Smart Pills: A New Method Of Targeted Drug Delivery System

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Abstract:

Smart pill technology represents a groundbreaking advancement in healthcare, integrating miniature electronic components into ingestible pills to revolutionize medication delivery, diagnostics, and monitoring. This comprehensive overview delves into the components, functions, applications, considerations, and future directions of smart pill technology. The core components of smart pills include ingestible sensors, electronic modules, and power sources, enabling a range of functions. These functions encompass medication adherence monitoring, diagnostic imaging, physiological monitoring, and targeted drug delivery. Patients ingest smart pills orally, and as they traverse the gastrointestinal tract, they wirelessly transmit data to external devices for analysis by healthcare providers. Smart pills offer numerous benefits across various healthcare domains. They enhance medication adherence and disease management for chronic conditions, facilitate non-invasive diagnostic screening of the gastrointestinal tract, and serve as valuable tools in clinical research. However, ensuring the safety, regulatory approval, and privacy of patient data are critical considerations in the deployment of smart pill technology. Future directions for smart pill technology focus on miniaturization, integration, and expanded applications. Continued advancements aim to make smart pills more compact, efficient, and user-friendly, while interdisciplinary collaboration drives innovation and addresses challenges in development and adoption. Smart pills hold promise beyond gastrointestinal diagnostics and drug delivery, extending to personalized medicine, targeted cancer therapy, and neurology.

Keywords: Technology, Gastrointestinal, Delivery, Diagnostic, Ingestible, Data receiver, Consent, Adherence, Monitoring, Localization, etc

Introduction:

Medication adherence is a significant global challenge, with approximately 50% of people with chronic diseases in developed countries not following their prescribed treatment plans, according to the World Health Organization (WHO). In Canada, the nonadherence rate is around 52%, contributing to 5% of hospital admissions and physician visits, which adds $4 billion in healthcare costs annually. Poor adherence leads to ineffective treatment, increased emergency visits, hospitalizations, and worsened health outcomes. WHO defines medication adherence as the extent to which a patient's behavior aligns with healthcare provider recommendations. Adherence involves three phases: initiation, implementation, and discontinuation of therapy, with nonadherence potentially occurring at any phase. This could include not filling prescriptions, incorrect usage, or prematurely stopping medication without consulting a healthcare provider.[1-7] Drug delivery systems (DDS) are developing to enhance pharmaceutical administration and get around systemic drug constraints, thereby enabling individualized treatment.[8] By modifying dosages for each patient and focusing on particular areas based on real-time monitoring by smart capsules with sensors, personalized drug delivery can improve therapeutic efficacy, especially in the treatment of gastrointestinal (GI) disorders like gastroesophageal reflux disease (GERD). [9] The perfect swallowable capsule would be self-sufficient, able to move to facilitate diagnosis, send information, and receive wireless commands to deliver medication therapies efficiently.[10] The goal of oral medicine administration is to effectively treat and prevent disease by delivering the proper dose at the right time and location. Traditional oral dosage forms are still the favored option, although they have drawbacks such as poor absorption of macromolecules like peptides, limited patient adherence to frequent prescriptions like HIV regimens, and difficulties delivering many pharmaceuticals at precise amounts. Osmotic-controlled Release Oral Systems (OROS) are one example of a technology that helps

reduce dose frequency; yet, because standard dosage forms have a limited residence time, adherence issues persist. Furthermore, semaglutide, which yields just around 1% bioavailability in oral peptide delivery, shows that macromolecule bioavailability remains poor even with permeation enhancers (PEs).[11]

1. Smart Pill:

Gastrointestinal (GI) motility (GIM) is critical for the efficient transit of contents through the digestive system, and abnormalities in this process can lead to significant discomfort in patients with GI symptoms. These GIM disorders can cause abdominal pain, bloating, constipation, or diarrhea, impacting both quality of life and contributing to socioeconomic burdens. Conventional treatments sometimes fall short, which underscores the need for more precise diagnostic methods, particularly for patients who do not respond to empirical therapies. The Smart Pill motility testing system (Medtronic, Minneapolis, MN, USA) offers a promising diagnostic tool for investigating GIM disorders. This system allows for precise, standardized, and reproducible measurements of GI motor activity, while maintaining a patient-friendly approach in terms of invasiveness. [15,16,17] Traditionally, GI motility (GIM) testing has been targeted at specific regions of the GI tract where abnormalities are suspected. For instance, testing might focus solely on the stomach, small intestine, or colon. However, emerging evidence indicates that GIM disorders are often more complex and not always confined to a single region of the GI tract. In many cases, the dysfunction might span multiple regions. For example, some patients suffering from slow transit constipation not only have issues with colonic dysmotility but also display delayed gastric emptying or small bowel motility disturbances. This broad dysfunction suggests that motility issues in one region can affect others, complicating diagnosis and treatment. This highlights the need for comprehensive motility testing that can evaluate the entire GI tract rather than isolated regions. The Smart Pill system is well-suited for such evaluations, providing a more complete picture of motility across different segments of the GI tract. [18,19] This insight emphasizes how crucial a thorough GIM assessment is in order to inform more precise diagnosis and customized treatment plans. The Smart Pill device consists of a single-use, ingestible, wireless motility capsule (WMC) measuring multiple vital parameters while it travels through the gastrointestinal tract, measuring 26.8 mm by 11.7 mm. [20,21]

2. Drug release mechanism of smart pill:

Drugs can be administered via active methods or delivered passively. Drugs delivered by passive methods are only exposed to their surroundings. They mostly include chemical or physical interactions (like diffusion), which are brought on by certain environmental factors like pH and temperature. The release is subject to certain requirements being met at the intended site. On the other hand, active mechanisms describe the capsule's ability to release the medicine from a reservoir after the release mechanism is triggered. FIGURES 4 and 5 provide a concise summary of the mechanisms that are really in use, while the paragraph that follows provides more specifics.[12]
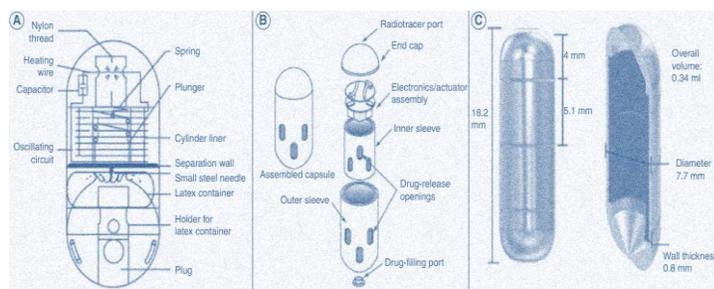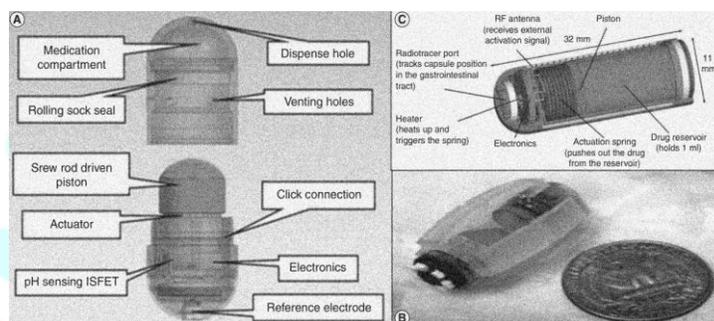

Figure:4

Figure:5

3. Smart pill container or box:

Sensor-equipped pillboxes and pill bottles have been developed to monitor medication adherence. MedTracker, an early approach by Hayes et al., used a 7-day pillbox with plungers to detect lid openings, transmitting data via Bluetooth. However, it mistakenly assumes lid openings equal medication intake and has limited battery life. Aldeer et al.'s Pill Sense improves accuracy by combining a magnetic switch, accelerometer, and load cell to track cap removal, pill pickup, and bottle weight changes, enhancing validation and energy efficiency. Lee and Dey developed a similar pillbox to monitor elderly patients' medication habits using wireless technology, but like other systems, it does not verify pill ingestion. These systems prioritize comfort and accuracy while avoiding direct body sensors, though ingestion confirmation remains a challenge.[13] Smart pill boxes, or "electronic medication-packaging devices," are designed to track medication use through timers, alarms, or Bluetooth functionality, monitoring whether the box has been opened. However, these devices face criticism for not verifying actual pill ingestion. Several randomized controlled trials (RCTs) have tested the effectiveness of smart pill boxes on medication adherence, yielding conflicting results. For example, Choudry et al. conducted a large 4-arm trial involving over 53,000 participants but found no significant difference in adherence across groups using different devices or no device. Similarly, in a multicenter RCT by Kooy et al., the use of smart pill boxes, either with or without counselling, did not result in significantly higher medication adherence compared to controls. These studies suggest that the effectiveness of smart pill boxes may depend on additional interventions that ensure consistent usage by patients.[14]

4. Smart pills used for diagnosis:

Various smart pills have been developed to improve the diagnosis of GI diseases and enhance understanding of their causes. These pills can be categorized into two types: those that use imaging technologies (e.g., optical, auto fluorescent imaging) and those that use sensors to detect changes in the GI environment, such as pressure, pH, or chemical analytes. However, most of these smart pills are still in the early stages of development, and their clinical efficacy has yet to be fully established due to ongoing technical challenges.[22]

5. Future direction:

5.1. For diagnostic smart pills:

The development of smart pills that integrate several sensors and imaging technologies presents opportunities to enhance diagnostic capabilities and overcome constraints in existing capsule endoscopy (CE) techniques. Many of these technologies, though, are still in their infancy and will need to undergo substantial clinical studies and more development before their efficacy can be established. Improved smart tablets with the ability to identify clinically significant biomarkers and precisely locate them in the gastrointestinal (GI) tract may make it possible to precisely identify illness sites and carry out focused medical procedures or therapeutic interventions. However, there is still a great deal of work to be done in creating chemical sensors that work consistently in the hostile GI environment.   [23,24]

In order to attain the required accuracy, sensitivity, and specificity for clinical diagnosis, developing effective smart tablets necessitates not only the advancement of individual sensors but also the exploration of sensor combinations.

Multimodal smart pills will affect onboard system integration, downsizing, and power management because they incorporate several sensors.

These medications will also produce enormous volumes of data, which will impact doctor workload and communications capacity.

Current capsule endoscopy (CE) devices produce thousands of images, leading to substantial time for review—up to 1 hour per examination—resulting in a 6–20% rate of missed pathologies. Thus, it is imperative to improve diagnostic

accuracy and data management. [25,26,27]

5.2. For therapeutic smart pills:

Two major technological issues that need to be resolved for smart pills to be employed for pharmaceutical or non-pharmacological treatment are anchoring and localization. The term "anchoring" describes the smart pill's capacity to withstand peristaltic and other stresses while remaining stationary in the gastrointestinal (GI) tract during therapy. A constant therapeutic distribution of the pill is ensured by effective anchoring, which lowers patient variability in transit time. This stability increases the efficacy of therapy by enabling the exact administration of medications or non-pharmacological treatments at specific areas. Numerous anchoring methods, such as biomimetic adhesives, magnets, microneedles,

and needles, have been proposed.[28,29,30,31]One of the biggest challenges for smart tablets that provide pharmaceutical treatments is the onboard storage volume, which usually falls between 0.3

and 1 ml.This restriction results from the fact that batteries, sensors, actuators, telemetry, electronics, and other necessary parts take up space inside the tablet.There will be limitations on the dosages that these devices can carry as they develop and grow more complex through the integration of cuttingedge mechanical and electrical systems.This constraint may necessitate more potent pharmaceuticals or developments in downsizing technologies, like microfluidics or microelectromechanical systems (MEMS), in order to reduce the component size.[32] Furthermore, the cost of production may climb as these systems get more integrated, which could prevent this technology from being widely used until economies of scale lower the costs. The sustainability of smart pills is also a worry because of their one-time usage and potential for bodily excretion, which could add to the growing amount of electronic trash. Although the research of biodegradable materials for electronic components is still in its infancy, addressing this issue may necessitate a shift in materials.[33]

Conclusion:

Drug delivery technology has advanced significantly with the introduction of smart tablets, which have the ability to provide accurate, targeted, and controlled medicine administration. Smart tablets can release medication in reaction to stimuli such as pH, temperature, or enzymes, distribute pharmaceuticals to precise areas, and actively monitor physiological variables through the integration of sensors, microelectronics, and responsive materials. This breakthrough should increase patient compliance, lessen adverse effects, and improve treatment efficacy. Nonetheless, there are still difficulties, especially with regard to maintaining safety, creating trustworthy monitoring systems, and managing regulatory procedures. The full medical potential of smart pills will require ongoing study and technical advancements.

Acknowledgment:

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