Al-Ameed Journal for Medical Research and Health Sciences

Volume 1 | Issue 1 Article 3

2023

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Recommended Citation

Shaker, Lina M.; Al-Amiery, Ahmed A.; and Kadhum, Abdul Amir H. (2023) "Advances in Drug Delivery Systems: A Mini-Review," *Al-Ameed Journal for Medical Research and Health Sciences*: Vol. 1 : Iss. 1 , Article 3.
Available at: https://doi.org/10.61631/3005-3188.1002

REVIEW

Advances in Drug Delivery Systems: A Mini-review

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Abstract

Drug delivery systems (DDS) refer to technologies designed to improve the safety and efficacy of drugs by controlling their release, absorption, and distribution in the body. DDS has gained significant attention due to its potential to enhance the therapeutic outcomes of various drugs. This mini-review article provides an overview of the current status of DDS. The article begins with a brief introduction to DDS, highlighting its importance in drug development and delivery. It also provides a historical background of DDS to provide context to its current developments. Next, the mini-review focuses on the various types of DDS, including oral, transdermal, injectable, inhalation, and implantable delivery systems. Each system is discussed, highlighting its advantages and limitations. The article then provides an in-depth discussion of recent advances in DDS, with particular emphasis on nanoparticle-based DDS. It covers the latest developments in smart, targeted, 3D printed, and controlled DDS, and highlights the challenges and future directions in these areas. Additionally, the article explores the safety concerns associated with DDS and the regulatory challenges in DDS development and approval. Finally, the mini-review concludes by discussing future trends in DDS and their potential impact on drug delivery and therapeutic outcomes. Overall, this mini-review provides a comprehensive overview of the current state of DDS and its potential to revolutionize drug delivery.

Keywords: Oral drug delivery, Immediate-release formulations, Modified-release, Transdermal drug, TDDS

Introduction

Drug delivery systems refer to the methods and techniques used to administer therapeutic agents to patients in a controlled and targeted manner. These systems can be used to improve the efficacy, safety, and convenience of drug therapy by delivering drugs directly to their site of action, reducing side effects, and optimizing drug dosing (Paunovska, Loughrey, & Dahlman, 2022). Drug delivery systems have evolved significantly over the years, with new technologies and approaches being developed to address the challenges associated with drug delivery. These technologies include nano-sized drug carriers, implantable devices, and controlled-release formulations, among others (Ansari et al., 2022). Advancements in drug delivery systems have revolutionized the field of medicine, allowing for more precise and effective drug administration. This mini-review aims to provide an overview of recent advances in drug delivery systems, highlighting their potential applications in various therapeutic areas (Sun et al., 2023). Drug delivery systems (DDS) play a vital role in the effective and targeted delivery of pharmaceutical agents to the desired site of action in the body. With the advent of nanotechnology and advancements in material science, there have been significant advances in the design and development of DDS, leading to improved therapeutic outcomes and reduced side effects. The application of DDS has become increasingly important in the treatment of diseases such as cancer, diabetes, and cardiovascular disorders, among others (Tiwari et al., 2012). The mini-review provides an overview of the recent developments in DDS. The article discusses various types of DDS, including liposomes, dendrimers, nanoparticles, and microspheres, and their

Received 10 March 2023; revised 24 March 2023; accepted 5 May 2023.
Available online 28 July 2023

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https://doi.org/10.61631/3005-3188.1002

applications in drug delivery. The mini-review also highlights the challenges and future directions of DDS research (Li et al., 2023b). The importance of DDS in the pharmaceutical industry and healthcare cannot be overstated, as it plays a crucial role in improving patient outcomes and reducing healthcare costs. This mini-review article provides a concise summary of the current state of DDS research and highlights the potential for further advancements in the field (Tabakoglu et al., 2023). Drug delivery systems have come a long way since the early days of medicine, when treatments were crude and often ineffective. The use of advanced drug delivery systems has revolutionized the field of pharmaceuticals, allowing for the targeted delivery of drugs to specific cells or tissues in the body. This has led to more effective treatments, improved patient outcomes, and reduced side effects (Wang et al., 2023). The history of drug delivery systems dates back to ancient times, with the use of plant extracts and other natural remedies to treat a range of ailments. However, it was not until the 19th century that modern drug delivery systems began to emerge, with the introduction of hypodermic needles and the development of injectable medications (Hari et al., 2023). Over the past century, drug delivery systems have continued to evolve and improve, with the introduction of new technologies. These advances have allowed for more precise drug targeting and controlled release, as well as the ability to bypass biological barriers that can limit the effectiveness of some medications (Langer & Peppas, 2003). This mini-review provides a brief overview of the history of drug delivery systems, as well as an examination of some of the most recent advances in this field. The article draws on a range of sources, including peer-reviewed research articles and other academic publications, to provide a comprehensive overview of this important area of pharmaceutical research. Table 1, represents a comparison of drug delivery systems.

Types of drug delivery systems

Oral drug delivery systems

Oral drug delivery systems are the most common route of drug administration due to its ease of use, non-invasive nature, and patient compliance. The oral route of drug administration involves delivering drugs to the gastrointestinal tract, where they undergo various processes of absorption, distribution, metabolism, and excretion. Different types of oral drug delivery systems are designed to overcome the challenges encountered in drug delivery, such as poor solubility, instability, and low bioavailability. This review article summarizes the different types of oral drug delivery systems and their advantages and limitations (Ahsan et al., 2023; Kong et al., 2023). Table 2, representing the different types of oral drug delivery systems.

Immediate-release formulations

Immediate-release formulations are the simplest and most common type of oral drug delivery system. They are designed to deliver drugs rapidly and achieve a desired therapeutic effect quickly. These formulations are available in various dosage forms such as tablets, capsules, and liquids. They disintegrate rapidly in the gastrointestinal tract to release the drug for absorption. However, immediate-release formulations have limitations, such as a short duration of action, frequent dosing, and potential side effects. Table 3 represents the types of Transdermal Drug Delivery Systems.

Modified-release formulations

Modified-release formulations are designed to overcome the limitations of immediate-release formulations. They release drugs slowly and achieve a sustained therapeutic effect over a prolonged period. These formulations are available in various types, such as delayed-release, extended-release,

Table 1. Drug delivery systems comparison (Aburahma, 2016; Dang & Guan, 2020; Dhiman et al., 2021).

Aspect	Liposomes	Polymeric Nanoparticles	Solid Lipid Nanoparticles	Ref.
Size	50–1000 nm	10–500 nm	50–1000 nm	Aburahma (2016)
Composition	Phospholipids	Polymeric materials (e.g. PLA, PLGA)	Lipids (e.g. triglycerides, fatty acids)	Aburahma (2016)
Stability	Unstable at high temperatures	Stable at high temperatures	Stable at high temperatures	Dang and Guan (2020)
Drug loading capacity	High	Moderate	High	Dang and Guan (2020)
Drug release profile	Can be tailored	Controlled release	Controlled release	Dang and Guan (2020)
Targeting capabilities	Limited	Can be enhanced with surface modifications	Limited	Dhiman et al. (2021)
Immunogenicity	Can induce immune responses	Low immunogenicity	Low immunogenicity	Dhiman et al. (2021)

Table 2. Different types of oral drug delivery systems (He et al., 2020; Hussain et al., 2020; Liu & Huang, 2019).

Types of Drug Delivery Systems	Description	Ref.
Immediate-Release Formulations	These formulations are designed to release the drug immediately upon ingestion. They are typically used for drugs that require rapid onset of action or have a short half-life. Examples include tablets, capsules, and syrups.	Liu and Huang (2019)
Modified-Release Formulations	These formulations are designed to release the drug over a prolonged period of time. They can be used to maintain a constant drug concentration over an extended period, improve drug efficacy, or reduce adverse effects. Examples include extended-release tablets, delayed-release capsules, and sustained-release pellets.	Hussain et al. (2020)
Targeted Drug Delivery Systems	These systems deliver drugs specifically to the site of action, while minimizing systemic exposure and reducing adverse effects. Examples include enteric-coated tablets, mucoadhesive systems, and pH-responsive nanoparticles.	He et al. (2020)
Nanoparticulate Drug Delivery Systems	These systems use nanoparticles to improve drug solubility, stability, and bioavailability.	He et al. (2020)

and controlled-release formulations. The delayed-release formulations are designed to release drugs in a specific part of the gastrointestinal tract, such as the small intestine or colon. The extended-release formulations release drugs slowly over an extended period, while the controlled-release formulations maintain drug levels within a narrow therapeutic range.

Targeted drug delivery systems

Targeted drug delivery systems are designed to deliver drugs to a specific site or tissue within the body. These systems can be achieved by various methods, such as ligand-targeted systems, pH-sensitive systems, and time-dependent systems. Ligand-targeted systems utilize specific ligands that bind to receptors on the target cells or tissues. pH-sensitive systems release drugs in response to changes in pH within the gastrointestinal tract. Time-dependent systems release drugs at a specific time after administration.

Nanoparticulate drug delivery systems

Nanoparticulate drug delivery systems involve the use of nanoparticles to deliver drugs to the gastrointestinal tract. These systems have advantages, such as improved drug solubility, enhanced bioavailability, and reduced toxicity. Nanoparticles can be made of various materials, such as lipids, polymers, and metals. These systems can also be functionalized to achieve targeted drug delivery to specific sites within the body.

Oral drug delivery systems have evolved over the years to overcome the challenges encountered in drug delivery. The different types of oral drug delivery systems offer advantages, such as improved drug solubility, enhanced bioavailability, reduced toxicity, and targeted drug delivery. However, each system has its limitations, and the choice of system depends on various factors, such as the physicochemical properties of the drug, the target site of action, and the desired therapeutic effect.

Transdermal drug delivery systems

Transdermal drug delivery systems (TDDS) are a type of drug delivery system that enables drugs to be absorbed through the skin for systemic effect. This route of administration is advantageous because it bypasses the gastrointestinal system and

Table 3. Types of transdermal drug delivery systems (Akhtar et al., 2020; Gheibi Hayat & Darroudi, 2019; Mishra & Bonde, 2020).

Type of Transdermal Drug Delivery System	Description	Examples	Ref.
Matrix system	Drug is embedded in a polymer matrix that controls the rate of drug release.	Nicotine patches, Fentanyl patches	He et al. (2020)
Reservoir system	Drug is contained in a reservoir compartment that is separated from the skin by a rate-controlling membrane.	Estradiol patches, Scopolamine patches	He et al. (2020)
Microelectronic system	Uses microelectronics to control drug release.	Iontophoresis patches	Mishra and Bonde (2020)
Osmotic system	Drug is released through a semipermeable membrane due to osmotic pressure generated by an osmotic agent.	Clonidine patches	Gheibi Hayat and Darroudi (2019)
Transfersome	Lipid vesicles that can penetrate the stratum corneum and release drugs in the deeper layers of the skin.	Lidocaine patches	Akhtar et al. (2020)

the first-pass effect, which can result in reduced drug efficacy and potential side effects. In this article, we will discuss the types of transdermal drug delivery systems, their advantages and limitations, and recent advancements in this field (Duong et al., 2023; He et al., 2023; Kolawole & Cook, 2023; Pardeshi et al., 2023).

Types of transdermal drug delivery systems

Matrix systems. These are the most common type of TDDS, in which the drug is dispersed within a polymeric matrix. The drug is released by diffusion through the polymer and absorption through the skin. Examples of matrix systems include patches for nicotine, fentanyl, and clonidine.

Reservoir systems. In this type of TDDS, the drug is contained within a reservoir and released through a membrane. The membrane controls the rate of drug delivery, and the drug is absorbed through the skin. Examples of reservoir systems include patches for nitroglycerin, estradiol, and testosterone.

Microstructured systems. These TDDS consist of microstructured arrays that are designed to penetrate the skin's outermost layer, the stratum corneum. This allows for improved drug absorption and increased drug delivery efficiency. Examples of microstructured systems include microneedle patches for insulin and vaccines.

Advantages and limitations of TDDS. TDDS have several advantages over other routes of administration. They provide controlled drug delivery, eliminate the need for frequent dosing, reduce the risk of gastrointestinal side effects, and improve patient compliance. Additionally, TDDS are non-invasive, making them more convenient and comfortable for patients. However, TDDS also have limitations. They are limited in the types of drugs that can be delivered, as only drugs with appropriate physicochemical properties can be absorbed through the skin. TDDS also have a limited drug loading capacity, and they may cause skin irritation or sensitization.

Recent advancements in TDDS. Recent advancements in TDDS include the use of novel materials and technologies to improve drug delivery efficiency and patient comfort. Examples include: Transdermal patches with smart release mechanisms, such as microneedles or electrical stimuli, to improve drug absorption.

Novel materials, such as hydrogels, nanoparticles, and liposomes, that can improve drug solubility and permeability. Combination therapy patches that deliver multiple drugs simultaneously.

Inhalation drug delivery systems

Inhalation drug delivery systems are medical devices used to administer medication directly into the lungs through inhalation. They are commonly used for the treatment of respiratory diseases such as asthma, chronic obstructive pulmonary disease (COPD), and cystic fibrosis. The advantage of inhalation drug delivery is that it allows for targeted delivery of medication directly to the site of action, thereby reducing systemic side effects and improving efficacy.

There are various types of inhalation drug delivery systems, including (Fink et al., 2012; Jude et al., 2023; Li et al., 2023a; Rau, 2015)

Metered-dose inhalers (MDIs). MDIs are handheld devices that deliver a measured dose of medication in aerosol form. They consist of a canister containing the medication, a propellant to generate the aerosol, and a metering valve to control the dose. MDIs are commonly used for the treatment of asthma and COPD.

Dry powder inhalers (DPIs). DPIs deliver medication in a dry powder form that is activated by the user's inhalation. DPIs do not require a propellant and are therefore more environmentally friendly than MDIs. DPIs are commonly used for the treatment of asthma and COPD.

Nebulizers. Nebulizers deliver medication in the form of a mist or aerosol that is generated by a compressor or ultrasonic device. Nebulizers are typically used for the treatment of severe asthma, COPD, and cystic fibrosis.

Soft mist inhalers (SMIs). SMIs are a newer type of inhaler that deliver medication in a slow-moving mist. They are designed to be more effective than MDIs and DPIs, particularly for patients with poor inhalation technique.

There are also various factors that can affect the efficacy of inhalation drug delivery systems, including the particle size and shape of the medication, the flow rate and volume of inhalation, and the design and performance of the inhaler device.

Implantable drug delivery systems

Implantable drug delivery systems (DDS) are a type of drug delivery system designed to provide sustained

and controlled release of therapeutic agents over an extended period by implanting a device or a system in the body. These systems have been developed for a variety of applications, including cancer treatment, pain management, hormonal therapy, and insulin delivery (Cong et al., 2023; Liu et al., 2023; Yoo et al., 2023; Zhang et al., 2023).

There are several types of implantable drug delivery systems, including

Implantable pumps. Implantable pumps are designed to deliver drugs continuously over an extended period. The pump is surgically implanted into the body and is programmed to release drugs at a specific rate and time interval. Examples of implantable pumps include osmotic pumps, electronically controlled pumps, and peristaltic pumps.

Implantable depots. Implantable depots are drug reservoirs that release drugs over an extended period. These depots can be designed to release drugs at a specific rate or in response to a trigger, such as a change in pH or temperature. Examples of implantable depots include biodegradable depots, non-biodegradable depots, and hydrogel depots.

Implantable microchips. Implantable microchips are small devices that are implanted under the skin and are programmed to release drugs in response to wireless signals. These microchips are currently being developed for the treatment of chronic diseases, such as diabetes and osteoporosis.

Implantable drug delivery systems offer several advantages over traditional drug delivery methods, including improved patient compliance, reduced side effects, and increased efficacy. However, these systems also have several challenges, including the risk of infection, the need for surgical implantation, and the potential for device failure.

Recent advances in drug delivery systems

Drug delivery systems (DDS) are used to improve the therapeutic efficacy of drugs by controlling their pharmacokinetics, pharmacodynamics and bioavailability. Over the past few decades, significant advances have been made in the development of novel drug delivery systems, including nanoparticles, liposomes, dendrimers, and hydrogels. These systems have been designed to overcome various biological barriers, such as the blood-brain barrier, and to target specific organs or tissues (Cong et al., 2023; Peng et al., 2023; Sandler et al., 2021; Sun et al., 2023; Tiwari et al., 2012; Zhang et al., 2023).

This mini-review will focus on recent advances in drug delivery systems, including their design, mechanisms, and applications.

Nanoparticles

Nanoparticles are submicron-sized particles that are typically composed of biodegradable and biocompatible materials such as polymers, lipids, and metals. They can be designed to deliver drugs to specific sites within the body, including tumors and the brain. Advances in nanoparticle technology have led to the development of several clinically approved drugs, including Doxil, Abraxane, and Onivyde (Barman et al., 2023).

One of the major challenges in nanoparticle drug delivery is achieving efficient drug release at the target site. Recently, a new class of nanoparticles, called stimulus-responsive nanoparticles, has been developed. These nanoparticles are designed to release drugs in response to specific stimuli, such as changes in pH, temperature, or light. For example, a recent study developed a pH-sensitive nanoparticle system that can selectively release drugs in response to the acidic environment of tumors.

Liposomes

Liposomes are spherical vesicles composed of phospholipids and cholesterol that can encapsulate hydrophilic or hydrophobic drugs. They are biodegradable, biocompatible, and can be modified to target specific cells or tissues. Several liposome-based drugs, such as Doxil and Myocet, have been approved for clinical use. Recent advances in liposome technology have focused on improving their stability and drug release kinetics. One approach is to modify the liposome surface with polyethylene glycol (PEG), a hydrophilic polymer that can increase the liposome circulation time in the bloodstream. Another approach is to use lipid bilayers that can respond to specific stimuli, such as temperature or light, to release drugs (Peng et al., 2023).

Dendrimers

Dendrimers are highly branched, nanoscale polymers that can encapsulate drugs within their interior or on their surface. They have a high degree of structural uniformity and can be modified with targeting ligands to deliver drugs to specific cells or tissues. Dendrimers have shown promise in drug delivery applications for cancer, inflammation, and infection. Recent advances in dendrimer technology have focused on improving their biocompatibility and

stability. One approach is to modify the dendrimer surface with hydrophilic polymers, such as PEG, to reduce their immunogenicity and improve their circulation time in the bloodstream. Another approach is to use biodegradable dendrimers that can be metabolized by the body into non-toxic products.

Hydrogels

Hydrogels are three-dimensional networks of hydrophilic polymers that can absorb large amounts of water. They have a high degree of biocompatibility and can be designed to release drugs in a controlled manner over extended periods of time. Hydrogels have shown promise in drug delivery applications for wound healing, tissue engineering, and drug delivery to the eye. Recent advances in hydrogel technology have focused on improving their mechanical properties and drug release kinetics. One approach is to incorporate nanoparticles or fibers into the hydrogel matrix to improve its strength and elasticity. Another approach is to use stimuli-responsive hydrogels that can release drugs in response to specific stimuli, such as temperature, pH, or light.

Smart drug delivery systems

Smart drug delivery systems (SDDS) are advanced drug delivery systems that can target and release drugs at specific sites in the body with high specificity and efficiency. SDDS can be designed to respond to internal or external stimuli, which may include pH, temperature, light, enzymes, and magnetic or electric fields. The use of SDDS offers many advantages, including improved drug efficacy, reduced toxicity, and minimized side effects. This article provides an overview of SDDS, their classification, and the principles behind their design and development (Barman et al., 2023; Kim & Matsunaga, 2017; Maja et al., 2020; Peng et al., 2023; Thirupathi et al., 2023).

Classification of smart drug delivery systems

SDDS can be classified based on their mode of drug release, target site, and triggering mechanism. Based on the mode of drug release, SDDS can be categorized as passive or active. Passive systems rely on the drug diffusion mechanism to release the drug, while active systems involve external stimuli to trigger drug release. Based on the target site, SDDS can be classified as systemic or localized. Systemic SDDS targets organs such as the liver or lungs, while localized SDDS is designed to deliver drugs to specific sites, such as tumors or inflamed tissues. Based on the triggering mechanism, SDDS can be classified as physical, chemical, or biological.

Design and development of smart drug delivery systems

The design and development of SDDS involve the selection of appropriate materials and stimuli-responsive mechanisms. SDDS can be designed using various materials. The selection of material depends on the specific application, as well as the desired drug release profile. Stimuli-responsive mechanisms include pH-sensitive, temperature-sensitive, and enzyme-sensitive mechanisms, among others. For example, pH-sensitive systems can release drugs in response to changes in pH levels, such as the low pH environment of tumors. Temperature-sensitive systems can release drugs in response to changes in temperature, such as the hyperthermic conditions of inflamed tissues.

Applications of smart drug delivery systems

SDDS has many potential applications in medicine, including cancer therapy, diabetes treatment, and gene therapy. In cancer therapy, SDDS can target tumors specifically and release drugs in response to the acidic tumor microenvironment. In diabetes treatment, SDDS can release insulin in response to changes in glucose levels. In gene therapy, SDDS can deliver therapeutic genes to specific sites in the body and release them in response to specific triggers.

Smart drug delivery systems represent a significant advancement in drug delivery technology. The design and development of SDDS require a deep understanding of the specific application, as well as the materials and mechanisms involved. SDDS has the potential to improve drug efficacy and reduce toxicity, and its applications in medicine are widespread.

Targeted drug delivery systems (Jain et al., 2018; Kumari et al., 2016; Zhao et al., 2020)

Targeted drug delivery (TDD) is a rapidly growing field that involves the development of drug delivery systems that selectively deliver therapeutic agents to specific target sites in the body. TDD systems have shown tremendous potential in improving drug efficacy, reducing side effects, and enhancing patient outcomes. This mini-review provides an overview of TDD systems, including their classification, advantages, limitations, and applications in various disease conditions.

Classification of TDD systems

TDD systems can be broadly classified into two categories: passive and active targeting systems. Passive targeting systems rely on the inherent physiological properties of the target site, such as permeability and

retention, to accumulate the drug at the desired site. Examples of passive targeting systems. On the other hand, active targeting systems use specific ligands, antibodies, or receptors to target the drug to the desired site. Examples of active targeting systems include antibody-drug conjugates, peptide-targeted nanoparticles, and aptamer-targeted drug delivery systems.

Advantages of TDD systems

TDD systems offer several advantages over traditional drug delivery methods, including:

Improved drug efficacy. TDD systems can deliver drugs directly to the target site, thereby reducing the dose required for therapeutic effect and minimizing systemic toxicity.

Reduced side effects. TDD systems can minimize off-target effects, reducing the risk of adverse reactions and improving patient compliance.

Enhanced drug stability. TDD systems can protect drugs from degradation and clearance, thereby prolonging their half-life and improving their pharmacokinetics.

Better disease control. TDD systems can improve disease control by providing sustained drug release and overcoming drug resistance.

Limitations of TDD systems

Despite their potential advantages, TDD systems face several challenges, including:

Complexity of design and synthesis. TDD systems require complex design and synthesis processes, which can be time-consuming and expensive.

Lack of specificity. TDD systems may not always achieve the desired level of specificity, leading to off-target effects.

Clearance by the reticuloendothelial system (RES). TDD systems may be cleared by the RES before reaching the target site, reducing their efficacy.

Immunogenicity. TDD systems that use biological ligands or antibodies may elicit an immune response, limiting their therapeutic potential.

Applications of TDD systems

TDD systems have shown promise in a wide range of disease conditions, including cancer, inflammatory diseases, cardiovascular diseases, and neurological disorders. Examples of TDD systems in clinical development or use include:

Abraxane®. A nanoparticle-based formulation of paclitaxel used in the treatment of breast and non-small cell lung cancer.

Mylotarg®. An antibody-drug conjugate used in the treatment of acute myeloid leukemia.

Depo-Provera®. A long-acting injectable contraceptive that uses biodegradable microspheres for sustained release of the contraceptive agent.

Nanoxel®. A nanoformulation of docetaxel used in the treatment of advanced breast cancer.

3D printing in delivery systems drug (Goyanes et al., 2015; Pawar & Edgar, 2017; Sandler et al., 2021; Ventola, 2014)

3D printing technology has revolutionized the way drugs are delivered, as it allows the manufacture of complex and customized drug delivery systems with high precision and reproducibility. 3D printing enables the production of drug delivery systems with various geometries, shapes, sizes, and controlled release patterns. This mini-review article will discuss the current state of 3D printing in drug delivery systems, the various techniques used in 3D printing, and their applications.

3D printing techniques in drug delivery

Several 3D printing techniques are currently being used in drug delivery systems, including fused deposition modeling (FDM), stereolithography (SLA), and inkjet printing. FDM is a commonly used technique that melts a thermoplastic material and deposits it layer-by-layer to create a solid object. SLA uses a liquid resin that is selectively cured by a laser to create a 3D object. Inkjet printing is a technique that deposits droplets of a liquid drug formulation onto a substrate to create a patterned layer. Other 3D printing techniques used in drug delivery include selective laser sintering (SLS), powder bed fusion (PBF), and binder jetting.

Applications of 3D printing in drug delivery

3D printing technology has enabled the development of drug delivery systems with precise dosing, personalized treatment, and controlled release patterns. 3D printing can also improve patient compliance by reducing the number of doses needed and improving drug stability. One

significant application of 3D printing in drug delivery is the development of patient-specific implants, such as dental implants, orthopedic implants, and stents. These implants can be designed and printed to fit the patient's anatomy, reducing the risk of complications and improving treatment outcomes. 3D printing has also been used to develop dosage forms with multiple drugs, enabling the simultaneous delivery of drugs with different release rates and profiles.

Challenges and future directions

Despite the potential benefits of 3D printing in drug delivery, several challenges remain. One of the main challenges is the lack of regulatory guidelines for 3D printed drug delivery systems, which can slow down the approval process. Another challenge is the limited availability of materials that can be used for 3D printing drug delivery systems, and the need for specialized equipment and expertise to produce these systems. In the future, the development of new materials and equipment, as well as the establishment of regulatory guidelines, will enable the widespread use of 3D printing in drug delivery.

Controlled drug delivery systems (Bastioli, 2020; Patil & Sawant, 2014; Wu et al., 2019)

Controlled drug delivery systems refer to techniques that are employed to maintain a constant release of drugs in a patient's body for an extended period. The main objective of controlled drug delivery systems is to ensure that a therapeutic dose of medication is delivered to a patient's system at the right time, in the right place, and in the right amount. This approach offers several advantages over conventional drug delivery methods, such as reducing toxicity and side effects, improving patient compliance, and increasing drug efficacy. In this mini-review, we will discuss the different types of controlled drug delivery systems and their applications.

Types of Controlled Drug Delivery Systems: There are several types of controlled drug delivery systems, which can be classified into two broad categories: oral and non-oral drug delivery systems.

Oral controlled drug delivery systems

Oral controlled drug delivery systems are used to deliver drugs via the gastrointestinal tract. These systems can be divided into three main types:

a. Immediate Release Systems: Immediate release systems release the drug rapidly after ingestion, allowing for quick onset of action.
b. Delayed Release Systems: Delayed release systems are designed to delay the release of the drug until it reaches a specific part of the gastrointestinal tract.
c. Controlled Release Systems: Controlled release systems are designed to release the drug over an extended period, ensuring that the patient receives a constant dose of medication.

Non-oral controlled drug delivery systems

Non-oral controlled drug delivery systems are used to deliver drugs through routes other than the gastrointestinal tract. Some of the common non-oral controlled drug delivery systems include:

a. Transdermal Drug Delivery Systems: Transdermal drug delivery systems are used to deliver drugs through the skin. These systems can provide a constant dose of medication over a prolonged period.
b. Implantable Drug Delivery Systems: Implantable drug delivery systems are surgically implanted devices that release drugs directly into the bloodstream or a specific area of the body.
c. Inhalation Drug Delivery Systems: Inhalation drug delivery systems are used to deliver drugs through the respiratory tract. These systems are commonly used to treat respiratory diseases such as asthma.

Applications of controlled drug delivery systems

Controlled drug delivery systems have several applications in the field of medicine, some of which include:

i. Cancer Treatment: Controlled drug delivery systems are commonly used in cancer treatment to deliver chemotherapy drugs directly to the tumor site, reducing toxicity and improving efficacy.
ii. Pain Management: Controlled drug delivery systems are used to provide long-lasting pain relief for patients suffering from chronic pain.
iii. Hormone Replacement Therapy: Controlled drug delivery systems are used to provide a constant dose of hormones to patients undergoing hormone replacement therapy.
iv. Diabetes Management: Controlled drug delivery systems are used to provide a constant dose of insulin to diabetic patients, improving blood sugar control.

Controlled drug delivery systems offer several advantages over conventional drug delivery

methods. They can provide a constant dose of medication, reduce toxicity and side effects, improve patient compliance, and increase drug efficacy. The development of new and improved controlled drug delivery systems is crucial to the advancement of medicine and the improvement of patient outcomes.

Challenges and future directions (Arya et al., 2021; Farokhzad & Langer, 2019; Kumar & Kharb, 2021; Li et al., 2018)

Drug delivery systems (DDS) are used to enhance the therapeutic efficacy of drugs and improve patient compliance. DDS can be classified into several categories, including oral, transdermal, inhalation, intravenous, and subcutaneous. However, the safety concerns associated with DDS remain a major challenge for their successful implementation in clinical practice. This mini-review article discusses the safety concerns associated with DDS and the future directions for their development.

Safety concerns associated with drug delivery systems

Toxicity

DDS may cause toxicity due to the release of high concentrations of drugs into the body. This can result in adverse effects, such as organ damage, allergic reactions, and even death. The toxicity of DDS can be reduced by optimizing the drug dosage, reducing the particle size of the drug, and using biocompatible materials.

1. Drug-drug interactions: DDS may interact with other drugs taken by the patient, leading to adverse drug reactions. The interactions may be pharmacodynamic or pharmacokinetic in nature. The risk of drug-drug interactions can be minimized by careful selection of drugs and close monitoring of the patient's response.
2. Device-related complications: DDS devices, such as pumps, catheters, and needles, may cause complications, such as infection, tissue damage, and mechanical failure. The risk of device-related complications can be minimized by proper training of healthcare providers and patients, regular maintenance of devices, and strict adherence to aseptic techniques.
3. Patient-related factors: Patient-related factors, such as age, weight, and comorbidities, may affect the safety and efficacy of DDS. Elderly patients, for example, may have reduced renal or hepatic function, which may alter the pharmacokinetics of drugs. Patients with comorbidities, such as heart disease or diabetes, may be more susceptible to drug interactions and adverse effects.

Future directions for DDS development

1. Targeted drug delivery: Targeted drug delivery aims to deliver drugs to specific tissues or cells, thereby reducing the risk of toxicity and improving efficacy. Targeted drug delivery can be achieved using various approaches.
2. Personalized medicine: Personalized medicine aims to tailor drug therapy to individual patients based on their genetic and molecular characteristics. DDS can play a key role in personalized medicine by delivering drugs in a patient-specific manner.
3. Smart drug delivery systems: Smart drug delivery systems use sensors and feedback mechanisms to control drug release based on physiological signals, such as pH, temperature, or glucose levels. Smart drug delivery systems can improve drug efficacy and safety by reducing the risk of over- or under-dosing.
4. Biodegradable materials: Biodegradable materials can reduce the risk of device-related complications by eliminating the need for device removal. Biodegradable materials can also reduce the risk of toxicity by eliminating the need for long-term drug exposure.

Regulatory challenges in drug delivery systems (Ahn et al., 2018; Bawa et al., 2013; Torchilin, 2000)

Regulatory challenges in drug delivery systems can be broadly classified into two categories: preclinical and clinical challenges.

Preclinical challenges involve the development and testing of drug delivery systems before they are tested in humans. Preclinical testing involves the evaluation of the safety and efficacy of drug delivery systems in animals. The regulatory challenges associated with preclinical testing include the lack of standardized testing protocols, the need for appropriate animal models, and the assessment of the long-term safety of drug delivery systems.

Clinical challenges involve the testing of drug delivery systems in humans. Clinical testing is a critical step in the development of drug delivery systems and is necessary to evaluate the safety and efficacy of these systems in humans. The regulatory challenges associated with clinical testing include the selection of appropriate patient populations, the

design of clinical trials, and the evaluation of long-term safety and efficacy.

In addition to preclinical and clinical challenges, drug delivery systems may face additional regulatory challenges related to manufacturing, labeling, and marketing. These challenges include the need for appropriate quality control measures, the evaluation of manufacturing processes, and the development of appropriate labeling and marketing strategies.

Future directions

To overcome the regulatory challenges associated with drug delivery systems, several future directions can be explored. These directions include:

1. Standardization of preclinical testing protocols: The development of standardized testing protocols can help ensure that drug delivery systems are evaluated consistently and accurately in preclinical studies.
2. Use of appropriate animal models: The selection of appropriate animal models is critical to the success of preclinical studies. The use of relevant and predictive animal models can help improve the translatability of preclinical data to humans.
3. Evaluation of long-term safety: The evaluation of long-term safety is critical for the development of drug delivery systems. Long-term safety studies can help identify potential safety concerns and improve the overall safety profile of drug delivery systems.
4. Development of personalized drug delivery systems: Personalized drug delivery systems can improve therapeutic efficacy and reduce side effects by tailoring drug delivery to individual patients.
5. Collaboration between industry, academia, and regulators: Collaboration between industry, academia, and regulators can help identify and address regulatory challenges associated with drug delivery systems. This collaboration can also help facilitate the development and commercialization of new drug delivery systems.

Future trends in drug delivery systems (Domb & Khan, 2017; Peer et al., 2007; Wang et al., 2019)

Targeted drug delivery systems

Targeted drug delivery (TDD) systems aim to improve drug efficacy and reduce toxicity by delivering drugs to specific sites in the body. TDD systems can be divided into two categories: passive and active targeting. Passive targeting is achieved by the use of nanocarriers that exploit the unique features of tumor tissue such as the enhanced permeability and retention (EPR) effect. Active targeting is achieved by the use of ligands that bind to specific receptors expressed on the surface of cancer cells. The development of TDD systems has the potential to revolutionize cancer treatment by improving drug efficacy while reducing side effects. Several TDD systems have been developed, which have shown promising results in preclinical and clinical studies.

Implantable devices

Implantable devices are another promising area of DDS that provides long-term drug delivery. These devices can be implanted in various parts of the body, including the brain, to deliver drugs directly to the site of action. Recent advances in nanotechnology have led to the development of implantable devices that can release drugs in a controlled manner for extended periods. These devices can be remotely controlled, allowing for precise drug delivery.

Biodegradable polymers

Biodegradable polymers are becoming increasingly popular in DDS due to their biocompatibility and ability to release drugs in a controlled manner. Biodegradable polymers can be designed to degrade at specific rates, allowing for sustained drug release over a defined period. The use of biodegradable polymers in DDS has the potential to improve patient compliance by reducing the frequency of drug administration.

3D printing

3D printing has gained significant attention in recent years in the pharmaceutical industry. 3D printing can be used to produce customized drug delivery devices, such as tablets and implants, with specific drug release profiles. The use of 3D printing in DDS has the potential to revolutionize drug development and manufacturing by enabling the rapid production of personalized drug delivery devices.

DDS has the potential to revolutionize drug development and improve patient outcomes. The future of DDS is focused on advanced technologies that aim to increase therapeutic efficacy while minimizing drug toxicity and side effects. Targeted drug delivery, implantable devices, biodegradable polymers, and 3D printing are among the most promising areas of DDS. These technologies have the potential to transform the pharmaceutical industry by enabling the development of more effective and personalized drug delivery systems.

The differences between extended release tablets, delayed-release capsules, and sustained-release pellets

Extended-release tablets, delayed-release capsules, and sustained-release pellets are all different types of drug formulations designed to release medication slowly over time. However, there are some important differences between them (Aburahma, 2016). Extended-release tablets are designed to release medication over an extended period of time, usually between 8 and 12 h. These tablets have a special coating that slowly dissolves in the stomach, releasing medication in a controlled manner. The active ingredient is usually mixed with a substance that swells when it comes into contact with stomach acid, which helps to control the release of the medication (Dang & Guan, 2020; Dhiman et al., 2021). Delayed-release capsules, on the other hand, are designed to release medication at a specific point in the digestive tract, usually in the small intestine. These capsules have a special coating that is resistant to stomach acid, allowing the medication to pass through the stomach and release in the intestine. Delayed-release capsules are often used for medications that can be destroyed by stomach acid, or for drugs that are intended to act on the small intestine (He et al., 2020; Hussain et al., 2020; Liu & Huang, 2019). Sustained-release pellets are a form of drug formulation that involves small pellets or beads that are coated with layers of medication. The pellets are designed to release medication over an extended period of time, usually between 12 and 24 h. The layers of medication are designed to dissolve at different rates, which helps to control the release of the medication (Akhtar et al., 2020; Gheibi Hayat & Darroudi, 2019; Mishra & Bonde, 2020).

In summary, extended-release tablets, delayed-release capsules, and sustained-release pellets are all drug formulations designed to release medication slowly over time, but they differ in terms of their release mechanism and target location within the digestive tract.

Conclusion

In conclusion, the field of drug delivery systems has made significant progress over the years in addressing the challenges associated with drug administration. Continuous research and development have resulted in the development of novel drug delivery systems that can significantly improve patient outcomes. However, the complexity of drug delivery systems requires a multidisciplinary approach involving researchers, clinicians, and other stakeholders. Collaborative efforts between these groups are essential to developing safe and effective drug delivery systems that can revolutionize the way we treat diseases. The future of drug delivery systems is promising, and we can expect to see further advancements in this field in the coming years.

Funding

Universiti Kebangsaan Malaysia provided funding for a portion of the study.

Acknowledgments

The support provided by Universiti Kebangsaan Malaysia (UKM) is acknowledged by the authors.

Conflicts of Interest

The authors claim they have no competing interests.

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