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Robotic Pills In Personalized Medicine: A Comprehensive Review

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Abstract: Robotic technologies are emerging as promising tools in pharmaceutical drug delivery to overcome long-standing challenges in global healthcare. Robotic pills are designed to bypass enzymatic degradation and first-pass metabolism, thereby enhancing systemic bioavailability and enabling the delivery of optimal therapeutic doses without reliance on frequent injections. This approach improves patient acceptance and reduces the burden associated with needle-based administration. Oral delivery of proteins and peptides, however, is hindered by toxicity concerns, high production costs, and poor stability in the gastrointestinal environment. Issues such as injection-related discomfort and treatment non-adherence can be minimized through innovative oral delivery systems. Because luminal mucus represents a major barrier to macromolecule absorption, advanced robotic capsules have been engineered to overcome this limitation. One such system, the RoboCap, is an ingestible robotic capsule designed to enhance drug mixing, clear the mucus layer, and deposit drug directly onto the intestinal surface to improve absorption. These innovations demonstrate the potential of robotic pills to provide a safe, effective, and patient-friendly alternative to parenteral administration of bio therapeutics.

Keywords: Robotic pills, oral drug delivery, Bio therapeutics, mucus –penetrating systems

I. INTRODUCTION

The use of biotherapeutics has been increasing exponentially since the U.S. FDA approved insulin, the first therapeutic recombinant protein. However, due to their susceptibility to enzymatic degradation and poor absorption across the gastrointestinal tract, these molecules are typically administered parenterally. Frequent injections, however, reduce patient compliance and quality of life, which has driven the development of orally ingestible robotic pills as an alternative (1).

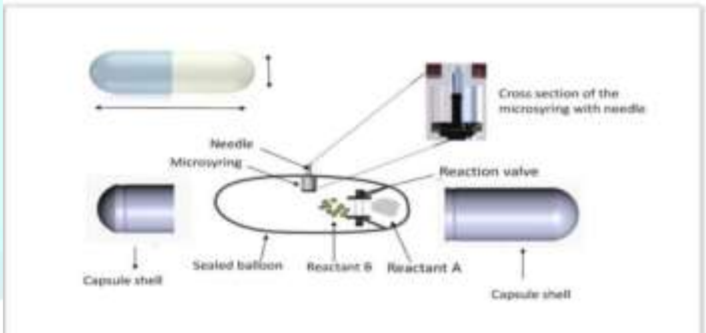
These robotic oral drug delivery systems are designed to improve mixing, clear the mucus layer, and enhance local absorption. Each pill typically contains an internal drug reservoir and a pH-sensitive outer coating that dissolves after reaching the stomach, exposing mechanisms for controlled drug release (2).

Biologic drugs hold immense promise for medical treatments, but their oral delivery remains a daunting challenge due to the harsh digestive environment and restricted gastrointestinal absorption. Inspired by biological systems such as the porcupinefish—which inflates itself and deploys spines for defense—

researchers have developed intestinal microneedle robots capable of inflating within the gut and injecting drug-loaded microneedles into the intestinal wall for efficient absorption (3,6).

Devices like the SOMA and LUMI pills demonstrate how self-orienting and microneedle-based systems can bypass biological barriers and deliver biologics such as insulin and mRNA directly into targeted tissues, achieving effects comparable to injections while remaining non-invasive (3).Although conventional oral peptide formulations such as semaglutide have achieved limited success, their bioavailability is constrained by passive transport mechanisms. Hence, active robotic systems that combine precision engineering with biological inspiration represent a major advancement toward achieving targeted, efficient, and patient-friendly oral delivery of biotherapeutics (4,5,6).By combining pharmaceutical technology with drug delivery expertise, robotic pills can be created effectively utilised to improve drug adherence and penetration through the GI tract's mucous membrane resulting in medication delivery at the intended location. Patients may not need daily needles or visit the hospital to acquire their medications thanks to Robo Cap. The current challenge of administering numerous cutting-edge and novel treatments orally is intended to be addressed by the novel idea known as Robo Cap (7).

II. Structure And Functions



The robotic pill is incorporated within a size 000 hydroxypropyl methylcellulose (HPMC) capsule, engineered for safe swallowing and resistance to stomach conditions. Inside, a polyethylene balloon approximately 75 mm long and 21–25 mm in diameter when expanded serves as the main carrier for the delivery system. Attached to the balloon is a small cylindrical polyethylene microsyringe containing a solid drug load, coupled with a hollow, dissolvable polyethylene glycol needle designed to inject the drug through the intestinal wall. The capsule's enteric coating, typically composed of pH-sensitive polymers such as methacrylic acid copolymers, protects the device in the stomach and dissolves in the intestinal environment, ensuring targeted delivery. A dissolvable reaction valve made from polyethylene oxide separates potassium bicarbonate and citric acid reactants; when exposed to intestinal fluids, these reactants produce gas to inflate the balloon, positioning the device for microneedle deployment (8)(9).Materials used in the device are FDA-recognized as food grade, inactive ingredients, or generally regarded as safe (GRAS), supporting the biocompatibility and regulatory acceptance for oral administration. Materials used in the device are FDA-recognized as food grade, inactive ingredients, or generally regarded as safe (GRAS), supporting the biocompatibility and regulatory acceptance for oral administration (10). EX: Rani pill

- **Drug Delivery :**

This flowchart depicts the oral robotic pill's delivery mechanism:

Capsule enters stomach, protected by pH-sensitive coating

⇓

Coating dissolves in intestinal pH environment

⇓

Balloon inflates releasing gas, clearing mucus barrier

⇓

Microsyringe injects the drug-loaded microneedle into intestinal wall

⇓

Drug absorption into systemic circulation bypassing harsh GI environment

Functions:

- Enable precise drug release in the intestine using pH-sensitive coatings and mechanical activation.
- Deliver biologics, peptides, and proteins directly past mucosal barriers via microneedle or injector technology.
- Improve patient comfort and adherence by providing a non-invasive alternative to injections.
- Protect acid-sensitive medicines from degradation in the stomach, allowing controlled release in the gut.
- Allow site-specific, timed, and responsive drug administration based on intestinal environment signals(8)(9).

III. MATERIALS AND METHODS

Capsule Shell and Coating:

Robotic pills are formulated using size 000 hydroxypropyl methylcellulose (HPMC) capsules due to their superior stability, low moisture content, and compatibility with pharmaceutical excipients and enteric coatings (11). For targeted intestinal delivery, a pH-sensitive polymeric coating (e.g., methacrylic acid copolymer, Eudragit, or advanced multi-layered coatings) is applied using automated coating equipment (12) (14)

Internal Device Design:

The pill incorporates a polyethylene balloon (about 75 mm by 21–25 mm when expanded) and a micro-syringe system containing a dissolvable polyethylene glycol microneedle preloaded with solid drug. The balloon inflates via reaction between potassium bicarbonate and citric acid, separated by a valve made from polyethylene oxide (15).

Materials Selection:

All materials—including balloon, micro-syringe, and microneedle, shell, and reaction valve—are selected for FDA GRAS status or as approved food-grade components, assuring biocompatibility for oral use. (16)

Device Assembly:

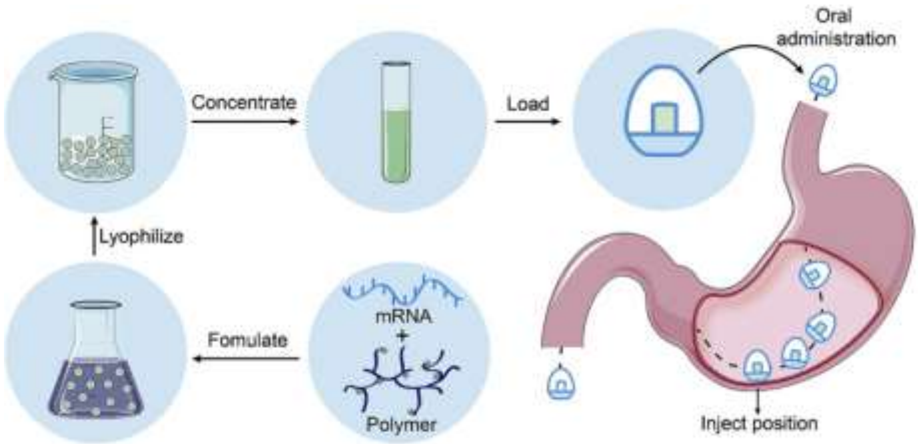
Each pill is assembled under sterile conditions, with automated equipment loading the drug payload and integrating micro-components. Quality control includes weight, integrity, and coating uniformity checks (11).

In Vitro and In Vivo Testing:

Drug release and activation profiles are evaluated in simulated gastric and intestinal fluids using dissolution apparatus and image analysis for deployment confirmation. Where appropriate, Phase I safety and performance trials are conducted in human volunteers (15).

EMERGING USES: ORAL DELIVERY OF MRNA THERAPEUTICS AND BIOLOGICS

Recent research has also explored robotic pill platforms for the oral delivery of mRNA therapeutics, which traditionally require injection due to instability and poor GI absorption. In experimental studies, robotic capsules equipped with protective coatings and microneedle systems succeeded in delivering mRNA directly to intestinal tissues, resulting in measurable protein expression and immunogenic response in animal models. This approach opens possibilities for non-invasive gene therapy, cancer vaccination, or treatment of genetic diseases. Similarly, robotic pills are being investigated for targeted oral administration of GLP-1 receptor agonists and monoclonal antibodies, offering new options for chronic disease management without injections (17).



Schematic process of orally delivering mRNA via robotic pill: Formulation, lyophilization, concentration, capsule loading, oral administration, and targeted intestinal injection to enhance absorption and therapeutic effect.

PREPARATION AND ADMINISTRATION OF MRNA-LOADED ROBOTIC PILLS IN THE GI TRACT:

Recent developments in robotic capsule engineering have enabled oral delivery of a wide range of macromolecules, such as mRNA, peptides, monoclonal antibodies, and small molecule drugs, making therapy more convenient and patient-friendly . SOMA capsules, pioneered by research teams including Abramson et al., utilize a self-orienting system inspired by the leopard tortoise to ensure rapid stabilization in the stomach. This design facilitates swift injection of medication-loaded microneedle tips directly into the gastric lining, triggered by dissolution of a targeted sugar-based actuator. Results show effective transfer of insulin and other biologic agents to the mucosa shortly after administration .Advancements have extended this technology to systemic delivery of larger molecules, including monoclonal antibodies and peptides, via oral capsules, reaching therapeutic blood levels in as little as thirty minutes, comparable to injection-based methods . Other innovative devices such as the LUMI system use unfolding microneedle arms to contact and deliver medication across the intestine. Additionally, kirigami-inspired stents are being explored for gradual, site-specific drug release, further reducing adverse effects and improving efficacy. Collectively, these robotic pill systems represent a significant step toward simple, non-invasive delivery of mRNA therapies and vaccines through the gastrointestinal tract.(18)

III. ADVANTAGES, APPLICATIONS, LIMITATIONS:

Advantages:

- Enables oral delivery of biologics and drugs previously restricted to injection.
- Improves patient compliance, comfort, and quality of life.
- Reduces risk of needle-stick injuries and associated infections.
- Allows site-specific and controlled drug release within the GI tract.
- Supports innovation in personalized medicine and chronic disease management .

Limitations:

- Limited long-term clinical trial data and regulatory approvals so far.
- Possible device retention or malfunction in rare cases.
- Challenges with large-scale manufacture and cost effectiveness.
- Drug load and capsule size restrictions for certain therapies **.**

APPLICATIONS:

Pill for oral delivery of biotherapeutics : -

The discomfort and inconvenience of frequent injections contribute to poor patient compliance and inadequate disease treatment, despite the high effectiveness of biotherapeutics. Despite numerous attempts, oral biotherapeutic administration remains ineffectual due to intestinal absorption problems and GI environment degradation. We developed an oral robotic pill (RP) that blocks the GI system from breaking down the biotherapeutic medication payload when it is delivered.

The promising clinical results show that this versatile, oral drug delivery method could make it possible to safely and reliably distribute biotherapeutics that are currently administered parenterally.

IV. CURRENT AND FUTURE CLINICAL APPLICATIONS

Current Applications:

- Oral insulin delivery for diabetes management.
- Non-invasive administration of antibiotics and therapeutic peptides.
- Emergency drug release in GI disorders .

Future Prospects:

Oral mRNA and gene therapy delivery for cancer and rare diseases.

Targeted vaccines and immunotherapies.

Personalized dosing, smart pill integration with digital health .

V. SAFETY, REGULATORY, AND ETHICAL ASPECTS

Safety and Tolerability:

Clinical and animal studies report favorable tolerability profiles for robotic pill platforms, with minimal gastrointestinal irritation and rare events of device retention or malfunction .

Regulatory Landscape:

Most robotic pills are in advanced preclinical or Phase I/II trials; standard approvals require demonstration of efficacy, safety, and device reliability. Regulatory agencies focus on quality control, biocompatibility, and patient monitoring .

Ethical Considerations:

Issues around patient consent, remote monitoring, and device failure management are under discussion as these technologies progress to market .

VI. Recent Innovations and Smart Capsules

Wireless Capsule Endoscopy:

Latest designs use sensors and wireless communication for internal monitoring, diagnostics, and responsive drug release .Magnetic and Programmable Capsules:

Research into capsules guided by magnetic fields or programmed for multi-stage release shows potential for precise, timed, and patient-specific therapy .Personalized Medicine Applications:

Custom drug cocktails, tailored release profiles, and data-driven

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