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Smart drug delivery systems: The integration of wearable and implantable technologies for precision medicine

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Abstract

Smart drug delivery systems (DDS) represent a transformative approach to modern healthcare by integrating advanced technologies such as nanotechnology, biomaterials, and wearable devices. These systems address limitations of traditional DDS, including poor bioavailability, systemic side effects, and non-specific targeting, by enabling precise, controlled, and targeted drug release. Wearable and implantable technologies, such as insulin pumps, transdermal patches, microneedle arrays, and electroceutical devices, enhance patient compliance and therapeutic outcomes through automated and non-invasive drug administration. Nanotechnology-based carriers like liposomes and nanoparticles improve drug solubility and stability while enabling site-specific action. Stimuli-responsive DDS further refine precision by releasing drugs in response to physiological triggers such as pH or temperature changes. The integration of artificial intelligence (AI), 3D printing, and biodegradable materials is paving the way for personalized medicine by enabling patient-specific formulations and programmable drug delivery. These advancements are particularly impactful in treating chronic diseases, cancer, and genetic disorders. By minimizing off-target effects and optimizing pharmacokinetics, smart DDS improve safety and efficacy while reducing dosing frequency. This review highlights the evolution of DDS from conventional systems to cutting-edge wearable technologies and explores their mechanisms, advantages, and future scope in revolutionizing healthcare efficiency

Keywords: Smart Drug Delivery Systems; Nanotechnology-based Carriers; Wearable Drug Delivery Devices; Stimuli-responsive Drug Release; Personalized Medicine

1. Introduction

In recent years, the paradigm of healthcare has shifted from a one-size-fits-all approach to a more individualized and patient-centric model known as precision medicine. This approach aims to tailor medical treatment to the individual characteristics of each patient, taking into account genetic, environmental, and lifestyle factors. A critical component in realizing the full potential of precision medicine is the development of smart drug delivery systems that can offer personalized, controlled, and responsive therapeutic interventions.

Conventional drug delivery methods, such as oral or injectable formulations, often suffer from limitations including poor bioavailability, lack of site-specific targeting, frequent dosing requirements, and an inability to adapt to the patient's real-time physiological conditions. These challenges not only reduce therapeutic efficacy but also increase the risk of adverse effects and reduce patient compliance. To address these issues, researchers and biomedical engineers have turned to the integration of wearable and implantable technologies into drug delivery platforms.

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Wearable drug delivery devices—such as smart patches, microneedle systems, and portable infusion pumps—offer non-invasive or minimally invasive options for continuous or on-demand drug administration. These systems often incorporate sensors that monitor physiological parameters like glucose levels, body temperature, or heart rate, enabling real-time feedback and adaptive dosing. On the other hand, implantable drug delivery systems, including microchips, osmotic pumps, and biodegradable implants, provide long-term, site-specific, and programmable drug release capabilities, often within deep tissue environments. The integration of these advanced technologies with wireless communication, biosensors, and artificial intelligence further enhances the autonomy, precision, and safety of drug delivery. Such systems are particularly valuable in the management of chronic diseases like diabetes, cancer, and cardiovascular disorders, where long-term monitoring and adaptable treatment strategies are essential.

This manuscript provides a comprehensive overview of the current landscape of smart drug delivery systems, focusing on the design, functionality, and application of wearable and implantable devices. It also explores the technological advancements, clinical benefits, challenges, and regulatory considerations associated with these systems, highlighting their potential to transform the future of precision medicine.

2. Overview of Drug Delivery Systems

Drug delivery systems (DDS) are designed to administer therapeutic agents efficiently, ensuring optimal drug absorption, distribution, and release while minimizing side effects(1). These systems enhance treatment efficacy by controlling the rate, time, and site of drug release, improving patient compliance and safety(2). Traditional DDS include oral tablets, capsules, injectables, and topical formulations, which rely on passive diffusion and systemic circulation(3). However, advanced drug delivery technologies have emerged to address limitations such as poor bioavailability and frequent dosing(4). Controlled-release systems, such as transdermal patches, biodegradable implants, and osmotic pumps, allow for prolonged and steady drug release, reducing dosing frequency and enhancing patient convenience(5). Targeted DDS, including monoclonal antibody-conjugated nanoparticles and liposomes, deliver drugs selectively to diseased tissues or cells, minimizing off-target effects and improving therapeutic outcomes(6). Nanotechnology-based carriers, such as micelles, dendrimers, and solid lipid nanoparticles, enhance drug solubility, stability, and permeability, particularly for poorly water-soluble drugs(7). Stimuli-responsive DDS release drugs in response to specific physiological triggers like pH, temperature, or enzymes, ensuring precise and timely drug action(8). Gene delivery systems utilizing viral and non-viral vectors are also being developed for advanced therapies, including genetic disorders and cancer treatment(9). As research progresses, the integration of biotechnology, 3D printing, and smart materials is expected to revolutionize DDS, enabling personalized medicine and improved therapeutic precision(10). The continuous advancement in drug delivery technology will significantly enhance drug efficacy, patient outcomes, and overall healthcare efficiency(11).

2.1. Smart Drug Delivery in Modern Healthcare

In modern healthcare, the need for smart drug delivery systems is more critical than ever(12). Traditional drug delivery methods often suffer from limitations such as poor bioavailability, systemic side effects, and non-specific targeting(13). Smart drug delivery systems address these challenges by ensuring precise, controlled, and targeted drug release, thereby enhancing therapeutic efficacy while minimizing side effects(14). One key advantage of smart drug delivery is its ability to deliver drugs specifically to the affected site, reducing damage to healthy tissues(15). This is particularly crucial in treating diseases like cancer, where targeted therapy can improve patient outcomes and reduce toxicity(16). Additionally, these systems can provide controlled drug release, maintaining optimal therapeutic levels over extended periods, which improves patient compliance and reduces dosing frequency(17). Advancements in nanotechnology, biomaterials, and responsive carriers (such as pH-sensitive or temperature-sensitive systems) have further improved drug delivery precision(18), for example, nanoparticles and liposomes enable enhanced drug penetration in targeted tissues, while For hydrogels and microneedles allow for localized and sustained drug release(19). Gene therapy and biologics also benefit from smart carriers that protect delicate molecules from degradation and enhance cellular uptake(20). The growing burden of chronic diseases, antibiotic resistance, and the demand for personalized medicine further highlight the importance of smart drug delivery(21). By integrating nanotechnology, biomaterials, and artificial intelligence, the future of drug delivery promises safer, more effective, and patient-friendly therapeutic solutions, ultimately revolutionizing modern medicine(22).

The primary objective of this review is to explore and analyze advancements in drug delivery systems (DDS) to enhance therapeutic efficacy, safety, and patient compliance. This review aims to provide a comprehensive understanding of various DDS, their mechanisms, and their impact on modern healthcare. The key objective is to assess conventional and advanced DDS, including oral, injectable, transdermal, and implantable systems. By comparing these systems, this review highlights their advantages, limitations, and applications in various medical fields. Additionally, it aims to examine controlled and targeted drug delivery approaches, focusing on technologies that improve drug stability, bioavailability, and site-specific action. This review seeks to provide insights into future directions in DDS research, fostering innovation and advancements that can improve drug administration, treatment outcomes, and overall healthcare efficiency.

3. Smart Drug Delivery Systems: Concept and Evolution

A drug delivery system (DDS) refers to a technology designed to transport a pharmaceutical compound to a specific site in the body, ensuring controlled drug release, enhanced therapeutic efficacy, and minimized side effects(23). DDS encompasses various formulations and devices that regulate the rate, time, and location of drug administration, thereby optimizing drug absorption, distribution, metabolism, and excretion(24). The working principle of a DDS depends on its design and mechanism of action. Conventional systems, such as tablets, capsules, and injectables, rely on passive diffusion, where the drug dissolves and enters systemic circulation. However, advanced DDS are engineered for controlled, sustained, or targeted release(25). Controlled-release systems, such as transdermal patches and polymer-based implants, release drugs at a predetermined rate, maintaining steady plasma drug levels and improving patient compliance(26). Targeted drug delivery utilizes ligands, antibodies, or nanoparticles to direct drugs specifically to diseased cells or tissues, minimizing off-target effects(27).

Nanotechnology-based DDS, such as liposomes, micelles, and dendrimers, enhance drug solubility and stability, allowing efficient drug transport across biological barriers(28). Stimuli-responsive systems release drugs in response to physiological changes, such as pH variations, temperature shifts, or enzymatic activity, ensuring site-specific and controlled drug action(29), the principle behind DDS is to optimize drug pharmacokinetics and pharmacodynamics, improving therapeutic outcomes while reducing toxicity(30). Continuous advancements in materials science, biotechnology, and nanomedicine are further refining DDS, making drug therapy more effective, personalized, and patient-friendly(31).

Table 1 Classification of Smart Drug Delivery Systems Based on Device Type, Functional Features, and Therapeutic Applications

Drug Delivery System	Examples	Advantages
Oral Delivery	Tablets, Capsules	Convenient, non-invasive, patient-friendly
Injectable Delivery	IV, IM, SC injections	Fast drug action, high bioavailability
Transdermal Systems	Nicotine patches, Hormonal patches	Continuous drug release, non-invasive
Nanoparticle-based Delivery	Liposomes, Micelles, Dendrimers	Improved bioavailability, targeted delivery
Wearable Drug Delivery	Insulin pumps, Wearable injectors	Real-time monitoring, automated dosing
Implantable Systems	Microchip implants, Osmotic pumps	Long-term drug release, reduced dosing frequency
Gene Therapy Delivery	Viral & Non-viral vectors	Precise genetic modification, potential for disease cure

3.1. Historical development and Milestones of Drug Delivery Systems

The evolution of drug delivery systems (DDS) has progressed from simple formulations to advanced, targeted therapies. The earliest drug delivery methods date back to ancient civilizations, where herbs and natural extracts were administered orally or topically(32). The 19th and early 20th centuries, the development of basic dosage forms like tablets, capsules, and injectables, marking a significant advancement in drug administration(33). A major milestone was the introduction of controlled-release systems in the mid-20th century. In the 1950s, polymer-based DDS emerged, enabling sustained drug release(34). The 1970s, the development of transdermal patches, providing a non-invasive and controlled drug release method for conditions like pain management and hormonal therapy(35). The 1980s and 1990s witnessed groundbreaking advancements in nanotechnology, leading to the introduction of liposomes for drug encapsulation, enhancing drug stability and targeted delivery(36). The approval of the first liposomal drug, Doxil, in

1995, marked a milestone in cancer treatment. Around the same time, microspheres and biodegradable implants were developed, further revolutionizing drug release control(37). The 21st century has seen rapid growth in gene therapy, personalized medicine, and smart DDS. Nanoparticles, micelles, and dendrimers have been widely explored for targeted drug delivery, while stimuli-responsive systems release drugs based on environmental triggers(38). Advances in 3D printing and AI-driven drug formulation are shaping the future of DDS(39). The continuous innovations in DDS have transformed drug therapy, improving treatment efficacy, reducing side effects, and paving the way for more personalized and precise medicine(40).

3.2. Current Trends and Future Scope of Drug Delivery Systems

The field of drug delivery systems (DDS) is evolving rapidly, driven by advancements in nanotechnology, biotechnology, and personalized medicine(41). Current trends focus on targeted, controlled, and smart drug delivery to enhance therapeutic efficacy while minimizing side effects(42). One significant trend is the development of nanotechnology-based carriers, such as liposomes, nanoparticles, micelles, and dendrimers, which improve drug solubility, bioavailability, and precision in targeting specific cells(43). These systems are widely used in cancer therapy, gene therapy, and neurological disorders(44). Another key advancement is stimuli-responsive DDS, which release drugs in response to physiological changes such as pH, temperature, or enzyme activity, ensuring precise and localized drug action(45). The integration of biodegradable polymers in controlled-release formulations, including transdermal patches, implants, and injectable hydrogels, is also gaining momentum(46). 3D printing technology is emerging as a game-changer, enabling the fabrication of patient-specific drug formulations with precise dosing and release profiles(47), the future of DDS lies in personalized medicine, where artificial intelligence (AI) and big data will help design customized drug delivery strategies based on an individual's genetic and metabolic profile(48). Gene and cell-based drug delivery is another promising area, with advancements in viral and non-viral vectors enhancing the precision of gene therapies(49). Additionally, the development of wireless, implantable drug delivery devices and biodegradable electronic systems will revolutionize real-time, programmable drug administration. As research continues, DDS will play a crucial role in enhancing therapeutic outcomes, reducing drug resistance, and improving overall healthcare efficiency(50).

4. Wearable Technologies and their mechanisms and working principles in Drug Delivery:

Wearable drug delivery devices are medical technologies designed to administer medications in a controlled, efficient, and patient-friendly manner(51). These devices improve adherence, minimize side effects, and enhance therapeutic outcomes. The most common types include:

- Insulin Pumps: Widely used by diabetic patients, insulin pumps deliver a continuous or bolus dose of insulin subcutaneously, mimicking natural insulin secretion. These pumps often integrate with continuous glucose monitors (CGMs) to adjust insulin delivery based on real-time glucose readings(52). These devices deliver insulin subcutaneously through a catheter. They use programmed infusion rates or real-time glucose feedback from continuous glucose monitors (CGMs) to regulate insulin doses. The pump releases rapid-acting insulin in basal (continuous) and bolus (on-demand) modes to maintain blood glucose levels(53).
- Transdermal Patches: These patches deliver drugs through the skin into systemic circulation. Examples include nicotine patches for smoking cessation, fentanyl patches for pain relief, and hormonal patches for contraception(54). Some patches utilize microneedles or iontophoresis to enhance drug absorption(55). These patches rely on passive diffusion to transport drugs across the skin barrier into systemic circulation. The drug is stored in a reservoir or matrix and slowly released over time. Some patches incorporate enhancement techniques like microneedles or iontophoresis to increase skin permeability and improve absorption(56).
- Wearable Injectors: Also known as on-body delivery systems, these devices administer high-viscosity biologic drugs over extended periods(57). They are commonly used for conditions like rheumatoid arthritis and cancer, allowing self-administration without frequent hospital visits(58). Also known as on-body delivery systems, these devices use mechanical or electronic infusion mechanisms to deliver drugs subcutaneously over a controlled period. They are often prefilled with biologic drugs and automatically administer precise doses upon activation(59).
- Electroceutical Drug Delivery Devices: These patches use mild electrical currents (iontophoresis) to increase skin permeability, enhancing drug penetration. This technology is used for localized pain management and transdermal drug administration(60). These patches use iontophoresis, applying a low electrical current to push charged drug molecules through the skin. This method enhances drug penetration, particularly for localized pain relief and dermatological treatments(61).
- Micro-needle Patches: These contain tiny, dissolvable or hollow microneedles that painlessly penetrate the skin to deliver drugs directly into the bloodstream. They are emerging as an alternative to traditional injections for

vaccines and insulin delivery(62). These patches contain tiny microneedles that painlessly penetrate the skin's outer layer, allowing rapid drug absorption into capillaries. They can be dissolvable (biodegradable) or hollow (drug-filled) for controlled release(63).

Wearable drug delivery devices are revolutionizing patient care by offering non-invasive, automated, and efficient medication administration, ultimately improving treatment outcomes and quality of life(64). Each mechanism ensures targeted, efficient, and sustained drug delivery, minimizing side effects and improving patient compliance(65).

4.1. Advantages of Wearable Drug Delivery Devices

Wearable drug delivery devices offer significant advantages in modern healthcare by providing automated, controlled, and efficient medication administration. These benefits enhance treatment effectiveness, improve patient comfort, and reduce the burden of frequent hospital visits.

- Real-time Monitoring: Many wearable devices integrate with digital health platforms and wireless sensors, allowing continuous tracking of drug administration and physiological responses. Insulin pumps, for example, connect with continuous glucose monitors (CGMs) to adjust insulin levels in real time. This helps prevent complications like hypoglycaemia or hyperglycaemia. Smart patches and wearable injectors can also record and transmit data to healthcare providers, enabling remote monitoring and timely interventions(66).
- Improved Patient Adherence: Automated and scheduled drug delivery reduces the risk of missed doses, especially for chronic diseases like diabetes, cardiovascular conditions, and pain management. Non-invasive systems, such as transdermal patches and micro-needle arrays, make medication administration more comfortable, leading to better adherence compared to traditional injections or oral drugs. Additionally, reminders and alerts integrated into wearable devices help patients stay on track with their treatment(67).
- Personalized Dosing: Advanced wearable systems can adjust drug delivery based on individual needs, optimizing therapeutic outcomes. Insulin pumps, for instance, use machine learning and AI algorithms to regulate insulin release according to a patient's lifestyle and glucose fluctuations. Personalized drug delivery reduces over- or under-dosing risks, enhancing both safety and efficacy(39).

4.2. Challenges and Limitations of Wearable Drug Delivery Devices

Despite their numerous advantages, wearable drug delivery devices face several challenges and limitations that impact their widespread adoption and effectiveness. These issues range from technical and economic concerns to patient-related factors(68).

- High Cost: Wearable drug delivery systems, such as insulin pumps and on-body injectors, are expensive due to advanced technology, smart sensors, and precision mechanisms. This limits accessibility, especially in low-income populations and regions with inadequate healthcare funding(69).
- Device Malfunctions: Mechanical failures, battery depletion, or software glitches can lead to under- or overdosing, posing serious health risks. For example, an insulin pump malfunction could result in life-threatening hypoglycaemia or hyperglycaemia(70).
- Skin Irritation and Allergic Reactions: Prolonged use of transdermal patches or microneedle systems can cause skin irritation, redness, or allergic reactions. Some patients may develop sensitivity to adhesives used in patches or wearable injectors(71).
- Complexity and Patient Training: Many wearable devices require proper training for safe and effective use. Older adults and individuals with limited technological literacy may find it difficult to operate these systems correctly, leading to improper medication administration(72).
- Battery Life and Maintenance: Most electronic wearable drug delivery devices rely on batteries or rechargeable power sources, requiring regular maintenance. Power failures or inadequate charging could disrupt drug delivery, affecting treatment efficacy(73).
- Regulatory and Safety Concerns: Since these devices involve automated drug administration, they require strict regulatory approvals to ensure safety and accuracy. Long-term effects of continuous drug exposure via wearables also need further research(65).

5. Implantable Drug Delivery Systems

5.1. Classification of Wearable Drug Delivery Devices

Wearable drug delivery devices represent a major advancement in modern medicine, providing automated, controlled, and patient-friendly medication administration. These devices enhance drug bioavailability, minimize side effects, and improve adherence by offering continuous or on-demand delivery. They can be classified into different categories based on technology, mechanism, and material composition(74).

5.1.1. Microchip-Based Drug Delivery Systems

Microchip drug delivery devices use programmable silicon-based chips containing multiple drug reservoirs. These devices allow precise, controlled release of medication at predetermined times or in response to physiological signals. Microchip implants can be activated remotely, enabling personalized dosing for conditions like osteoporosis and cancer therapy(75).

5.1.2. Osmotic Pumps

Osmotic pumps use osmotic pressure gradients to regulate drug release. These systems consist of a drug core surrounded by a semipermeable membrane, which absorbs water from bodily fluids, creating pressure that pushes the drug out through a small opening. Osmotic pumps ensure a steady, long-term drug release, making them suitable for chronic disease management(76).

5.1.3. Polymeric Implants

Polymeric implants are biodegradable or non-biodegradable drug delivery systems designed for sustained-release therapy. These implants slowly degrade or dissolve over time, releasing drugs at a controlled rate. Examples include contraceptive implants (e.g., Nexplanon), chemotherapy implants, and long-term pain management systems(77).

Each of these wearable or implantable systems offers unique advantages, such as precision dosing, reduced side effects, and improved patient compliance, making them crucial for modern personalized medicine and chronic disease management(78).

5.2. Mechanisms and Advancements in Controlled Release

Controlled drug release systems are designed to deliver medications at a predetermined rate, for a specific duration, and to a targeted site in the body. These mechanisms help maintain optimal drug levels, minimize side effects, and improve patient adherence(65).

5.2.1. Mechanisms of Controlled Release

- Diffusion-Controlled Systems: Drug release occurs via passive diffusion through a polymer matrix or membrane. Examples include polymeric implants and transdermal patches(79).
- Osmotic-Controlled Systems: These use osmotic pressure to push the drug out through a small opening, ensuring steady, long-term release. Osmotic pumps (e.g., DUROS system) are widely used in chronic pain management(80).
- Erosion and Biodegradation: Some polymeric drug carriers gradually degrade or dissolve in the body, allowing controlled drug release. PLGA-based implants are an example(81).
- Stimuli-Responsive Release: Smart drug delivery systems respond to external triggers such as pH, temperature, enzymes, or ultrasound to release drugs on demand. pH-sensitive hydrogels are used in cancer therapy(82).

5.2.2. Recent Advancements

- Nanotechnology: Nano-carriers (liposomes, micelles, dendrimers) enhance drug solubility and targeted delivery.
- Microchip-Based Delivery: Implantable programmable microchips release drugs at precise times via wireless activation.
- AI-Integrated Pumps: Insulin pumps now use AI algorithms to adjust insulin release based on real-time glucose levels(83).
- These advancements in controlled release mechanisms enhance efficacy, safety, and patient convenience, revolutionizing drug delivery in chronic diseases, cancer, and personalized medicine(84).

- Case Studies: Applications in Chronic Disease Management and Pain Therapy

Wearable and implantable drug delivery devices have found significant application in chronic disease management and pain therapy, offering patients more precise control over their treatment regimens.

5.2.3. Chronic Disease Management

Diabetes: Insulin pumps are commonly used to manage type 1 and type 2 diabetes. These devices deliver continuous, precise doses of insulin based on real-time glucose monitoring, reducing the need for frequent injections and helping patients maintain stable blood sugar levels. For example, Medtronic's MiniMed insulin pump integrates continuous glucose monitoring (CGM) for personalized insulin delivery(85).

- Cardiovascular Diseases: Osmotic pumps are used for antihypertensive drug delivery to maintain steady blood pressure control. These pumps offer long-term management, reducing the risk of complications associated with irregular drug intake(86).

5.2.4. Pain Therapy

- Cancer Pain Management: Fentanyl patches, a type of transdermal patch, provide long-lasting pain relief for cancer patients. The patch delivers fentanyl continuously, bypassing the gastrointestinal system and avoiding peaks in plasma concentration(87).
- Post-Surgical Pain: Wearable injectors like Biosensors' On-body injector deliver controlled doses of pain relief drugs such as morphine or local anesthetics over extended periods post-surgery. These systems are designed to improve patient recovery by maintaining consistent pain relief(88).

These case studies demonstrate the power of wearable drug delivery devices in improving patient outcomes by enhancing treatment precision, convenience, and adherence in managing chronic conditions and pain(51).

5.3. Potential Risks and Biocompatibility Concerns

Despite their advantages, wearable drug delivery systems present several potential risks and biocompatibility concerns. These must be carefully evaluated to ensure patient safety and device efficacy(89).

5.3.1. Potential Risks

- Overdose or Underdose: Device malfunctions, such as pump failure, incorrect dosing, or sensor errors, could lead to under- or overdosing, which can result in severe health consequences. For example, insulin pumps could deliver too much insulin, causing hypoglycemia, or too little, leading to hyperglycemia(90).
- Infections and Skin Irritation: Prolonged use of transdermal patches or subcutaneous implants may lead to skin irritation, allergic reactions, or infections at the site of application or implantation(91).
- Biofilm Formation: In implantable devices, bacteria can form biofilms on the surface, increasing the risk of infection and affecting the drug release rate(92).

5.3.2. Biocompatibility Concerns

- Toxicity of Materials: The polymeric materials used in many devices must be carefully selected to ensure they are non-toxic, non-immunogenic, and compatible with the body's biological environment. Materials like PLGA or silicone are commonly used for their biodegradability and low toxicity(93).
- Long-Term Safety: The long-term implantation of devices, such as osmotic pumps or microchip-based systems, requires thorough evaluation to ensure they do not induce chronic inflammation or other adverse immune responses(94).
- Cellular Interaction: Nanomaterials in drug delivery systems must be assessed for potential cellular toxicity, genotoxicity, and their ability to interact with immune cells(95).

These risks highlight the need for rigorous biocompatibility testing, regular monitoring, and fail-safe mechanisms in wearable and implantable drug delivery systems to ensure patient safety(96).

6. Role of AI and IoT in Smart Drug Delivery

6.1. Integration of Artificial Intelligence (AI) and Internet of Things (IoT)

The integration of Artificial Intelligence (AI) and the Internet of Things (IoT) into wearable drug delivery systems has transformed how we manage chronic conditions and administer medications. These technologies enable intelligent, adaptive, and real-time drug delivery systems that personalize treatment for individual patients(97).

AI algorithms process vast amounts of real-time data collected from IoT-enabled devices like continuous glucose monitors, heart rate sensors, and wearable injectors. These systems can identify patterns, make predictions, and adjust drug delivery based on data inputs. For example, smart insulin pumps use AI to predict fluctuations in glucose levels, adjusting insulin delivery without patient intervention. This not only improves efficacy but also minimizes human error(64). IoT enhances this by creating connected healthcare ecosystems. Wearable devices can transmit data directly to cloud platforms, where healthcare providers can monitor patient status remotely. This enables doctors to track a patient's progress and intervene proactively without needing frequent in-person visits. Additionally, IoT facilitates data collection from a range of sources, enabling holistic health monitoring and more personalized care plans(98).

Together, AI and IoT enable real-time, data-driven decision-making, improving patient outcomes, increasing treatment efficiency, and providing better management of complex diseases like diabetes, heart disease, and chronic pain. The combination also offers the promise of reducing healthcare costs by decreasing hospital visits and complications related to disease mismanagement(99).

Table 2 Advantages and Challenges of Smart Drug Delivery Systems

Feature	Advantages	Challenges
Targeted Drug Delivery	Reduces side effects, enhances efficacy	Requires complex formulation
Controlled Release	Steady plasma drug levels, improved compliance	Potential device failure risks
Wearable Devices	Automated dosing, remote monitoring	High cost, battery life concerns
Biodegradable Implants	Eliminates need for removal, long-term therapy	Regulatory approval complexities
Nanocarriers	Enhanced drug solubility, improved tissue penetration	Potential toxicity concerns
AI-Integrated Systems	Personalized dosing, real-time adjustments	Data privacy and security risks

6.2. Remote Monitoring and Automated Adjustments in Drug Dosing

One of the most impactful innovations in healthcare is the ability to provide remote monitoring and automated adjustments in drug dosing through wearable drug delivery systems. These technologies enhance the ability to manage chronic conditions in real time, reduce human error, and improve treatment adherence(100).

For example, insulin pumps that integrate with continuous glucose monitors (CGMs) can automatically adjust insulin delivery based on real-time blood glucose levels, ensuring that patients receive the right amount of insulin at the right time(101). These adjustments can happen without the need for manual input, reducing the chance of errors and offering greater control over disease management. Similarly, pain management pumps can be programmed to adjust opioid doses for chronic pain, offering a more precise, consistent method of managing pain while minimizing the risk of over- or under-dosing(102).

Remote monitoring is particularly advantageous for patients who are homebound, live in remote areas, or have limited access to healthcare facilities(103). Healthcare providers can track patient progress through IoT-connected devices, identifying any potential issues before they become critical(104). In emergency scenarios, remote systems can alert medical professionals, enabling them to intervene promptly(105).

Automated drug delivery systems, when integrated with real-time data analysis, ensure that patients receive optimal care with minimal effort. These systems also reduce healthcare burden, as fewer in-person appointments are required, and patient adherence improves, leading to better disease management and outcomes(67).

6.3. Data Security and Privacy Concerns

With the rise of AI and IoT in wearable drug delivery devices, the importance of data security and privacy has become a pressing concern(106). These devices continuously collect sensitive medical data, such as glucose levels, drug dosage, and patient vitals, which need to be stored and transmitted securely(107).

Data security is vital to protect this sensitive information from unauthorized access, hacking, or tampering. Encrypted communication channels and secure cloud storage are essential to ensure that patient data is kept safe from cyber threats(108). Devices must comply with strict regulations like HIPAA (Health Insurance Portability and Accountability Act) in the United States, ensuring that patient information is kept confidential and used only for legitimate purposes(109).

Moreover, data privacy concerns arise as patients may worry about how their personal health information is used and shared. It is crucial for patients to have clear consent mechanisms where they are fully informed about how their data will be used, who has access to it, and how long it will be stored(110).

Additionally, wearable devices connected to the internet may be vulnerable to cyberattacks. Hackers could potentially gain control over drug delivery systems, manipulating drug doses or causing device malfunctions. This highlights the need for robust cybersecurity measures such as multi-factor authentication and encryption protocols to prevent unauthorized access(111).

In summary, while AI and IoT offer incredible benefits in personalized healthcare, ensuring data security, privacy, and regulatory compliance is essential to maintain trust and protect patient welfare in these advanced systems(112).

6.4. Clinical Applications and Case Studies

6.4.1. Diabetes Management (Insulin Pumps with Glucose Monitoring)

Diabetes management has greatly benefited from insulin pumps integrated with continuous glucose monitoring (CGM) systems. Insulin pumps deliver precise doses of insulin to diabetic patients, improving blood sugar control while reducing the burden of multiple daily injections(113). These devices, especially when paired with CGMs, provide a continuous feedback loop, allowing real-time adjustments to insulin delivery based on current glucose levels(114).

For instance, Medtronic's MiniMed 670G system integrates an insulin pump with a CGM, creating an automated insulin delivery system often referred to as an “artificial pancreas.” This device can automatically increase or decrease insulin doses based on real-time blood glucose levels, enhancing glucose control. The CGM sensors track glucose fluctuations, and the insulin pump adjusts insulin delivery accordingly, even during periods of fasting or after meals(115).

These systems significantly reduce the risk of hypoglycemia (low blood sugar) and hyperglycemia (high blood sugar), common complications of diabetes. Additionally, insulin pumps with CGMs improve patient quality of life by minimizing the need for frequent finger-stick blood tests, offering a more comfortable and efficient way to manage diabetes(116). Studies show that insulin pumps combined with glucose monitoring lead to better glycemic control, reduced A1C levels, and improved patient adherence to treatment regimens(117).

6.4.2. Neurological Disorders (Parkinson’s Disease, Epilepsy)

Wearable drug delivery devices also play a pivotal role in the management of neurological disorders like Parkinson’s disease and epilepsy. These devices offer continuous, non-invasive delivery of medication, improving symptoms and enhancing quality of life(118).

For Parkinson’s disease, patients often suffer from motor fluctuations as the disease progresses. One promising example is the Duopa system, which uses an intestinal gel pump to deliver levodopa directly to the small intestine, bypassing the gastrointestinal tract for more efficient absorption(119). This system provides continuous levodopa delivery, reducing the “off” times when symptoms become more severe. It offers patients a more consistent response compared to oral medication, which is subject to fluctuating blood levels(120).

For epilepsy, wearable devices that monitor seizures and provide stimulus-responsive drug delivery are being developed. Some of these systems use responsive neurostimulation (RNS) to detect seizure activity and deliver medications or electrical impulses to interrupt the seizure(121). An example is the NeuroPace RNS System, which helps prevent or reduce the frequency of seizures by monitoring brain activity and delivering electrical stimulation. In addition, wearable patches can provide antiepileptic drug delivery during or post-seizure, helping to reduce seizure frequency and severity over time(122).

6.4.3. Oncology (Targeted Chemotherapy via Implantable Devices)

In the field of oncology, wearable and implantable drug delivery devices enable targeted chemotherapy, reducing side effects and improving therapeutic outcomes. These devices allow direct, controlled delivery of chemotherapeutic agents to tumor sites, minimizing systemic exposure and toxicity to healthy tissues(123).

One example is the implantable infusion pump used in intraperitoneal chemotherapy for abdominal cancers, such as ovarian cancer. These pumps deliver chemotherapy directly into the peritoneal cavity, where the tumor resides, ensuring that the drug reaches the cancerous tissue in high concentrations while minimizing its effects on other organs(124). The Port-A-Cathsystem, often used in cancer treatments, delivers continuous chemotherapy through a central venous catheter, which is implanted under the skin(125).

Another promising advancement in oncology is the use of nanoparticles and nanocarriers for targeted drug delivery. Nanoparticles can be engineered to recognize and bind to specific tumor markers, delivering chemotherapy directly to cancer cells while sparing healthy cells(126). For example, Doxil, a liposomal formulation of doxorubicin, uses liposomes to encapsulate the chemotherapy drug and enhance targeted drug delivery to tumors. These systems improve efficacy while reducing side effects such as nausea, fatigue, and hair loss, which are common with traditional chemotherapy(127).

6.4.4. Cardiovascular Diseases (Antihypertensive Drug Implants)

Wearable and implantable drug delivery systems have proven highly beneficial in managing cardiovascular diseases, particularly hypertension (high blood pressure). Antihypertensive drug implants offer continuous, controlled release of medication, ensuring steady management of blood pressure levels and reducing the risk of complications such as stroke or heart failure(128).

One such system is the osmotic pump used to deliver antihypertensive medications like lisinopril or atenolol. These pumps provide slow, continuous drug release, eliminating the need for daily oral doses and improving patient compliance(129). The osmotic mechanism ensures precise, controlled delivery, preventing fluctuations in drug levels that can lead to under- or overdosing(130).

Implantable drug delivery systems like the Corline Vascular Bioactive Stent are designed to release antihypertensive agents directly to the arterial wall over a long period, helping to reduce blood pressure at the site of the condition. This localized delivery reduces the need for systemic treatments and helps patients achieve better control over their condition with fewer side effects(131).

These drug delivery systems not only offer better efficacy but also improve patient quality of life by providing a more comfortable and consistent treatment approach for those with chronic cardiovascular conditions. Additionally, they have the potential to reduce healthcare costs by minimizing the frequency of doctor visits and hospitalizations(132).

6.5. Regulatory Challenges and Ethical Considerations

6.5.1. FDA and EMA Guidelines for Wearable and Implantable Drug Delivery Systems

The FDA (Food and Drug Administration) in the United States and the EMA (European Medicines Agency) in Europe have set rigorous guidelines for wearable and implantable drug delivery systems to ensure safety, efficacy, and patient protection(133). These regulatory bodies classify drug delivery devices based on their level of risk, with devices that involve implantation or continuous drug administration falling under more stringent scrutiny(134).

For example, the FDA requires manufacturers to demonstrate that wearable drug delivery devices meet performance standards, are biocompatible, and are free of risks such as infection or toxic reactions(135). The devices are subjected to clinical trials to prove their safety and effectiveness in the target population. In addition to this, the FDA mandates post-market surveillance to track device performance over time(136).

Similarly, the EMA adheres to medical device regulations (MDR), ensuring devices undergo thorough evaluation and approval before they are marketed in Europe(137). Clinical evaluations, including risk assessments, are required to confirm that devices do not pose significant harm to patients. Both the FDA and EMA also emphasize quality control in manufacturing and traceability of devices through unique device identification (UDI)(138).

As wearable and implantable drug delivery systems grow in complexity and connectivity (e.g., integration with IoT and AI), these regulatory frameworks are continuously evolving to address emerging challenges in data security, wireless communication, and interoperability(139).

6.5.2. Patient Consent, Safety, and Ethical Concerns

Patient consent and safety are critical ethical concerns when developing wearable and implantable drug delivery systems(140). Obtaining informed consent is vital, ensuring that patients understand the potential risks, benefits, and limitations of these technologies. This includes providing clear explanations about the functionality of the devices, side effects, and possible complications like infections, device failure, or adverse reactions to drugs(141).

Additionally, safety is paramount, as these devices are often designed for long-term use, with some being implanted into the body. Manufacturers must prove that devices are biocompatible and will not cause chronic inflammation, immune responses, or toxicity(142). Clinical trials help assess the long-term safety of these devices. Ensuring patient safety also involves monitoring the system's performance over time and implementing mechanisms for failure detection and emergency intervention(143).

Another ethical consideration is the autonomy of patients in their decision-making process. They must have control over whether to use these devices, understanding their role in managing their condition and any risks involved(144). As devices become more complex (e.g., those powered by AI), it is important that patients are educated on how decisions may be made autonomously by the device and what that means for their treatment(145).

Lastly, ethical concerns also extend to the privacy of patient data, as wearable devices continuously collect sensitive health information. Securing patient data and ensuring data protection are crucial in preserving patient rights and maintaining trust in these technologies(146).

6.5.3. Market Adoption and Cost-Effectiveness

The adoption of wearable and implantable drug delivery systems is a multifaceted challenge that involves not only technical feasibility but also cost-effectiveness and market access. From a market adoption perspective, one key challenge is the high initial cost of developing and producing these advanced technologies(147). Many devices, particularly implantable drug pumps or those incorporating AI and IoT, require significant research and development investment. This can lead to high market prices, which may limit access, particularly for patients in low-income regions(148).

However, as demand for personalized medicine grows and technologies become more widely used, economies of scale could lower production costs, making these devices more affordable(149). Furthermore, the integration of AI and IoT can drive operational efficiencies, optimizing drug delivery and reducing the need for frequent doctor visits or hospitalizations. This may offset initial costs by improving patient adherence, reducing complications, and enhancing long-term outcomes(150).

From a cost-effectiveness standpoint, health authorities and insurers are increasingly evaluating these devices based on their ability to improve patient outcomes and reduce healthcare spending. For example, insulin pumps, when compared to regular insulin injections, can help patients better manage diabetes, potentially reducing the incidence of diabetic complications and their associated healthcare costs(151).

Nonetheless, convincing healthcare providers and insurance companies to cover the costs of these technologies remains a challenge. Regulatory agencies are working to streamline approval processes and ensure that cost-effectiveness studies are conducted to evaluate the economic benefits of wearable and implantable drug delivery systems, helping to foster wider adoption in the healthcare market(152).

6.6. Future Perspectives and Research Directions

6.6.1. Next-Generation Smart Drug Delivery Systems

The future of smart drug delivery systems lies in developing highly personalized, adaptive, and self-regulating technologies that offer real-time, precise delivery of medications based on individual patient needs. These next-generation systems will likely integrate advanced sensors, AI algorithms, and biomaterials to create a seamless connection between patient health status and drug administration. Such systems will be capable of monitoring critical health parameters, such as blood glucose levels, heart rate, and biomarker concentrations, and adjusting the drug release accordingly. For example, future insulin pumps may become even more autonomous by using AI-driven predictive models to anticipate fluctuations in glucose levels and adjust insulin dosing in real-time, significantly improving the management of chronic diseases like diabetes.

Moreover, next-gen systems will have enhanced capabilities in patient monitoring and data sharing. Wearable devices will not only deliver drugs but also transmit data to healthcare providers, enabling remote monitoring and timely intervention. This could be particularly beneficial in managing complex diseases such as cancer, neurological disorders, and cardiovascular conditions. These intelligent systems will offer greater flexibility, minimize human error, and improve patient adherence, all of which will contribute to better health outcomes and a higher quality of life.

The future vision of these systems includes integrating advanced feedback loops that adjust dosing based on a wide range of personalized health metrics, ultimately enabling truly individualized care.

6.6.2. Innovations in Nanotechnology and Bioelectronics

Nanotechnology and bioelectronics hold transformative potential in advancing drug delivery systems. The application of nanotechnology to drug delivery allows for the design of nanocarriers like liposomes, micelles, and nanoparticles, which can be engineered to deliver drugs more effectively to specific target sites in the body(153).These nanoparticles can improve solubility, bioavailability, and targeting, particularly for poorly soluble drugs or those with narrow therapeutic windows. By manipulating materials at the nanoscale, these carriers can also be used to deliver multiple drugs simultaneously, offering more efficient and synergistic treatments for complex diseases such as cancer or autoimmune disorders(154).

Moreover, innovations in bioelectronics are enabling the development of smart drug delivery devices that are not only capable of delivering drugs but also monitoring physiological signals and responding to changes in the body(155). Bioelectronic devices such as wearable patches and implantable sensors can communicate with external controllers, providing real-time feedback on drug absorption, tissue response, and efficacy. These devices can also be powered by bioenergy, eliminating the need for external power sources and enabling continuous monitoring without frequent maintenance(156).

Future advancements in these fields could lead to the miniaturization of drug delivery devices, creating invisible, highly efficient systems that seamlessly integrate with the body to deliver medications on-demand and targeted with minimal side effects(157).

6.6.3. Potential for Fully Autonomous Drug Administration

The development of fully autonomous drug administration systems represents one of the most promising future directions in healthcare. These systems aim to eliminate the need for human intervention by combining real-time data collection, AI decision-making, and automated drug delivery to continuously adjust treatment based on a patient's ever-changing health status(158). With advancements in sensors that track physiological markers like glucose levels, blood pressure, and neurotransmitter levels, autonomous systems can be designed to respond instantly to these metrics without the need for direct patient involvement(159).

For instance, a fully autonomous insulin delivery system could continually monitor a patient's blood glucose levels and adjust insulin dosage through a connected insulin pump, all while considering factors like meal timing, exercise, and stress levels(160).Similarly, in pain management, a neurostimulator could automatically adjust electrical stimulation levels based on real-time data from a brain-computer interface, providing pain relief without the need for patient control(161).

In addition to chronic disease management, these systems could revolutionize the acute care setting by delivering medications for emergency situations, such as anaphylaxis or stroke(162). Autonomous drug delivery could potentially improve patient outcomes by delivering the right amount of drug at the right time, tailored to the individual's specific needs, reducing the risk of overdosing or underdosing(163). The implementation of fully autonomous systems would require overcoming challenges related to data security, device reliability, and regulatory approval, ensuring that these systems remain safe, ethical, and reliable for widespread use in clinical practice(164).

7. Conclusion

Smart drug delivery systems have revolutionized personalized medicine by enabling precise, patient-specific treatments. The integration of wearable devices, implantable systems, and AI-powered technologies has introduced real-time monitoring and adaptive dosing, significantly enhancing treatment efficacy and patient adherence. Devices such as insulin pumps, neurostimulation systems, and oncology-specific delivery tools exemplify how on-demand drug administration can improve quality of life and clinical outcomes. Nanotechnology has further refined targeted drug delivery, allowing medications to reach diseased tissues with greater accuracy while minimizing systemic side effects. In parallel, advancements in bioelectronics have enhanced the performance of wearable and implantable devices, offering continuous health monitoring and improved therapeutic control.

These innovations are particularly impactful in managing chronic conditions like diabetes, cardiovascular diseases, and neurological disorders. In oncology, targeted systems have improved chemotherapy precision, reducing toxicity to healthy cells. Smart systems also empower patients by reducing hospital visits and enabling more consistent self-management. However, widespread clinical adoption faces challenges. Regulatory frameworks are still evolving, with safety, biocompatibility, and efficacy remaining critical concerns. High development and implementation costs hinder accessibility, especially in low-resource settings. Data security and privacy also pose significant issues, as these systems handle sensitive health data. Ensuring transparency and reliability in AI-driven decision-making is essential to build trust among patients and healthcare providers.

Despite these barriers, the future is promising. As costs decrease and regulations become clearer, smart systems driven by AI, IoT, and nanotechnology—could offer fully autonomous drug delivery for various diseases. These technologies hold the potential to redefine treatment paradigms by delivering dynamic, real-time therapies tailored to individual needs. Ultimately, smart drug delivery systems are poised to become a cornerstone of modern, patient-centric healthcare.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors do not have any conflict of interest.

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