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Controlled Drug Delivery Systems: Mechanisms, Drug Selection, and Formulation Approaches

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ABSTRACT

Controlled Drug Delivery Systems (CDDS) are pharmaceutical formulations designed to regulate the rate and duration of drug release to maintain therapeutic drug concentrations over an extended period. Compared with conventional dosage forms, these systems aim to reduce fluctuations in drug concentration, decrease the frequency of drug administration, and improve patient compliance. This review discusses the major principles and mechanisms involved in controlled drug delivery, including dissolution-controlled, diffusion-controlled, erosion-controlled, ion-exchange-controlled, and osmotic systems. It also highlights the importance of selecting suitable drug candidates based on their physicochemical, biopharmaceutic, pharmacokinetic, and pharmacodynamic properties. Factors such as molecular weight, aqueous solubility, partition coefficient, drug stability, absorption characteristics, biological half-life, metabolism, therapeutic range, and therapeutic index influence the suitability of a drug for controlled release. Understanding these properties is essential for selecting an appropriate drug delivery approach and designing formulations capable of providing predictable and sustained drug release. Overall, controlled drug delivery offers an important approach to improving dosage convenience and maintaining therapeutic effectiveness, although its success depends on appropriate drug selection and formulation design.

1. INTRODUCTION

Drug delivery systems play an important role in the administration of therapeutic agents for the prevention and treatment of various diseases. Among the different routes of drug administration, the oral route is widely preferred because of its convenience, ease of administration, and patient acceptability. Conventional dosage forms, particularly tablets and capsules, are extensively used for oral drug delivery. However, these dosage forms have certain limitations associated with dosing frequency, fluctuations in plasma drug concentrations, and maintenance of therapeutic activity over an extended period. Following the administration of a conventional dosage form, the drug is released and absorbed into the systemic circulation, resulting in an increase in plasma drug concentration. As the drug undergoes distribution, metabolism, and elimination, its

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concentration gradually decreases. When the plasma concentration falls below the minimum effective concentration, the desired therapeutic effect may no longer be maintained, necessitating the administration of another dose. Conversely, excessive drug concentrations may exceed the therapeutic range and produce undesirable effects or toxicity. Consequently, conventional dosage forms may produce fluctuations in plasma drug concentrations, which can affect therapeutic efficacy and drug safety.[1]

Controlled drug delivery systems (CDDS): have been developed to overcome some of the limitations associated with conventional dosage forms by regulating the rate and duration of drug release. These systems are designed to deliver a drug at a predetermined rate over a specified period, with the objective of maintaining its concentration within the desired therapeutic range. Depending on the formulation design, controlled drug delivery may also regulate the time or location of drug release. The development of controlled drug delivery systems is based on the modification of drug-release characteristics through appropriate formulation approaches. The release of a drug may be regulated by mechanisms such as diffusion, dissolution, ion exchange, and osmotic pressure. The selection of a suitable delivery system depends on the physicochemical properties of the drug, its pharmacokinetic characteristics, the intended route of administration, and the desired therapeutic response.

Controlled drug delivery systems offer several potential advantages over conventional dosage forms, including reduced dosing frequency, improved patient compliance, reduced fluctuations in plasma drug concentrations, and prolonged therapeutic activity. However, their performance depends on appropriate formulation design, and limitations such as dose dumping, formulation complexity, manufacturing costs, and difficulties in predicting in vivo drug-release behaviour must also be considered.

Therefore, understanding the fundamental principles of controlled drug delivery, the mechanisms governing drug release, and the physicochemical and biological properties of drug candidates is essential for the rational development of these formulations. These considerations provide the basis for selecting suitable drugs and designing delivery systems capable of achieving the intended drug-release profile.[1-2]

Bioavailability Profile of Drug after Oral Administration; After oral administration, the drug is absorbed into the bloodstream, causing its plasma concentration to increase. When the concentration reaches the Minimum Effective Concentration (MEC), the therapeutic effect begins. The concentration rises to its maximum level (Cmax) at a particular time (tmax). Subsequently, metabolism and elimination cause the concentration to decrease. The therapeutic effect continues as long as the concentration remains above the MEC. The area under the curve (AUC) represents the extent of systemic drug exposure, while the Maximum Safe Concentration (MSC) indicates the upper safe concentration limit shown in the figure.1

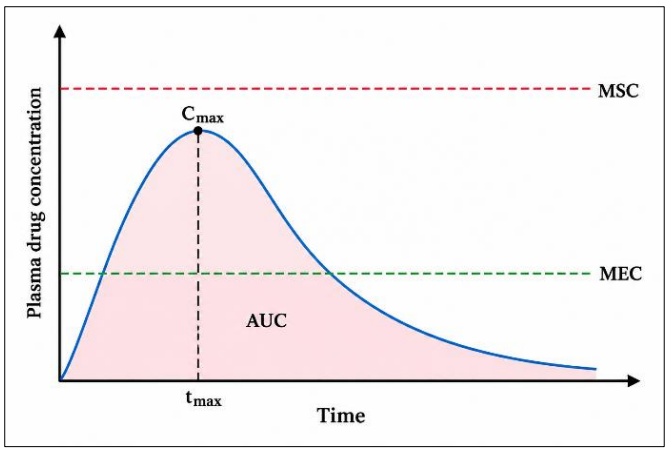


Figure 1.1: Bioavailability profile of drug after oral administration. The curve plotted between plasma drug concentration vs. time, showing all the pharmacokinetic parameters, where; MEC-minimum effective

concentration; MSC- maximum safe concentration; AUC- area under curve; Cmax maximum drug concentration and tmax maximum time.

Following the administration of conventional dosage forms, the plasma drug concentration increases during absorption and decreases during elimination. Repeated administration produces fluctuations in drug concentration, resulting in a peak-and-valley pattern. The drug concentration may fall below the minimum effective concentration (MEC), reduce therapeutic effectiveness, or rise excessively, increasing the risk of adverse effects. Therefore, repeated doses are required to maintain the drug concentration within the therapeutic range.[1-3]

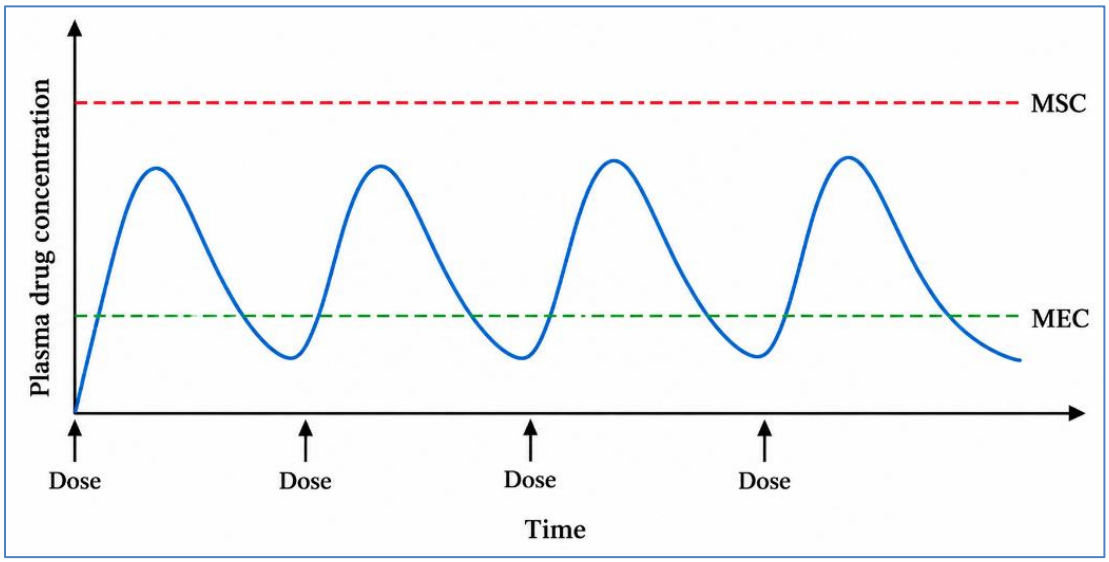


Figure 1.2: Fluctuation in Plasma Concentration of Drug Following Conventional Dosage Forms

Rationale of Controlled Drug Delivery Systems (CDDS): The primary objective of controlled drug delivery is to modify the pharmacokinetic and pharmacodynamic properties of a drug. This can be achieved by developing a novel drug delivery system or by modifying the drug's molecular structure and physiological parameters. A properly designed dosage form should maintain drug action over an extended period. The main aim of controlled drug delivery is to ensure drug safety, improve therapeutic efficacy, and enhance patient compliance through better regulation of plasma drug concentrations and reduced dosing frequency. In conventional dosage forms, the dose and dosing interval are the main parameters that can be adjusted. Each drug has a specific therapeutic window. When the plasma drug concentration falls below the minimum effective concentration (MEC), the desired therapeutic effect may not be achieved. Conversely, when the concentration exceeds the maximum safe concentration (MSC), toxic effects may occur. The therapeutic index is expressed as the ratio of the median lethal dose (LD_{50}) to the median effective dose (ED_{50}).

1. **To provide location-specific action within the gastrointestinal tract (GIT):** To deliver the drug to a particular site within the GIT where its action is required.
2. **To avoid undesirable local action within the GIT:** To prevent unwanted local effects of the drug within the gastrointestinal tract.
3. **To provide a programmed delivery pattern:** To release the drug according to a predetermined pattern.
4. **To increase the rate and extent of absorption and bioavailability:** To improve the rate and amount of drug absorbed into the body.
5. **To extend the duration of drug action:** To prolong the therapeutic action of the drug over a longer period.[4]

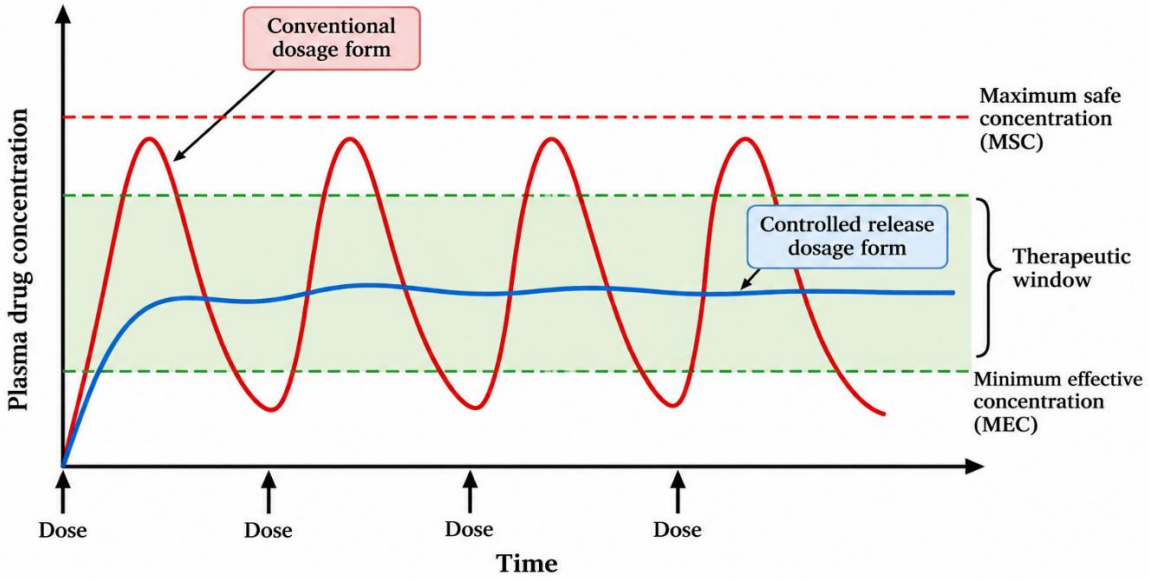


Figure 1.3: No fluctuation in plasma concentration of drug following controlled release dosage form

General Advantages of Controlled Drug Delivery Systems (CDDS)

1. Maintenance of drug concentration: Maintains drug concentration within the desired therapeutic range for an extended period.
2. Reduced dosing frequency: Reduces the frequency of drug administration, improving convenience for patients.
3. Improved patient compliance: Simplifies the dosing regimen and helps improve patient adherence to treatment.
4. Reduced overdosage and underdosage: Helps prevent fluctuations in drug concentration associated with conventional dosage forms.
5. Reduced adverse effects: Minimizes local and systemic side effects by maintaining drug concentrations within the desired range.
6. Improved therapeutic efficacy and safety: Provides better control of plasma drug concentrations, helping improve the effectiveness and tolerability of treatment.
7. Reduced total drug consumption: May reduce the total amount of drug required to achieve the desired therapeutic effect.
8. Reduced drug accumulation: Helps minimize excessive drug accumulation in the body.
9. Improved bioavailability: May improve the bioavailability of certain drugs.
10. Prolonged duration of action: Extends the therapeutic action of the drug and may reduce the need for frequent administration.[1,5]

Disadvantages of Controlled Drug Delivery Systems (CDDS)

1. High cost: Controlled drug delivery systems are generally more expensive than conventional dosage forms.
2. Unpredictable performance: Their performance may be difficult to predict, and correlations between in vitro and in vivo drug release may be poor.
3. Risk of dose dumping: Failure of the drug-release system may result in the rapid release of a large amount of drug, potentially causing toxic effects.

4. Limited dose adjustment: These systems offer less flexibility for adjusting the dose once administered.
5. Increased first-pass clearance: Some drugs may undergo increased first-pass clearance, which can reduce their systemic availability.
6. Poor systemic availability: Certain controlled-release formulations may result in poor systemic availability of the drug.
7. Limited release duration: For some oral controlled-release formulations, drug release may be limited by the residence time of the dosage form in the stomach and gastrointestinal tract.
8. Delayed onset of action: Controlled-release formulations may take longer to produce the desired therapeutic effect than conventional dosage forms.
9. Limited drug suitability: Not all drugs are suitable for incorporation into controlled drug delivery systems.[1,5]

Selection of Drug Candidates for Controlled-Release Dosage Forms: Not all drugs are suitable for formulation as controlled-release dosage forms. The selection of a suitable drug candidate depends on several characteristics, including its elimination half-life, therapeutic index, absorption rate, absorption mechanism, and first-pass effect.

1. Very short elimination half-life: The elimination half-life of a drug is an important consideration when selecting candidates for controlled-release formulations. Drugs with a very short elimination half-life require particular consideration because their duration in the body is limited.
2. Very long elimination half-life: Drugs with a very long elimination half-life must also be evaluated when designing controlled-release dosage forms, as their elimination characteristics influence the suitability of prolonged drug delivery.
3. Narrow therapeutic index: The therapeutic index is an important parameter in drug selection. It represents the relationship between a drug's toxic and effective doses. Drugs with a narrow therapeutic index require careful consideration because maintaining drug concentrations within the appropriate therapeutic range is important.
4. Rate of absorption: The rate at which a drug is absorbed influences the design of a controlled-release formulation. Therefore, the absorption rate must be considered when selecting a drug candidate.
5. Mechanism of absorption: The mechanism by which a drug crosses biological membranes is another important consideration. Understanding the absorption mechanism helps determine the suitability of the drug for controlled-release delivery.
6. First-pass effect: The first-pass effect must be considered when selecting a drug for controlled-release formulation because it influences the amount of drug that reaches the systemic circulation after administration.[7]

Approaches to the Design of Controlled-Release Formulations: The design and development of controlled-release formulations primarily involve two approaches: modification of the drug molecule and modification of the dosage form. These approaches form the basis for developing controlled-release and sustained-release dosage forms. The chapter further indicates that oral controlled-release formulations are predominantly designed using physical mechanisms, whereas chemical degradation, enzymatic degradation, and prodrug approaches are used less frequently. Depending on the release mechanism, controlled-release formulations may be designed using a single mechanism or a combination of mechanisms to achieve the desired drug-release characteristics.

The modified-release dosage form can be categorized into the following;

- Delayed release
- Extended-release
- Sustained release
- Controlled release
- Timed release
- Prolonged release

Broadly the modified release dosage form can be classified as below (Fig. 1.4),[4,8]

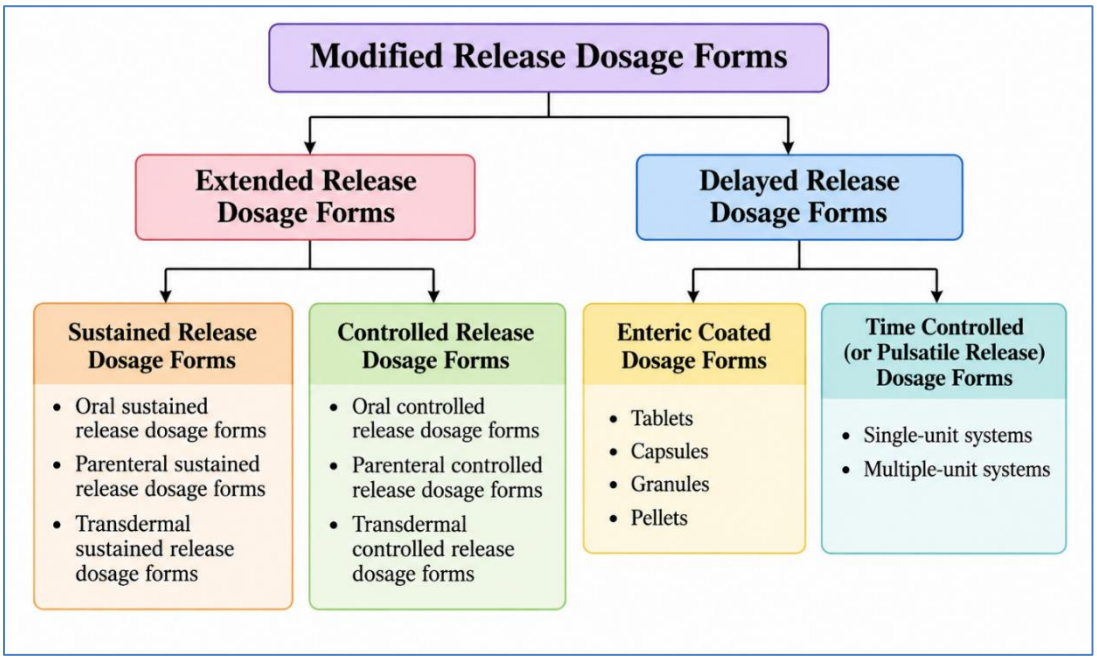


Figure 1.4: Classification of Modified-Release Dosage Forms

Based on the mechanism of drug release and the carrier used, modified-release dosage forms can be classified into the following six categories:

1. Diffusion-Sustained Systems
   - (a) Reservoir type
   - (b) Matrix type
2. Dissolution-Sustained Systems
   - (a) Reservoir type
   - (b) Matrix type
3. Ion-Exchange Methods
4. Methods Using Osmotic Pressure
5. pH-Independent Formulations
6. Altered-Density Formulations[9]

Dissolution-Controlled Release: Dissolution-controlled release systems are commonly prepared as sustained-release oral formulations in which the dissolution of the drug determines the rate of release. When

a drug dissolves rapidly, it is combined with a carrier that dissolves slowly and formulated into a tablet to maintain or control drug release.

When dissolution is controlled by the diffusion layer, the rate-limiting step is the movement of the drug from the solid surface into the bulk solution through an unstirred liquid film. Under steady-state conditions, this process can be expressed using the Noyes–Whitney equation.

Two approaches are used to prepare dissolution-controlled formulations:

1. Dissolution-controlled encapsulated or coated systems.
2. Dissolution-controlled matrix systems.

Dissolution-Controlled Encapsulation: In this approach, individual drug particles or granules are coated with a material that dissolves slowly. The coated particles are then directly compressed into tablets. Space Tabs and Spansules are examples of this type of formulation.[9,10]

Dissolution-Controlled Matrix: In this method, the drug is combined with a slowly dissolving carrier to form a matrix, which is subsequently compressed into a tablet. Drug bioavailability is regulated by the penetration of the dissolution medium into the matrix. This penetration is influenced by the porosity of the tablet matrix, the presence of hydrophilic materials, tablet wettability, and particle surface area. Poorly water-soluble drugs, classified as BCS Class II and IV, naturally tend to exhibit sustained release. For water-soluble drugs, a water-insoluble carrier is incorporated into the formulation to decrease the dissolution rate of the drug particles. These particles may be precoated with materials such as polyethylene glycol. In such formulations, a disintegrating agent may not be included because it could interfere with the intended delayed-release effect.[11]

Erosion-Controlled Systems: Erosion-controlled drug delivery systems are also known as stimuli-induced systems. Their release mechanism is activated by an external stimulus, such as pH, temperature, enzymes, or osmotic pressure. The drug is released as the surface or bulk of the formulation undergoes erosion. When the surrounding pH is unsuitable for drug dissolution, the drug may remain unreleased, as occurs with pH-sensitive dosage forms. Polymers are commonly used to coat these formulations. Acrylates, including methacrylic acid copolymers, and cellulose esters, such as cellulose acetate phthalate, are used for coating pH-sensitive systems. These polymers may also be employed in the preparation of matrix systems.[12-13]

Hybrid Systems: Hybrid systems combine the robust matrix structure of matrix systems with the constant-release characteristics of reservoir systems. The drug is incorporated or entrapped within a release-controlling matrix, which is subsequently coated with a polymer. High-molecular-weight compounds may also be incorporated into these systems.

Advantages of hybrid systems:

- They are cost-effective.
- They are easy to manufacture.
- They can be prepared using conventional processes and equipment.

Diffusion-Controlled Release

Diffusion-controlled systems can be divided into two types:

1. Diffusion-controlled encapsulation.
2. Systems in which osmotic pressure is the rate-limiting factor.

Diffusion-Controlled Encapsulation

In diffusion-controlled formulations, drug molecules pass through a polymer membrane or polymer matrix and are released. Depending on whether the polymer forms a surrounding membrane or is distributed throughout the formulation, these systems are classified into:

- Reservoir systems.
- Monolithic systems.

In nonporous reservoir systems, drug molecules move through the polymer membrane. In microporous reservoir systems, the drug is released through micropores, which are generally filled with water or oil.

Diffusion-controlled monolithic systems can further be classified according to the concentration of the incorporated drug. In these systems, the drug is loaded into a polymer matrix by soaking the polymer in a drug solution. The drug concentration within the matrix cannot exceed its solubility in the polymer. When the drug loading exceeds its solubility, the system is referred to as a monolithic dispersion.[12-15]

Fick's Law of Diffusion: Fick's law describes the flux of a drug, expressed as the amount passing through a unit area per unit time, across a membrane in the direction of decreasing concentration. The release rate of a drug from a diffusion-controlled system depends on its diffusion through the inner and outer insoluble membrane barriers.[15]

Reservoir Type: In a reservoir system, a drug-containing core is enclosed within a water-insoluble polymeric material that controls the release rate. When the dosage form comes into contact with the surrounding fluid, the fluid enters the polymer membrane, exchanges with the surrounding medium, and allows the drug to diffuse through the polymer toward the exterior. Ethyl cellulose and polyvinyl acetate are commonly used polymers in these systems.

Advantages

- Zero-order drug delivery can be achieved.
- The release rate can be varied by changing the polymer type.

Disadvantages

- The system must be physically removed from the implantation site.
- Delivery of high-molecular-weight compounds is difficult.
- The cost per dosage unit is generally increased.
- Toxicity may occur if the system fails.[16-17]

Matrix Type; In a matrix system, a solid drug powder is uniformly distributed throughout an insoluble, rate-controlling matrix. Materials such as beeswax, carnauba wax, hydrogenated castor oil, and other suitable waxes are used to prepare these matrices.

These waxes regulate drug dissolution by controlling the rate at which the drug dissolves in the surrounding fluid and subsequently penetrates the matrix. The medium affects matrix porosity, while the tablet's wettability or dissolution characteristics also influence the release rate.

Drug release from such matrices generally follows first-order kinetics. The matrix may be prepared by dispersing the drug in molten wax, followed by solidification and granulation. The release rate is influenced by drug diffusion rather than solely by the rate of dissolution.[17]

Advantages

- Matrix systems are easier to produce than reservoir or encapsulated systems.
- They can deliver high-molecular-weight compounds.

Disadvantages

- Zero-order drug release cannot be achieved.
- The remaining matrix must be removed when the system is implanted.[17-18]

Osmosis-Based Formulations: Osmosis is the movement of a solvent, such as water, from a region of higher solvent concentration to a region of lower solvent concentration through a semipermeable membrane. In drug delivery, this principle is used to develop systems capable of providing zero-order drug release. Osmotic formulations are prepared by enclosing an osmotic drug core, containing an osmotically active drug or a mixture of an osmotically inactive drug with an osmotically active salt such as sodium chloride (NaCl), within a semipermeable membrane made of biocompatible polymers, such as cellulose acetate. When an osmotic pressure gradient develops, water continuously enters the tablet through the membrane. The dissolved drug is then pumped out through a delivery orifice. This process can continue for an extended period, approximately 24 hours. The drug-release rate is independent of the gastrointestinal environment but depends on the osmotic pressure of the release medium. The manufacturing process for osmotic systems is complex.

Basic Osmotic Systems

Basic osmotic systems can deliver only water-soluble drugs. Water-insoluble drugs may be delivered using push-pull osmotic systems.

In push-pull systems, a non-swelling solubilizing agent enhances the solubility of the insoluble drug, while a non-swelling agent increases the contact surface area between the drug and the incoming aqueous liquid distributed throughout the formulation.

Different polymer membranes have different water-vapour transmission values. The selection of a semipermeable membrane therefore depends on the intended application.[18-22]

Types of Osmotic Systems

Type A: Drug present in the osmotic core: The drug is incorporated directly into the osmotic core, which is surrounded by a semipermeable rigid membrane.

Type B: Osmotic core without drug: The osmotic core does not directly contain the drug; instead, the drug is present in a separate solution within a flexible membrane.

Types of Osmotic Pumps

- **Basic osmotic pump:** Water enters the osmotic drug core through the membrane, and the drug solution exits through the delivery orifice.
- **Push-pull osmotic pump:** Water enters the system, while the push layer helps expel the drug through the delivery orifice.[22]

Ion-Exchange-Controlled Drug Release: Ion-exchange resins are used to regulate the release of drugs. These resins are water-insoluble polymeric materials containing ionic groups. Through electrostatic interactions, drug molecules bind to oppositely charged ionic groups present on the resin. Drug molecules can exchange with other ions carrying the same charge. As a result, the drug is released from the ion-exchange resin. This principle is used to prepare controlled-release dosage forms containing either anionic or cationic drugs.

Method of Preparation

The preparation of ion-exchange-controlled drug formulations involves the following steps:

1. Drug absorption: The ionized drug is absorbed onto ion-exchange resin granules. For example, codeine base (drug) is absorbed onto Amberlite (resin).
2. Filtration: The drug-loaded resin is separated from the alcoholic medium by filtration.
3. Polymer coating: The filtered drug–resin complex granules are coated with a water-permeable polymer, such as a modified copolymer of polyacrylic and methacrylic ester, using the spray-drying method.[23]

Mechanism of Drug Release: In the gastrointestinal tract, the drug is released when appropriately charged ions replace the drug bound to the resin. The released drug then diffuses out of the resin.

Drug release depends on:

- The strength and type of the ionic environment: This includes pH and electrolyte concentration.
- The properties of the resin.

Factors Controlling the Rate of Diffusion

The rate of drug diffusion from the resin is controlled by three factors:

1. Area of diffusion.
2. Length of the diffusion path.
3. Rigidity of the resin.

Advantages

- Protective effect: The system provides protection by temporarily changing the substrate.
- Suitability for susceptible drugs: It is suitable for drugs that are highly susceptible to degradation by enzymatic processes.

Limitations

- The drug-release rate is proportional to the concentration of ions present near the resin granules at the site of administration.
- The release rate varies depending on diet, water intake, and intestinal contents.[23-24]

Processes Used to Prepare Controlled-Release Formulations: Oral controlled-release (CR) formulations are developed using drug-release mechanisms such as dissolution, diffusion, and osmosis.

The approaches or technologies used to prepare these formulations can be broadly classified into three types:

1. Matrix tablets
2. Multiparticulate formulations
3. Osmotic tablets

Drug Selection for Controlled Drug Delivery Systems (CDDS): The selection of a suitable drug for a controlled drug delivery system depends on its physicochemical, pharmacokinetic, and pharmacodynamic properties.[25-27]

Physicochemical Properties: These properties determine the drug's solubility, diffusion, membrane permeability, and suitability for controlled release.

1. Molecular weight: Drugs with a molecular weight below 1000 Da are generally considered suitable because molecular size influences their ability to diffuse through membranes.
2. Aqueous solubility: The drug should have adequate water solubility to dissolve in body fluids and become available for absorption. Drugs with extremely low solubility can be difficult to formulate into controlled-release dosage forms.
3. Apparent partition coefficient: This describes the distribution of a drug between oil and water. An appropriate partition coefficient is important for drug movement through lipid membranes. Both excessively high and low values may affect absorption and drug release.
4. pKa and ionization: The pKa of a drug and the pH of its surrounding medium determine its degree of ionization. The unionized form generally crosses lipid membranes more readily than the ionized form.
5. Drug stability: The drug should remain sufficiently stable in the gastrointestinal environment. Drugs that degrade in gastrointestinal fluids may be unsuitable for conventional oral controlled-release formulations.
6. Mechanism and site of absorption: The drug's absorption mechanism and the region of the gastrointestinal tract where absorption occurs influence its suitability. Drugs absorbed throughout the gastrointestinal tract are generally more suitable than those absorbed only at a specific site.
7. Route of administration: The route must be appropriate for the drug's properties and the intended release pattern. The chapter discusses oral, parenteral, and transdermal routes in relation to controlled drug delivery.[28-32]

Biological Properties: Biological properties are divided into pharmacokinetic and pharmacodynamic properties.

A. Pharmacokinetic Properties

Pharmacokinetics describes what the body does to a drug, including its absorption, distribution, metabolism, and elimination.

1. Absorption rate: The drug should be absorbed at an appropriate rate after its release from the dosage form. Its absorption characteristics influence the duration and effectiveness of controlled drug delivery.
2. Biological half-life: This is the time required for the drug concentration in the body to decrease by half. According to the chapter, drugs with a half-life of approximately 2–4 hours are ideal candidates for controlled-release formulations. Drugs with very long half-lives are generally less suitable.
3. Rate of metabolism: The rate at which the body metabolizes a drug influences its concentration and duration of action. Drugs that undergo excessively rapid metabolism or alter their own metabolism may be unsuitable for controlled release.
4. Drug distribution: The distribution of a drug throughout the body affects its concentration at the site of action and its elimination. Therefore, distribution characteristics must be considered when selecting a drug for controlled release.
5. Drug–protein binding: Drugs bind to proteins in plasma to varying degrees. Extensive protein binding may prolong the drug's half-life and make it less suitable for sustained- or controlled-release formulations.
6. Dosage form index: This is the ratio of the maximum steady-state concentration to the minimum steady-state concentration. A value close to 1 indicates less fluctuation between maximum and minimum steady-state drug concentrations.[33]

B. Pharmacodynamic Properties

Pharmacodynamics describes the relationship between drug concentration and its effects on the body.

1. **Therapeutic range:** This is the range of drug concentrations between the minimum effective concentration and the concentration at which toxicity may occur. A sufficiently wide therapeutic range is desirable because variations in drug release are less likely to produce toxic concentrations.
2. **Therapeutic index:** The therapeutic index indicates the safety margin of a drug. A higher therapeutic index indicates a wider safety margin, whereas drugs with a very low therapeutic index are less suitable for controlled-release formulations.
3. **Plasma concentration–response relationship:** This describes how changes in plasma drug concentration influence its pharmacological effect. Drugs whose effects are independent of their concentration, such as reserpine according to the chapter, are considered poor candidates for controlled-release systems.[34]

CONCLUSION

Controlled Drug Delivery Systems (CDDS) represent an important advancement in pharmaceutical formulation, designed to regulate the rate, duration, and, where appropriate, site of drug release to achieve the desired therapeutic effect. Unlike conventional dosage forms, which generally release the drug more rapidly, controlled-release formulations aim to maintain drug concentrations within the therapeutic range for a prolonged period and reduce fluctuations in plasma drug levels. The successful design of CDDS depends on the careful selection of a suitable drug based on its physicochemical, pharmacokinetic, and pharmacodynamic properties. Factors such as molecular weight, aqueous solubility, partition coefficient, drug stability, absorption characteristics, biological half-life, metabolism, therapeutic range, and therapeutic index play important roles in determining the suitability of a drug for controlled release. A thorough understanding of these characteristics helps in selecting an appropriate formulation strategy and release mechanism. Overall, CDDS can help reduce the frequency of drug administration, improve patient compliance, minimize fluctuations in drug concentrations, and maintain therapeutic effectiveness over an extended period. However, their successful application depends on appropriate drug selection, rational formulation design, and consideration of the limitations associated with individual drugs and delivery systems. Therefore, the integration of drug properties with suitable formulation technologies is fundamental to the development of safe, effective, and reliable controlled drug delivery systems.

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