Review Articles

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Digital Pills and Ingestible Biosensors: Redefining Drug Adherence Science

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ABSTRACT

Background Medication non-adherence remains a critical global healthcare challenge, contributing to poor clinical outcomes, increased hospitalizations and rising healthcare costs. Conventional adherence assessment tools self-reports, pill counts, pharmacy refills are indirect and error-prone. Digital pills integrated with ingestible biosensors have emerged as a disruptive innovation offering objective, real-time confirmation of drug ingestion. **Objective** This review critically examines the scientific principles, technological architectures, clinical applications, regulatory landscape and ethical considerations of digital pills and ingestible biosensors, with a focus on research trends from 2020-2025. **Methods** A narrative and trend-based systematic review was conducted using PubMed, Scopus and Web of Science databases following PRISMA-informed principles. Peer-reviewed articles published between January 2020 and June 2025 were analyzed. **Results** Ingestible biosensors demonstrate high accuracy in detecting medication ingestion and physiological parameters, particularly in psychiatry, cardiology, tuberculosis and transplant medicine. However, challenges persist related to cost, data privacy, patient autonomy, scalability and long-term clinical validation. **Conclusion** Digital pills represent a paradigm shift in adherence science, transitioning from probabilistic estimates to direct biological confirmation. Future research must prioritize patient-centered design, ethical governance and integration with digital health ecosystems.

1. Introduction

Medication non-adherence is estimated to affect nearly 50% of patients with chronic diseases worldwide, accounting for approximately USD 300–500 billion in avoidable healthcare expenditure annually [1]. The World Health Organization recognizes poor adherence as a major barrier to effective disease management, particularly in chronic and psychiatric disorders. The inability of traditional adherence metrics to accurately capture real-time drug ingestion has catalyzed interest in bio-integrated technologies[2]. Digital pills pharmaceutical formulations embedded with ingestible sensors offer a fundamentally new approach by directly confirming ingestion events through physiological activation within the gastrointestinal tract. This review explores how ingestible biosensors are redefining adherence science by converging pharmacology, materials science, electronics and digital medicine [3]. This figure 1 illustrates the global burden of medication non-adherence and its clinical and economic consequences, including disease progression, increased hospitalizations, and substantial avoidable healthcare costs. Conventional adherence assessment methods, such as pill counts and patient self-reports, are highlighted as indirect and unreliable proxies of true drug ingestion. The lower panel depicts an innovative digital pill system in which pharmaceutical formulations are integrated with ingestible sensors that activate upon exposure to the gastrointestinal environment. These sensors generate physiological signals confirming ingestion events, which are transmitted wirelessly to external devices and cloud-based platforms for real-time monitoring by clinicians. Collectively, the figure 1 underscores how bio-integrated ingestible technologies bridge pharmacology, electronics and digital health to enable objective, real-time measurement of medication adherence and redefine adherence science.

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Fig. 1 - Digital Pills and Ingestible Biosensors as a Paradigm Shift in Medication Adherence Monitoring

Figure 1 overview illustrating the global challenge of medication non-adherence and the role of digital pills in this gap. Medication non-adherence affects nearly 50% of patients with chronic diseases, leading to disease progression, increased hospitalizations and an estimated USD 300–500 billion in avoidable healthcare costs annually. Conventional adherence assessment methods, such as pill counts and patient self-reports, lack reliability and real-time verification. Digital pills, composed of pharmaceutical formulations integrated with ingestible biosensors are activated upon contact with gastrointestinal fluids following ingestion. The resulting physiological signal is transmitted to an external wearable or mobile device and relayed to secure cloud-based platforms, enabling real-time confirmation of drug intake for clinicians and healthcare systems. This bio-integrated approach redefines adherence science by bridging pharmacology, sensor materials, electronics and digital medicine.

2. Methodology

2.1. Literature Search Strategy

A systematic literature search was conducted in PubMed, Scopus and Web of Science databases. Search terms included combinations of: "digital pill", "ingestible sensor", "medication adherence technology", "smart pills" and "biosensor-enabled pharmaceuticals" [4].

Table 1 - Literature search strategy and data sources used in this review

Component	Description	Ref.
Databases searched	PubMed, Scopus and Web of Science	[5]
Search approach	Systematic literature search	[6]
Core research concepts	Digital pills, ingestible sensors, medication adherence technologies	[7]
Primary search terms	“Digital pill”; “ingestible sensor”; “smart pills”	[8]
Secondary search terms	“Medication adherence technology”; “biosensor-enabled pharmaceuticals”	[9]
Search logic	Boolean operators (AND, OR) combining primary and secondary keywords	[10]
Research focus	Objective and real-time monitoring of medication ingestion events	[11]
Study type emphasis	Original research articles and relevant review papers	[12]
Language restriction	English-language publications only	[13]

2.2. Inclusion and Exclusion Criteria

2.2.1 Inclusion: Peer-reviewed original research articles, review papers and clinical trials published between 2020 and 2025 were included if they involved human participants, evaluated digital pills or ingestible biosensor technologies and were available as full-text publications in the English language [14][15].

2.2.2 Exclusion: Studies were excluded if they focused solely on non-ingestible, wearable-only medication adherence technologies were limited to animal models without human data, or were conference abstracts lacking accessible full-text publications [16].

2.3. Data Extraction and Synthesis

Data were extracted on sensor design, activation mechanism, clinical indication, outcomes, regulatory status and limitations. A thematic synthesis approach was applied [17].

3. Technological Architecture of Digital Pills

3.1. Ingestible Sensor Design and Materials

Most digital pills utilize millimeter-scale sensors composed of biocompatible materials such as silicon, magnesium, copper and food-grade polymers. Activation occurs upon contact with gastric fluid, generating a galvanic signal [18].

3.2. Signal Transmission and Data Flow

Upon activation, the sensor transmits a low-power signal to a wearable receiver (e.g., dermal patch), which relays ingestion data to cloud-based platforms accessible by clinicians [19]. This figure 2 when a patient swallows a digital pill it activates in the stomach and begins transmitting a wireless signal to a wearable patch on the patient’s body. The patch then relays the collected data to a cloud platform where cloud-based analytics process and analyze the information before presenting the results to clinicians through a dashboard.

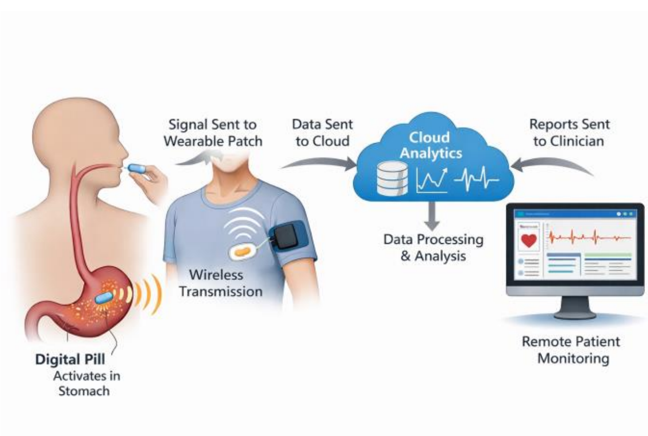

Fig. 2 - Conceptual architecture of a digital pill system

The Figure 2 illustrates how a digital pill works within a remote patient monitoring system. After ingestion the digital pill activates in the stomach, sending a wireless signal to a wearable patch on the patient. The patch then transmits data to the cloud where analytics and processing occur. Clinicians receive reports via a remote monitoring dashboard for ongoing patient assessment.

4. Clinical Applications and Evidence

4.1. Psychiatry and Neurology

The first FDA-approved digital pill (aripiprazole with ingestible sensor) demonstrated feasibility in schizophrenia and bipolar disorder. Studies report improved adherence monitoring, though patient acceptance varies [20].

4.2. Cardiovascular and Metabolic Disorders

Digital antihypertensive and antidiabetic formulations have shown potential in improving adherence in high-risk populations, particularly when integrated with telemonitoring programs [21].

4.3. Infectious Diseases and Transplant Medicine

In tuberculosis and post-transplant immunosuppression, ingestible biosensors offer objective adherence verification critical for preventing resistance and graft rejection [22].

5. Advantages, Limitations and Ethical Considerations

Table 1 - Comparative analysis of adherence assessment methods

Method	Accuracy	Real-time	Patient Burden	Key Limitations
Self-report	Low	No	Low	Recall bias
Pill count	Moderate	No	Moderate	Manipulation
Digital pill	High	Yes	Moderate	Cost, privacy

Ethical concerns include data ownership, informed consent, potential coercion and surveillance perceptions, particularly in vulnerable populations [22].

6. Regulatory Landscape and Commercialization

Regulatory agencies increasingly classify digital pills as combination products. Post-market surveillance, cybersecurity compliance and interoperability standards remain evolving challenges [23].

7. Future Perspectives and Research Gaps

Key research gaps include long-term outcome validation, cost-effectiveness analyses, miniaturization, battery-free sensing and integration with artificial intelligence-driven adherence prediction models [24].

8. Conclusion

Digital pills and ingestible biosensors represent a transformative advancement in adherence science, offering unprecedented accuracy and clinical insight. Their successful adoption will depend on balancing technological innovation with ethical responsibility and patient trust.

Declaration:

A.1. Abbreviations

AI: Artificial Intelligence
FDA: Food and Drug Administration
GI: Gastrointestinal
mHealth: Mobile Health

A.2. Declaration of competing interest

The authors declare that they have no conflicts of interest.

A.3. Acknowledgements

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