How to Cite:
Hamzy, I. A., Alqhoson, A. I., Aljarbou, A. M., & Alhajri, M. A. (2022). An in-depth overview of controlled drug delivery systems: Present developments and prospective advancements. *International Journal of Health Sciences*, *6*(S10), 1755–1770. https://doi.org/10.53730/ijhs.v6nS10.15096

An in-depth overview of controlled drug delivery systems: Present developments and prospective advancements

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***Abstract*---Background:** Drug delivery systems (DDS) are crucial in modern medicine for optimizing the therapeutic efficacy and safety of pharmaceutical agents. Traditionally, direct use of active pharmaceutical ingredients (APIs) poses challenges such as dosing accuracy, stability, and patient compliance. Controlled drug delivery systems have emerged to address these issues by releasing drugs at a controlled rate, thereby enhancing therapeutic outcomes and minimizing side effects. **Aim:** This article aims to provide a comprehensive overview of current advancements and future prospects in controlled drug delivery systems. It explores various DDS technologies, their mechanisms, and their impact on drug efficacy and patient adherence. **Methods:** The review synthesizes data from recent research on drug delivery systems, focusing on their classification, design considerations, and performance. It discusses the pharmacokinetics of drug release, including absorption, distribution, metabolism, and excretion, and evaluates different controlled release mechanisms such as dissolution-controlled, diffusion-controlled, and osmotic pressure-controlled systems. **Results:** Controlled DDS have evolved significantly from the first-generation systems that relied on basic mechanisms like dissolution and diffusion to advanced technologies involving stimuli-responsive biomaterials. These systems now include innovations such as nanoparticle-based delivery, self-regulating devices, and long-term non-invasive methods for proteins and nucleic acids. The development of biomaterials and smart polymers has further enhanced the precision and efficacy of drug

Manuscript submitted: 01 Jan 2022, Manuscript revised: 09 Jan 2022, Accepted for publication: 15 Jan 2022

delivery. **Conclusion:** Controlled drug delivery systems represent a significant advancement in pharmaceutical technology, offering improved management of drug release rates and better patient outcomes. Future developments will likely focus on refining these systems for broader applications and integrating advanced biomaterials to address specific therapeutic needs and challenges.

***Keywords*---**Controlled drug delivery systems, pharmaceutical technology, drug release kinetics, biomaterials, nanocarriers, stimuli-responsive polymers.

Introduction

A drug, or active pharmaceutical ingredient (API), is defined as a substance officially recognized in pharmacopoeias and intended for application in the diagnosis, treatment, alleviation, or prevention of disease according to FDA guidelines. Drug delivery encompasses methods of administering medication to a patient in a manner that selectively enhances the drug concentration in specific body regions compared to others [1]. The primary objective of any delivery system is to prolong, localize, and direct the drug to the affected tissue while ensuring a protected interaction. Each dosage form integrates APIs with non-drug components known as excipients or additives. APIs are the chemical entities directly responsible for therapeutic effects [2]. Drug delivery systems (DDS) are favored over the direct clinical use of active pharmaceutical ingredients (APIs) due to several challenges. Direct application of APIs is infrequent because handling and accurate dosing can be problematic for highly potent drugs, particularly those requiring very low milligram or microgram amounts [3]. Administering drugs into body cavities, such as the rectal or vaginal routes, can be impractical due to potential degradation at the site of administration (e.g., acidic conditions in the stomach) and the risk of local irritation or injury from high drug concentrations [3]. Some APIs are sensitive to environmental factors such as light, moisture, temperature, and pH, necessitating stabilization to prevent chemical instability. Additionally, APIs often possess undesirable organoleptic properties (taste, smell) that can decrease patient compliance [2].

Therefore, APIs are formulated with excipients. Excipients or additives are used for various purposes: to impart specific structure and shape to the formulation, enhance stability, mask unpleasant tastes, increase palatability, bulk up formulations with potent ingredients, facilitate accurate dosing, assist in handling the active substance, and improve the manufacturing process [4]. Moreover, excipients contribute to bioavailability, enhance the safety and function of the dosage form during storage and use, and improve patient acceptability [5]. Common excipients utilized in formulations include coloring agents, suspending agents, binding agents, solvents, lubricants, perfumes, sweetening agents, flavoring agents, solubilizing agents, and antioxidants [4]. Fillers are added to increase the size of tablets (e.g., lactose) when the quantity of active ingredient is too small to handle without a filler. Binders are used to maintain tablet integrity post-compression and prevent disintegration into separate pieces (e.g., starch, HPMC) [6]. Disintegrants facilitate the breakdown of dosage forms into smaller

fragments upon ingestion, aiding in rapid dissolution and absorption [6]. Glidants reduce particle friction and prevent lump formation, thereby improving the flowability of tablet granules or powders. Anti-adherents prevent powder from sticking to manufacturing equipment, while lubricants ensure a smooth tablet surface by minimizing friction during ejection. Flavoring agents mask unpleasant odors, and colorants enhance recognition and aesthetics [7].

The Biopharmaceutics Classification System (BCS) categorizes drugs into four classes based on their intestinal permeability and solubility [8]. Class I drugs exhibit high permeability and high solubility, resulting in efficient absorption, with absorption rates exceeding excretion (e.g., metoprolol, paracetamol). Class II drugs have high permeability but low solubility, with bioavailability limited by solvation rate (e.g., glibenclamide, aceclofenac). Class III drugs possess low permeability but high solubility, where rapid solvation is offset by limited permeation rate. If the formulation does not alter permeability or gastrointestinal transit time, Class I criteria apply (e.g., cimetidine). Class IV drugs are characterized by low permeability and low solubility, resulting in poor absorption and high variability in bioavailability (e.g., Bifonazole) [8].

Dosage forms can be administered via various routes depending on the target site, treatment duration, and the drug's physicochemical properties [9]. Common dosage forms include tablets, capsules, pills, ointments, syrups, and injections. The choice of administration route is influenced by factors such as the targeted area of the body, the drug's mechanism of action, and its solubility and permeability. For instance, some drugs are degraded by stomach acids when administered orally, leading to poor bioavailability, necessitating parenteral administration for optimal efficacy. Intravenous administration ensures 100% bioavailability [9].

Classification of Dosage Forms: Dosage forms are categorized based on the route of administration, the origin of the compound (natural or synthetic), and the physical form of the final delivery systems.
Classification of Solid Dosage Forms: Solid dosage forms are divided into two primary categories based on dose type: unit dose and bulk dose.
(a) **Unit Dose:** Each dose is individually formulated as a separate unit, and the patient consumes one unit per dose. Examples include tablets, capsules, pills, lozenges, chewable tablets, effervescent tablets, and dry powder inhalers in metered-dose containers.
(b) **Bulk Dose:** This category consists of loose, solid powders without individual dosing [10,11]. Bulk powders face challenges such as dose dumping but are typically used for surgical or injury dressing powders. Examples include insufflation powders and dressing powders [10].

Tablets:

Tablets are solid unit dosage forms manufactured through compression or granulation in various shapes (round, oval, square). Excipients such as binders, glidants, and lubricants are added for effective tabletting, while disintegrants enhance tablet breakdown in the digestive tract. Coatings with pigments, sweeteners, and flavoring agents mask undesirable tastes and improve

swallowability, provide environmental protection, and extend shelf life [10,12]. Sublingual and buccal tablets are also solid unit dosage forms, administered under the tongue or between the gum and cheek. These tablets dissolve rapidly and are absorbed through oral mucous membranes, bypassing stomach acids and liver metabolism [10,12]. Effervescent tablets release carbon dioxide upon contact with water, disintegrating within minutes. These tablets, consisting of acids (e.g., citric or tartaric acid) and carbonates or bicarbonates, dissolve quickly in water, mimicking the taste of carbonated drinks (e.g., antacids). Chewable tablets, intended for mastication before swallowing, are useful for children and the elderly (e.g., vitamin supplements) [10,12].

Capsules, Lozenges, Pills, and Granules: Capsules are unit solid dosage forms with drug components enclosed in a soluble shell, which helps mask unpleasant tastes and limits interaction with excipients. Capsules are classified into hard-shelled (for dry powders) and soft-shelled (for hydrophobic or oily substances). Lozenges are chewable solid forms where the drug is embedded in a caramel base, providing slow release for oral applications [10]. Pills are solid dosage forms created by compressing APIs with adhesives into rounded masses for oral use. Granules are dry aggregates provided in single-dose sachets, either taken directly with water or dissolved in water before ingestion. Effervescent granules, similar to effervescent tablets, release carbon dioxide upon contact with water [10].

Bulk Solid Dosage Forms: Bulk powders are multidose formulations consisting of loose, dry particles of varying fineness. They may include active ingredients with or without excipients and, if necessary, coloring and flavoring agents. Packaged in wide-mouthed, airtight containers, these powders are used for both internal and external administration. They are generally formulated with non-potent drugs (e.g., laxatives, antacids) due to issues with dosage accuracy [10].

Semisolid Dosage Forms

Semisolid dosage forms have a semi-solid consistency and are intended for application to the skin or mucous membranes (e.g., nasal, vaginal, rectal) for therapeutic, protective, or cosmetic purposes. These include ointments, creams, gels/jellies, lotions, pastes, and transdermal patches [13]. They are used externally and locally, reducing the likelihood of side effects, and are suitable for patients who cannot take oral medications or require a more stable formulation than liquids [14].

Ointments: Ointments are oil-based semisolid formulations, typically containing less than 20% water and volatile substances, and more than 50% hydrocarbons (e.g., waxes, polyols). They provide a high retention time and are less spreadable, making them suitable for applying drugs over prolonged periods [14,15].

Creams: Creams are semisolid, easily spreadable forms containing over 20% water and volatile substances, and less than 50% hydrocarbons. Cream bases are emulsions classified as either oil-in-water (O/W) or water-in-oil (W/O). O/W creams have small oil droplets in an aqueous phase and are less greasy, while W/O creams contain water droplets in an oily phase, offering more moisturizing properties [14,15].

Gels (Jellies) and Lotions: Gels are semisolid systems with a liquid phase trapped in a 3D polymeric matrix, used in medicine, cosmetics, and as drug carriers (e.g., spermicides). Lotions are aqueous fluid preparations for external use, applied directly to the skin or onto dressings to reduce evaporation [14,16].

Pastes: Pastes are ointments with a high percentage of insoluble solids, which stiffen the formulation. They offer lower permeability and provide a protective barrier on the skin. Pastes can neutralize harmful chemicals and are less greasy compared to ointments [14,16].

Transdermal Patches: Transdermal patches are adhesive drug delivery systems placed on the skin to release medication into the bloodstream. They are particularly useful for patients who cannot take oral medications or experience intolerable side effects from oral drugs. Patches consist of a backing film, a drug-containing layer, a membrane controlling drug diffusion, and an adhesive layer. They are classified into matrix, reservoir, multilaminate, and drug-in-adhesive types, based on the drug loading and release mechanism [17,18,19]. The first commercial transdermal patch was scopolamine for motion sickness [20].

Suppositories:

Suppositories are small, solid or semisolid dosage forms intended to be inserted into body cavities (such as the rectum or vagina), where they dissolve or melt to release their active ingredients. They are used for local or systemic effects and offer certain advantages over oral administration, particularly in bypassing the hepatic first-pass metabolism due to direct absorption into the systemic circulation through the highly vascularized rectal or vaginal mucosa.

Key Components:

- **Base Materials:** Suppositories are commonly made from natural fats (like cocoa butter) or synthetic polymers (such as polyethylene glycol). Glycerol may also be used. The choice of base affects the melting point and the release of the drug.
- **Drug Release:** Upon insertion, suppositories melt or dissolve, allowing the drug to be absorbed into the bloodstream or act locally.

Advantages:

- **Rapid Onset of Action:** The rectum's rich blood supply facilitates quick absorption of the drug.
- **Bypass Hepatic Metabolism:** Drugs avoid first-pass metabolism in the liver, potentially increasing bioavailability.

Uses:

- **Local Effects:** Such as in treating hemorrhoids or vaginal infections.
- **Systemic Effects:** When oral administration is not feasible, such as in cases of nausea, vomiting, or when the patient is unconscious [14,22].

Liquid Dosage Forms:

Liquid dosage forms are formulations in which the active pharmaceutical ingredient (API) is dissolved or dispersed in a suitable liquid medium. They are

designed for easy administration, particularly for patients who have difficulty swallowing solid forms.

Types and Subtypes:

- **Monophasic Liquids:** These include solutions where the API is completely dissolved in the solvent.
- **Biphasic Liquids:** These include suspensions and emulsions, where the API is not completely dissolved but dispersed in a liquid medium.

Oral Liquid Forms:

1. **Solutions:** Clear, homogenous liquids where APIs are dissolved in a solvent. Examples include oral solutions and syrups.
2. **Suspensions:** Biphasic liquids where APIs are dispersed as solid particles in a liquid medium. These need to be shaken before use to ensure uniformity.
3. **Emulsions:** Biphasic liquids where the API is dispersed in an oil-in-water or water-in-oil system. They are used to deliver drugs that are poorly soluble in water.
4. **Syrups:** Concentrated aqueous solutions containing a high percentage of sugar, which may be flavored to mask the taste of the API.
5. **Elixirs:** Clear, sweetened liquids containing alcohol and water, used to improve the palatability of bitter drugs.
6. **Linctuses:** Viscous liquids with demulcent properties used to soothe the throat, often taken in small doses.

Topical and Other Liquid Forms:

1. **Oral Drops:** Concentrated solutions or suspensions for administration in very small volumes, often used for pediatric dosing.
2. **Gargles and Mouthwashes:** Aqueous solutions used for oral hygiene and to treat conditions of the mouth and throat. Gargles are diluted before use, while mouthwashes are ready-to-use.

Pharmacokinetics of Drug Delivery Systems:

Pharmacokinetics involves the study of how drugs are absorbed, distributed, metabolized, and excreted by the body. It encompasses the time course of drug concentration in the bloodstream and tissues.

1. **Absorption:**
    - **Passive Transport:** Drugs move from areas of higher concentration (like the gastrointestinal tract) to lower concentration (the bloodstream) without energy. The rate depends on drug properties such as lipid solubility and molecular size.
    - **Active Transport:** Requires energy to move drugs against a concentration gradient. This is facilitated by specific transporters in the intestine and can involve drugs mimicking endogenous substances.
2. **Distribution:**
    - The drug moves from the bloodstream to various tissues and organs. Factors influencing distribution include blood flow, drug lipophilicity, molecular size, and protein binding.

- **Blood-Brain Barrier:** A selective barrier that restricts access of certain drugs to the central nervous system. Lipophilic and small drugs can cross this barrier more easily.

3. **Metabolism:**
   - Drugs are chemically modified in the liver or gut to form metabolites, which are often less active or inactive. This process can significantly reduce the drug's concentration before it reaches systemic circulation. The liver enzyme system, particularly cytochrome P450, plays a major role in drug metabolism.
4. **Excretion:**
   - The removal of drugs or their metabolites from the body, primarily through urine, bile, sweat, saliva, tears, or feces. The efficiency of excretion affects the drug's duration of action and potential for toxicity.
5. **Bioavailability:**
   - The fraction of an administered drug that reaches systemic circulation in an active form. Drugs administered intravenously have 100% bioavailability, while oral drugs may have reduced bioavailability due to factors such as first-pass metabolism.

Each of these stages is crucial for understanding the drug's efficacy and safety profile, influencing dosage regimens and therapeutic strategies [29-41].

Drug Release Kinetics: Basic Concepts:

Drug release kinetics is a critical aspect of pharmacology and drug formulation. It describes how a drug is released from its dosage form and absorbed into the bloodstream over time. The release profile is often illustrated as a plot of plasma drug concentration versus time.

Key Concepts:

1. **Minimum Effective Concentration (MEC):**
   - The lowest concentration of a drug in the bloodstream is required to achieve the desired therapeutic effect.
2. **Toxic Concentration:**
   - The concentration of a drug that causes harmful or undesirable side effects.
3. **Therapeutic Window:**
   - The range of drug concentrations between the MEC and toxic concentration, where the drug is effective without causing toxicity.

Release Kinetics:

1. **Zero-Order Release:**
   - **Definition:** The drug is released at a constant rate, independent of its concentration. This means that a fixed amount of drug is released per unit of time.
   - **Advantage:** Maintains drug concentrations within the therapeutic window for a prolonged period, potentially improving efficacy and reducing the need for frequent dosing.
   - **Example:** Certain controlled-release formulations designed to provide a steady drug level over time.

2. **First-Order Release:**
    - **Definition:** The release rate of the drug is proportional to its concentration. As the concentration decreases, the rate of release also decreases.
    - **Characteristic:** The drug release follows an exponential decay, where a higher concentration leads to a faster release rate.
    - **Example:** Immediate-release tablets where the drug is quickly absorbed and then rapidly metabolized.
3. **Sustained Release:**
    - **Definition:** Designed to release a drug slowly over an extended period after administration of a single dose. This approach helps in maintaining drug levels within the therapeutic window.
    - **Advantage:** Reduces the need for multiple dosing, improving patient compliance and potentially minimizing side effects.
    - **Example:** Extended-release tablets or implants.

Therapeutic Index (TI) and Therapeutic Window:

1. **Therapeutic Index (TI):**
    - **Definition:** A measure of a drug's safety, calculated as the ratio between the dose that causes adverse effects (TD50) and the dose that provides the desired therapeutic effect (ED50).
    - **High TI:** Indicates a larger margin of safety between effective and toxic doses.
    - **Low TI:** Indicates a smaller margin of safety, requiring more precise dosing.
2. **Therapeutic Window:**
    - **Definition:** The range of drug doses that provide therapeutic efficacy without causing toxicity.
    - **Importance:** A narrower therapeutic window requires careful dose management to avoid adverse effects.

Conventional vs. Controlled Drug Delivery Systems (DDS):

1. **Conventional DDS:**
    - **Characteristics:** Includes tablets, capsules, and syrups. These forms often lead to rapid fluctuations in plasma drug levels, with a sharp rise and fall in concentration after administration.
    - **Disadvantages:** Requires frequent dosing to maintain drug levels within the therapeutic window, which can lead to non-compliance and fluctuations in efficacy.
2. **Controlled Release DDS:**
    - **Characteristics:** Designed to release the drug at a constant rate, maintaining therapeutic levels for extended periods.
    - **Advantages:** Reduces the need for frequent dosing, maintains drug levels within the therapeutic window, and improves patient compliance.
    - **Disadvantages:** Can be more complex to design and may have a higher cost.

Summary: Understanding drug release kinetics is essential for designing effective drug delivery systems that provide therapeutic benefits while minimizing side

effects. Controlled and sustained release systems are particularly valuable for maintaining drug levels within the therapeutic window and improving patient adherence to treatment regimens [43].

Controlled Drug Delivery Systems:

Controlled drug delivery systems (DDS) are designed to maintain a constant level of a drug in the blood and tissue over an extended period. Conventional DDS, such as oral tablets or injections, show typical bolus PK with multiple dosing, resulting in fluctuating drug levels above and below the minimum effective concentration (MEC). Conversely, controlled DDS exhibit zero-order PK, with a single dose maintaining drug levels consistently within the therapeutic window [47].

Controlled DDS achieve constant drug plasma levels by releasing a specific dose at predetermined intervals. This approach reduces the dose and dosing frequency, enhancing patient compliance and minimizing drug toxicity and adverse effects. The overall efficacy of the dosage form is improved [43].

Design Considerations for Controlled Release Drug Delivery Systems
Designing a controlled release DDS involves several factors. Parameters are classified into formulation-related and drug-related categories:

- **Formulation-Related Parameters:**
  - Biomaterial properties (biocompatibility, surface chemistry, hydrophilicity, degradation, mechanical and rheological properties).
  - Route of administration.
  - Pharmacokinetics and stability enhancement.
- **Drug-Related Parameters:**
  - Drug binding efficiency with plasma proteins.
  - Ability of the drug to cross biological barriers.
  - Regulatory aspects.

Biomaterial properties such as pH and temperature stability are crucial. For instance, rectal administration requires biomaterials with a melting point at or above 37 °C or solubility at that pH. Stability enhancement is critical for drugs like peptides, proteins, and genes that are unstable under harsh conditions. This can be achieved by incorporating drugs into specialized carrier systems [48]. Targeting the drug to specific sites to prevent unwanted effects is essential. Techniques include antibody tagging, ligand attachment, and localized delivery. Biological barriers such as the blood-brain barrier, bone, and testicles can be crossed using permeation enhancers and nanocarriers. Establishing suitable animal models is necessary for bridging in vitro and in vivo results [49,50].

Classification of Controlled Release Drug Delivery Systems

Controlled release DDS are classified based on the mechanism of drug release:

1. **Dissolution-Controlled Drug Delivery Systems:**
   - **Definition:** Drugs are coated with or encapsulated within slowly dissolving polymeric membranes (reservoir systems) or matrices (monolithic systems). The rate-limiting step is dissolution [52].

- **Example:** Immediate-release tablets and pills.

2. **Diffusion-Controlled Drug Delivery Systems:**
   - **Definition:** Drugs are trapped in and released via diffusion through inert water-insoluble polymeric membranes or matrices. Release is governed by Fick's laws of diffusion [53,54].
   - **Example:** Membrane-controlled reservoir systems and monolithic matrix systems.
3. **Water Penetration-Controlled Drug Delivery Systems:**
   - **Osmotic Pressure-Controlled Systems:**
     - **Definition:** Uses osmotic pressure for drug delivery. Basic components include the drug, osmogen, a semipermeable membrane, and an outer coating material. Advantages include increased efficacy and reduced dosing frequency [55,56].
     - **Example:** Cardura® XL, Covera-HS®, Sudafed®, Procardia XL® [56,57].
   - **Swelling-Controlled Systems:**
     - **Definition:** Drug dispersed in a hydrophilic polymer matrix. Water penetration causes the matrix to swell and release the drug slowly [61].
4. **Chemically Controlled Drug Delivery Systems:**
   - **Polymer-Drug Dispersion Systems:**
     - **Definition:** Drug dispersed in a biodegradable polymer, released through polymer degradation. Includes bulk erosion and surface erosion [62].
   - **Polymer-Drug Conjugate Systems:**
     - **Definition:** Drug chemically conjugated to a polymer, released through cleavage of polymer-drug bonds [62].

Controlled Release Dosage Form Design: Practical Considerations:

The primary goal of controlled drug delivery systems (DDS) is to minimize drug dose and frequency, reduce blood plasma level fluctuations, enhance patient compliance, and decrease drug toxicity and adverse effects. In contrast to immediate-release systems, which rely on the body's absorption physiology to maintain drug availability, controlled DDS ensure that drug administration rates are carefully managed through their design. This approach typically involves two components: a loading dose for a rapid onset of effect, and a maintenance dose for sustained drug release, following zero-order kinetics to maintain therapeutic levels [2,47]. Achieving these goals requires designing an ideal DDS, though many existing products do not fully meet these criteria [17].

Evolution of Controlled Release Dosage Forms

First Generation (1950–1980): The initial generation of controlled release dosage forms introduced four key mechanisms: dissolution, osmosis, diffusion, and ion exchange. These mechanisms were mainly applied in oral and transdermal formulations. The success of this generation stemmed from the development of these routes and a clear understanding of the correlation between in-vitro and in-

vivo formulations. No significant biological barriers were identified during this period [63].

Second Generation: This generation was less successful compared to the first. It included prolonged-release formulations using biodegradable polymers for proteins and peptides and the development of pulmonary delivery systems for insulin. Due to its lower bioavailability, insulin required much higher doses for pulmonary delivery compared to parenteral injections, leading to adverse effects. The last decade saw the exploration of nanoparticles for targeting genes and tumors [47].

Third Generation: New technologies in this generation focus on delivering poorly water-soluble drugs, long-term non-invasive methods for proteins/nucleic acids/peptides, targeted delivery using nanoparticles, and self-regulating drug delivery systems [47, 63,64].

Concept of Biomaterials in Controlled Drug Delivery: Biomaterials play a crucial role in modulating drug pharmacokinetics in DDS. A biomaterial is an engineered substance designed to interact with biological systems for therapeutic or diagnostic purposes. Choosing the right biomaterials—such as polymers, polysaccharides, proteins, lipids, and peptides—is essential for designing DDS with specific physicochemical properties and drug release profiles. Biomaterials should be biocompatible, biodegradable, non-toxic, hydrophilic, mucoadhesive, and possess adequate mechanical strength. Biodegradable polymers are preferred for controlled DDS as they prevent the accumulation of toxic remnants. Non-biodegradable systems may require additional measures like chelators to disintegrate if complications arise [48].

Stimuli-Responsive Biomaterials: Stimuli-responsive or smart polymers can react to physical or chemical external stimuli. These polymers are pivotal in nanomedicine development. They can be classified into single stimuli-responsive and dual or multiple stimuli-responsive types. Single stimuli polymers respond to factors like temperature, electric pulse, magnetic fields (exogenous stimuli), and enzyme concentrations, hormone levels, pH, and redox potential (endogenous stimuli). Strategies for controlling drug release from these polymers include using nanocarriers to activate the release or designing polymers with charged surfaces for targeted cell internalization [65].

Conclusion

The landscape of drug delivery systems (DDS) has witnessed substantial transformation with the advent of controlled release technologies. These advancements address critical challenges associated with traditional dosage forms, including the accuracy of dosing, stability of active pharmaceutical ingredients (APIs), and patient compliance. Controlled DDS, characterized by their ability to release drugs at a predetermined rate over extended periods, have revolutionized pharmaceutical practices by maintaining therapeutic drug levels and reducing the frequency of dosing. Controlled release systems operate on various principles, including dissolution, diffusion, and osmotic pressure. These systems ensure that the drug is delivered at a consistent rate, overcoming the

limitations of conventional methods that often lead to fluctuating drug levels and variable efficacy. Recent developments have introduced sophisticated technologies such as stimuli-responsive biomaterials and nanoparticle-based systems, which enhance the precision of drug delivery and target specific sites within the body. The evolution of DDS has been marked by three distinct generations. The first generation focused on basic release mechanisms and paved the way for oral and transdermal applications. The second generation attempted to tackle more complex issues such as protein stability and pulmonary delivery but faced challenges with bioavailability and patient tolerability. The third generation has seen the integration of advanced materials and self-regulating systems, promising improved performance and broader therapeutic applications. Future advancements in DDS are likely to involve further refinement of biomaterials, development of smart polymers, and exploration of novel delivery methods. These innovations hold the potential to enhance drug efficacy, minimize side effects, and offer tailored therapeutic solutions for diverse medical conditions. The ongoing research and development in this field will continue to drive the evolution of drug delivery technologies, improving patient care and therapeutic outcomes across various medical domains.

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نظرة معمقة على أنظمة توصيل الأدوية المتحكم بها: التطورات الحالية والتقدم المستقبلي

الملخص:

خلفية: تعد أنظمة توصيل الأدوية (DDS) أساسية في الطب الحديث لتحسين الفعالية العلاجية وسلامة العوامل الدوائية. تقليديًا، يواجه استخدام المكونات الصيدلانية النشطة (APIs) بشكل مباشر تحديات مثل دقة الجرعات، الاستقرار، والامتثال لدى المرضى. ظهرت أنظمة توصيل الأدوية المتحكم بها لمعالجة هذه المشكلات عن طريق تحرير الأدوية بمعدل متحكم به، مما يعزز النتائج العلاجية ويقلل من الآثار الجانبية.

الهدف: يهدف هذا المقال إلى تقديم نظرة شاملة على التقدمات الحالية والتوقعات المستقبلية في أنظمة توصيل الأدوية المتحكم بها. يستكشف المقال تقنيات DDS المختلفة وآلياتها وتأثيرها على فعالية الأدوية وامتثال المرضى.

الطرق: يجمع الاستعراض بين بيانات الأبحاث الحديثة حول أنظمة توصيل الأدوية، مع التركيز على تصنيفها، اعتبارات تصميمها، وأدائها. يناقش الدوائية لإطلاق الدواء، بما في ذلك الامتصاص، التوزيع، الأيض، والإفراز، ويقيم الآليات المختلفة للإفراج المتحكم فيه مثل الأنظمة المتحكم فيها بالذوبان، المتحكم فيها بالانتشار، والمتأثرة بالضغط الأسموزي.

النتائج: تطورت أنظمة DDS المتحكم بها بشكل كبير من الأنظمة من الجيل الأول التي اعتمدت على آليات أساسية مثل الذوبان والانتشار إلى تقنيات متقدمة تتضمن مواد حيوية تستجيب للمؤثرات. تشمل هذه الأنظمة الآن ابتكارات مثل توصيل الجزيئات النانوية، الأجهزة ذاتية التنظيم، والطرق غير الغازية طويلة الأمد للبروتينات والأحماض النووية. كما أن تطوير المواد الحيوية والبوليمرات الذكية قد عزز من دقة وفعالية توصيل الأدوية.

الخلاصة: تمثل أنظمة توصيل الأدوية المتحكم بها تقدمًا كبيرًا في التكنولوجيا الصيدلانية، حيث تقدم تحسينًا في إدارة معدلات إطلاق الدواء ونتائج أفضل للمرضى. من المحتمل أن تركز التطورات المستقبلية على تحسين هذه الأنظمة لتطبيقات أوسع ودمج المواد الحيوية المتقدمة لمعالجة الاحتياجات والتحديات العلاجية المحددة.

الكلمات المفتاحية: أنظمة توصيل الأدوية المتحكم بها، التكنولوجيا الصيدلانية، حركية إطلاق الأدوية، المواد الحيوية، النواقل النانوية، البوليمرات المستجيبة للمؤثرات.