WJPMR, 2026, 12(11), 426-449

Review Article

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Impact Factor: 7.533

ISSN (O): 2455-3301

ISSN (P): 3051-2557

Coden USA: WJPMBB

FROM SWALLOWABLE DEVICES TO SMART THERAPEUTICS: ADVANCES IN ORALLY INGESTIBLE MEDICAL DEVICES AND SOMA-BASED BIOLOGIC DELIVERY

Saira Bhanu Shaik*[1], G. Akhila Bhanu Prasanna[2], M.A.V.D.S. Prajna[3], Ch. Siva Durga[4], Ch. Janush[5], P. Sai Srinu[6], A. Vara Lakshmi[7], M. Vamsi Vara Prasad[8]

[1]Assistant Professor, M.Pharm;(Ph.D), Dept. of Pharmaceutical Analysis, Koringa College of Pharmacy, Korangi, Kakinada, Andhra Pradesh, India.

[2-8]B.Pharm Scholar, Department of Pharmacy Practice, Koringa College of Pharmacy, Korangi, Kakinada, Andhra Pradesh, India.

***Corresponding Author: Saira Bhanu Shaik**

Assistant Professor, M.Pharm;(Ph.D), Dept. of Pharmaceutical Analysis, Koringa College of Pharmacy, Korangi, Kakinada, Andhra Pradesh, India.

DOI: https://doi.org/10.5281/zenodo.23914865

How to cite this Article: Saira Bhanu Shaik*[1], G. Akhila Bhanu Prasanna[2], M.A.V.D.S. Prajna[3], Ch. Siva Durga[4], Ch. Janush[5], P. Sai Srinu[6], A. Vara Lakshmi[7], M. Vamsi Vara Prasad[8]. (2026). From Swallowable Devices To Smart Therapeutics: Advances In Orally Ingestible Medical Devices and Soma-Based Biologic Delivery. World Journal of Pharmaceutical and Medical Research, 12(11), 426–449.

This work is licensed under Creative Commons Attribution 4.0 International license.

Article Received on 05/10/2026 **Article Revised on 25/10/2026** **Article Published on 01/11/2026**

ABSTRACT

Orally ingestible medical devices represent an emerging approach in modern healthcare, offering minimally invasive methods for drug delivery, sensing, sampling, imaging, diagnosis, and targeted therapy within the gastrointestinal (GI) tract. Unlike conventional oral dosage forms, these devices can perform specific functions after ingestion and may improve the localized delivery and monitoring of therapeutic agents. Recent advances in microengineering, robotics, biomaterials, and programmable systems have enabled the development of ingestible devices with applications ranging from gastrointestinal imaging and microbiome sampling to biological drug delivery. One notable example is the self-orienting millimeter-scale applicator (SOMA), an experimental ingestible device developed for the oral delivery of biologic therapeutics such as insulin. SOMA is designed to autonomously orient itself within the stomach and deploy a drug-loaded microneedle into the gastric tissue, thereby enabling drug delivery while avoiding conventional injections. Preclinical studies have demonstrated the feasibility of this approach, although SOMA is not currently an FDA-approved or marketed therapeutic device. Beyond insulin delivery, the underlying technology may have potential for delivering other biological medicines that are difficult to administer orally because of degradation and poor gastrointestinal permeability. This review discusses the classification and applications of orally ingestible medical devices, their mechanisms of action, major challenges in oral delivery of biologics, and the design and working principle of SOMA. It also highlights the potential advantages, limitations, and future prospects of ingestible devices in improving patient-friendly and minimally invasive delivery of therapeutic agents.

KEYWORDS: Orally ingestible medical devices; SOMA; self-orienting millimeter-scale applicator; oral drug delivery; gastrointestinal drug delivery; biologics; insulin delivery; ingestible devices; microneedle; targeted drug delivery; therapeutic delivery; drug delivery systems.

1. INTRODUCTION

Oral drug delivery is one of the most widely used routes for administering therapeutic agents because it is convenient, non-invasive, painless, and generally well accepted by patients. Tablets, capsules, powders, solutions, and suspensions are commonly administered through the oral route. Compared with injectable administration, oral delivery allows patients to administer medicines without specialized assistance and is particularly suitable for long-term treatment. These advantages have made the oral route an important focus

of pharmaceutical research and formulation development.[1,2]

1.1 Oral Drug Delivery: An Overview

Following oral administration, a drug passes through different regions of the gastrointestinal (GI) tract before reaching its site of absorption. The dosage form generally undergoes disintegration and dissolution, followed by release of the active pharmaceutical ingredient. The dissolved drug then interacts with the gastrointestinal environment and may cross the intestinal epithelial barrier to enter the systemic circulation. Therefore, oral drug absorption is influenced by drug solubility, dissolution rate, gastrointestinal stability, permeability, intestinal transit, and first-pass metabolism.[3]

The gastrointestinal tract is a highly complex physiological system rather than simply a passage for drug transport. It contains different pH environments, digestive enzymes, mucus layers, bile salts, intestinal fluids, epithelial cells, and microorganisms. These factors can influence the stability, release, absorption, and bioavailability of orally administered drugs.[4] Gastric emptying and intestinal motility can also produce variations in the time available for drug dissolution and absorption.

Conventional oral formulations work particularly well for many small-molecule drugs that possess adequate stability and permeability. However, the increasing development of peptides, proteins, antibodies, nucleic acids, vaccines, and other biological therapeutics has exposed important limitations of conventional oral dosage forms.[5]

1.2 Need for Advanced Oral Drug Delivery Systems

The growing number of complex therapeutic molecules has increased the demand for advanced oral drug delivery technologies. Conventional tablets and capsules generally depend on the passive release and subsequent absorption of the drug. This approach becomes inadequate when the therapeutic molecule is unstable in the GI tract, poorly soluble, poorly permeable, or requires delivery to a particular gastrointestinal region.[6]

An advanced oral drug delivery system should ideally protect the therapeutic agent from degradation, provide controlled drug release, improve intestinal absorption, and, where necessary, deliver the drug at a specific site.

Different approaches such as gastroretentive systems, mucoadhesive systems, nanoparticles, lipid-based carriers, permeation-enhancing systems, and other specialized delivery platforms have therefore been investigated.[7–9] Another important requirement is the ability to deliver drugs locally within the gastrointestinal tract. Local delivery can be useful when the therapeutic target is located in the GI tract because it may increase drug exposure at the desired site while potentially reducing unnecessary systemic exposure. This has encouraged the development of systems capable of controlling drug release according to gastrointestinal location and physiological conditions.[10]

1.3 Challenges in Oral Delivery of Biologics and Macromolecules

The oral delivery of biologics and macromolecules remains a major challenge in pharmaceutical science. Peptides, proteins, antibodies, nucleic acids, and other macromolecules are generally large, hydrophilic, and structurally complex. These characteristics make their transport across the intestinal epithelium difficult.[11]

One of the first barriers encountered after oral administration is the **acidic environment of the stomach**. Some biological molecules may undergo structural changes or degradation under acidic conditions. After entering the intestine, they are exposed to proteolytic and other digestive enzymes that can further degrade the therapeutic molecule.[12]

Another important barrier is the **intestinal mucus layer**. Mucus protects the intestinal epithelium from harmful substances and microorganisms, but it can also restrict the movement of therapeutic molecules and drug-delivery systems toward the epithelial surface.[13]

The **intestinal epithelial barrier** represents another major obstacle. The epithelial layer controls the movement of substances from the intestinal lumen into the body. Large hydrophilic macromolecules generally have limited ability to cross cell membranes by passive diffusion. Tight junctions between epithelial cells also restrict paracellular transport of large molecules.[14,15]

In addition, biological molecules may undergo **poor chemical and physical stability**, aggregation, and degradation during formulation, storage, and gastrointestinal transit. Their relatively low permeability and susceptibility to degradation can consequently result in very low oral bioavailability.[16]

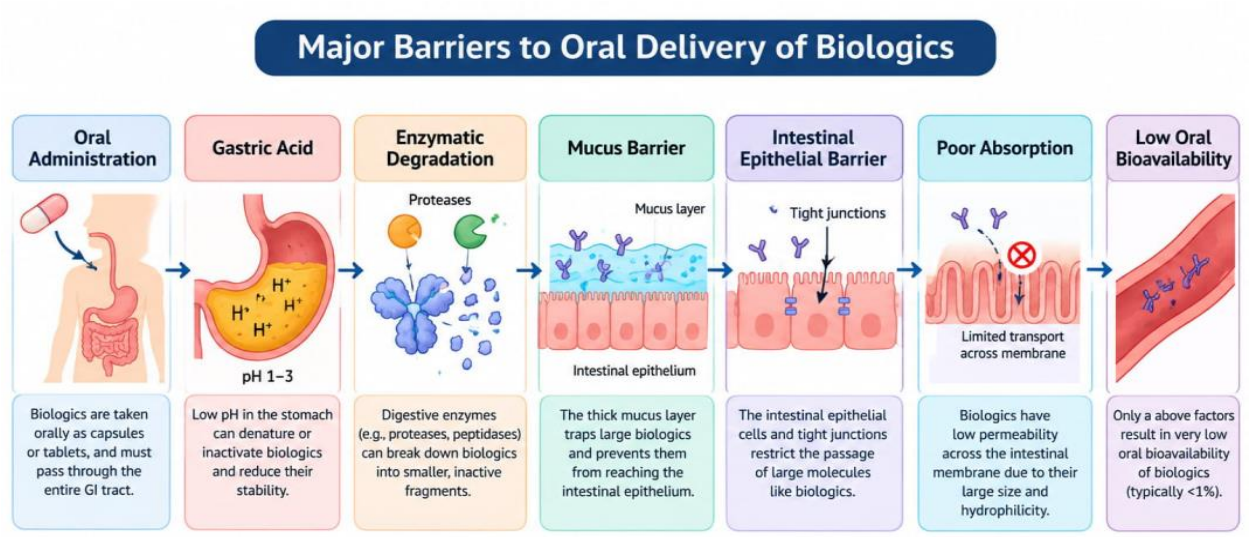
1.4 Major Barriers to Oral Delivery of Biologics

The major barriers can be summarized as:

- ✔ Oral administration
- ✔ Gastric acid
- ✔ Enzymatic degradation
- ✔ Mucus barrier
- ✔ Intestinal epithelial barrier
- ✔ Poor permeability
- ✔ Low absorption
- ✔ Low oral bioavailability

Because of these barriers, many biologic therapies are traditionally administered through parenteral routes. Although injections can provide effective systemic delivery, repeated administration may be inconvenient and uncomfortable for patients. Consequently, significant research has been directed toward developing

technologies that can deliver biologics through the oral route.[17]



1.5 Emergence of Orally Ingestible Medical Devices

Unlike conventional tablets or capsules, these systems can be engineered to perform functions such as **targeted drug delivery, biological sampling, sensing, imaging, diagnosis, monitoring, and localized therapeutic intervention.**[18,19] Some devices use mechanical components, sensors, electronics, microneedles, or other engineered structures to interact with specific regions of the GI tract.

One important development is the use of ingestible systems for the delivery of macromolecules. For example, self-orienting ingestible devices have been investigated for delivering therapeutic macromolecules through the gastrointestinal wall, demonstrating how an orally administered device can overcome some limitations of conventional passive absorption.[20]

Ingestible devices have also been developed for gastrointestinal sensing and biological monitoring. Capsule-based technologies can travel through the GI tract and collect information about the local physiological environment. Such approaches demonstrate the potential of the gastrointestinal tract as an accessible site for minimally invasive diagnosis and monitoring.[21]

2. ORALLY INGESTIBLE DRUG DELIVERY DEVICES

Orally ingestible drug delivery devices are an emerging class of drug delivery technologies designed to be swallowed and transported through the gastrointestinal (GI) tract to perform a specific therapeutic function. Unlike conventional tablets and capsules, which mainly depend on drug dissolution followed by passive absorption, ingestible devices can be engineered to control the location, timing, and mechanism of drug delivery. These systems are particularly important for therapeutic agents that are difficult to administer orally, including peptides, proteins, and other macromolecules.[22,23]

2.1 Definition and Concept of Ingestible Devices

An orally ingestible medical device can be described as a swallowable device that enters the gastrointestinal tract and performs a predefined medical function. Depending on its design, the device may be used for drug delivery, biological sampling, sensing, imaging, diagnosis, monitoring, or localized treatment.[24]

The basic concept of an ingestible drug delivery device is to use the gastrointestinal tract not merely as a pathway for drug transport but as an **active site for therapeutic intervention**. After swallowing, the device travels through the stomach and intestine and may respond to physiological or anatomical conditions to perform its intended function.For conventional oral dosage forms, the general process is drug release followed by dissolution and absorption. In contrast, an ingestible device can incorporate mechanical, chemical, electronic, or programmable components that allow the therapeutic agent to be released at a selected location or through a specific mechanism.[25]

This approach is particularly valuable for biologics. Large therapeutic molecules generally have poor intestinal permeability and are susceptible to degradation by gastrointestinal enzymes. An ingestible device can potentially protect the therapeutic molecule and facilitate its delivery close to or across the intestinal barrier.[26] important example is the **self-orienting millimeter-scale ingestible device** developed for oral delivery of macromolecules. The device was designed to orient itself within the gastrointestinal tract and deploy a drug through the tissue, demonstrating the possibility of

delivering macromolecules by an orally administered device.[27]

2.2 Evolution of Ingestible Drug Delivery Technologies

The next stage involved **modified-release and gastro retentive systems**, which attempted to control the rate or location of drug release. Enteric-coated formulations, for example, were designed to prevent drug release in the stomach and promote release in the intestine.

Gastro retentive systems were developed to increase residence time within the stomach and improve drug absorption for suitable drugs.[28]

Further development resulted in **advanced carrier-based systems**, including nanoparticles, polymeric carriers, lipid-based systems, and permeation-enhancing formulations. These technologies were developed to improve drug stability, solubility, intestinal permeability, and bioavailability.[29]

A major development was the introduction of ingestible systems capable of delivering macromolecules through the gastrointestinal wall. Abramson and colleagues demonstrated a self-orienting ingestible system capable of delivering macromolecules through the stomach wall, providing an important proof of concept for device-mediated oral delivery of biologics.[30] At the same time, capsule-based technologies were being developed for purposes other than drug delivery. Wireless capsule endoscopy demonstrated that a swallowable device could acquire images while passing through the gastrointestinal tract, establishing an important foundation for modern ingestible medical devices.[31]

More recent systems have incorporated **miniaturized sensors, electronics, wireless communication, microneedles, and programmable mechanisms**. These technologies have expanded the potential applications of ingestible devices from drug delivery to physiological monitoring, biological sampling, diagnosis, and gastrointestinal research.[32]

✔ Thus, the evolution of the field can be summarized as:

- **Conventional oral dosage forms**
- **Controlled-release systems**
- **Advanced carrier systems**
- **Device-based drug delivery**
- **Smart and multifunctional ingestible devices**

The major change during this evolution has been the transition from **passive drug release to active interaction with the gastrointestinal environment**.

2.3 Classification of Oral Ingestible Devices

Oral ingestible devices can be classified according to their primary function. Since some modern systems perform multiple functions, a single device may fall into more than one category.

2.3.1 Ingestible Drug Delivery Devices

These devices are specifically designed to administer therapeutic agents within the gastrointestinal tract. They may provide controlled, targeted, or localized delivery and are particularly relevant to drugs that have poor oral bioavailability.

Drug delivery devices may use different mechanisms, including mechanical deployment, microneedles, controlled-release compartments, or other engineered structures. These systems have been investigated for the delivery of peptides, proteins, and other macromolecules.[33]

2.3.2 Ingestible sensing Devices

Ingestible sensing devices contain sensors capable of detecting physiological or chemical parameters within the GI tract. Depending on their design, they can measure parameters such as temperature, pressure, pH, gases, or specific biological signals.

These systems can provide information about the gastrointestinal environment and may support disease monitoring and physiological research.[34]

2.3.3 Ingestible Sampling Devices

Sampling devices are designed to collect biological material from specific regions of the gastrointestinal tract. The collected material can subsequently be analyzed for microorganisms, metabolites, proteins, inflammatory markers, or other biological components.

This approach is particularly useful for investigating the **spatial variation of the gut microbiome**, because microbial composition may differ between different regions of the GI tract.[35]

2.3.4 Ingestible Imaging Devices

Ingestible imaging devices are designed to capture images during passage through the gastrointestinal tract. The best-established example is **capsule endoscopy**, in which a patient swallows a small capsule containing a miniature camera, light source, battery, and image-transmission system.

The capsule travels through the GI tract and transmits images to an external recording system, allowing visualization of gastrointestinal regions without conventional endoscopic insertion.

2.3.5 Ingestible Diagnostic Devices

Diagnostic ingestible devices are designed to obtain information that can assist in the detection or monitoring of disease. These systems may combine sensing, sampling, or imaging functions to identify physiological or biochemical changes within the gastrointestinal tract.[36]

2.3.6 Ingestible Therapeutic Devices

Some ingestible devices are designed to provide a therapeutic action directly within the GI tract. Instead of simply releasing a drug into the lumen, these systems may interact with tissues or provide localized treatment.

Such approaches are being investigated for conditions in which local gastrointestinal intervention may be beneficial.[37]

2.3.7 Robotic and Programmable Ingestible Devices

Recent advances have introduced robotic and programmable functions into ingestible medical devices. These systems may incorporate miniature actuators, sensors, motors, or programmable components that enable controlled movement, orientation, activation, or drug deployment.

The incorporation of these technologies has increased the possibility of developing **smart ingestible devices capable of performing multiple predetermined functions inside the gastrointestinal tract.**

Classification of Oral Ingestible Devices

Type	Primary function
Drug delivery devices	Delivery of therapeutic agents
Sensing devices	Detection of physiological or biochemical parameters
Sampling devices	Collection of GI biological samples
Imaging devices	Visualization of the GI tract
Diagnostic devices	Detection or monitoring of disease-related changes
Therapeutic devices	Localized therapeutic intervention
Robotic/programmable devices	Controlled or programmed medical actions

Overall, orally ingestible devices have evolved from relatively simple drug-containing systems into sophisticated platforms capable of performing **drug delivery, sensing, sampling, imaging, diagnosis, and therapeutic functions**. This evolution has created new possibilities for overcoming biological barriers and improving the delivery of therapeutics that are difficult to administer using conventional oral dosage forms

2.4 TYPES OF ORALLY INGESTIBLE MEDICAL DEVICES

Orally ingestible medical devices are designed to perform specific medical functions after being swallowed and entering the gastrointestinal (GI) tract. Depending on their intended application, these devices can be broadly classified into **drug delivery devices, diagnostic and monitoring devices, sampling devices, therapeutic devices, and sensing devices**. Among these, drug delivery devices have received considerable attention because they can overcome several limitations associated with conventional oral administration, particularly for peptides, proteins, and other biological therapeutics.

1. DRUG DELIVERY DEVICES

Orally ingestible drug delivery devices are engineered systems that deliver a therapeutic agent at a predetermined site and/or time within the gastrointestinal tract. Unlike conventional tablets and capsules, these systems can provide controlled, targeted, or mechanically assisted delivery.

Some devices use electronic systems, mechanical actuation, springs, reservoirs, or microneedles to improve drug administration. These approaches are particularly important for macromolecular drugs that are poorly absorbed or degraded in the GI tract.[38,39]

The major orally ingestible drug delivery devices include **SOMA, L-SOMA, LUMI, RaniPill, and IntelliCap**.

1.1 SOMA Device

SOMA (Self-Orienting Millimeter-scale Applicator) is an ingestible device developed for the oral delivery of macromolecular drugs such as insulin. The major challenge addressed by SOMA is that large biological molecules generally have poor oral bioavailability because they are degraded in the GI tract and have difficulty crossing the intestinal epithelium.

The SOMA device is designed to **self-orient inside the stomach** so that its drug-delivery mechanism faces the gastric wall. It contains a small amount of drug and a spring-loaded mechanism connected to a dissolvable needle. After the device reaches the stomach, its shape and mass distribution allow it to orient appropriately. The needle then penetrates the gastric tissue and releases the drug directly into the tissue.

One of the important features of SOMA is that the patient does not need to control the orientation or position of the device. After administration, the device performs the delivery automatically. Preclinical studies demonstrated successful delivery of insulin in large-animal models, showing the potential of ingestible systems for systemic delivery of biologics.[40]



1.2 L-SOMA Device

L-SOMA (Long-acting SOMA) represents an extension of the SOMA concept designed to provide **longer-lasting drug delivery**. While the conventional SOMA system is primarily intended to deliver a drug dose through a single administration event, the L-SOMA concept focuses on extending the duration of therapeutic exposure.

The basic principle is based on the self-orienting mechanism of SOMA, while incorporating a formulation or delivery strategy capable of providing prolonged drug release. Such systems are particularly useful for biological drugs that normally require frequent injections. The development of long-acting ingestible systems is an important direction in oral biologic delivery because it combines the convenience of oral administration with approaches normally associated with parenteral long-acting formulations.[41,42]



1.3 LUMI Device

LUMI is an ingestible drug-delivery platform developed to enable controlled administration of therapeutic agents within the gastrointestinal tract. The device concept is based on placing the drug in a protected internal reservoir and releasing it at a selected location in the GI tract.

LUMI-type systems demonstrate how ingestible devices can combine **drug protection, site-specific delivery, and controlled release** within a single swallowed platform. These characteristics are especially relevant for drugs that require delivery beyond the stomach or that have limited stability in the gastrointestinal environment.[43]



1.4 RaniPill Device

RaniPill is an orally ingestible platform developed for the delivery of biologic drugs, including peptides and proteins that are difficult to administer effectively by conventional oral dosage forms. The system is designed to transport the drug through the stomach and release it after reaching the intestine.

A key feature of the RaniPill technology is its use of **self-deploying microneedles**. RaniPill therefore represents an important approach for converting injectable biologics into a swallowable dosage form. Its development demonstrates the potential of mechanical and microneedle-based systems for improving the oral delivery of macromolecular therapeutics.[44,45]

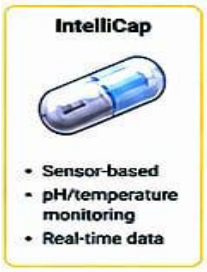


1.5 IntelliCap Device

IntelliCap is a programmable, electronically controlled ingestible drug-delivery capsule. Unlike conventional capsules, which generally release their contents according to formulation properties, IntelliCap can provide **controlled and programmable drug release**.

The device contains a drug reservoir and an electronic control system that regulates drug release. The release profile can be programmed according to the required treatment conditions, allowing drug administration to be modified with respect to **time, dose, and location** within the gastrointestinal tract.

IntelliCap illustrates the transition from passive oral dosage forms toward **active, programmable ingestible drug-delivery systems**, in which electronic and mechanical components can be integrated with pharmaceutical formulations.[46]



2. SENSING DEVICES

Sensing devices are an important category of orally ingestible medical devices designed to measure physiological conditions inside the gastrointestinal (GI) tract. After swallowing, these devices can collect information such as **pH, pressure, temperature, gastrointestinal transit time, gas composition, and intestinal motility**.

The collected data are transmitted to an external receiver or stored for later analysis. Unlike conventional diagnostic procedures, ingestible sensors can provide information from different regions of the GI tract without requiring repeated invasive procedures.[47]

2.1 SmartPill

The **SmartPill** is an ingestible wireless gastrointestinal monitoring capsule developed to assess GI tract function. It contains sensors that can measure **pH, temperature, and pressure** as the capsule passes through the gastrointestinal tract.

After the capsule is swallowed, the recorded information helps determine **gastric emptying time, small-intestinal transit time, colonic transit time, and whole-gut transit time**. Pressure measurements can also provide information about gastrointestinal motility.

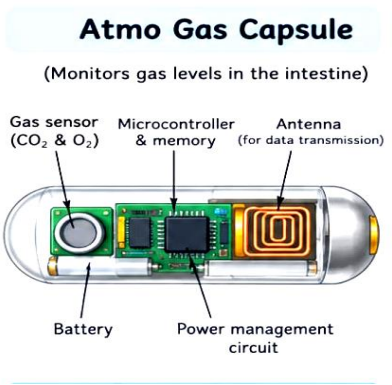
The SmartPill therefore provides a non-invasive method for evaluating gastrointestinal motility and transit abnormalities. It has been investigated particularly in patients with suspected disorders such as **gastroparesis, constipation, and other gastrointestinal motility disorders**. The device demonstrates how a small ingestible sensor can continuously monitor physiological changes throughout the GI tract.[48]

2.2 Atmo Gas Capsule

The **Atmo Gas Capsule** is an ingestible sensing system designed to analyse **intestinal gases** and provide information about gastrointestinal physiology. After ingestion, the capsule travels through the GI tract and detects gases produced within the intestinal environment.

The device can measure changes in gases such as **hydrogen, oxygen, and carbon dioxide**, which can reflect microbial activity and physiological processes occurring in different regions of the intestine. The measurements are transmitted wirelessly to an external receiver for analysis.

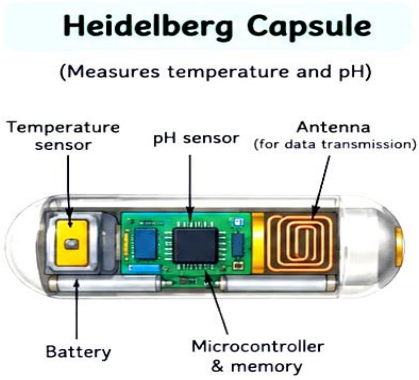
This approach provides an opportunity to study the GI environment directly and may help researchers understand **gut microbiota activity, digestion, fermentation, and gastrointestinal disorders**.[49]



2.3 Heidelberg Capsule

The **Heidelberg pH capsule**, also known as the **Heidelberg capsule**, is an ingestible device primarily used for measuring **gastrointestinal pH**. The capsule contains a pH-sensitive sensor and transmits measurements to an external receiver as it passes through the GI tract.

The continuous pH profile obtained from the capsule can provide information about the **acidic environment of the stomach and the transition from the stomach to the intestine**. It has been used in the assessment of gastric acid secretion and in studies evaluating the effect of acid-suppressing treatments.[50]



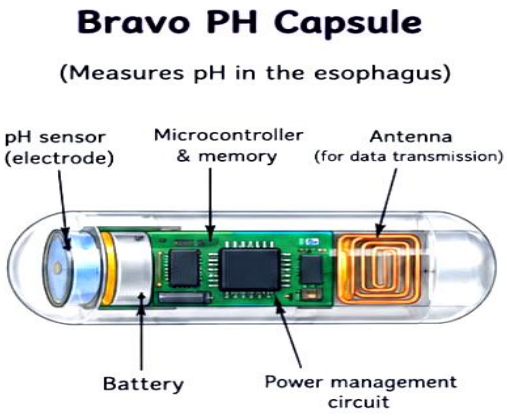
2.4 Bravo pH Capsule

The **Bravo pH capsule** is a wireless ingestible pH monitoring system mainly used for evaluating **gastroesophageal reflux disease (GERD)**. Unlike a conventional pH catheter, the Bravo capsule is temporarily attached to the oesophageal mucosa during an endoscopic procedure.

The capsule continuously measures oesophageal pH and wirelessly transmits the data to a receiver worn by the patient.

The system allows prolonged monitoring of acid exposure, commonly over approximately **48 hours**, depending on the specific system and protocol.

The recorded data can help determine the frequency and duration of acid reflux episodes and can support the evaluation of patients with suspected GERD.



Because there is no transnasal catheter during the monitoring period, the system can provide a more comfortable alternative for prolonged ambulatory oesophageal pH monitoring.[51]

3. SAMPLING DEVICES

Sampling devices are orally ingestible medical devices designed to **collect biological samples from specific regions of the gastrointestinal (GI) tract**. These devices can collect intestinal contents, microorganisms, metabolites, and other biological materials without requiring repeated endoscopic procedures. They are particularly useful for studying the **gut microbiome**, gastrointestinal physiology, and regional changes in intestinal composition.

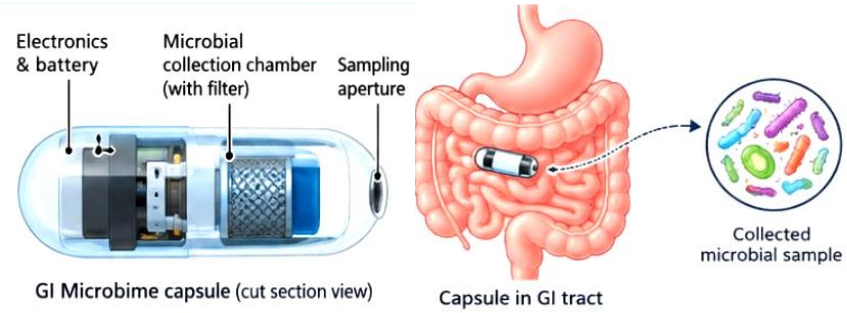
An important advantage of ingestible sampling systems is their ability to obtain samples from regions that are difficult to access using conventional endoscopy. Therefore, they provide an opportunity for more detailed and region-specific investigation of the GI tract.[52]

3.1 GI Microbiome Sampling Capsules

GI microbiome sampling capsules are ingestible devices developed to collect microorganisms and intestinal contents from different regions of the gastrointestinal tract. After swallowing, the capsule travels through the GI tract and collects a sample from its surrounding environment.

The collected material can contain **bacteria, microbial DNA, metabolites, and other components of the intestinal environment**. After recovery of the capsule, the sample can be analysed using microbiological and molecular techniques such as **DNA sequencing and metagenomic analysis**.

A major advantage of these capsules is that they can provide information about the microbiome at different locations within the GI tract. This is important because the composition of microorganisms can vary considerably between the stomach, small intestine, and colon. Therefore, ingestible sampling can provide a more detailed picture of the **spatial distribution of the gut microbiome** than stool analysis alone.[53]

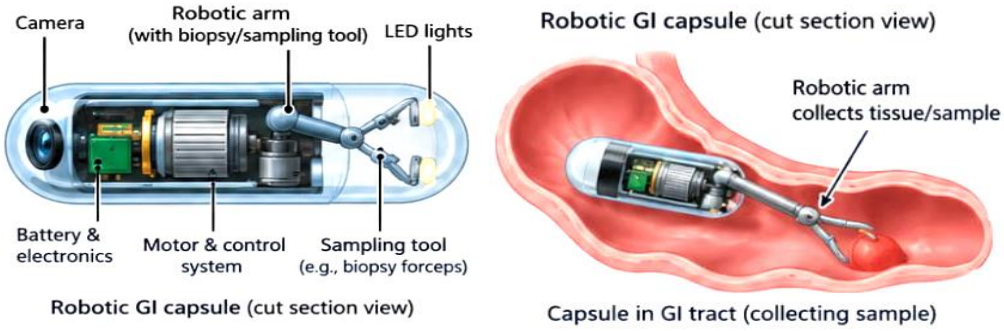


3.2 Robotic GI Sampling Capsules

Robotic gastrointestinal sampling capsules are advanced ingestible systems designed to collect biological samples from selected regions of the GI tract. These systems combine capsule technology with **miniaturized robotic or mechanically actuated components**.

After reaching the target region, the capsule can activate a sampling mechanism that collects intestinal fluid or mucosal material. Some designs incorporate controlled opening, suction, mechanical collection, or other actuation mechanisms to obtain the sample and protect it inside the capsule.

The major advantage of robotic sampling systems is the possibility of obtaining **site-specific samples** while the capsule moves naturally through the GI tract. This can reduce dependence on invasive sampling procedures and may be useful for investigating regional differences in microbiota, metabolites, and intestinal biomarkers. Such systems are still an emerging area of ingestible medical-device research.[54]

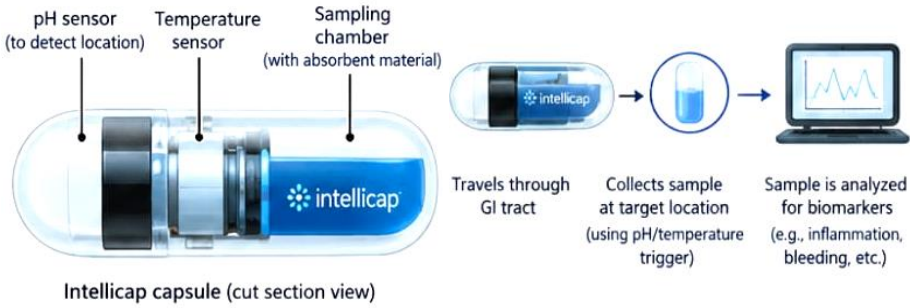


3.3 IntelliCap Sampling Systems

IntelliCap platform is primarily known as a programmable ingestible drug-delivery system, but related ingestible capsule technologies demonstrate the possibility of integrating **sampling and sensing functions** with controlled gastrointestinal operation.

An ingestible sampling system based on programmable capsule technology can be designed to control **when and where a sample is collected**. The capsule may remain closed during transit and activate its sampling mechanism at a predetermined time or GI location. The collected material can then be retained inside the device for subsequent laboratory analysis.

Integration of programmable control with sampling is important because it can improve the precision of GI investigations. This approach may support research into **microbiome composition, intestinal biomarkers, drug–microbiome interactions, and gastrointestinal diseases.**[55]



4. IMAGING DEVICES

Imaging devices are an important group of orally ingestible medical devices used to obtain **visual images of the gastrointestinal (GI) tract**. These devices are generally designed as small swallowable capsules containing a miniature camera, light source, battery, image sensor, and wireless transmission system. As the capsule travels naturally through the GI tract, it captures images and transmits them to an external recording device.

The major advantage of capsule-based imaging is that it allows visualization of regions of the GI tract that may be difficult to examine using conventional endoscopy, particularly the **small intestine**. It is a minimally invasive approach and does not require the patient to swallow or tolerate a conventional endoscopic tube.[56]

4.1 PillCam SB

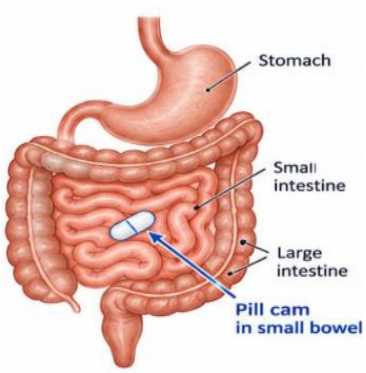
PillCam SB (Small Bowel) is a capsule endoscopy system specifically designed for imaging the **small intestine**. The capsule contains a miniature camera and illumination system that capture images as the capsule moves through the gastrointestinal tract.

After swallowing, the capsule passes naturally through the stomach and small intestine. Images are transmitted wirelessly to a recorder worn by the patient. The recorded images can subsequently be reviewed by a healthcare professional.

PillCam SB has been used particularly for the investigation of **small-bowel bleeding, Crohn's disease, small-intestinal lesions, and other mucosal abnormalities**. It provides visualization of the small bowel without the need for conventional invasive endoscopy.[57]



Pill cam **SB** (small bowel capsule)



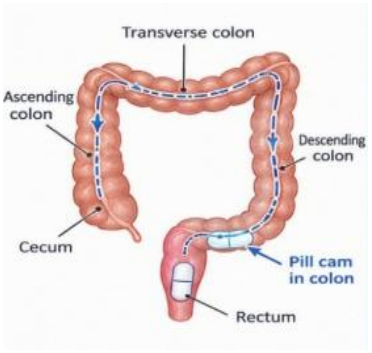
4.2 PillCam COLON

PillCam COLON is a capsule endoscopy system developed primarily for imaging the **colon and colorectal mucosa**. It contains cameras that allow visualization of the intestinal mucosal surface as the capsule travels through the gastrointestinal tract. The capsule captures images from different regions of the colon and transmits them to an external recording system. PillCam COLON has been investigated as a non-invasive or minimally invasive alternative for **colorectal evaluation and detection of colonic polyps and other mucosal abnormalities**.

An important advantage of colon capsule endoscopy is that it can visualize the colon without the insertion of a conventional colonoscope. However, adequate bowel preparation is still required, and the technique has limitations related to incomplete capsule transit and image interpretation.[58]



Pill cam **COLON** (colon capsule)



4.3 PillCam ESO

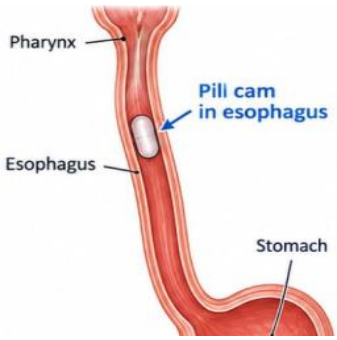
PillCam ESO (Esophagus) is a capsule endoscopy system designed for imaging the **oesophagus**. It contains miniature cameras positioned to capture images of the oesophageal mucosa as the capsule passes through the upper gastrointestinal tract.

The device can capture multiple images per second from the oesophageal region and transmit them wirelessly to an external recorder. It has been investigated for the detection and evaluation of **oesophageal mucosal abnormalities and conditions associated with gastroesophageal disease**.

PillCam ESO demonstrates how capsule endoscopy can be adapted for specific anatomical regions by modifying the camera arrangement and image-capture characteristics of the ingestible device.[59]



Pill cam **ESO** (esophageal capsule)



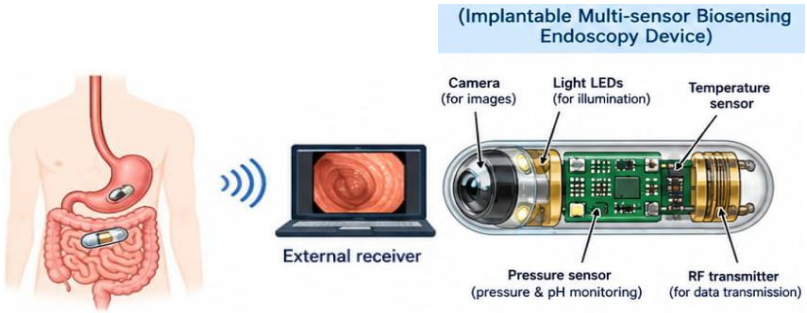
5. DIAGNOSTIC DEVICES

Orally ingestible diagnostic devices are designed to obtain information about the gastrointestinal tract and help in the detection or assessment of disease-related changes. These devices may incorporate **biosensors, cameras, chemical sensors, optical systems, and wireless communication components** to identify abnormalities during their passage through the GI tract.

Compared with conventional diagnostic methods, ingestible diagnostic devices can provide information from areas that are difficult to access using standard endoscopy. They can also support continuous or site-specific monitoring of physiological and pathological conditions.[60]

5.1 IMBED

IMBED represents an ingestible biosensing approach in which a swallowed device can detect biological or chemical information within the gastrointestinal environment. The basic concept of such systems is to combine a miniature sensing element with an ingestible platform so that measurements can be performed directly inside the GI tract. Depending on the sensor incorporated into the device, different parameters such as **chemical substances, gases, metabolites, pH, or disease-related biomarkers** can potentially be detected. The measured information can be stored within the device or transmitted wirelessly to an external receiver.The development of ingestible biosensors is important because many gastrointestinal processes cannot be accurately assessed using measurements obtained outside the body. Direct sensing within the GI tract may therefore provide more localized information about gastrointestinal physiology and disease processes.[61]

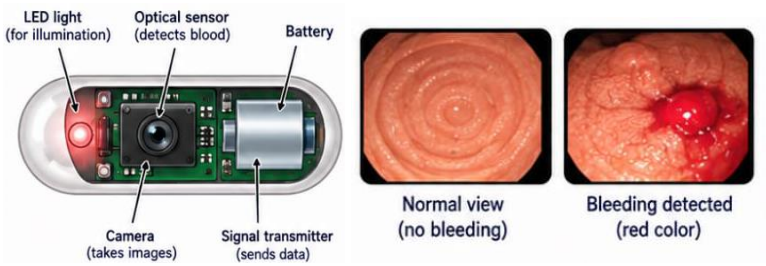


5.2 GI Bleeding Detection Capsule

A **GI bleeding detection capsule** is an ingestible diagnostic system designed to identify the presence and, in some approaches, the location of **blood within the gastrointestinal tract**.

The capsule may use optical imaging or blood-sensitive sensing mechanisms to detect changes associated with bleeding. As it travels through the GI tract, the device can identify blood or bleeding-related visual characteristics and transmit the information to an external recording system.

Such technology may be useful in the investigation of **obscure gastrointestinal bleeding**, particularly when the bleeding source is difficult to identify using conventional upper GI endoscopy or colonoscopy. The development of dedicated bleeding-detection capsules may improve the ability to identify bleeding episodes and potentially determine their approximate anatomical location.[62]

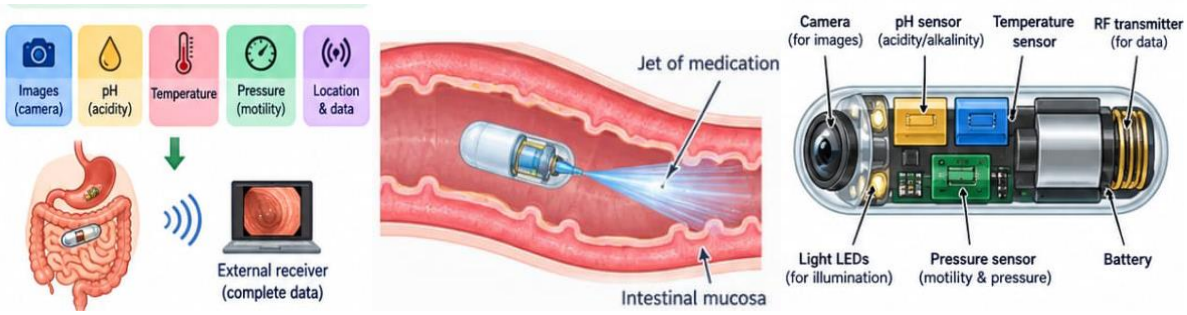


5.3 Multimodal Diagnostic Capsule

A **multimodal diagnostic capsule** combines more than one diagnostic function within a single ingestible platform. Instead of depending only on conventional imaging, these capsules may integrate **optical imaging with chemical sensing, pH measurement, temperature sensing, gas detection, or other biosensing technologies**.

The major advantage of multimodal systems is that different types of information can be obtained simultaneously. For example, imaging can provide structural information about the intestinal mucosa, while chemical or biological sensors can provide information about the local physiological environment.

Such integration can improve the characterization of gastrointestinal abnormalities because structural changes and biochemical changes can be assessed together. Multimodal capsules are therefore being investigated as next-generation platforms for **early disease detection, gastrointestinal monitoring, biomarker analysis, and personalized diagnosis.**[63,64]



6. THERAPEUTIC DEVICES

Therapeutic orally ingestible medical devices are designed not only to monitor or diagnose gastrointestinal conditions but also to **produce a therapeutic effect after ingestion**. These devices can use mechanical, physical, or electrical mechanisms to act on the gastrointestinal tract or facilitate the administration of therapeutic agents.

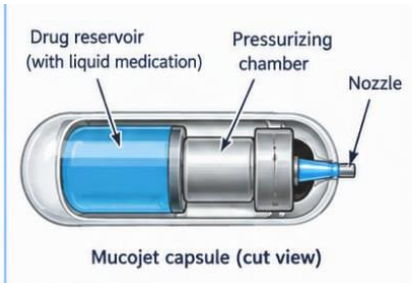
Unlike conventional oral dosage forms, therapeutic ingestible devices can perform an active function inside the GI tract. Important examples include **MucoJet, JetCap, and ingestible electrical-stimulation devices**.

6.1 MucoJet

MucoJet is an ingestible drug-delivery device designed to deliver therapeutic agents directly to the gastrointestinal mucosa. It was developed to overcome the barrier presented by the mucus layer and intestinal epithelium, which can limit the absorption of biological drugs.

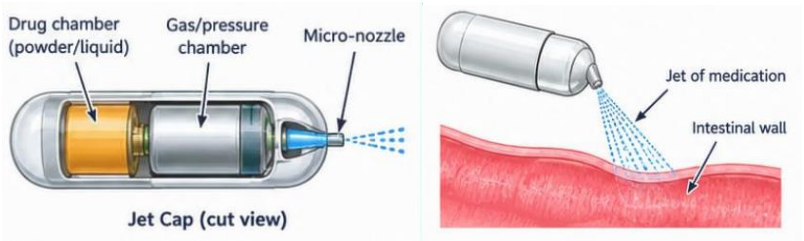
The MucoJet system uses a **high-pressure liquid jet** to propel the drug formulation toward the mucosal surface. When the device reaches the desired location, an internal mechanism generates pressure that forces the drug through a small nozzle. The resulting jet can penetrate the mucus layer and deliver the formulation directly onto or into the mucosal tissue.

This approach is particularly relevant for **macromolecules and biological therapeutics**, which generally show poor absorption after conventional oral administration. MucoJet therefore represents a mechanically assisted approach to improving local or systemic delivery through the gastrointestinal mucosa.[65]



6.2 JetCap

JetCap is an ingestible jet-based delivery system designed to administer a drug formulation through the gastrointestinal mucosal barrier. The device uses a controlled **liquid jet mechanism** to deliver the drug from the capsule toward the intestinal tissue.After reaching the target region, the device generates sufficient pressure to expel the drug through a small opening. The resulting jet provides a localized delivery mechanism and can help overcome the protective mucus layer.



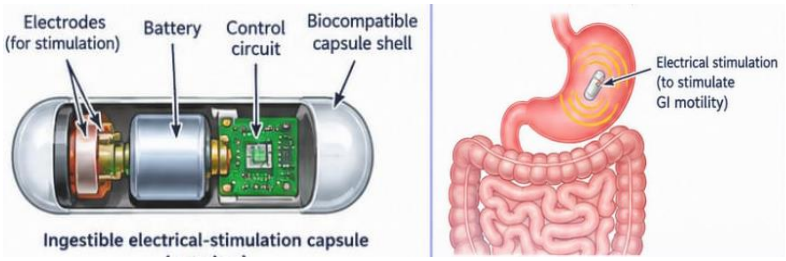
Jet-based ingestible systems are particularly interesting for the delivery of drugs that have difficulty crossing the GI epithelium by passive diffusion. They provide an alternative to conventional tablets and capsules by using **mechanical force rather than relying entirely on drug dissolution and passive absorption.**[66]

6.3 Ingestible Electrical-Stimulation Devices

Ingestible electrical-stimulation devices are swallowable systems that deliver controlled electrical signals to tissues within the gastrointestinal tract. These devices generally contain miniature electronic circuits, electrodes, a power source, and control components. After ingestion, the device can stimulate the surrounding gastrointestinal tissue using programmed electrical pulses.

Depending on the target and stimulation parameters, electrical stimulation may influence **gastrointestinal motility, neural activity, secretion, or other physiological functions**.

One potential application is the modulation of gastrointestinal motility in conditions where normal GI movement is impaired. Ingestible electrical systems are also being investigated as platforms for neuromodulation and other bioelectronic therapeutic approaches.

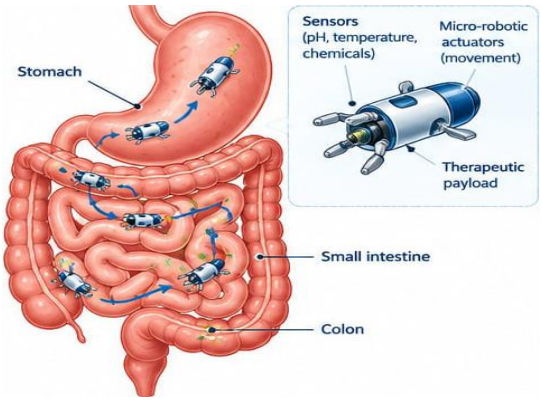


These devices represent an emerging transition from conventional pharmaceutical treatment toward **bioelectronic medicine**, in which electrical signals are used to modify physiological functions. Their major advantages include the possibility of localized stimulation and temporary treatment without permanent implantation.[67,68]

7. ROBOTIC/PROGRAMMABLE DEVICES

Robotic and programmable ingestible devices represent an advanced generation of orally ingestible medical technologies. Unlike passive capsules that mainly travel through the gastrointestinal tract with natural peristalsis, these systems can incorporate **actuation, sensing, wireless communication, magnetic control, and programmable mechanisms**.

The main purpose of these devices is to provide greater control over the movement, sensing, sampling, drug delivery, or therapeutic activity of the capsule. Such technologies have the potential to improve the precision and functionality of gastrointestinal interventions.[69]

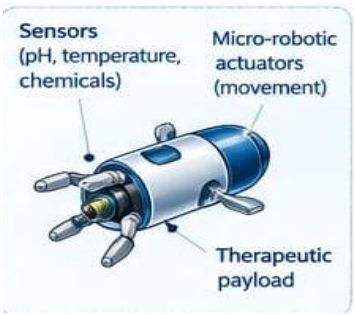


7.1 GI Microrobots

Gastrointestinal microrobots (GI microrobots) are miniature robotic systems designed to operate within the gastrointestinal tract. These devices may be swallowed as capsules or introduced through minimally invasive approaches and can perform functions such as **movement, sensing, drug delivery, sampling, and localized therapy**.

GI microrobots can be designed with small-scale actuators and sensors that allow them to interact with the intestinal environment. Some systems use external magnetic fields or other forms of remote control to influence their movement.

An important advantage of microrobotic systems is their potential to perform **localized and targeted functions** within the GI tract. Instead of relying entirely on passive gastrointestinal transit, future microrobots may allow clinicians to control the position and therapeutic action of the device. These systems are still largely in the research and development stage.[70]



7.2 Magnetic Capsule Robots

Magnetic capsule robots are ingestible robotic devices whose movement or operation can be controlled using an external magnetic field. A magnet incorporated into the capsule interacts with an externally generated magnetic field, allowing the capsule to be moved, rotated, or positioned within the gastrointestinal tract.

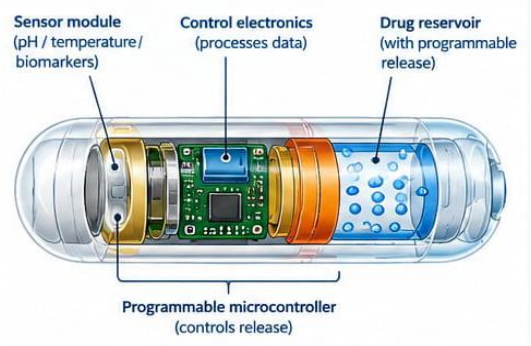
Magnetic control can provide advantages over conventional passive capsule systems because it can potentially allow **targeted positioning and controlled navigation**. Magnetic capsule robots have been investigated for applications including gastrointestinal imaging, targeted drug delivery, biopsy or tissue interaction, and other minimally invasive procedures.

The use of external magnetic control also reduces the requirement for complex onboard propulsion systems. This makes magnetic actuation an attractive approach for developing small and remotely controllable gastrointestinal robots.[71,72]

7.3 Programmable Smart Capsules

Programmable smart capsules are ingestible systems that combine sensors, electronic components, drug reservoirs, and programmable control mechanisms. Their operation can be adjusted according to predetermined parameters or external commands.

Depending on their design, smart capsules can control **drug release, sampling, sensing, imaging, or other therapeutic functions** at specific times or locations in the GI tract.



Wireless communication can also allow information to be transmitted between the capsule and an external monitoring device.

The major advantage of programmable capsules is their ability to perform **time-controlled and location-specific functions** rather than simply releasing a drug or collecting information passively. This approach can support personalized drug delivery, gastrointestinal monitoring, and controlled diagnostic procedures. Programmable ingestible systems therefore represent a transition from conventional capsules toward multifunctional robotic platforms capable of sensing their environment and responding according to programmed instructions.[73]

8. SOMA (Self-Orienting Millimeter-scale Applicator)

8.1 Introduction

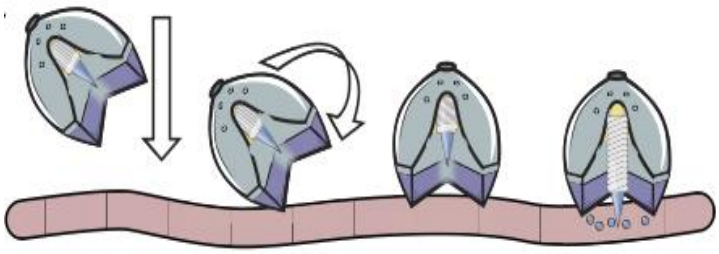
The **Self-Orienting Millimeter-scale Applicator (SOMA)** is an innovative ingestible drug-delivery device developed to provide an alternative route for the administration of macromolecular drugs such as insulin. Conventional oral delivery of proteins and peptides is difficult because these molecules can undergo degradation in the gastrointestinal tract and have poor permeability across the intestinal epithelium.[74,75]

SOMA addresses these limitations by using a small ingestible device that can self-orient inside the stomach and mechanically deliver the drug directly into the gastric tissue. The device was developed to combine the convenience of oral administration with the effectiveness of tissue-based delivery, providing a potential needle-free approach for systemic administration of biological medicines.[76]



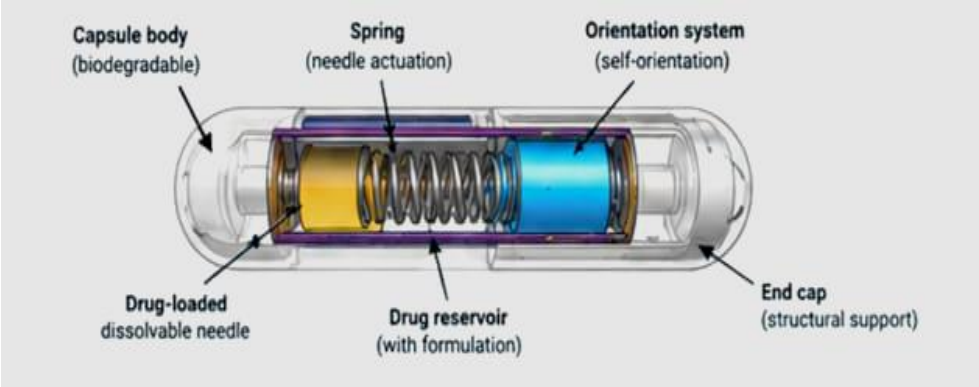
8.2 Design of SOMA

The design of SOMA is based on the principle of **self-orientation followed by mechanical drug delivery**. The device has a specially engineered shape and mass distribution that allow it to naturally orient toward the gastric wall after reaching the stomach. This feature is important because the drug-delivery mechanism needs to be positioned correctly before the drug can be introduced into the tissue.[76]



SOMA contains a **drug-loaded dissolvable needle, a spring-loaded actuation mechanism, structural components, and an orientation system**. The drug is incorporated into a small dissolvable needle that functions as the delivery element. A compressed spring stores mechanical energy inside the device, which is later released to push the needle into the gastric tissue.[76] The external geometry of SOMA is designed to provide stable orientation within the stomach. Its shape helps the device settle against the gastric wall in a predictable manner despite changes in its initial position after swallowing. This self-orienting capability reduces the dependence on external positioning or electronic control and is one of the major design features of the system.[76]

The **dissolvable needle** is another important component of the SOMA design. When the delivery mechanism is activated, the needle penetrates the gastric tissue and deposits the drug below the tissue surface. The needle is designed to dissolve after insertion, allowing the drug to be released into the tissue while avoiding the need for removal of a conventional needle.[76]



Overall, SOMA integrates **device geometry, controlled mechanical force, dissolvable microneedle technology, and drug formulation** into a single ingestible platform. This integrated design allows a biologic drug to be delivered through the gastric wall rather than relying solely on conventional gastrointestinal absorption.[77,78]

8.3 Use and Working of SOMA Applicator

The **Self-Orienting Millimeter-scale Applicator (SOMA)** is designed to function as an ingestible therapeutic device capable of transporting a biological drug to the stomach and delivering it directly into the gastric tissue. Unlike conventional oral dosage forms, which release the drug into the gastrointestinal lumen for subsequent absorption, SOMA combines drug storage, self-orientation, mechanical actuation, and tissue penetration within a single miniaturized platform. Such integration represents an important direction in the development of ingestible medical devices for active drug delivery.[79,80]

8.3.1 Administration of SOMA

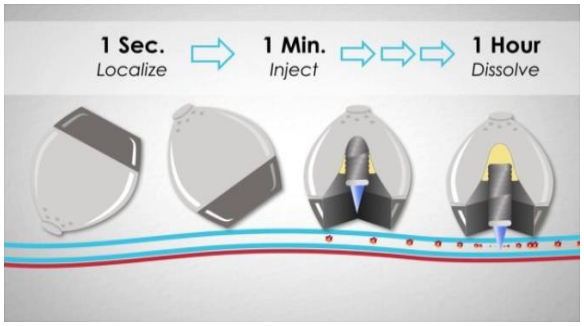
SOMA is intended to be swallowed orally as a compact ingestible device. After administration, it passes through the upper gastrointestinal tract and reaches the stomach, where the device interacts with the gastric environment. Ingestible medical devices are increasingly being designed to perform functions beyond simple drug release, including sensing, sampling, imaging, and active therapeutic intervention.[79,80]

The important feature of SOMA is that its operation does not require the patient to manually position the device after swallowing. Its specially engineered structure allows it to establish a preferred orientation inside the stomach. This principle is related to the broader development of ingestible systems in which device geometry, physical forces, and miniaturized mechanisms are used to achieve specific functions within the gastrointestinal tract.[79,81]

8.3.2 Self-Orientation

After entering the stomach, SOMA undergoes **self-orientation** so that the drug-delivery component is directed toward the gastric wall. Predictable positioning is particularly important for an ingestible tissue-delivery system because the orientation of the device determines the direction of mechanical deployment.

The concept of controlling the position and movement of gastrointestinal devices has also been explored using magnetic actuation and other forms of external manipulation.

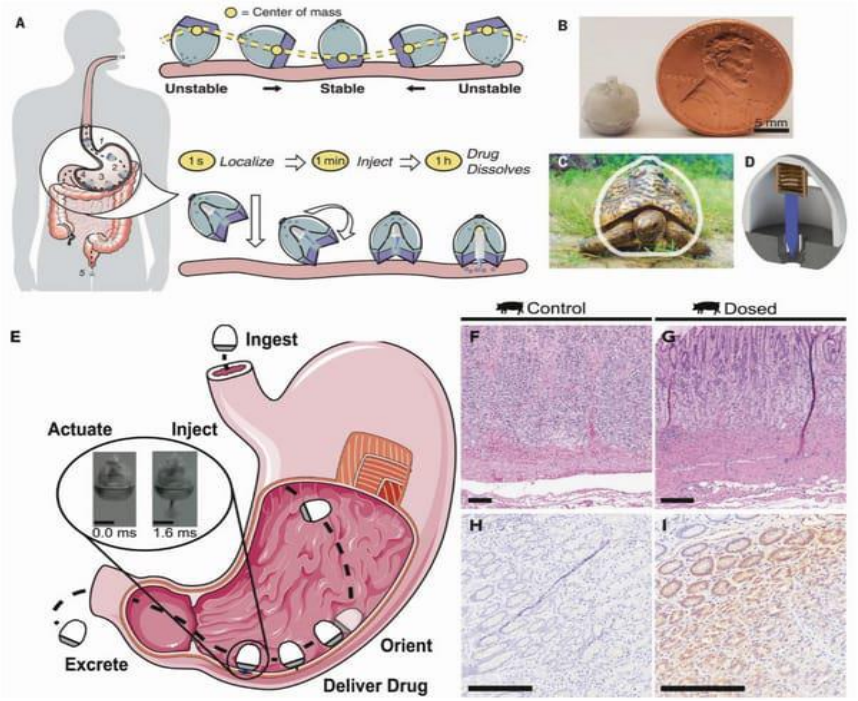


However, passive self-orientation offers the potential advantage of reducing dependence on external positioning equipment and simplifying administration.[81,82]

8.3.3 Mechanical Drug Delivery

Following appropriate orientation, the SOMA applicator uses a stored mechanical force to activate its delivery mechanism. The mechanical system drives the drug-containing dissolvable needle into the gastric tissue. This converts the device from a passive capsule into an **active tissue-delivery system**.

Mechanical actuation is an important principle in miniature biomedical devices because controlled forces can be generated within a small device to perform specific biological functions. Similar engineering principles have been investigated in microrobotic and ingestible systems designed for interaction with tissues and organs.[82,83]



8.3.4 Drug Deposition

The dissolvable needle acts as the interface between the device and the gastric tissue. When the needle penetrates the tissue, the incorporated drug is deposited at the site of insertion. The subsequent dissolution of the needle allows the therapeutic molecule to become available within the local tissue environment. This approach is particularly relevant for biological medicines because many peptides and proteins have limited ability to cross gastrointestinal barriers following conventional oral administration. Active tissue delivery therefore provides an alternative strategy in which the therapeutic molecule is introduced beyond the luminal barrier rather than relying entirely on passive epithelial absorption.[84]

8.3.5 Completion of Drug Delivery

After the drug has been deposited, the dissolvable delivery element is designed to disappear through dissolution, while the remaining device components can continue through the gastrointestinal tract. The use of dissolvable delivery elements is advantageous because it avoids the requirement for retrieval of a sharp delivery needle after administration.

From a pharmaceutical perspective, the performance of the system depends on the interaction between **drug formulation, dissolvable needle material, mechanical force, tissue penetration, and drug-release characteristics**. Therefore, the applicator should be considered a combination of pharmaceutical and biomedical engineering technologies rather than simply a modified capsule.

8.3.6 Significance of the SOMA Applicator

The major significance of SOMA is its ability to transform oral administration into a form of **mechanically assisted tissue delivery**. This concept provides a possible solution to one of the major limitations of oral biologic therapy, where gastrointestinal degradation and low epithelial permeability can prevent therapeutically useful systemic exposure.

The broader field of ingestible medical devices has demonstrated that small swallowed systems can be engineered to interact with the gastrointestinal tract for diagnostic, sensing, and therapeutic purposes. SOMA extends this concept toward active delivery of biological medicines by incorporating a tissue-penetrating mechanism within the ingestible platform.

9. Beyond Insulin: Can SOMA Deliver Other Drugs?

Although SOMA was originally developed and experimentally demonstrated for insulin delivery, its basic mechanism is not limited to insulin. The platform is designed to deliver a drug-containing dissolvable needle into gastric tissue; therefore, in principle, it could be investigated for other **peptides, proteins, hormones, and selected biological medicines** that are difficult to administer by the conventional oral route. However, these applications remain investigational and would require optimization according to the dose, molecular size, stability, pharmacokinetics, pharmacodynamics, and therapeutic target of each drugs.

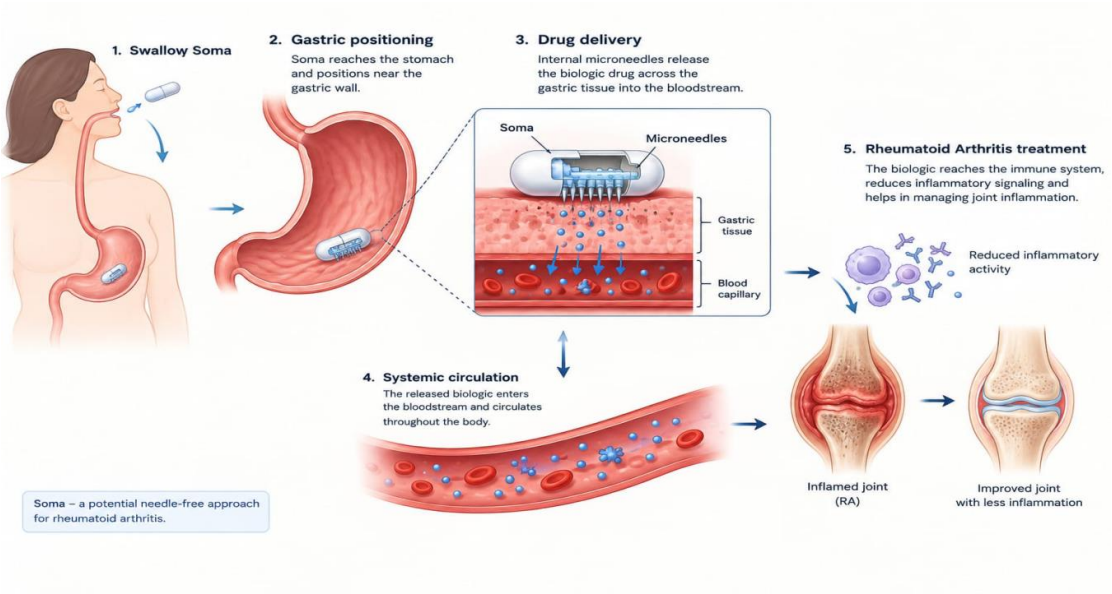
9.1 SOMA for Rheumatoid Arthritis: A Potential Needle-Free Approach

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease in which the immune system causes persistent inflammation of the synovial tissues surrounding joints.

Important biological targets in RA include **tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and other inflammatory pathways**. Biological medicines such as monoclonal antibodies and recombinant proteins are widely used to block these inflammatory mediators, but many require parenteral administration.[85,86] SOMA could theoretically provide an alternative oral route for selected biological medicines used in RA. After swallowing, the device would reach the stomach, self-orient toward the gastric wall, and mechanically insert a drug-loaded dissolvable needle into the gastric tissue. The therapeutic protein would then be released into the tissue and enter the local circulation, followed by systemic distribution.

Mechanism

SOMA Ingestion
↓
Stomach
↓
Drug Delivery
↓
Systemic Circulation
↓
Binds to Inflammatory target
↓
Reduces the Inflammatory Activity



For example, if a suitable **anti-TNF biological agent** were incorporated into a future SOMA formulation, the delivered antibody would theoretically enter systemic circulation and bind circulating or tissue-associated TNF-α. TNF-α blockade reduces downstream inflammatory signaling and can decrease production of inflammatory mediators involved in synovial inflammation. Similarly, an IL-6 pathway inhibitor could theoretically act by interfering with IL-6-mediated inflammatory signaling.

The important point is that **SOMA itself does not treat rheumatoid arthritis**. SOMA functions as the delivery platform, while the biological drug provides the pharmacological activity. Therefore, the feasibility of this application would depend on whether the required dose of the RA biologic can be incorporated into the device and whether sufficient systemic exposure can be achieved.

9.2 SOMA in Crohn's Disease: Expanding Oral Biological Delivery

Crohn's disease is a chronic inflammatory disorder of the gastrointestinal tract involving dysregulated immune responses and intestinal inflammation. Biological therapies used in Crohn's disease include agents directed against inflammatory mediators such as **TNF-α and interleukin pathways**, as well as other immune targets.[87,88] SOMA could potentially be investigated for oral administration of selected biological therapies in Crohn's disease. Following gastric delivery, the drug would be introduced into the gastric tissue and subsequently absorbed into the circulation. The biological medicine could then reach inflamed intestinal tissues through systemic distribution.

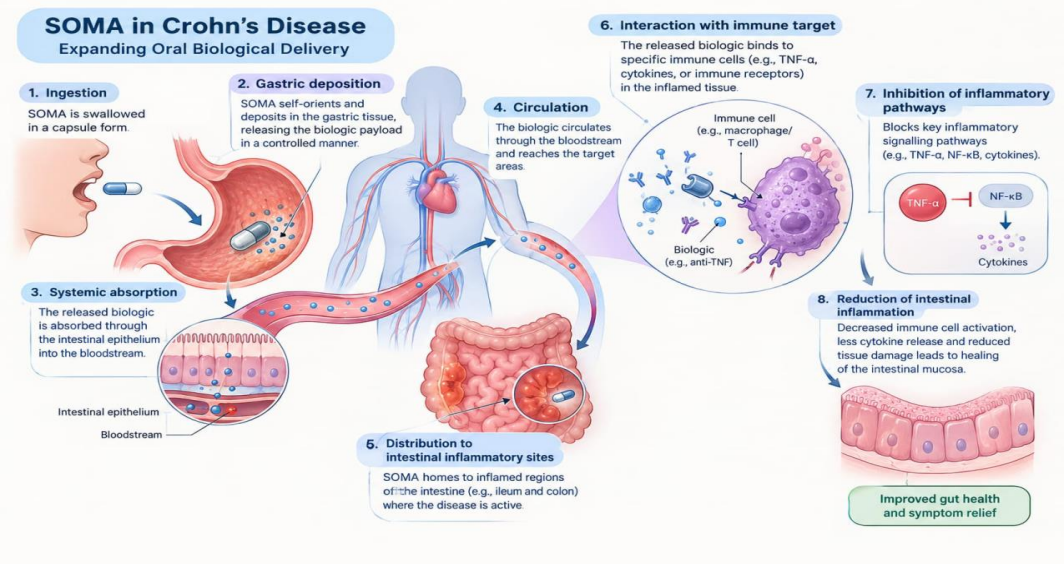
Mechanism

SOMA
↓
Gastric tissue deposition
↓
Systemic absorption
↓
Circulation
↓
Distribution to intestinal inflammatory sites
↓
Interaction with immune target
↓
Inhibition of inflammatory pathway
↓
Reduction of intestinal inflammation

nFor an anti-TNF therapeutic, the expected pharmacological mechanism would involve binding to TNF-α and reducing TNF-mediated activation of inflammatory cells and downstream cytokine signaling. This could theoretically reduce inflammatory activity associated with Crohn's disease.

However, Crohn's disease also highlights an important distinction between **local and systemic delivery**. If the therapeutic objective is specifically to act within the intestinal lumen or directly on intestinal mucosa, gastric-wall delivery may not necessarily provide the desired local concentration. In contrast, for biologics whose principal therapeutic action requires systemic exposure, SOMA could theoretically be more suitable.

Therefore, SOMA should not automatically be considered a treatment for Crohn's disease. Its potential role would depend on the pharmacological target and whether systemic delivery provides an adequate therapeutic concentration at the sites of inflammation.



9.3 Beyond Diabetes: SOMA for Autoimmune Therapies

The potential application of SOMA extends beyond diabetes because many autoimmune diseases are treated with **peptides, proteins, monoclonal antibodies, and other biological medicines**. Examples include rheumatoid arthritis, inflammatory bowel disease, psoriasis, multiple sclerosis, and other immune-mediated disorders.[89] The major concept is that SOMA could potentially replace repeated injections for selected biologics by introducing the therapeutic molecule into gastric tissue. Once absorbed, the drug could reach its pharmacological target through systemic circulation. For example, a biological medicine designed to inhibit a circulating cytokine would first be deposited into gastric tissue by SOMA.

After Absorption Mechanism

Drug deposition
↓
Systemic absorption
↓
Plasma distribution
↓
Target binding
↓
Inhibition of inflammatory signaling
↓
Reduction in disease-associated immune activity

In the case of a monoclonal antibody, the antibody would retain its specific binding activity after reaching the systemic circulation. It could recognize its target antigen or cytokine and interfere with the biological signaling pathway responsible for inflammation.

This concept is particularly attractive for chronic autoimmune diseases because patients may require repeated administration over long periods. An orally administered delivery device could potentially reduce dependence on conventional injections. Nevertheless, biologics often require relatively large doses, making **drug-loading capacity** one of the major challenges for adapting SOMA to monoclonal antibodies.

9.4 SOMA for Peptide and Hormone Delivery

Peptides and hormones represent another important group of molecules that could potentially benefit from SOMA-based delivery. Many peptide therapeutics have poor oral bioavailability because they are susceptible to enzymatic degradation and generally have limited permeability across gastrointestinal epithelial barriers.[90,91]

Potentially relevant peptide or hormone classes include **peptide hormones, therapeutic peptides, and protein-based endocrine medicines**. Examples may include selected hormone-replacement agents or peptide therapeutics where systemic exposure is required.

The proposed **mechanism** would involve incorporation of the peptide or hormone into the dissolvable needle followed by tissue deposition:

SOMA administration
↓
Gastric self-orientation
↓
Needle insertion
↓
Peptide/hormone release
↓
Tissue uptake
↓
Systemic circulation
↓
Receptor binding
↓
Physiological response

Once absorbed into the circulation, the therapeutic molecule would act according to its normal pharmacological mechanism. For example, a hormone

would bind to its specific receptor and initiate the appropriate intracellular signaling pathway. Therefore, SOMA does not change the fundamental pharmacological action of the hormone; instead, it changes **how the hormone reaches the systemic circulation**.

For peptide therapeutics, the major advantage of this approach is the possibility of avoiding extensive gastrointestinal degradation before systemic absorption. However, the peptide must remain structurally and pharmacologically active during formulation, storage, needle fabrication, and release.

9.5 The Wider Potential of SOMA for Biological Medicines

The broader significance of SOMA is its potential application as a **platform technology for oral delivery of biological medicines**. Biological drugs include peptides, proteins, enzymes, hormones, antibodies, and other macromolecules whose administration is often restricted by poor oral absorption.[92]

The potential sequence for a biological medicine can be represented as:

Ingestible SOMA
↓
Gastric positioning
↓
Mechanical tissue penetration
↓
Drug deposition
↓
Tissue uptake
↓
Systemic circulation
↓
Target tissue distribution
↓
Molecular target interaction
↓
Pharmacological response

The final pharmacological effect would depend entirely on the therapeutic molecule. For a receptor agonist, the drug would activate its receptor; for an antagonist, it would block receptor signaling; for an antibody, it could bind a specific antigen or soluble mediator; and for an enzyme replacement therapy, the delivered protein would need to reach the appropriate biological compartment and retain enzymatic activity.

Therefore, SOMA can be viewed as a **delivery technology rather than a therapeutic agent itself**. Its major contribution is to provide an alternative route for introducing biological molecules into the body.

10. SOMA vs Conventional Drug Delivery: What Could Change?

Conventional drug delivery systems have been highly successful for many small-molecule drugs, but the oral administration of peptides and proteins remains difficult. These molecules are generally large, chemically and enzymatically unstable, and poorly transported across the gastrointestinal epithelium. As a result, many biological medicines are administered by subcutaneous, intramuscular, or intravenous injection. The development of orally ingestible systems such as the Self-Orienting Millimeter-scale Applicator (SOMA) represents a different approach in which the device itself assists drug administration rather than depending only on conventional formulation strategies.[93,94]

11. Difference in the Basic Drug Delivery Approach

In conventional oral delivery, the drug must survive the acidic gastric environment, resist digestive enzymes, dissolve or remain available at the absorption site, cross the intestinal barrier, and finally enter systemic circulation. These barriers become particularly important for peptides and proteins because they can undergo extensive degradation before reaching the bloodstream.[95]

This represents a conceptual change from **"improving the drug formulation so that it can cross the GI tract"** to **"using an ingestible device to actively deliver the drug through the GI tissue."** Such a strategy may be particularly useful for biological medicines for which conventional oral absorption is extremely low.

11.1 Conventional Oral Delivery vs SOMA-Based Delivery

Conventional oral delivery mainly depends on passive or formulation-assisted absorption. Formulation technologies may include protective coatings, nanoparticles, permeation enhancers, enzyme inhibitors, mucoadhesive systems, and other approaches designed to improve the stability or permeability of the drug.[95,96]

SOMA represents a more mechanical approach. The drug is placed within a device that can autonomously orient itself inside the stomach. After appropriate positioning, the device uses a spring-loaded mechanism to introduce the drug into the stomach wall. Therefore, the device can potentially bypass some of the major epithelial and enzymatic barriers associated with conventional oral delivery.

11.2 Effect on Patient Convenience

The route of administration can strongly influence the practical experience of long-term treatment. Injectable therapies require preparation, appropriate injection technique, and repeated administration.

An orally ingestible system could potentially make administration easier because the patient would swallow

the device rather than directly inserting a needle into the body.

For this reason, device-based oral delivery may offer an alternative approach for patients who require repeated administration of biological medicines. The potential improvement in convenience is one of the important motivations behind research into oral biologic delivery.[97]

11.3 Possibility of Delivering Peptides and Proteins

Peptide and protein therapeutics have become an important part of modern medicine. However, their oral administration remains challenging because of enzymatic degradation, poor epithelial permeability, and unfavorable physicochemical properties.[98]

The same general concept could potentially be investigated for other peptide or protein medicines. However, each drug would require independent evaluation because molecular size, stability, potency, dose requirements, pharmacokinetics, and tissue distribution can differ substantially between biological medicines.[98]

11.4 Influence on Drug-Development Strategies

SOMA also demonstrates how drug-delivery technology can influence pharmaceutical development. Traditional drug development often focuses mainly on discovering a suitable active molecule and then developing a formulation that provides adequate exposure. For difficult-to-deliver biological molecules, the delivery device itself may become an integral component of the therapeutic system.[98]

12. Future Role of SOMA in Drug Delivery

SOMA should therefore be viewed as a platform that demonstrates a possible new route for administering difficult-to-deliver biological medicines rather than as a replacement for all conventional drug-delivery systems. Conventional oral formulations will continue to be appropriate for many drugs, while injectable administration remains important for numerous biological therapies.

The major contribution of SOMA is the demonstration that an ingestible device can actively deliver a macromolecule into gastrointestinal tissue. This concept may encourage the development of other orally ingestible systems capable of combining drug formulation, mechanical actuation, sensing, and targeted delivery.[98]

13. Future Advantages and Scope: Could SOMA Transform Drug Delivery?

The development of the Self-Orienting Millimeter-scale Applicator (SOMA) represents an important step toward transforming the way difficult-to-deliver medicines may be administered. Conventional oral dosage forms are highly convenient, but their application is limited for many biological drugs because peptides and proteins are vulnerable to gastrointestinal degradation and generally show poor absorption. SOMA introduces a different concept in which an ingestible device can actively deliver a drug into gastrointestinal tissue rather than depending entirely on conventional intestinal absorption. This concept creates several potential future advantages for oral delivery of biological medicines.

1. Expansion of Oral Delivery to Biological Medicines

One of the most important future advantages of SOMA is its potential to expand oral administration beyond conventional small-molecule drugs. Many modern therapies are peptides, proteins, antibodies, nucleic-acid-based medicines, or other macromolecules that are difficult to administer orally. Their large molecular size, enzymatic instability, and limited membrane permeability make conventional oral delivery challenging.[99,100]

2. Potential Improvement in Patient Acceptability

For chronic diseases requiring repeated administration, this could potentially improve treatment acceptability and simplify administration. Patient-centered drug delivery is increasingly important because the effectiveness of a therapy depends not only on pharmacological activity but also on whether patients can use the treatment consistently.[101]

3. Integration with Sensing Technologies

Another important future direction is the combination of drug delivery with sensing. Ingestible sensors have already demonstrated the ability to collect information about gastrointestinal conditions such as gases, pressure, temperature, and other physiological parameters.[102]

4. Scope for Next-Generation Ingestible Devices

SOMA can be viewed as part of a larger movement toward intelligent ingestible medical devices. Research in this field is increasingly exploring systems that can sense, diagnose, sample, image, stimulate, and deliver therapeutic agents within the gastrointestinal tract.[103,104]

14. Overall Future Scope

The future scope of SOMA extends beyond the delivery of a single biological drug. It represents a broader strategy for integrating pharmaceutical formulations with ingestible medical-device engineering. The platform may potentially support oral administration of selected peptides and proteins, reduce dependence on injections for some therapies, enable active gastrointestinal delivery, and provide a foundation for future smart ingestible systems. The ultimate impact of SOMA will depend on whether its promising preclinical concept can be translated into safe, reproducible, scalable, and clinically useful products. If these challenges are successfully addressed, SOMA-like technologies could become an important component of next-generation oral drug delivery and could contribute to expanding the

range of therapeutic molecules that can be administered through the gastrointestinal route.

15. CONCLUSION

Orally ingestible medical devices represent an emerging area of pharmaceutical and biomedical technology that combines drug delivery, sensing, diagnosis, sampling, imaging, and therapeutic intervention within ingestible systems. These devices have the potential to overcome several limitations of conventional oral dosage forms and may provide new ways to interact with different regions of the gastrointestinal tract. Technologies such as capsule endoscopy, ingestible sensors, microbiome-sampling devices, robotic capsules, and drug-delivery systems demonstrate the increasing capabilities of orally ingestible medical devices.

Among these technologies, the Self-Orienting Millimeter-scale Applicator (SOMA) represents an important advancement in the oral delivery of biological medicines. Conventional oral administration of peptides and proteins is difficult because of gastrointestinal degradation, poor permeability, and limited absorption. SOMA addresses this challenge through an active device-assisted delivery mechanism in which the ingestible system autonomously positions itself and delivers the drug into gastrointestinal tissue. The preclinical demonstration of this concept has provided an important proof of principle for the possibility of administering macromolecular drugs through an ingestible device.

Overall, orally ingestible medical devices are moving drug delivery from a **passive dosage-form concept toward active interaction between a medical device and the gastrointestinal tract**. SOMA is an important example of this transition. Although it should currently be regarded as a developing research technology rather than a clinically established replacement for injectable therapy, its underlying concept provides a promising foundation for future drug-delivery systems. Continued advances in pharmaceutical sciences, microengineering, robotics, materials science, electronics, and biomedical engineering may eventually enable safer, smarter, and more personalized ingestible therapeutic devices.

The future of orally ingestible medical devices is therefore likely to involve multifunctional systems capable of **sensing, targeting, sampling, diagnosing, and delivering therapy within the gastrointestinal tract**. With continued research and successful clinical translation, these technologies could broaden the range of medicines and medical functions that can be performed through a simple ingestible platform and contribute significantly to the development of next-generation patient-centered healthcare.

REFERENCES

1. Aulton ME, Taylor KMG. *Aulton's Pharmaceutics: The Design and Manufacture of Medicines*. 6th ed. Elsevier, 2022.
2. Kumar A, et al. Oral drug delivery: challenges and opportunities. *International Journal of Pharmaceutics*.
3. Dressman J, Reppas C. In vitro–in vivo correlations for lipophilic, poorly water-soluble drugs. *European Journal of Pharmaceutical Sciences*, 2000; 11(2): S73–S80.
4. Lennernäs H. Intestinal permeability and its relevance for absorption and elimination. *Xenobiotica*, 2007; 37(10–11): 1015–1051.
5. Moroz E, Matoori S, Leroux JC. Oral delivery of macromolecular drugs: Where we are after almost 100 years of attempts. *Advanced Drug Delivery Reviews*, 2016; 101: 108–121.
6. Park K. Controlled drug delivery systems: Past forward and future back. *Journal of Controlled Release*, 2014; 190: 3–8.
7. Ensign LM, Cone R, Hanes J. Oral drug delivery with polymeric nanoparticles: The gastrointestinal mucus barriers. *Advanced Drug Delivery Reviews*, 2012; 64(6): 557–570.
8. Lopes CM, Bettencourt C, Rossi A, Buttini F, Barata P. Overview on gastroretentive drug delivery systems for improving drug bioavailability. *International Journal of Pharmaceutics*, 2016; 510(1): 144–158.
9. Brayden DJ, Hill TA, Fairlie DP, Maher S, Mrsny RJ. Systemic delivery of peptides by the oral route. *Nature Reviews Drug Discovery*, 2020; 19: 127–148.
10. Wilson CG, Washington N. *Physiological Pharmaceutics: Biological Barriers to Drug Absorption*. 2nd ed. CRC Press.
11. Antosova Z, Mackova M, Kral V, Macek T. Therapeutic application of peptides and proteins: Parenteral vs. oral delivery. *Trends in Biotechnology*, 2009; 27(10): 628–635.
12. Bernkop-Schnürch A. The use of enzyme inhibitors to protect peptide drugs from gastrointestinal proteolysis. *Journal of Controlled Release*, 1998; 52(1–2): 1–16.
13. Ensign LM, Cone R, Hanes J. Oral drug delivery with polymeric nanoparticles: The gastrointestinal mucus barriers. *Advanced Drug Delivery Reviews*, 2012; 64(6): 557–570.
14. Vllasaliu D, Thanou M, Stolnik S, Fowler R. Recent advances in oral delivery of biologics: A review. *Pharmaceutical Research*, 2014; 31: 123–138.
15. Maher S, Mrsny RJ, Brayden DJ. Intestinal permeation enhancers for oral peptide delivery. *Advanced Drug Delivery Reviews*, 2016; 106: 277–319.
16. Daugherty AL, Mrsny RJ. Emerging technologies for the oral delivery of proteins and peptides. *Current Opinion in Chemical Biology*, 2000; 4(5): 593–598.

17. Buckley ST, Bækdal TA, Vegge A, et al. Transcellular uptake of a delivery system for oral administration of semaglutide. *Science Translational Medicine*, 2018; 10(467): eaar7047.
18. Kalantar-Zadeh K, Ha N, Ou JZ, Berean KJ. Ingestible sensors and devices for monitoring the gastrointestinal tract. *Advanced Functional Materials*, 2017; 27(7): 1604146.
19. Choi J, Rogers JA. Recent advances in the development of ingestible medical devices. *Advanced Materials*, 2018; 30(31): 1705368.
20. Abramson A, Caffarel-Salvador E, Khang M, et al. An ingestible self-orienting system for oral delivery of macromolecules. *Science*, 2019; 363(6427): 611–615.
21. Mimee M, Nadeau P, Hayward A, et al. An ingestible bacterial-electronic system to monitor gastrointestinal health. *Science*, 2018; 360(6391): 915–918.
22. Moroz E, Matoori S, Leroux JC. Oral delivery of macromolecular drugs: Where we are after almost 100 years of attempts. *Advanced Drug Delivery Reviews*, 2016; 101: 108–121.
23. Choi J, Rogers JA. Recent advances in the development of ingestible medical devices. *Advanced Materials*, 2018; 30(31): 1705368.
24. Kalantar-Zadeh K, Ha N, Ou JZ, Berean KJ. Ingestible sensors and devices for monitoring the gastrointestinal tract. *Advanced Functional Materials*, 2017; 27(7): 1604146.
25. Traverso G, Schoellhammer CM, Schroeder A, et al. Microneedles for drug delivery via the gastrointestinal tract. *Journal of Controlled Release*, 2015; 218: 46–53.
26. Brayden DJ, Hill TA, Fairlie DP, Maher S, Mrsny RJ. Systemic delivery of peptides by the oral route. *Nature Reviews Drug Discovery*, 2020; 19: 127–148.
27. Abramson A, Caffarel-Salvador E, Khang M, et al. An ingestible self-orienting system for oral delivery of macromolecules. *Science*, 2019; 363(6427): 611–615.
28. Lopes CM, Bettencourt C, Rossi A, Buttini F, Barata P. Overview on gastroretentive drug delivery systems for improving drug bioavailability. *International Journal of Pharmaceutics*, 2016; 510(1): 144–158.
29. Ensign LM, Cone R, Hanes J. Oral drug delivery with polymeric nanoparticles: The gastrointestinal mucus barriers. *Advanced Drug Delivery Reviews*, 2012; 64(6): 557–570.
30. Maher S, Mrsny RJ, Brayden DJ. Intestinal permeation enhancers for oral peptide delivery. *Advanced Drug Delivery Reviews*, 2016; 106: 277–319.
31. Iddan G, Meron G, Glukhovsky A, Swain P. Wireless capsule endoscopy. *Nature*, 2000; 405: 417.
32. Mimee M, Nadeau P, Hayward A, et al. An ingestible bacterial-electronic system to monitor gastrointestinal health. *Science*, 2018; 360(6391): 915–918.
33. Caffarel-Salvador E, Kearney MC, McCarthy HO, et al. Oral, controlled release delivery of macromolecules using ingestible systems. *Advanced Drug Delivery Reviews*.
34. Kalantar-Zadeh K, Berean KJ, Ha N, et al. A human pilot trial of ingestible sensors for monitoring gastrointestinal physiology. *Nature Electronics*, 2018; 1: 79–87.
35. Desai A, Yan Y, et al. Ingestible devices for gastrointestinal sampling and microbiome analysis. *Advanced Drug Delivery Reviews*.
36. Choi J, Rogers JA. Ingestible medical devices for gastrointestinal monitoring and diagnosis. *Advanced Materials*, 2018.
37. Caffarel-Salvador E, Abramson A, Langer R, Traverso G. Oral delivery of biologics using drug delivery systems. *Advanced Drug Delivery Reviews*, 2019.
38. Moroz E, Matoori S, Leroux JC. Oral delivery of macromolecular drugs: Where we are after almost 100 years of attempts. *Advanced Drug Delivery Reviews*, 2016; 101: 108–121.
39. Brayden DJ, Hill TA, Fairlie DP, Maher S, Mrsny RJ. Systemic delivery of peptides by the oral route. *Nature Reviews Drug Discovery*, 2020; 19: 127–148.
40. Abramson A, Caffarel-Salvador E, Khang M, et al. An ingestible self-orienting system for oral delivery of macromolecules. *Science*, 2019; 363(6427): 611–615.
41. Traverso G, Schoellhammer CM, Schroeder A, et al. Microneedles for drug delivery via the gastrointestinal tract. *Journal of Controlled Release*, 2015; 218: 46–53.
42. Caffarel-Salvador E, Kearney MC, McCarthy HO, et al. Oral, controlled release delivery of macromolecules using polymeric systems. *Advanced Drug Delivery Reviews*. [Reference details should be matched with the specific source used for L-SOMA.]
43. Choi J, Rogers JA. Recent advances in the development of ingestible medical devices. *Advanced Materials*, 2018; 30(31): 1705368.
44. Traverso G, Azagury DE, Hooper G, et al. Microneedles for drug delivery via the gastrointestinal tract: Development and applications. *Journal of Controlled Release*, 2015; 218: 46–53.
45. Rani Therapeutics. RaniPill® oral biologic delivery platform: development and preclinical evaluation. [Company/platform information; use a peer-reviewed RaniPill paper if required by the journal.]
46. Brambilla D, Luciani P, Leroux JC. The IntelliCap® system for programmable oral drug delivery. [Reference details should be matched with the original IntelliCap publication used in your review.]
47. Kalantar-Zadeh K, Ha N, Ou JZ, Berean KJ. Ingestible sensors and devices for monitoring the

gastrointestinal tract. *Advanced Functional Materials*, 2017; 27(7): 1604146.
48. Rao SSC, Kuo B, McCallum RW, et al. Investigation of colonic and whole-gut transit with wireless motility capsule and radiopaque markers in constipation. *Clinical Gastroenterology and Hepatology*, 2009; 7(5): 537–544.
49. Kalantar-Zadeh K, Berean KJ, Ha N, et al. A human pilot trial of ingestible electronic capsules capable of sensing different gases in the gut. *Nature Electronics*, 2018; 1: 79–87.
50. Read NW, Al-Janabi MN, Bates TE, et al. Simultaneous measurement of gastric pH and gastric emptying using an ingestible pH-sensitive capsule. *Gut*. [Heidelberg capsule methodology/reference; exact edition should be matched to the source used.]
51. Pandolfino JE, Richter JE, Ours T, Joehl RJ, Hawn M, Kahrilas PJ. Ambulatory esophageal pH monitoring using a wireless system. *American Journal of Gastroenterology*, 2003; 98(4): 740–749.
52. Kalantar-Zadeh K, Ha N, Ou JZ, Berean KJ. Ingestible sensors and devices for monitoring the gastrointestinal tract. *Advanced Functional Materials*, 2017; 27(7): 1604146.