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# From Conventional to Smart: A New Dawn in Oral Drug Administration

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**Abstract:** This review explores the evolution from conventional to smart technologies in oral drug administration, ushering in a new era of personalized healthcare. The journey from traditional dosage forms to smart drug delivery systems represents a paradigm shift, promising improved therapeutic outcomes and enhanced patient engagement. The abstract provides a succinct overview of the key aspects covered in the review, including the emergence of smart pills, connected drug delivery devices, benefits, challenges, case studies, and future directions. The convergence of pharmaceuticals and technology in oral drug administration signals a transformative phase in healthcare, emphasizing the potential for more effective, patient-centric treatment modalities.

**Keywords:** Smart drug delivery, oral drug administration, smart pills, connected devices, personalized healthcare, therapeutic outcomes, patient engagement, healthcare technology.

## 1. Introduction

The history of oral drug administration unveils a fascinating narrative, tracing its origins from ancient civilizations to contemporary pharmaceutical breakthroughs. In antiquity, ancient cultures like the Egyptians and Greeks relied on orally administered herbal remedies for medicinal purposes [1]. As time progressed, medieval herbalism contributed to the development of tinctures and extracts. The Renaissance marked a pivotal shift, steering the focus toward early pharmaceuticals and standardized formulations. The subsequent centuries witnessed the introduction of pills and powders, while the late 19th century saw advancements in compressed tablets and coated pills, revolutionizing drug stability. The mid-20th century solidified oral administration as the predominant route, emphasizing convenience and patient acceptance. In recent decades, technological integration has ushered in smart pills and nanotechnology, propelling oral drug administration into an era of precision and innovation. This historical journey underscores the evolution and significance of administering medications through the oral route [2,3] (Figure 1).

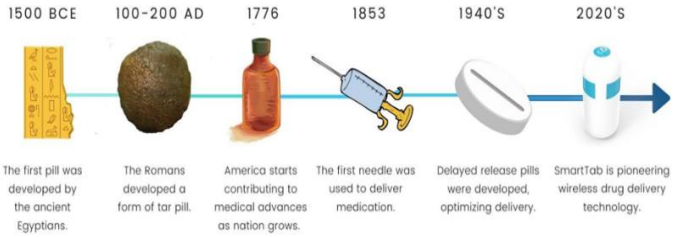


*Figure 1: Historical Journey of Oral Route*

Prior to 1950, all drugs were formulated into pills or capsules, releasing the loaded drug immediately upon contact with water, lacking control over release kinetics. In 1952, Smith Klein Beecham introduced the pioneering sustained release formulation, employing Spansule technology, enabling precise control over drug release kinetics for a sustained 12-hour efficacy [4]. This marked a significant advancement in controlled drug delivery. Early on, various terms like sustained release, timed release, and extended release were introduced to describe these novel formulations. Over time, the term "sustained release" gained more widespread usage. The controlled drug delivery field's history, detailed in Table 1, outlines developments from 1950 to 1980, with the first generation (1G) identifying key drug release mechanisms, including dissolution-controlled and diffusion-controlled systems. Although osmosis-based formulations briefly gained popularity, the majority continue to rely on dissolution- or diffusion-controlled mechanisms, especially in oral once-a-day formulations. The convenience of oral delivery ensures the continued success of sustained release formulations [5-7].

**Table 1:** Outlining the key milestone in the history of oral drug delivery system [1, 8-10]

| Year | Milestone in Oral Drug Delivery System |
|---|---|
| Ancient Times | Utilization of oral herbal remedies and potions in ancient civilizations |
| 19th Century | Emergence of compressed tablets and coated pills for improved dosing. |
| 1950 | Introduction of Spansule technology, the first sustained-release formulation. |
| 1970s | Proliferation of controlled-release formulations, including sustained release and timed release. |
| 1980s | Advancements in oral drug delivery technologies, including microspheres and liposomes. |
| 1990s | Introduction of biodegradable implants and nanoparticles for enhanced drug release. |
| 2000s | Rise of RNA-based therapeutics and nanomedicine for targeted drug delivery. |
| 2010s | Integration of smart drug delivery systems and gene editing technologies. |
| 2020s | Rapid development of mRNA vaccines, exemplified by COVID-19 vaccines. |
| Future | Ongoing innovations, including nanorobotics and implantable devices for precise drug delivery. |

Conventional dosage forms play a pivotal role in pharmaceutical delivery, offering diverse options for administering medications. Tablets, one of the most prevalent forms, are solid and compressed, typically containing powders or granules with additional components like binders and coatings. Capsules, encapsulating drug substances in gelatin or polymer shells, provide an alternative to tablets and are often more easily swallowed. Powders, consisting of fine particles, can be administered as is or reconstituted into liquids. Liquid formulations, including solutions, suspensions, and syrups, offer easy administration and are suitable for patients who have difficulty swallowing solid forms. Topicals, such as creams, ointments, and patches, are applied externally for localized treatment. Suppositories, designed for rectal or vaginal administration, melt at body temperature, facilitating drug release. Inhalers deliver aerosols or dry powder medications for respiratory conditions, targeting the lungs. Lastly, injections, administered intravenously, intramuscularly, or subcutaneously, provide a rapid onset of action by delivering drugs directly into the bloodstream or tissues. Each of these conventional dosage forms caters to specific patient needs and routes of administration, contributing to the versatility of pharmaceutical treatments (Table 2). [11, 12]

**Table 2:** Brief overview of conventional dosage forms [11, 12]

| Dosage form | Description | Characteristics |
|---|---|---|
| Tablets | Solid, Compressed Dosage form | Compressed powders or granules. May include disintegrates, binders, and coatings. Convenient for oral use. |
| Capsules | Gelatin or polymer shells enclosing drug substance. | Available in hard or soft forms. Can contain powders, granules, or liquids. Easier to swallow than tablets. |
| Powders | Fine particles of drug substance. | Often mixed with a diluent for accurate dosing. Can be reconstituted into a liquid or taken directly. |
| Liquids | Solutions, suspensions, or syrups. | Easy administration, suitable for those who have difficulty swallowing solids. May require refrigeration. |

| | | |
|---|---|---|
| Topicals | Creams, ointments, gels, patches. | Applied externally on the skin. Effective for localized treatment. Various bases for different applications. |
| Suppositories | Solid dosage forms inserted into body cavities. | Rectal or vaginal administration. Melts at body temperature, facilitating drug release. |
| Inhalers | Aerosol or dry powder devices for inhalation. | Used for respiratory conditions. Delivers medication directly to the lungs. |
| Injections | Intravenous, intramuscular, subcutaneous. | Delivers drugs directly into the bloodstream or tissues. Rapid onset of action. |

**Evolution of Oral Drug Administration**

Traditional dosage forms, encompassing tablets, capsules, and other conventional formulations, have long been the cornerstone of drug delivery in the pharmaceutical realm. However, these conventional forms are not without their limitations and challenges. Patient compliance poses a significant hurdle as these forms may necessitate frequent dosing, leading to potential lapses in adherence. Immediate-release formulations might offer a rapid onset, but sustaining therapeutic effects over time can be challenging [10]. Variability in absorption, first-pass metabolism, and gastrointestinal irritation further add to the complexities. To address these challenges, the pharmaceutical landscape has witnessed a transformative influence from technological advancements. The advent of nanotechnology has paved the way for nanoscale drug delivery, offering improved bioavailability and targeted release. Smart drug delivery systems, incorporating sensors and responsive materials, provide precision in drug administration. Biotechnology, mRNA technology, 3D printing, and microfluidics contribute to personalized medicine, allowing tailored drug formulations and innovative delivery methods. Implantable devices, targeted drug delivery, AI, and continuous manufacturing mark the integration of cutting-edge technologies, reshaping drug delivery paradigms. This synergistic interplay between traditional forms and technological advancements heralds a new era in pharmaceuticals, addressing challenges and ushering in unprecedented opportunities for efficacy, precision, and patient-centric care [13-15] (Figure 2).

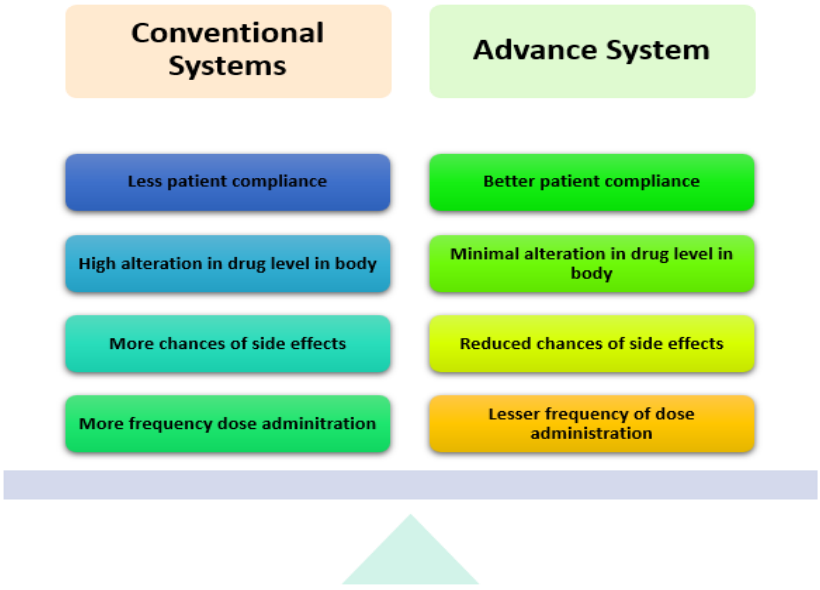


*Figure 2: Conventional system vs Advance system*

**Smart Pills**

Smart pills, also known as digital pills or ingestible sensors, are innovative drug delivery systems equipped with electronic components that facilitate communication between the pill and external devices. These pills are designed

to enhance medication adherence, monitor physiological parameters, and provide valuable data for healthcare professionals. The key feature of smart pills is their ability to transmit real-time information about medication ingestion and physiological metrics, offering a novel approach to patient care and disease management [16].

Smart pills incorporate ingestible sensors that are typically composed of biocompatible materials. These sensors can detect and transmit signals in response to various stimuli. They are equipped with wireless communication capabilities, enabling them to transmit data to external devices. This communication is often facilitated through technologies like Bluetooth or other wireless protocols. The primary function of smart pills is to monitor and transmit data related to medication adherence and physiological parameters. This data may include the time of ingestion, drug release patterns, and specific physiological responses within the body [17].

Smart pills often integrate with mobile applications or other digital platforms. These apps allow patients and healthcare providers to access real-time data, set medication reminders, and track treatment progress. To ensure safety and minimize environmental impact, some smart pills are designed to be biodegradable. Once the intended functions are completed, the pill can naturally break down within the body. They have integrated power sources such as small batteries or, in some cases, derive power wirelessly. Efficient power management is crucial to sustain the functionality of the electronic components. A key characteristic is the ability to monitor medication adherence. Smart pills provide insights into whether patients are taking their medications as prescribed, aiding in treatment optimization. Some smart pills are designed with diagnostic features, allowing them to collect data on specific health parameters or conditions. This can be particularly useful in chronic disease management. Given the sensitive nature of health data, smart pills incorporate privacy and security measures to protect patient information. Encryption and secure data transmission protocols are commonly employed. Future developments may include smart pills with the capability for targeted drug delivery, releasing medications at specific locations within the gastrointestinal tract for optimized therapeutic effects [18,19].

Smart pills represent a cutting-edge intersection of medicine and technology, offering a promising avenue for improving patient care, medication adherence, and disease monitoring. As technology continues to advance, smart pills are likely to evolve with enhanced features and applications.

Smart pills utilize various mechanisms to enhance drug delivery precision, providing a targeted and controlled approach to medication administration. The incorporation of electronic components and advanced technologies enables these mechanisms, contributing to improved therapeutic outcomes. Here are key mechanisms employed by smart pills for enhanced drug delivery precision:

Smart pills are equipped with wireless communication capabilities, enabling them to transmit signals and data to external devices. This wireless connectivity allows healthcare professionals to remotely monitor the status of medication ingestion and adjust treatment plans as needed.

Ingestible sensors within smart pills can monitor physiological parameters in real time. These sensors may detect specific biomarkers, pH levels, or other indicators within the gastrointestinal tract, providing valuable insights into the patient's response to the medication.

Some smart pills incorporate feedback mechanisms that allow for bidirectional communication. This means that not only can data be transmitted from the smart pill to external devices, but instructions or adjustments can also be sent back to the pill, enabling dynamic control over drug release.

Advanced smart pills have the capability for on-demand drug release. This feature allows for precise control over when and where the medication is released within the body. External triggers, such as a signal from a mobile app or a specific physiological condition, can initiate drug release.

Smart pills often integrate with mobile applications that serve as a control interface. Patients and healthcare providers can use these apps to set parameters, receive notifications, and remotely manage drug delivery schedules based on real-time data provided by the smart pill.

Closed-loop systems involve continuous monitoring of physiological parameters, and the smart pill adjusts drug release accordingly. For example, if a patient's condition changes or deviates from the expected response, the smart pill can adapt the drug delivery profile to maintain therapeutic efficacy.

Smart pills are designed with biocompatible materials to ensure safety within the gastrointestinal environment. Additionally, coatings on the smart pill may control drug release rates, protect electronic components, and provide targeted drug delivery to specific regions of the digestive tract.

Efficient power management is crucial for the sustained functionality of smart pills. Power sources, such as small batteries, must be designed to last throughout the intended duration of drug delivery. Some smart pills also explore alternative power options, such as harvesting energy from the body or wireless sources.

Smart pills with diagnostic features can collect real-time data on specific health parameters. This information can be used to tailor drug delivery schedules based on the patient's individual response and health status.

By incorporating these mechanisms, smart pills aim to revolutionize drug delivery precision, ensuring that medications are administered in a targeted, patient-specific manner, ultimately improving treatment outcomes and patient adherence [20-23].

**Connected Drug Delivery Devices**

Connected drug delivery devices refer to a class of innovative medical devices that integrate drug administration with digital technologies, allowing for enhanced monitoring, control, and communication between the device, patients, and healthcare providers. These devices are designed to improve medication adherence, provide real-time data on treatment progress, and enable personalized healthcare solutions. Here are key aspects and features of connected drug delivery devices [24-26] (Figure 1):

**1. Wireless Connectivity**

Connected drug delivery devices are equipped with wireless communication capabilities, enabling seamless data transfer between the device and external platforms such as smartphones, tablets, or cloud-based systems [27].

**2. Smart Sensors**

These devices often incorporate smart sensors that monitor various parameters, including drug administration, dosage timing, physiological responses, and patient interactions with the device. These sensors provide real-time data for comprehensive treatment management [28].

**3. Mobile Applications**

Many connected drug delivery devices integrate with mobile applications, allowing patients to receive reminders, track medication schedules, and access personalized health information. Healthcare providers can also remotely monitor patient adherence and treatment outcomes through these apps [29].

**4. Data Logging and Reporting**

Connected devices collect and log data related to medication adherence, dosing history, and patient responses. This information can be compiled into comprehensive reports that offer insights into treatment efficacy and potential adjustments [30].

**5. Remote Monitoring**

Healthcare professionals can remotely monitor patients' medication adherence and health status through connected platforms. This remote monitoring capability enables timely interventions, adjustments to treatment plans, and improved patient care [31].

**6. Real-Time Feedback**

Patients receive real-time feedback on their medication adherence and health metrics through connected interfaces. This immediate feedback can motivate patients to stay on track with their treatment plans.

**7. Adaptive Dosing and Personalization**

Some connected drug delivery devices offer adaptive dosing features, allowing for personalized treatment plans based on individual responses. This adaptability enhances the precision of drug delivery and improves therapeutic outcomes.

**8. Security and Privacy Measures**

Connected devices prioritize security and privacy, incorporating encryption and other measures to protect patient data. Compliance with data protection regulations ensures the safe and confidential handling of health information.

**9. Integration with Electronic Health Records (EHR)**

To facilitate comprehensive healthcare management, some connected drug delivery devices integrate with electronic health record systems. This integration ensures that healthcare providers have access to a complete patient profile for informed decision-making [32].

**10. Patient Engagement and Education**

Connected drug delivery devices often include features to engage and educate patients about their treatment. Interactive interfaces provide information on medications, potential side effects, and lifestyle recommendations.

**11. Remote Software Updates**

To maintain device functionality and security, connected drug delivery devices may support remote software updates. This ensures that the devices remain up-to-date with the latest features and security patches.

Connected drug delivery devices represent a significant advancement in healthcare technology, offering a holistic approach to medication management and patient care. These devices aim to empower patients, enhance treatment outcomes, and streamline communication between patients and healthcare providers.

**Benefits of Smart Oral Drug Administration**

Smart oral drug administration, facilitated by innovative technologies and connected devices, brings about several benefits that contribute to improved patient outcomes, enhanced treatment adherence, and more personalized healthcare. Here are key benefits associated with smart oral drug administration:

**1. Enhanced Medication Adherence**

Smart oral drug administration devices provide features such as reminders and real-time monitoring, significantly improving medication adherence. Patients receive timely alerts, reducing the likelihood of missed doses.

**2. Real-Time Monitoring and Feedback**

Patients and healthcare providers have access to real-time data on medication ingestion and patient responses. This information facilitates immediate feedback, allowing for timely interventions and adjustments to treatment plans.

**3. Personalized Treatment Plans**

Smart oral drug administration devices can adapt to individual patient responses, enabling personalized treatment plans. This adaptability ensures that patients receive the right dosage at the right time, optimizing therapeutic outcomes.

**4. Data-Driven Healthcare**

The continuous monitoring capabilities of smart devices generate valuable data that can be used for data-driven decision-making. Healthcare providers can analyze patient-specific data to tailor treatment strategies and optimize medication regimens.

**5. Remote Patient Monitoring**

Healthcare professionals can remotely monitor patient adherence and health metrics, reducing the need for frequent in-person visits. This remote monitoring capability is particularly beneficial for individuals with chronic conditions.

**6. Improved Patient Engagement**

Smart oral drug administration devices often include interactive interfaces and educational features, engaging patients in their treatment. Informed and engaged patients are more likely to adhere to prescribed regimens.

**7. Timely Interventions**

The ability to monitor patient data in real-time allows healthcare providers to intervene promptly in case of issues such as missed doses or adverse reactions. This proactive approach contributes to better patient care.

**8. Efficient Healthcare Delivery**

Remote monitoring and data-driven insights enable more efficient healthcare delivery. Healthcare providers can prioritize interventions based on patient needs, streamlining the allocation of resources and reducing unnecessary visits.

**9. Security and Privacy Measures**

Smart oral drug administration devices incorporate security measures to protect patient data and ensure privacy. Compliance with data protection regulations builds trust and confidence in the use of these technologies.

**10. Optimized Treatment Plans**

The wealth of data collected from smart devices allows for the optimization of treatment plans. Healthcare providers can adjust dosages, delivery schedules, or switch medications based on individual patient responses and evolving health conditions.

**11. Increased Patient Empowerment**

Patients actively participating in their treatment through smart devices become more empowered and accountable for their health. The knowledge that their adherence is being monitored can motivate patients to adhere to prescribed regimens.

**12. Reduced Healthcare Costs**

By improving medication adherence, optimizing treatment plans, and reducing the need for frequent in-person visits, smart oral drug administration contributes to overall cost reduction in healthcare.

Smart oral drug administration represents a transformative approach to medication management, leveraging technology to create a more patient-centric, efficient, and data-informed healthcare ecosystem [33-36].

## Challenges

### Regulatory Considerations in the Adoption of Smart Technologies

The integration of smart technologies in healthcare, including smart oral drug administration, raises several regulatory considerations. Regulatory bodies play a crucial role in ensuring the safety, efficacy, and ethical use of these technologies. Regulatory agencies need to establish clear approval processes for smart oral drug administration devices. This involves evaluating the safety and effectiveness of these technologies before they can be introduced to the market. It should define quality and manufacturing standards for smart devices. This ensures that these technologies meet established criteria for reliability, accuracy, and consistency. Regulations must address data security and privacy concerns associated with smart technologies. Clear guidelines on the storage, transmission, and protection of patient data are essential to safeguard patient privacy. As smart devices often interface with other healthcare systems, regulatory bodies should establish interoperability standards. This ensures seamless communication between different devices and platforms.

Regulatory agencies need mechanisms for post-market surveillance to monitor the ongoing safety and performance of smart technologies. This involves tracking adverse events, user feedback, and device malfunctions. Comprehensive labeling and user instructions are critical for safe and effective use. Regulatory requirements should mandate clear and user-friendly instructions to minimize the risk of user error. Regulatory frameworks should support ongoing monitoring of technological advancements. Updates and modifications to smart devices should be subject to regulatory scrutiny to ensure continued safety and effectiveness [37-39].

### Ethical Concerns Related to Patient Privacy and Data Security

The adoption of smart technologies in healthcare, including smart oral drug administration, introduces ethical considerations pertaining to patient privacy and data security. Patients must provide informed consent for the collection, storage, and use of their health data. Ethical considerations emphasize transparency regarding how patient data will be utilized. Patients should have control over their health data. Ethical frameworks should address issues of data ownership, allowing patients to decide who has access to their information and for what purposes. Ethical guidelines should encourage the de-identification and anonymization of patient data to protect individual privacy. Striking a balance between data utility for research and protecting patient identities is crucial. Ethical considerations emphasize the implementation of robust security measures to safeguard patient data from unauthorized access, breaches, or cyber threats. Patients should have the right to request the deletion of their health data when it is no longer necessary for the intended purpose. This "right to be forgotten" aligns with ethical principles of autonomy and privacy [40-42].

### Technological Challenges and Limitations

The adoption of smart oral drug administration technologies faces certain technological challenges and limitations that must be addressed:

Ensuring the reliability and accuracy of smart technologies is a challenge. Technological advancements are needed to enhance the precision of drug administration and data monitoring.

Smart devices may face challenges related to interference with other electronic devices and compatibility issues. Robust design and testing are necessary to address these challenges.

Smart devices often rely on batteries or alternative power sources. Efficient power management solutions are crucial to ensure the sustained functionality of these devices.

Designing user-friendly interfaces is essential for patient acceptance and adherence. Addressing usability challenges and ensuring accessibility for diverse user populations are ongoing considerations.

The cost of smart technologies may be a barrier to widespread adoption. Technological advancements and economies of scale are necessary to reduce costs and make these innovations more accessible.

Seamless integration with existing healthcare systems poses a challenge. Standardization and interoperability solutions are needed to ensure compatibility and smooth data exchange.

The continuous monitoring capabilities of smart technologies may generate large volumes of data. Effective data management and analytics solutions are required to derive meaningful insights without overwhelming healthcare providers.

Addressing these regulatory, ethical, and technological considerations is essential to foster the responsible and effective adoption of smart oral drug administration technologies in healthcare. Balancing innovation with patient safety and ethical principles is key to realizing the full potential of these advancements [43, 44].

**Case Studies and Applications**

Below in table 3 is a simplified representation of a table outlining case studies on smart oral drug delivery systems.

**Table 3:** Case Studies on Smart Oral Drug Delivery Systems

| Case study | Application Area | Key Features | Outcomes and Impact |
|---|---|---|---|
| Diabetes Management with Smart Pill Dispensers [45] | Chronic Disease | Reminder Functions, Connectivity | Improved Medication Adherence, Enhanced Glycemic Control |
| Precision Oncology with Targeted Therapies [46] | Oncology | Targeted Drug Release, Minimal Side Effects | Increased Effectiveness, Personalized Cancer Treatment |
| Psychiatric Medication Management [47] | Mental Health | Adherence Support, Monitoring Patient Responses | Improved Outcomes in Schizophrenia Treatment |
| Infectious Disease Treatment and Monitoring [48] | Infectious Diseases | Precision Drug Delivery, Real-time Monitoring | Enhanced Treatment Efficacy, Monitoring of Disease Progress |
| Pediatric Medication Adherence Solutions [49] | Pediatrics | Child-friendly Interface, Parental Oversight | Improved Adherence Among Pediatric Patients |
| Remote Monitoring for Elderly Populations [50] | Geriatrics | Remote Monitoring, Adjustment of Treatment Plans | Better Adherence Management in Polypharmacy |
| Customized Treatment Approaches in Rheumatology [51] | Rheumatology | Personalized Dosing Schedules, DMARD Delivery | Improved Disease Control in Rheumatoid Arthritis |
| Neurological Disorders and Wearable Connectivity [52] | Neurology | Wearable Integration, Real-time Data Collection | Optimized Treatment Adjustments in Parkinson's Disease |

Minaam et. al. (2018), introduced a smart pillbox prototype designed to address medication administration challenges, particularly in hospitals or retirement homes. The innovative pillbox autonomously sorts pills and offers advanced features, easing the burden on caregivers dealing with a large volume of medications. The programmable device allows customization of pill quantity, timing, and service times for daily medication routines. With nine separate sub-boxes, users can manage information for various pills, receiving timely reminders through sound and light cues. Unlike traditional pillboxes, this smart solution minimizes the need for frequent reloading, providing a more efficient and user-friendly approach for patients and caregivers [53].

Alqahtani et al., (2021) said that the oral route stands as the predominant and preferred mode for drug administration, offering non-invasiveness, patient compliance, and convenient drug intake. Successful oral drug absorption hinges on factors such as drug solubility, mucosal permeability, and stability in the gastrointestinal environment. Efforts to surmount these challenges have delved into understanding physicochemical, biochemical, metabolic, and biological barriers limiting overall drug bioavailability. Diverse pharmaceutical technologies and drug delivery systems, including nanocarriers, micelles, cyclodextrins, and lipid-based carriers, have been explored to enhance oral drug absorption. This review comprehensively addresses the physiological and pharmaceutical barriers influencing drug bioavailability via the oral route. It examines both conventional and novel drug delivery strategies, shedding light on the challenges and developmental considerations in pediatric formulations [54].

Bayan et al., (2022) focused on developing a smart colonic drug delivery system to address limitations in conventional oral formulations, which are primarily absorbed in the small intestine. The smart system aims to improve therapeutic efficacy, reduce dosing frequency, minimize potential side effects, and enhance patient acceptance, particularly in diseases requiring topical drug action at the colon's inflammation site. The system is designed to delay or inhibit drug release during the approximately 5 to 6 hours it takes for oral medication to reach the colon in healthy individuals, followed by controlled release afterward. pH-sensitive polymeric formulations, synthesized through free-radical bulk polymerization, are loaded with a model drug (5-amino salicylic acid) and a bioavailability enhancer (Capmul MCM C8). Characterization studies include measuring glass transition temperature, tensile strength, Young's modulus, and tensile elongation at break. In vitro swelling and release studies demonstrate the system's potential to regulate drug release in conditions resembling the stomach, small intestine, and colon, suggesting its promising application as a smart colonic drug delivery system [55].

Liu et al., (2022) explored the significance of oral drug administration as a convenient and safe strategy, particularly for patients with needle fear and swallowing difficulties. The intraoral drug delivery system emerges as an attractive option for macromolecule absorption, bypassing gastrointestinal degradation and first-pass metabolism. Despite its advantages, challenges such as limited bioavailability, short retention time, and poor reproducibility hinder conventional intraoral drug delivery systems. Recent advancements in chemical, material, and engineering techniques offer opportunities to enhance fabrication and applications of intraoral systems. The review systematically summarizes recent developments in smart intraoral drug delivery systems, encompassing various formulations. Challenges and prospects for clinical and industrial applications are discussed, highlighting the potential of smart intraoral systems to significantly impact human life in the near future [56].

Milián-Guimerá et al., (2023) addressed challenges in traditional oral dosage forms, emphasizing issues of adherence and limited bioavailability, particularly for peptide- and protein-based drugs. The last decade has seen substantial research and development in novel oral drug delivery strategies. Two main approaches are explored: lumen-release methods, including 3D-printed capsules and prolonged gastric residence forms for personalized medicine, and mucus interfacing strategies, such as gastrointestinal patches and epithelium injections, to enhance biologic macromolecule permeability. Despite being in early stages, these methods show promising results for personalized medicine and improved bioavailability. The review critically examines current and potential millimeter-sized devices and technologies for oral drug delivery in clinical use and anticipated for the future market [16].

Lou et al., (2023) said that the oral route remains the most favored avenue for systemic and local drug delivery, yet it encounters challenges from the gastrointestinal environment, impacting bioavailability and targeted design. This review delves into the anatomical, biochemical, and physiological factors influencing oral drug delivery. Innovative

pharmaceutical approaches, including nanoparticulate formulations, biomimetic drug formulations, and microfabricated devices, are explored to optimize drug targeting and bioavailability. The review emphasizes recent advancements in both conventional and novel oral drug delivery strategies, aiming to enhance bioavailability and targeting precision. Challenges and future opportunities in the realm of oral drug delivery systems are also discussed [57].

**Future Directions**

The future of smart drug delivery is poised to witness transformative developments driven by emerging trends, potential breakthroughs, and the integration of artificial intelligence (AI). Emerging trends suggest a shift towards more patient-centric and personalized drug delivery solutions. Innovations in materials science, nanotechnology, and biotechnology are expected to play a pivotal role, enabling precise control over drug release kinetics and targeted delivery. Advanced sensors and connectivity features will enhance real-time monitoring, ensuring optimal therapeutic outcomes. Potential breakthroughs may include the development of self-regulating drug delivery systems capable of adapting to individual patient responses, further optimizing treatment efficacy. Artificial intelligence is set to revolutionize the landscape by offering predictive modeling for drug release patterns, personalized dosing recommendations, and predictive analysis of patient responses. The convergence of these trends and breakthroughs heralds a future where smart drug delivery systems not only enhance adherence and efficacy but also contribute to a more intelligent and responsive healthcare ecosystem.

**Conclusion**

In conclusion, the transition from conventional to smart oral drug administration represents a groundbreaking shift in pharmaceutical approaches, offering enhanced precision, patient compliance, and therapeutic outcomes. The integration of smart technologies, such as ingestible devices, intelligent formulations, and interconnected drug delivery systems, has opened new avenues for personalized medicine. The advent of artificial intelligence has further propelled the evolution of oral drug administration, paving the way for real-time monitoring, adaptive dosing, and data-driven treatment strategies. While facing regulatory considerations, ethical concerns, and technological challenges, the future of smart oral drug administration holds immense promise. As advancements continue to unfold, the potential breakthroughs and innovations in this field are poised to redefine the landscape of drug delivery, ushering in a new era of efficiency and efficacy in patient care.

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