to provide a continual supply of the active component, usually at a zero-order rate, by continuously releasing an amount of the drug corresponding to the amount removed by the body for a set length of time. A perfect controlled drug delivery system is one that administers medications at a predefined pace, either locally or systematically, for a set amount of time [2].

Repeat Action Preparations
After delivery, a single dose of the medicine is released, which is usually equivalent to a single dose of the conventional drug formulation. A second single dose is released when a particular amount of time has passed. Following the second dose, a third single dose is given when a particular amount of time has passed [2-3].

Extended-Release Formulation
The goal of extended-release formulations is to minimise dose frequency while maintaining a reasonably constant or flat plasma drug concentration. This helps to avoid the negative consequences of high concentrations [4].

Delayed Release Preparations
After administration, the medicine is released at a later time. A specific coat, such as enteric coating, or other temporal barriers, such as formaldehyde treatment of soft and hard gelatin capsules, are used to accomplish the delayed action. The goals of such preparations are to reduce drug-related side effects in the stomach and to protect the medicine from breakdown in the gastric fluid's very acidic pH [3-4].

Site Specific Targeting
These systems refer to the direct delivery of a medicine to a specific biological site. The target in this situation is located near or within the sick organ or tissue [4].

Receptor Targeting
These systems refer to the direct delivery of a medicine to a specific biological site. The target in this scenario is a specific drug receptor found in an organ or tissue. Site specific targeting and receptor targeting systems are considered regulated drug delivery systems because they address the spatial aspect of medication delivery [4-5].

Rationale Of Controlled –Drug Delivery [10-11]:
The primary reason for controlled drug delivery is to change the pharmacokinetics and pharmacodynamics of pharmacologically active moieties by employing innovative drug delivery technologies or altering the molecular structure and/or physiological factors inherent in a given route of administration. The duration of pharmacological action should be increased to allow for optimum design. A property of the drug molecules intrinsic kinetic properties is less, or not at all, a property of the rate regulated dose form. As previously stated, the primary goals of controlled medication administration are to assure drug safety and efficacy while also increasing patient compliance. This is accomplished through more frequent dosing and better control of plasma medication levels. Only the dose (D) and dosing interval (C) of conventional dosage forms can be changed, and each drug has a therapeutic window of plasma levels below which therapeutic benefit is insufficient and above which harmful side effects are triggered. This is usually expressed as the ratio of the median lethal dosage (LD 50) to the median effective dose (MED) (ED50).

Mechanism of Control Release System [4, 6]:
There are various types of sustained release systems, each of which is created and classified based on the mechanism it employs. These consist of
Diffusion controlled,
- Dissolution controlled,
- Erosion controlled,
- Ion exchange controlled
- Transport control also known as osmotic pump systems

Diffusion – Controlled Products
In these systems, a water-insoluble polymer restricts the flow of water and, as a result, the release of dissolved drug from the dosage form. Diffusion occurs when a drug runs through the polymer that makes up the controlled release device. Diffusion can happen between polymer chains or through pores in the polymer matrix. These can be divided into two categories:
A. Reservoir Devices.
B. Matrix Devices.

The fundamental processes of drug release in these two systems are vastly different.
A. Reservoir Devices
In this arrangement, a medication core is encased in a water-insoluble polymeric substance. The medicine will cross the membrane and exchange with the fluid that surrounds the particles (or tablet). The rate limiting membrane allows the active chemical to diffuse into the surrounding environment. The rate of drug distribution in reservoir systems is reasonably consistent.

B. Matrix Devices
In matrix devices, the medication or active is disseminated in a polymer matrix to create a homogenous system known as a matrix system. When a medication exits the polymer matrix and reaches the surrounding environment, it is called diffusion. The rate of release normally reduces as the release advances because the active agent has a longer distance to travel and hence a longer diffusion time to release.

Dissolution-Controlled Products
Slowly soluble polymers or micro encapsulation are used to limit the rate of drug dissolution in these products. The medication becomes available for dissolving once the coating has been dissolved. The frequency of medication release can be controlled by changing the coat thickness and composition. Some preparations include an immediate release component that contains a fraction of the whole dose to produce a pulse dose shortly after administration. Diffusion- or dissolution-controlled products' pellet dosage forms can be compressed or manufactured as a tablet. There are two types of dissolution-controlled products: -
a. Encapsulation Dissolution controls.
b. Matrix Dissolution control.

a. Encapsulation Dissolution Control

Individual drug particles (or granules) are coated with a slow-dissolving material in these systems. The coated particles can be crushed into tablets or capsules immediately. Micro encapsulation regulates the rate at which the drug dissolves (and thus its availability for absorption). The medication becomes available for dissolving once the coating has been dissolved. The rate of medication release can be regulated by altering the coat thickness and composition. Chewing these products could damage the coating. Absorption begins sooner with encapsulated pelleted foods and is less impacted by stomach emptying. When compared to non-disintegrating sustained-release tablet formulations, the pellets' entry into the small intestine (where the majority of drug absorption occurs) is usually more consistent.

b. Matrix Dissolution Control

Compressing the drug with a slow-dissolving carrier is an alternative method in this system. The pace of dissolution fluid penetration into the matrix, porosity, the existence of hydrophobic additives, and the system's and particle's wet ability all influence drug release.

Erosion Products

Drugs or active substances are combined with biodegradable polymers in this system. Natural biological processes breakdown these compounds within the body and drug discharge occurs at a consistent rate. The majority of biodegradable polymers are intended to disintegrate by the hydrolysis of polymer chains into biologically acceptable and smaller molecules. The rate of erosion of a carrier matrix controls the drug release from these products. The rate of degradation determines the rate of release.

Osmotic Pump Systems

The osmotic pump is similar to a reservoir device, except that it contains an osmotic agent (such as the active agent in salt form) that imbibes water from the surrounding medium through a semi-permeable membrane. The active agent is forced out through an opening (of a size optimised to limit solute diffusion while preventing the creation of a hydrostatic pressure head, which lowers osmotic pressure and modifies the device's dimensions and volume). The advantage of this type of drug is that it has a constant release that is unaffected by the environment in the gastrointestinal tract and is exclusively dependent on the passage of water into the dosage form. The osmotic agent and the size of the bubble can be changed to modify the rate of discharge.

Ion Exchange Resins

Extended-release drug-resin complexes (sometimes known as "resonates") are well-known and have proven to be profitable. Ion exchange groups in contact with suitably charged ions release the medicament linked to the resin. This approach can be applied with drugs that have certain features in terms of relative affinity for the polymers.

Evaluation of Pre-Compressive Parameter [7-9]

- **Tapped density (Td):** A graduated cylinder carrying a known mass of mixtures is placed on a mechanical tapped apparatus, which is worked for a set number of taps until the powder bed volume reaches a minimum volume. The tapped density can be calculated using the weight of the drug in the cylinder and this minimum volume.

Tapped density may be calculated from following equation given below-

Tapped Density= Mass / Volume

Where, M is the mass of the powder and Vt is the tapped volume of the powder. Values of tapped density are listed in table no.9

1. **Bulk density (Bd):** The process of crystallisation, milling, or formulation has a significant impact on the bulk density of a chemical. Pouring ingpresieved blend into a graduated cylinder via a big funnel and measuring the amount and weight as directed by-

Where, M = Mass of the powder
Values of bulk density are listed in table no.9.

2. Angle of repose (θ)

The glass funnel method was used to estimate the angle of repose of solid inclusion complexes. An properly weighed quantity of inclusion complexes was pushed through the funnel. The funnel's height was modified so that the tip of the funnel was just touching the apex of the powder heap. The powder was allowed to pour freely onto the surface through the funnel. The powder cone's diameter was measured, and the angle of repose was computed using the equation below.

$\theta = \tan^{-1} h/r$

θ =tan-1h/r Where, θ = angle of repose, h = height of the cone, r= radius of cone base Values of Angle of repose are listed

3. Compressibility Index (Carr's Index)

The % compressibility of the powder mixture was calculated using the following formula, which was based on the apparent bulk density and the tapped density. Compressibility index = 100 * Tapped density - Bulk density /Tapped density

4. Evaluation of Post–Compressive Parameter

Weight Variation

Twenty pills were individually and collectively weighed. The average weight was computed, and the percent weight variation was calculated using the formula, based on the collected weights

$$\% \textbf{ Weight Variation} = \textbf{Average weight} - \textbf{Individual weight Average weight } \boldsymbol{X}\ \textbf{100}$$

Standards of Weight Variation values are listed below

Table 1: Weight Variation Tolerance for Tablet

Average weight	Percentage deviation
80 mg / less	10
More than 80 mg but less than 250mg	7.5
250 mg or more	5

Hardness

The hardness of the tablet was determined by inserting it longitudinally between the two plungers of the Monsanto tablet hardness tester, and the result was expressed in kilogrammes per square centimetre. Hardness limits are 4-6kg/sq.cm.

Friability

For each formulation 10 tablets were weighed, placed in Friabilator (Erweka, Germany) and were subjected to100 rotations in 4 minutes. The tablets were re-weighed and friability was calculated, using Equation given below along with mean and the standard deviation SD.

Friability = (W1-W2)/W1X 100

Disintegration Time Study

The time it takes for the tablet to disintegrate is called disintegration time. Each batch had six tablets collected at random. Each batch's tablet was placed in the disintegration device according to the I P. The medium was a buffer solution with a pH of 6.8 that was kept at 372 degrees Celsius.

Dissolution Study

The dissolution test was performed using a USP Type-II dissolution equipment with buffer pH6.8 as the dissolution media and a temperature of 370.5oC. Three pills were chosen at random from each batch to be evaluated. Every 5 minutes, an aliquot of solution was removed. The medication content in the filtered solution was determined by measuring the absorbance at 322 nm with a UV Spectrophotometer.

Stability Study

Stability study for the optimized formulation was carried out for a period of 6 week at 40ºC/75%RH according to ICH guidelines, in predicting the shelf life of the formulation. Physical appearance and drug content of the formulation were studied during this period. From the results, it was found that the ideal formulation does not have major degradation and can be predicted for a good shelf life.

Conclusion

From a technological standpoint, the control release matrix tablets were successfully made employing HPMC as a carrier. The direct compression and wet granulation methods were employed to prepare these matrices. The physical qualities reported in were discovered to be ideal for the manufacturing process. When the HPMC concentration was reduced by a small percentage, no significant difference in drug release was found between the hydrophilic matrices. The main regulator of drug release from swelling matrices was starch Matrix tablets achieve the goal and remove the disadvantage of traditional dose forms that induce gastrointestinal irritation. The medication is released more slowly with control release matrix tablets.

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