

A REVIEW ON CONCEPTS OF NOVEL DRUG DELIVERY SYSTEMS

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ABSTRACT

Novel drug delivery systems have great potential to enhance treatment effectiveness, minimize side effects, and support personalized medicine. As technology progresses, these systems are poised to transform healthcare, leading to improved therapeutic outcomes for patients. Novel drug delivery systems (NDDS) mark a significant breakthrough in medicine, addressing the shortcomings of traditional drug delivery methods. These systems enhance drug bioavailability, enable controlled release, provide targeted delivery, and minimize side effects, thereby improving therapeutic outcomes. NDDS are especially beneficial in managing complex diseases such as cancer, chronic conditions, and genetic disorders. With ongoing advancements in research and technology, NDDS are poised to become essential in personalized medicine, offering more efficient, effective, and patient-centered treatments. However, challenges related to manufacturing, regulatory approval, and scalability must be overcome to fully unlock their potential in clinical application

Key Words : Novel Drugs Different Delivery Systems Applications Trends

INTRODUCTION

Controlled Drug Delivery Systems (CDDS)

Controlled Drug Delivery Systems are innovative therapeutic approaches designed to release medications in a regulated manner over a specific time frame. This method enhances therapeutic outcomes and patient compliance. Below are the key aspects, types, mechanisms, advantages, challenges, applications, and future trends related to CDDS.

- **Purpose:** CDDS aim to maintain drug concentrations within a therapeutic range, which helps minimize side effects and enhance efficacy.
- **Kinetics:** These systems can be engineered to release drugs at a constant rate (zero-order kinetics), a variable rate (first-order kinetics), or in response to specific stimuli (stimuli-responsive systems).[1]
- **Formulation Components:**
 - **Polymers:** Biodegradable and biocompatible polymers are commonly used to encapsulate drugs and regulate their release.
 - **Active Ingredients:** The therapeutic agents can include small molecules, peptides, proteins, or nucleic acids.
 - **Excipients:** Non-active substances that help stabilize the formulation and improve performance.

Types of Controlled Drug Delivery Systems

1. Matrix Systems:

- **Homogeneous Matrices:** Drugs are uniformly distributed within a polymer matrix.

- **Reservoir Systems:** Drugs are contained within a core that is surrounded by a polymer membrane.
- 2. **Microencapsulation:** Involves coating drug particles with a polymer to modulate release rates.
- 3. **Transdermal Systems:** Medications are delivered through the skin using patches that provide controlled release.
- 4. **Implants:** Devices placed under the skin for prolonged drug delivery.
- 5. **Nanoparticles:** Nanoscale carriers that enhance drug solubility and target specific delivery sites.
- 6. **Smart Drug Delivery Systems:** These systems respond to stimuli such as pH, temperature, or light to release drugs as needed.

Mechanisms of Drug Release

- **Diffusion:** Drugs migrate through the polymer matrix.
- **Erosion:** The polymer matrix breaks down over time, facilitating drug release.
- **Osmosis:** Osmotic pressure drives drug release through a semi-permeable membrane.
- **Swelling:** The matrix expands upon contact with biological fluids, leading to drug release.

Advantages of Controlled Drug Delivery Systems

- **Enhanced Efficacy:** Maintains optimal drug levels, maximizing therapeutic effects.
- **Reduced Side Effects:** Lower peak drug concentrations decrease the likelihood of toxicity.
- **Improved Patient Compliance:** Fewer doses required can lead to better adherence.
- **Targeted Delivery:** Localized treatment reduces systemic exposure and potential side effects.

Challenges and Limitations

- **Complex Manufacturing:** The development process can be intricate and costly compared to traditional formulations.
- **Stability Issues:** Some formulations may face stability challenges that affect their shelf life and efficacy.
- **Patient Variability:** Differences in individual metabolism and absorption can influence system performance.
- **Regulatory Hurdles:** The complexity of CDDS can complicate regulatory approval processes.[2]

Applications

- **Chronic Diseases:** Used in the management of conditions such as diabetes (insulin delivery), cancer (chemotherapy), and cardiovascular diseases.
- **Pain Management:** Long-acting analgesics can be effectively delivered through implants or patches.
- **Vaccination:** Controlled release systems are being developed for vaccines.

Future Trends

- **Personalized Medicine:** CDDS can be tailored to individual patients based on genetic and metabolic profiles.
- **Integration with Digital Health:** Combining CDDS with smart technologies can enable real-time monitoring and adjustments to therapy.

Polymers in controlled drug delivery systems (CDDS), ensuring originality while retaining the essential information:

Polymers in Controlled Drug Delivery Systems

Polymers are vital components in the formulation of controlled drug delivery systems (CDDS). This overview explores the various types of polymers, their properties, mechanisms of action, and applications in drug delivery.

Polymers

Polymers are large molecules made up of repeated structural units called monomers, connected by covalent bonds. They can be categorized as natural or synthetic, and their classification often depends on their origin, structure, and specific properties.

Types of Polymers in Drug Delivery

1. Natural Polymers:

- **Examples:** Common natural polymers include chitosan, alginate, hyaluronic acid, gelatin, and collagen.
- **Properties:** These polymers are typically biocompatible and biodegradable, demonstrating good cell adhesion and bioactivity, which are essential for various biomedical applications.
- **Applications:** Natural polymers are widely used in drug delivery systems, particularly in tissue engineering and regenerative medicine.

2. Synthetic Polymers:

- **Examples:** Notable synthetic polymers include poly(lactic-co-glycolic acid) (PLGA), polycaprolactone (PCL), polyethylene glycol (PEG), and polyvinyl alcohol (PVA).
- **Properties:** These polymers offer tunable mechanical and degradation properties, allowing for customization based on specific therapeutic needs.
- **Applications:** Synthetic polymers are commonly utilized in the production of micro- and nanoparticles, implants, and hydrogels.[3]

Properties of Polymers

- **Biocompatibility:** Essential for drug delivery applications, polymers must not trigger adverse reactions in the body.
- **Biodegradability:** Many CDDS use biodegradable polymers that degrade into non-toxic byproducts, facilitating gradual drug release without the need for surgical removal.
- **Mechanical Properties:** The strength, flexibility, and elasticity of polymers influence the performance and stability of drug delivery systems.
- **Porosity and Permeability:** Polymer structures can be engineered to control these characteristics, directly impacting drug release rates.
- **Swelling Behavior:** Hydrogels that swell in aqueous environments are particularly advantageous for controlled release applications.

Mechanisms of Drug Release

1. **Diffusion-Controlled Release:** In this mechanism, drug molecules diffuse through the polymer matrix. The release rate is influenced by the polymer's porosity and the solubility of the drug.

2. **Erosion-Controlled Release:** This involves the gradual degradation of the polymer over time, leading to drug release. Erosion can occur via surface erosion (where the outer layer degrades first) or bulk erosion (where the entire matrix degrades).
3. **Swelling-Controlled Release:** Polymers that swell in the presence of water can facilitate drug release by forming a gel-like environment that allows drugs to diffuse out.
4. **Stimuli-Responsive Release:** Some polymers are designed to alter their properties in response to specific stimuli (e.g., pH, temperature, or light), enabling targeted drug release.

Applications of Polymers in Drug Delivery

- **Nanoparticles:** Polymers are used to form nanoparticles, enhancing drug solubility and enabling targeted delivery.
- **Hydrogels:** These water-swollen networks are utilized for controlled release in applications such as wound dressings and tissue engineering.
- **Microspheres and Microcapsules:** These structures encapsulate drugs for sustained release.
- **Implants:** Biodegradable polymer implants can provide long-term drug release, reducing the need for frequent dosing.
- **Transdermal Systems:** Polymer-based patches allow for controlled drug delivery through the skin, presenting an alternative to oral administration.

Future Directions

- **Smart Polymers:** Ongoing research aims to develop polymers that respond to specific biological signals, allowing for more precise control over drug release.
- **Combination Therapies:** Polymers can be engineered to co-deliver multiple drugs, targeting different biological pathways for enhanced therapeutic effects.
- **Personalized Drug Delivery:** Advances in polymer technology may lead to customized drug delivery systems tailored to individual patient profiles, optimizing treatment outcomes.

Microencapsulation

Microencapsulation is a versatile technique widely utilized in pharmaceuticals and various other industries, where active substances are enclosed within a protective coating. This process offers significant advantages for drug delivery, stability, and bioavailability. Below is a comprehensive exploration of microencapsulation, including its principles, methods, applications, and emerging trends.[4]

Microencapsulation

Microencapsulation involves the process of enveloping tiny particles or droplets of active materials—such as drugs, vitamins, or flavors—within a thin protective layer. The resulting microcapsules, typically ranging in size from 1 to 1000 micrometers, serve multiple purposes, including controlled release, protection from environmental degradation, and enhanced bioavailability.

Principles of Microencapsulation

1. **Core Material:** This refers to the active ingredient being encapsulated, which can include drugs, nutrients, or other bioactive compounds.

2. **Wall Material:** The protective coating that surrounds the core. Common wall materials include various polymers, lipids, and proteins. The selection of wall material significantly influences the release characteristics and stability of the microcapsules.
3. **Encapsulation Efficiency:** This metric indicates the proportion of the core material successfully encapsulated within the wall. High encapsulation efficiency is crucial for effective formulations.

Methods of Microencapsulation

Microencapsulation techniques can be classified into several categories:

1. **Physical Methods:**
 - **Spray Drying:** In this method, a solution containing the core material is atomized into a hot air chamber, where the solvent evaporates, resulting in solid microcapsules.
 - **Coacervation:** This technique involves phase separation of a polymer solution, forming a droplet around the core material that solidifies into a coating.
 - **Fluidized Bed Coating:** Particles are suspended in an air stream while a coating solution is sprayed onto them, creating a layer as the solvent evaporates.
2. **Chemical Methods:**
 - **Interfacial Polymerization:** This process involves the reaction of two monomers at the core's interface, forming a polymeric shell.
 - **Solvent Evaporation:** A mixture of core and wall materials is emulsified, and solvent evaporation results in the formation of microcapsules.
3. **Mechanical Methods:**
 - **Extrusion:** The core material is combined with wall materials and extruded through nozzles to form beads, which are then solidified into microcapsules.

Properties of Microencapsulated Systems

1. **Controlled Release:** Microencapsulation enables sustained or controlled release of the encapsulated substance, facilitating more effective dosing regimens.
2. **Protection:** The coating protects sensitive active ingredients from degradation due to environmental factors such as light, moisture, and oxygen.
3. **Improved Stability:** Encapsulation can enhance the stability of substances, extending their shelf life and maintaining efficacy.
4. **Taste Masking:** In pharmaceuticals, microencapsulation can effectively mask unpleasant flavors, improving patient compliance.
5. **Targeted Delivery:** Microcapsules can be designed to release their contents at specific sites within the body, enhancing therapeutic outcomes.

Applications of Microencapsulation

1. **Pharmaceuticals:** Microencapsulation is employed for controlled drug delivery, taste masking, and stabilizing sensitive formulations.
2. **Nutraceuticals:** Vitamins and supplements are encapsulated to enhance bioavailability and stability.
3. **Food Industry:** Flavor compounds are encapsulated to improve shelf life and prevent degradation of sensitive ingredients.
4. **Cosmetics:** Active ingredients are microencapsulated for sustained release and better skin penetration.

5. **Agriculture:** Pesticides and fertilizers are encapsulated for controlled release, reducing environmental impacts.[5]

Challenges and Limitations

1. **Production Costs:** Some microencapsulation methods can be expensive and time-consuming, which may limit their broader application.
2. **Scale-Up Issues:** Transitioning from laboratory-scale to industrial-scale production can be challenging, particularly in maintaining consistent quality.
3. **Release Control:** Achieving precise control over the release rates of the encapsulated materials can be complex.
4. **Compatibility:** Ensuring compatibility between the core and wall materials is essential for effective encapsulation and release.

Future Trends

1. **Smart Microcapsules:** Research is focusing on developing microcapsules that respond to specific stimuli (e.g., pH, temperature, or enzymatic activity) for targeted release.
2. **Personalized Medicine:** Advances in microencapsulation may enable the creation of tailored drug delivery systems suited to individual patient needs.
3. **Combination Therapies:** Microencapsulation facilitates the co-delivery of multiple drugs or therapeutics, enhancing overall treatment efficacy.
4. **Biodegradable Materials:** There is a growing emphasis on utilizing environmentally friendly and biodegradable materials for microencapsulation.

Mucosal Drug Delivery Systems (MDDS)

Mucosal drug delivery systems are innovative methods designed to administer therapeutics through various mucosal membranes, including those in the oral cavity, nasal cavity, gastrointestinal tract, and other mucosal sites. These systems offer distinct advantages such as enhanced bioavailability, rapid onset of action, and reduced systemic side effects.

Mucosal Drug Delivery Systems

MDDS take advantage of the rich vascular network and permeability characteristics of mucosal tissues to facilitate direct absorption of drugs into the bloodstream. This approach can effectively bypass first-pass metabolism, significantly improving the bioavailability of compounds that may be poorly absorbed or extensively metabolized when administered orally.

Types of Mucosal Drug Delivery Systems

1. **Oral Mucosal Delivery:**
 - **Sublingual:** Drugs are placed under the tongue for rapid absorption via the sublingual mucosa. Common examples include nitroglycerin.
 - **Buccal:** Drugs are administered between the gums and cheek, allowing for sustained release and absorption, as seen in buccal tablets and films.[6]
2. **Nasal Drug Delivery:**
 - This route utilizes nasal sprays or drops for quick absorption through the nasal mucosa, making it suitable for both systemic delivery (e.g., vaccines, peptides) and local treatments (e.g., nasal congestion).

3. **Rectal Drug Delivery:**
 - Suppositories and enemas provide a means to deliver drugs via the rectal mucosa, particularly beneficial for patients unable to take medications orally.
4. **Vaginal Drug Delivery:**
 - Formulations like creams, gels, and tablets allow for drug delivery through the vaginal mucosa, serving both local and systemic therapeutic purposes, such as hormone replacement therapy and antifungal treatments.
5. **Ocular Drug Delivery:**
 - Though not always categorized with other mucosal routes, ocular formulations (such as eye drops) utilize mucosal membranes for drug absorption.

Mechanisms of Drug Absorption

1. **Passive Diffusion:** This is the primary mechanism for small, non-polar molecules diffusing across the lipid bilayer of mucosal cells.
2. **Facilitated Diffusion:** Carrier proteins assist in transporting larger or polar molecules across the mucosal barrier.
3. **Endocytosis:** Some drugs can be internalized by cells through endocytosis, allowing transport across the mucosal barrier.
4. **Transcytosis:** This mechanism involves vesicular transport that allows drugs to cross the mucosal barrier.
5. **Permeation Enhancers:** These substances temporarily increase mucosal permeability, enhancing drug absorption.

Advantages of Mucosal Drug Delivery Systems

1. **Increased Bioavailability:** By bypassing first-pass metabolism, MDDS can significantly enhance the bioavailability of poorly absorbed drugs.
2. **Rapid Onset of Action:** The highly vascular nature of mucosal tissues facilitates quick absorption into the bloodstream.
3. **Improved Patient Compliance:** Mucosal administration can be more comfortable and convenient for patients compared to injections or frequent oral dosing.
4. **Localized Delivery:** MDDS allow for targeted delivery to specific sites, minimizing systemic side effects.
5. **Formulation Versatility:** These systems are compatible with a wide range of formulations, including solutions, gels, films, and tablets.

Challenges and Limitations

1. **Variability in Absorption:** Individual differences in mucosal health, thickness, and hydration can lead to inconsistent drug absorption.
2. **Limited Formulation Options:** Some drugs may face stability issues or poor solubility, making them unsuitable for mucosal delivery.
3. **Irritation and Sensitivity:** Certain formulations can cause irritation to mucosal tissues, limiting their applicability.
4. **Short Residence Time:** Formulations may be rapidly cleared from the mucosal surface, necessitating frequent administration.
5. **Regulatory Challenges:** The development and marketing of mucosal delivery systems often encounter rigorous regulatory scrutiny.

Future Perspectives

1. **Nanotechnology:** Incorporating nanoparticles and nanocarriers can enhance the stability and absorption of drugs through mucosal routes.
2. **Smart Delivery Systems:** Development of responsive systems that release drugs in response to specific physiological triggers (e.g., changes in pH) is an emerging area of research.
3. **Personalized Medicine:** Tailoring MDDS to meet individual patient needs based on genetic and physiological factors is gaining traction.
4. **Combination Therapies:** Mucosal systems can enable the simultaneous delivery of multiple drugs, enhancing therapeutic efficacy.
5. **Advancements in Formulation:** Continued research into novel excipients and formulation strategies aims to improve the effectiveness and safety of mucosal drug delivery.[7]

Implantable Drug Delivery Systems (IDDS)

IDDS are sophisticated therapeutic devices designed to release medications directly into the body over extended periods. These systems are particularly advantageous for managing chronic conditions that require consistent drug administration, ultimately improving patient compliance and treatment outcomes. Below is a comprehensive overview of implantable delivery systems, encompassing their types, mechanisms of action, advantages, challenges, and future perspectives.

Implantable Drug Delivery Systems

Implantable drug delivery systems are devices that are inserted into the body to provide either localized or systemic therapeutic effects. These systems can be engineered to release drugs at predetermined rates, allowing for controlled therapeutic responses while minimizing side effects associated with high plasma concentrations. Materials used for these implants can vary widely, including biodegradable and non-biodegradable polymers, metals, and ceramics.

Types of Implantable Delivery Systems

1. **Biodegradable Implants:**
 - **Description:** Composed of polymers that break down in the body over time, releasing drugs as they degrade.
 - **Examples:** Polylactic acid (PLA) and poly(lactic-co-glycolic acid) (PLGA).
 - **Applications:** Commonly used for hormone delivery, chemotherapy, and pain management.
2. **Non-Biodegradable Implants:**
 - **Description:** Designed to remain in the body long-term without degrading; drugs are released through diffusion or other mechanisms.
 - **Examples:** Silicone or metallic implants used for prolonged hormone therapy.
3. **Micro- and Nanoparticles:**
 - **Description:** Small particles encapsulating drugs to provide sustained release and improve the solubility and bioavailability of poorly soluble drugs.
4. **Reservoir Systems:**
 - **Description:** These systems consist of a drug reservoir encased by a rate-controlling membrane, allowing controlled diffusion of the drug.
5. **Matrix Systems:**
 - **Description:** Drugs are dispersed within a polymer matrix, with the release rate governed by polymer characteristics and drug diffusion.

6. Smart Implants:

- **Description:** Advanced systems that can modulate drug release rates in response to specific physiological conditions (e.g., pH, temperature, biomolecules).

Mechanisms of Drug Release

1. Diffusion-Controlled Release:

- Drug molecules diffuse through the polymeric matrix or membrane, with the rate influenced by drug size, polymer characteristics, and environmental conditions.

2. Erosion-Controlled Release:

- Implants degrade gradually, releasing drugs. This can be surface-controlled (outer layer degrades first) or bulk-controlled (entire implant degrades).

3. Osmotic Release:

- Osmotic pressure drives the drug release from a reservoir implant, allowing for a consistent release rate over time.

4. Swelling-Controlled Release:

- Some hydrophilic polymers swell in bodily fluids, facilitating drug diffusion as the polymer expands.[8]

Advantages of Implantable Drug Delivery Systems

1. Sustained Release:

- Provides continuous and controlled medication release, reducing the need for frequent dosing.

2. Improved Patient Compliance:

- Minimizes the daily medication burden, enhancing adherence to treatment regimens.

3. Localized Treatment:

- Enables targeted drug delivery, reducing systemic side effects and maximizing therapeutic effects at the desired site.

4. Enhanced Bioavailability:

- Improves the bioavailability of drugs that are poorly absorbed through traditional routes.

5. Reduced Side Effects:

- Maintains steady drug levels, minimizing peaks and troughs associated with conventional dosing.

Challenges and Limitations

1. Surgical Insertion:

- The necessity for surgical implantation can pose barriers, including increased costs and risks associated with the procedure.

2. Biocompatibility:

- Materials must be biocompatible and non-toxic to avoid adverse reactions in the body.

3. Stability Issues:

- Ensuring the stability of both the implant material and the drug is critical to prevent degradation prior to release.

4. Variable Release Rates:

- Achieving consistent and predictable release rates can be complicated by factors like tissue response, inflammation, and biological variability.

5. Removal Difficulties:

- Non-biodegradable implants may require surgical removal, leading to inconvenience and additional costs.

Future Perspectives

1. **Smart Delivery Systems:**
 - Development of implants that respond to specific physiological stimuli for on-demand drug release.
2. **Personalized Medicine:**
 - Advances in material science may facilitate the customization of implants based on individual patient profiles.
3. **Combination Therapies:**
 - The capacity to deliver multiple drugs simultaneously from a single implant can enhance treatment efficacy, particularly in areas like cancer therapy and pain management.
4. **Nanotechnology:**
 - Integration of nanoparticles can improve drug solubility, stability, and targeting within implantable systems.
5. **Regenerative Medicine:**
 - Combining implantable systems with tissue engineering techniques could enable local delivery of growth factors or stem cells to promote healing.

Transdermal Drug Delivery Systems (TDDS)

TDDS are advanced methods for administering drugs through the skin for systemic effects. This non-invasive approach bypasses the gastrointestinal tract and first-pass metabolism, enhancing drug bioavailability and providing several advantages over traditional delivery methods. Below is a comprehensive overview of TDDS, including their types, mechanisms, benefits, challenges, and future trends.

Transdermal Drug Delivery Systems

TDDS consists of a drug reservoir or matrix within a patch that adheres to the skin, allowing for controlled drug release over extended periods. This ensures steady plasma levels and minimizes side effects, making TDDS suitable for a range of medications, including hormones and analgesics.

Types of Transdermal Drug Delivery Systems

1. **Transdermal Patches:**
 - **Description:** Adhesive patches that contain either a drug reservoir or a polymer matrix impregnated with the drug.
 - **Examples:** Nicotine patches, fentanyl patches, and contraceptive patches.
2. **Microneedle Systems:**
 - **Description:** Patches with tiny needles that penetrate the outer layer of the skin to enhance drug delivery.
 - **Examples:** Vaccines and peptides delivered using microneedles.[9]
3. **Iontophoresis:**
 - **Description:** A technique that uses a small electric current to drive charged drugs through the skin.
 - **Applications:** Effective for delivering peptides and proteins.
4. **Sonophoresis:**

- **Description:** Utilizes ultrasound waves to increase skin permeability and facilitate drug delivery.
 - **Applications:** Often used for larger molecules, including certain vaccines.
5. **Chemical Enhancers:**
- **Description:** Formulations that include substances like alcohols or fatty acids to enhance skin permeability and drug absorption.

Mechanisms of Drug Absorption

1. **Passive Diffusion:**
 - The primary mechanism where drug molecules diffuse from a higher concentration in the patch to a lower concentration in the bloodstream.
2. **Enhanced Permeation:**
 - Involves using chemical enhancers or methods like microneedles to disrupt the stratum corneum, facilitating drug passage.
3. **Electrotransport:**
 - Iontophoresis and sonophoresis use electrical or ultrasonic energy to improve drug absorption through the skin.

Advantages of Transdermal Drug Delivery Systems

1. **Avoids First-Pass Metabolism:**
 - Bypasses the gastrointestinal tract and liver, enhancing bioavailability for many drugs.
2. **Controlled Release:**
 - Allows for sustained release of medication over hours or days, maintaining steady therapeutic levels.
3. **Non-Invasive:**
 - Offers a painless and convenient alternative to injections, improving patient compliance.
4. **Ease of Use:**
 - Patches are simple to apply and remove, making them suitable for self-administration.
5. **Local and Systemic Effects:**
 - Capable of delivering drugs for both localized (e.g., pain relief) and systemic effects (e.g., hormone therapy).[10]

Challenges and Limitations

1. **Skin Barrier:**
 - The stratum corneum poses a significant barrier to drug absorption, limiting the types and quantities of drugs suitable for transdermal delivery.
2. **Drug Characteristics:**
 - Only small, lipophilic, and non-irritating molecules can be effectively delivered; larger or hydrophilic drugs often face absorption difficulties.
3. **Variable Absorption:**
 - Individual differences in skin thickness, hydration, and health can lead to variability in drug absorption rates.
4. **Limited Formulation Options:**
 - Not all drugs can be formulated for transdermal delivery due to stability and solubility issues.
5. **Skin Irritation:**

- Some patients may experience irritation or allergic reactions to the adhesive or active ingredient.

Future Trends

1. **Nanotechnology:**
 - Using nanoparticles and nanocarriers to enhance drug solubility and absorption through the skin.
2. **Smart Delivery Systems:**
 - Development of patches that respond to physiological changes (e.g., temperature, pH) for controlled and on-demand drug release.
3. **Combination Therapies:**
 - Potential to deliver multiple drugs simultaneously for synergistic effects from a single transdermal system.
4. **Personalized Medicine:**
 - Advances may enable customization of transdermal patches based on individual patient needs and responses.
5. **Research on New Drug Candidates:**
 - Ongoing studies to identify new drugs suitable for transdermal delivery, including biologics and vaccines.

Gastrointestinal Drug Delivery Systems (GIDDS)

GIDDS are essential in modern therapeutics, designed to deliver medications directly to the gastrointestinal tract for local or systemic effects. This route of administration is widely favored due to its non-invasive nature, ease of use, and high patient compliance. Below is a detailed overview of GIDDS, including their types, mechanisms, advantages, challenges, and future trends.[11]

Gastrointestinal Drug Delivery Systems

GIDDS target various regions of the gastrointestinal tract (GI tract), such as the stomach, small intestine, and large intestine, to optimize drug absorption and bioavailability. These systems consider factors such as pH, enzyme activity, and food interactions to enhance therapeutic efficacy.

Types of Gastrointestinal Drug Delivery Systems

1. **Oral Dosage Forms:**
 - **Tablets and Capsules:** Standard forms that disintegrate in the GI tract to release the drug.
 - **Extended-Release Formulations:** Designed for slow, prolonged release, maintaining therapeutic levels and reducing the frequency of dosing.
2. **Sustained-Release Systems:**
 - **Matrix Systems:** Drugs are embedded in a polymer matrix, controlling release through diffusion and erosion.
 - **Coated Systems:** Protect drugs from the stomach's acidic environment, allowing release in the neutral pH of the intestines.
3. **Enteric-Coated Formulations:**
 - These are designed to resist stomach acidity and dissolve in the higher pH of the intestines, thereby protecting sensitive drugs and ensuring targeted release.
4. **Mucoadhesive Systems:**

- These formulations adhere to the mucosal lining of the GI tract, enhancing retention time and absorption.
- 5. **Targeted Delivery Systems:**
 - **Colonic Drug Delivery:** Specifically formulated to release drugs in the colon, useful for local treatments, such as inflammatory bowel diseases.
- 6. **Nanoparticle and Microparticle Systems:**
 - These enhance the solubility and stability of poorly soluble drugs and improve their absorption across intestinal membranes.[12]

Mechanisms of Drug Absorption

1. **Passive Diffusion:**
 - The primary mechanism where drugs move from areas of higher concentration in the GI tract to lower concentration in the bloodstream.
2. **Facilitated Diffusion:**
 - Involves carrier proteins aiding the transport of larger or polar molecules across cell membranes.
3. **Active Transport:**
 - Certain drugs are absorbed against their concentration gradient via specific transport proteins, crucial for nutrients and some pharmaceuticals.
4. **Endocytosis:**
 - Cells engulf drug particles, allowing larger molecules that cannot diffuse passively to be absorbed.

Advantages of Gastrointestinal Drug Delivery Systems

1. **Ease of Administration:**
 - Oral administration is non-invasive and widely accepted, making it convenient for patients.
2. **Cost-Effectiveness:**
 - Generally, oral formulations are less expensive to produce than injectable alternatives.
3. **Versatility:**
 - A broad range of drug forms and formulations can be developed for various therapeutic applications.
4. **Controlled Release:**
 - Sustained and controlled-release formulations help optimize therapeutic outcomes while minimizing side effects.
5. **Enhanced Bioavailability:**
 - Formulations can improve the solubility and absorption of poorly bioavailable drugs.[13]

Challenges and Limitations

1. **Gastric Environment:**
 - The acidic pH and enzymatic activity in the stomach can degrade some drugs, limiting their effectiveness.
2. **Variability in Absorption:**
 - Factors such as food intake, gastrointestinal motility, and individual patient differences can affect drug absorption rates.
3. **Limited Absorption:**
 - Only small, lipophilic, and non-irritating molecules are effectively absorbed; larger or hydrophilic drugs often face challenges.

4. First-Pass Metabolism:

- Drugs absorbed from the GI tract may undergo significant metabolism in the liver before reaching systemic circulation, reducing bioavailability.

5. Patient Compliance:

- Some patients may have difficulty swallowing pills or adhering to prescribed dosing regimens.[14]

Future Trends

1. Nanotechnology:

- Development of nanoparticles to enhance drug solubility, stability, and targeted delivery in the GI tract.

2. Personalized Medicine:

- Tailoring formulations based on individual patient characteristics, such as genetic and metabolic profiles.

3. Smart Delivery Systems:

- Formulations that respond to physiological changes (e.g., pH, temperature) to optimize drug release.

4. Combination Therapies:

- GIDDS may be designed to co-deliver multiple drugs to enhance therapeutic efficacy, especially in complex diseases.

5. Biologics and Biopharmaceuticals:

- Research into oral delivery systems for larger molecules, such as proteins and peptides, traditionally administered via injections.

Nasopulmonary Drug Delivery Systems

Nasopulmonary drug delivery systems are advanced therapeutic approaches designed to deliver medications through the nasal cavity directly to the lungs or pulmonary system. This route is particularly beneficial for treating respiratory diseases and conditions, offering rapid absorption and effective systemic delivery. Below is a comprehensive overview of nasopulmonary drug delivery systems, covering their types, mechanisms, advantages, challenges, and future trends.

Nasopulmonary drug delivery involves administering drugs via the nasal mucosa, enabling direct access to the lungs. This method takes advantage of the large surface area and rich vascularization of the nasal passages, facilitating efficient absorption into the bloodstream and pulmonary tissue. It is especially effective for systemic delivery of drugs such as vaccines, peptides, anesthetics, and for local treatments of respiratory conditions.

Types of Nasopulmonary Drug Delivery Systems

1. Nasal Sprays and Drops

- **Description:** Liquid formulations delivered via spray or dropper into the nasal cavity.
- **Examples:** Decongestants, corticosteroids, migraine medications.

2. Nasal Powders

- **Description:** Dry powder formulations that are inhaled through the nose.
- **Examples:** Some vaccines and analgesics.[15]

3. Aerosolized Solutions

- **Description:** Liquid formulations nebulized into fine droplets for inhalation.
- **Examples:** Asthma medications like albuterol.

4. **Microneedle Systems**
 - **Description:** Patches containing microneedles that penetrate the nasal mucosa to enhance drug delivery.
 - **Applications:** Useful for vaccines and biologics requiring deeper tissue penetration.
5. **Iontophoresis and Sonophoresis**
 - **Description:** Techniques utilizing electrical or ultrasonic energy to enhance drug delivery through the nasal mucosa.
 - **Applications:** Effective for delivering peptides and proteins.

Mechanisms of Drug Absorption

1. **Passive Diffusion**
 - Drugs move from higher to lower concentration areas in the nasal cavity to the bloodstream.
2. **Facilitated Diffusion**
 - Involves carrier proteins assisting in transporting larger or polar molecules across cell membranes.
3. **Active Transport**
 - Some drugs are absorbed against their concentration gradient via specific transport proteins.
4. **Endocytosis**
 - Nasal epithelial cells engulf drug particles, allowing for absorption of larger molecules.
5. **Permeation Enhancers**
 - Chemical agents that temporarily disrupt the nasal mucosa's barrier properties, facilitating increased drug absorption.

Advantages

1. **Rapid Onset of Action**
 - The rich vascularization of the nasal cavity allows for quick absorption and therapeutic effects.
2. **Bypass First-Pass Metabolism**
 - Nasal administration avoids degradation in the gastrointestinal tract and liver, enhancing bioavailability.
3. **Local and Systemic Delivery**
 - Effective for both local (e.g., nasal congestion) and systemic (e.g., analgesics, hormones) effects.
4. **Non-Invasive**
 - Provides a convenient and painless alternative to injections, improving patient compliance.
5. **Ease of Administration**
 - Nasal systems can be self-administered, making them user-friendly.[16]

Challenges and Limitations

1. **Nasal Mucosa Variability**
 - Individual differences in mucosal thickness, hydration, and health can affect drug absorption.
2. **Limited Formulation Options**
 - Not all drugs are suitable for nasal delivery due to stability and solubility issues.
3. **Irritation and Sensitivity**

- Some formulations may cause nasal irritation or allergic reactions.
- 4. **Short Residence Time**
 - Formulations can be quickly cleared from the nasal cavity, requiring frequent administration.
- 5. **Technical Complexity**
 - Some delivery systems (e.g., nebulizers, microneedles) may require specialized devices and training.

Future Trends

1. **Nanotechnology**
 - Utilizing nanoparticles to enhance drug solubility, stability, and targeting capabilities.
2. **Smart Delivery Systems**
 - Developing formulations that respond to physiological changes (e.g., pH, temperature) for controlled release.
3. **Personalized Medicine**
 - Tailoring nasal formulations based on individual patient characteristics to optimize therapeutic outcomes.
4. **Combination Therapies**
 - Co-delivery of multiple drugs from a single formulation to enhance efficacy, especially in chronic respiratory diseases.
5. **Research on New Drug Candidates**
 - Ongoing studies to identify new drugs suitable for nasal delivery, including biologics and vaccines.

Targeted Drug Delivery Systems (TDDS)

TDDS are innovative therapeutic strategies designed to deliver medications directly to specific sites within the body, thereby enhancing treatment efficacy while minimizing systemic side effects. These systems are especially significant in managing diseases such as cancer, where localized treatment is critical. Below is an in-depth overview of TDDS, covering their types, mechanisms, advantages, challenges, and future trends.

TDDS focus on improving drug distribution, bioavailability, and therapeutic outcomes by directing drugs to their intended site of action. This approach utilizes various mechanisms, including specific ligands, carriers, and technologies that recognize and bind to target cells or tissues.[17]

Types of Targeted Drug Delivery Systems

1. **Nanoparticle-Based Systems**
 - **Description:** These systems utilize nanoparticles (1-100 nm in size) to encapsulate and deliver drugs to targeted tissues.
 - **Examples:** Liposomes, dendrimers, and polymeric nanoparticles.
 - **Applications:** Particularly used in cancer therapy to deliver chemotherapeutic agents directly to tumor cells.
2. **Monoclonal Antibodies**
 - **Description:** Engineered antibodies designed to specifically bind to antigens on target cell surfaces.
 - **Examples:** Trastuzumab (Herceptin) for HER2-positive breast cancer.
 - **Applications:** Targeted therapies for various cancers and autoimmune diseases.

3. Ligand-Targeted Systems

- **Description:** These systems utilize ligands (e.g., peptides, sugars) that bind to receptors overexpressed on target cells.
- **Examples:** Folate-conjugated nanoparticles targeting cancer cells with high folate receptor expression.
- **Applications:** Targeting specific cell types in cancer, inflammation, or infectious diseases.

4. Smart Delivery Systems

- **Description:** Systems that release drugs in response to specific stimuli, such as pH, temperature, or biomolecules.
- **Examples:** pH-sensitive nanoparticles that release drugs in the acidic environment of tumor tissues.
- **Applications:** Cancer therapies where drug release is triggered by the tumor microenvironment.

5. Microspheres and Microcapsules

- **Description:** Spherical carriers designed to encapsulate drugs and facilitate controlled release.
- **Examples:** Biodegradable microspheres for sustained drug release.
- **Applications:** Used for chronic conditions requiring controlled drug release.

6. Implantable Systems

- **Description:** Devices implanted near the target area to release drugs over an extended period.
- **Examples:** Biodegradable implants for localized cancer treatment.
- **Applications:** Pain management, hormone delivery, and cancer therapies.

Mechanisms of Targeted Drug Delivery

1. Passive Targeting

- **Mechanism:** Utilizes the natural distribution of drugs in the body, enhanced by the leaky vasculature of tumors or inflamed tissues.
- **Applications:** Nanoparticles accumulate in tumor tissues due to the enhanced permeability and retention (EPR) effect.

2. Active Targeting

- **Mechanism:** Modifies drug carriers with specific ligands that bind to receptors on target cells, promoting cellular uptake.
- **Applications:** Antibody-conjugated drugs that bind directly to cancer cell markers.

3. Controlled Release

- **Mechanism:** Allows drugs to be released in a regulated manner based on specific triggers such as environmental changes.[18]
- **Applications:** Drug release from polymers in response to changes in pH or temperature.

4. Endocytosis

- **Mechanism:** Targeted carriers can be taken up by cells through endocytosis, allowing for intracellular delivery.
- **Applications:** Delivery of large molecules, including proteins and nucleic acids.

Advantages of Targeted Drug Delivery Systems

1. Enhanced Efficacy

- Higher concentrations of drugs delivered directly to target sites improve therapeutic effects.

2. Reduced Side Effects

- Minimizing systemic exposure reduces the risk of side effects associated with conventional therapies.
- 3. **Improved Patient Compliance**
 - Sustained release and localized treatment reduce the frequency of administration.
- 4. **Personalized Medicine**
 - Allows for tailoring treatments based on individual patient needs and disease characteristics.
- 5. **Overcoming Biological Barriers**
 - Targeting specific pathways enhances the ability of drugs to cross biological barriers, such as the blood-brain barrier.

Challenges and Limitations

1. **Complexity of Design**
 - Developing effective targeted delivery systems requires sophisticated engineering and design.
2. **Stability Issues**
 - Maintaining the stability of drug formulations can be challenging in biological environments.
3. **Limited Targeting Efficiency**
 - Variability in the expression of target receptors can lead to inconsistent targeting and efficacy.
4. **Potential for Immunogenicity**
 - Biological components, such as antibodies, may evoke immune responses in some patients.
5. **Regulatory Hurdles**
 - Extensive testing and validation are necessary before new targeted delivery systems can be approved for clinical use.[19]

Future Trends

1. **Advancements in Nanotechnology**
 - Continued development of novel nanoparticles and carriers to improve targeting, solubility, and stability.
2. **Combination Therapies**
 - Utilizing targeted delivery systems to co-administer multiple therapeutic agents for synergistic effects, particularly in cancer treatment.
3. **Personalized Targeting**
 - Leveraging genetic and molecular profiling to design targeted therapies tailored to individual patient tumors or conditions.
4. **Smart Therapeutics**
 - Developing smart delivery systems that release drugs in response to specific biological triggers or environmental changes.
5. **Integration with Diagnostic Tools**
 - Combining targeted delivery with diagnostic imaging to enhance treatment precision and monitor therapeutic responses in real time.

Ocular Drug Delivery Systems (ODDS)

ODDS are specialized methods designed to administer therapeutic agents directly to the eye. These systems are essential for treating various ocular conditions, including glaucoma, infections, inflammation, and retinal diseases. The unique anatomical and physiological characteristics of the eye present specific challenges that necessitate the development of effective delivery systems. Below is a comprehensive overview of ocular drug delivery systems, including their types, mechanisms, advantages, challenges, and future trends.

The primary goal of ocular drug delivery systems is to effectively deliver drugs to the eye, achieving therapeutic concentrations while minimizing systemic exposure and side effects. The eye's structure, particularly the corneal barrier, poses challenges for drug absorption, highlighting the need for effective delivery methods.

Types of Ocular Drug Delivery Systems

1. Topical Drops

- **Description:** Liquid formulations applied directly to the eye's surface.
- **Examples:** Eye drops for dry eye syndrome, glaucoma medications.
- **Applications:** Convenient for self-administration; however, they often suffer from low bioavailability due to rapid drainage and limited absorption.[20]

2. Ocular Ointments and Gels

- **Description:** Viscous formulations providing prolonged contact with the eye surface.
- **Examples:** Antibiotic ointments, lubricating gels.
- **Applications:** Increase residence time but may cause blurred vision and discomfort.

3. Intraocular Injections

- **Description:** Direct injection of drugs into the eye (e.g., anterior chamber, vitreous humor).
- **Examples:** Corticosteroids for uveitis, anti-VEGF injections for retinal diseases.
- **Applications:** Deliver high concentrations directly to target tissues; however, they are invasive and require professional administration.

4. Sustained-Release Systems

- **Description:** Devices or formulations designed to release drugs over extended periods.
- **Examples:** Intraocular implants and biodegradable systems.
- **Applications:** Reduce the frequency of administration and improve patient compliance.

5. Nanoparticle-Based Systems

- **Description:** Nanoparticles used to enhance drug solubility and targeting.
- **Examples:** Liposomes, solid lipid nanoparticles.
- **Applications:** Improve ocular bioavailability and targeting to specific ocular tissues.

6. Contact Lenses

- **Description:** Lenses that release drugs while worn on the eye.
- **Examples:** Drug-eluting contact lenses for sustained drug release.
- **Applications:** Provide continuous drug delivery and enhance patient compliance.[21]

Mechanisms of Ocular Drug Absorption

1. Passive Diffusion

- **Mechanism:** Drug molecules diffuse from a region of higher concentration (in the formulation) to lower concentration (in the eye).
- **Significance:** This is the primary pathway for many ocular drug absorption processes.

2. Facilitated Diffusion

- **Mechanism:** Involves carrier proteins that assist in transporting drugs across cell membranes.
- **Applications:** Enhances the absorption of larger or polar molecules.
- 3. **Active Transport**
 - **Mechanism:** Drugs are absorbed against their concentration gradient via specific transport proteins.
 - **Significance:** Important for the uptake of certain nutrients and drugs with specific transporters.
- 4. **Endocytosis**
 - **Mechanism:** Cells engulf drug particles, allowing for the absorption of larger molecules.
 - **Applications:** Useful for delivering biopharmaceuticals and gene therapies.

Advantages of Ocular Drug Delivery Systems

1. **Direct Targeting**
 - Allows for localized treatment, enhancing therapeutic efficacy for ocular diseases.
2. **Reduced Systemic Side Effects**
 - Minimizes the risk of systemic exposure and side effects associated with oral or injectable routes.
3. **Improved Patient Compliance**
 - Sustained-release formulations and user-friendly delivery systems can enhance adherence to treatment regimens.
4. **Enhanced Bioavailability**
 - Advanced formulations, such as nanoparticles and gels, can improve drug absorption and retention on the ocular surface.[22]

Challenges and Limitations

1. **Ocular Barriers**
 - The cornea, conjunctiva, and sclera present significant barriers to drug absorption, limiting bioavailability.
2. **Rapid Drainage**
 - Tears and the blink reflex can quickly clear topical formulations, necessitating frequent administration.
3. **Limited Formulation Options**
 - Not all drugs can be effectively formulated for ocular delivery due to solubility, stability, and irritation issues.
4. **Patient Discomfort**
 - Some formulations may cause irritation or discomfort, affecting patient compliance.
5. **Variability in Drug Response**
 - Individual differences in ocular anatomy and health can lead to variability in drug absorption and efficacy.

Future Trends

1. **Nanotechnology**
 - Continued exploration of nanoparticles and nanocarriers to enhance drug solubility, stability, and targeted delivery to ocular tissues.
2. **Smart Delivery Systems**

- Development of responsive formulations that release drugs in response to specific ocular conditions or stimuli.
- 3. **Personalized Medicine**
 - Tailoring ocular drug delivery systems based on individual patient characteristics and disease profiles.
- 4. **Combination Therapies**
 - Utilizing multifaceted approaches to co-deliver multiple therapeutics for synergistic effects, particularly in complex ocular diseases.
- 5. **Integration with Digital Health**
 - Incorporating digital health technologies, such as mobile apps, to monitor treatment adherence and improve patient education.

Intrauterine Drug Delivery Systems (IUDDS)

IUDDS are specialized devices designed to administer therapeutic agents directly into the uterine cavity. While primarily used for contraception, they also provide targeted treatment for various gynecological conditions such as endometriosis, menstrual disorders, and uterine fibroids. This overview explores the types, mechanisms, advantages, challenges, and future trends of intrauterine drug delivery systems.

IUDDS aim to achieve localized treatment within the uterus, delivering high drug concentrations at the target site while minimizing systemic exposure and side effects. These systems can be designed for both short-term and long-term use, allowing for sustained medication release over time.[23]

Intrauterine Drug Delivery Systems

1. **Intrauterine Devices (IUDs)**
 - **Description:** T-shaped devices inserted into the uterine cavity, often coated or embedded with hormones or drugs.
 - **Examples:**
 - **Copper IUDs** (e.g., ParaGard) for contraception.
 - **Hormonal IUDs** (e.g., Mirena) releasing levonorgestrel for both contraception and management of heavy menstrual bleeding.
 - **Applications:** Provide long-term contraception (3-10 years) and localized hormone therapy.
2. **Drug-Eluting Implants**
 - **Description:** Implants that release therapeutic agents over a specified duration.
 - **Examples:** Biodegradable polymer-based implants for conditions like endometriosis.
 - **Applications:** Facilitate sustained release for gynecological disorders.
3. **Intrauterine Tablets or Capsules**
 - **Description:** Solid dosage forms designed to dissolve and release drugs within the uterus.
 - **Examples:** Dexamethasone tablets for local treatment of endometrial conditions.
 - **Applications:** Enable localized drug delivery with controlled release.
4. **Microspheres and Nanoparticles**
 - **Description:** Tiny particles that encapsulate drugs for controlled release.
 - **Examples:** Polymer-based microspheres that deliver hormones or anti-inflammatory medications.
 - **Applications:** Enhance drug stability and targeted delivery within the uterine environment.

Mechanisms of Drug Absorption

1. Diffusion

- **Mechanism:** Drug molecules move from an area of higher concentration (the delivery system) to lower concentration (surrounding tissues).
- **Significance:** This is the primary pathway for drug release from IUDDS.

2. Bioadhesion

- **Mechanism:** Drug formulations adhere to the endometrial tissue, extending residence time and improving absorption.
- **Applications:** Enhances drug retention and localized therapeutic effects.

3. Controlled Release

- **Mechanism:** Formulations are designed to release drugs at a controlled rate, often via diffusion or polymer matrix erosion.
- **Significance:** Facilitates sustained therapeutic effects over time.

Advantages of Intrauterine Drug Delivery Systems

1. Localized Treatment

- Direct delivery enables high drug concentrations at the target site, enhancing therapeutic efficacy.

2. Reduced Systemic Side Effects

- Localized delivery minimizes systemic exposure and associated side effects from oral or injectable medications.[24]

3. Sustained Release

- Long-acting systems reduce the frequency of administration and improve treatment adherence.

4. Improved Patient Compliance

- Convenient, long-term options enhance adherence to prescribed regimens.

5. Versatility

- IUDDS can be used for a variety of applications beyond contraception, including the management of gynecological conditions.

Challenges and Limitations

1. Invasiveness

- Insertion of IUDs and implants requires a medical procedure, which can cause discomfort or anxiety.

2. Risk of Infection

- Intrauterine devices may increase the risk of pelvic inflammatory disease or other infections, particularly during insertion.

3. Device Expulsion

- There is a possibility that the device may be expelled from the uterus, especially in women with a history of expulsion.

4. Limited Drug Options

- Not all drugs are suitable for intrauterine delivery due to factors such as stability, solubility, and potential irritation.

5. Variability in Drug Response

- Individual differences in uterine anatomy and health can lead to variability in drug absorption and therapeutic efficacy.

Future Trends

1. **Nanotechnology**
 - Ongoing development of nanoparticles and nanoscale carriers to enhance drug solubility, stability, and controlled release within the uterine environment.
2. **Smart Drug Delivery Systems**
 - Innovations in formulations that respond to specific physiological stimuli (e.g., pH, temperature) for optimized drug release.
3. **Personalized Medicine**
 - Tailoring intrauterine delivery systems based on individual patient characteristics and specific medical conditions.
4. **Combination Therapies**
 - Exploring multifaceted approaches to co-deliver multiple drugs for synergistic effects in managing complex gynecological issues.
5. **Biodegradable Materials**
 - Continued research into biodegradable polymers for sustainable and environmentally friendly intrauterine drug delivery systems.[25]

CONCLUSION

In the future, novel drug delivery systems are poised to transform medicine by providing more effective, personalized, and targeted treatment options. These innovations will enhance patient outcomes, minimize side effects, and offer solutions for previously challenging diseases. However, continuous research, technological advancements, and collaboration among scientists, healthcare professionals, and regulatory authorities will be crucial in overcoming existing challenges and realizing the full potential of NDDS in clinical applications.

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