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Review Article

Artificial Intelligence and Machine Learning in GRDDS

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ABSTRACT

Gastroretentive Drug Delivery Systems (GRDDS) are designed to remain in the stomach for extended periods, releasing their drug payload in the gastric environment. These platforms are especially beneficial for drugs with limited absorption in the distal gastrointestinal tract, narrow absorption windows in the proximal small intestine, stability or solubility issues at alkaline intestinal pH, short biological half-lives, or local therapeutic activity in the upper small intestine. Research and development are hindered by the complexity of GRDDS design, which requires the integration of drug kinetics, materials science, patient physiology, and real-time data. To transform GRDDS research, this study proposes a revolutionary approach that leverages AI-augmented data platforms. These systems enable intelligent decision-making, enhanced formulation strategies, and rapid prototyping throughout the drug development pipeline by integrating machine learning, predictive modelling, and real-world data analytics. When it comes to improving crucial GRDDS performance metrics, such as floating lag time, buoyancy duration, and drug release kinetics, Artificial Intelligence (AI) and Machine Learning (ML) are revolutionary. These factors are crucial for ensuring that the formulation releases the medicine in a controlled and efficient manner and maintains its presence in the stomach for an extended period.

Keywords: Artificial Intelligence, Biological Half-Lives, Extended Period, Gastroretentive Drug Delivery Systems, Machine Learning.

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INTRODUCTION

Recent advances in materials, formulation technologies, and therapeutic applications of gastro-retentive drug delivery systems are reviewed, alongside outlining the challenges faced (Bardonnet *et al.*, 2006). Such systems prolong retention in the gastric region and constitute a valuable approach when the stomach or proximal small intestine is the site for local or systemic drug action. Floating, bioadhesive, swelling/expanding, and sinking systems rely on different mechanisms for gastro-retention and are less affected by gastric emptying rate as compared with conventional controlled-release systems (Pant *et al.*, 2016). Polymers are the main formulating materials, and their characteristics determine the preparation method, release pattern, and *in vivo* performance. Various natural and synthetic polymers are presented along with their key properties, and the principal formulation strategies for each type of gastro-retentive system are described (Landge *et al.*, 2023). *In vitro* and *in vivo* evaluation techniques are summarized, and the therapeutic categories that benefit from prolonged gastric residency span the treatment of chronic pathologies, the administration of drugs that are less soluble at neutral pH, the local eradication of *H. Pylori* and other bacteria, the targeting of drugs to the upper small intestine, and the delivery of nutraceuticals (Rathod *et al.*, 2016).

METHODOLOGY

The authors conducted an extensive literature review to identify and analyze published work on the application of Artificial Intelligence (AI) and Machine Learning (ML) in Gastroretentive Drug Delivery Systems (GRDDS). Major electronic databases, including PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar, were systematically searched using combinations of keywords and Boolean operators such as "Artificial Intelligence," "Machine Learning," "Deep Learning," "Neural Networks," "Gastroretentive Drug Delivery Systems," "GRDDS," "Floating Drug Delivery Systems," "Controlled Release," and "Formulation Optimization." The search was limited to publications from the last 10-15 years to capture recent advancements in AI-driven pharmaceutical research. The inclusion criteria encompassed studies reporting the use of AI or ML applications in pharmaceutical formulation, optimization, modeling, or drug delivery systems, with a focus on gastroretentive or controlled-release platforms. Original research papers, review articles, and relevant book chapters in English were considered,

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whereas studies irrelevant to drug delivery or lacking sufficient scientific detail were excluded. Additional relevant papers were identified through a manual review of the bibliographies in the selected articles. From the eligible studies, information regarding AI and ML techniques, formulation variables, modeling approaches, performance metrics, and reported limitations was extracted. The collected data were analyzed qualitatively and synthesized to highlight current trends, challenges, and future directions in the development of AI-enabled GRDDS.

Overview of Gastroretentive Systems

Several approaches have been extensively explored to achieve a prolonged gastric residence time for orally administered drugs (Lopes *et al*., 2016). Floating systems have gained considerable attention and form the core focus of most recent technological innovations in this area. Inventive efforts have led to various floating formulations incorporating multiple strategies to enhance gastric retention (Kumar *et al*., 2018). In addition to gas-propelled and effervescent floating systems, ion-exchange resin-loaded, hollow microsphere-based floatable drug delivery systems, raft systems, and low-density systems have been more recently developed. These diverse developments have materialized into commercial products, and the clinical benefits of these therapeutically efficacious systems have been demonstrated (Abdel Rahim *et al*., 2017).

Therapeutic systems employing other mechanisms of gastric retention, such as bioadhesive or mucoadhesive systems, have also garnered significant interest. Recent studies have emphasized the advantages of selected polymers and polymer combinations for their gastroretentive properties. Furthermore, the performance of these systems has been evaluated using both *in vitro* and *in vivo* techniques (Tripathi *et al*., 2019).

Mechanisms of Gastroretention

Gastroretentive Drug Delivery Systems (GRDDS) were developed to prolong the retention of dosage forms within the stomach, allowing for a complete release of the active drug in the gastric environment (Haas *et al*., 2002). Various mechanisms have been used to achieve this effect, including floating systems, high-density formulations, bio/mucoadhesive platforms, expandable systems, superporous hydrogels, and magnetic devices. The stomach is segmented into the fundus, body, and antrum, with the proximal region serving as a reservoir and the antrum facilitating mixing and gastric emptying (Awasthi *et al*., 2016). Drugs that benefit most from gastric retention typically exhibit poor absorption in the distal gastrointestinal tract, possess a narrow absorption window, have stability or solubility challenges at alkaline pH, exhibit a short half-life, or provide local activity in the upper intestine (Prinderre *et al*., 2011; Bhalla *et al*., 2013).

Types of Gastroretentive Drug Delivery Systems

The concept of the gastroretentive drug delivery system was first initiated in the late 1960s, which led to extensive dissemination of pharmaceutical drug carriers capable of prolonging the retention time of drugs in the stomach or the upper part of the small intestine (Streubel *et al*., 2006). The majority of both single and multiple unit dosage forms possessing the ability to remain in the stomach for a prolonged period of time can be classified as gastroretentive. Many of these formulations are floating drug delivery systems developed based on micro balloons and air compartment tablets, whereas other types of gastroretentive formulations such as expanding [antipode] and gastric resin beads also exist (Gopalakrishnan *et al*., 2011). Common approaches for achieving gastric retention include bio-adhesive or mucoadhesive systems, incorporate low-density floating systems, high-density, sedimentation, magnetic, modified shape systems, or systems that promote gastric emptying delay.

Over the past 20 years, there has been a rising interest in the development of oral sustained drug-delivery systems capable of remaining for prolonged periods of time in the pre-stomach of animals. There are several advantages of this system listed here as prolonged residence time; specific drug delivery site; increase in bioavailability; decreased number of administrations; improved patient compliance; commercial value; achievement of desired pharmacological action; and drug absorption from the upper part of the gastrointestinal tract, preventing its reach to the colon (Iannuccelli *et al*., 1988).

Floating Drug Delivery Systems

Various attempts have been made to develop gastroretentive systems, including floating drug delivery systems, swelling and expanding systems, polymeric bioadhesive systems, high-density systems, modified-shape systems, and other delayed gastric emptying devices (Tomar *et al.*, 2019).

Floating dosage forms have attracted considerable interest due to their capacity to achieve gastric retention and prolonged-release profiles. Such systems may help overcome the short gastric residence time and physiological variability associated with liquid formulations. Floating matrix tablets can be prepared by incorporating suitable ingredients or gas-generating agents into tablets or capsules (Arora *et al.*, 2005).

Floating Drug Delivery Systems (FDDS)

Floating Drug Delivery Systems (FDDS) are designed to prolong gastric residence time and improve bioavailability and therapeutic effectiveness. They target drugs with a narrow absorption window, limited solubility at alkaline pH, instability in intestinal or colonic fluids, or local activity in the stomach or proximal small intestine shown in Figure 1. Various approaches have been investigated to confer buoyancy, controlled-release kinetics, and sustained drug release. Some formulation strategies include hydrodynamically

balanced systems, raft-forming systems, highly porous systems, and alginate beads. Despite some technical and physiological hurdles, floating dosage forms represent a promising approach for gastroretention and controlled drug delivery (Namdev *et al.*, 2019; Setia *et al.*, 2018).

Bioadhesive Systems

Bioadhesion can be defined as the adhesion between two materials, at least one of which is of biological origin. The term bioadhesion refers specifically to sticking to biological tissue. Mucoadhesion refers to sticking to mucus, and mucosa-adhesion refers to sticking to any mucosal location within the body (Gopaiah *et al.*, 2023; Chavanpatil *et al.*, 2006). The mucoadhesive or bioadhesive formulation, when comes in contact with mucus covering the biological membrane of the site of application, adheres to it. The increased retention at the site of administration enhances the residence time of drugs at the absorption site, leading to maintenance of a consistent and effective level of the drug in the bloodstream with a reduction in dosing frequency. In addition, mucoadhesive delivery systems can limit inter- and intra-subject drug absorption variability and protect the drugs from challenging environments (Streubel *et al.*, 2006).

Figure 2 explains the several mechanisms have been suggested for mucoadhesion; interpenetration and fracture strength are the most frequently accepted. Mucoadhesion can be described in two broad phases: Phase I contact stage, where swelling of the polymer occurs leading to the formation of mucus-polymer mash; and Phase II consolidation phase, where adhesion occurs as a result of chemical bonding between mucus and polymers. Hydration of the polymer and mucus induces close contact and allows penetration of the mucoadhesive polymer into the mucus (More *et al.*, 2018).

Expandable Systems

Expandable systems can be engineered to grow or reconfigure in the stomach to dimensions exceeding that of the pyloric sphincter, thereby prolonging the duration of gastric retention. These systems must be sufficiently small for easy administration; subsequently, they increase their dimensions to prevent passage through the pylorus (Das *et al.*,2021). At the conclusion of drug delivery, a reduction in size facilitates evacuation from the gastric cavity. Due to their capacity to occlude the pyloric orifice, such systems are often referred to as "plug-type." Expansion mechanisms include swelling and unfolding, enabling concurrent changes in volume and shape. Swelling systems commonly incorporate hydrophilic polymers such as Hydroxypropyl Methylcellulose (HPMC), Polyethylene Oxide (PEO), and Carbopol, which are selected for their pronounced capacity to absorb water (Rajendra *et al.*,2020). In unfolding systems, the drug and polymeric components are initially contained within a capsule in a folded configuration; upon capsule dissolution in gastric fluids, the apparatus expands to its unfolded geometry shown in Figure 3. Key attributes of the selected polymers encompass molecular weight, viscosity, swelling behavior, and biodegradability, all of which influence the ability of the system to remain in the stomach and to release the therapeutic agent in a controlled manner (Kumar *et al.*,2018). An illustrative example features an expandable matrix devised for gabapentin delivery, in which gelatin is combined with hydrophobic polymers that act as release retardants. Such a formulation is capable of unfolding and expanding to a maximum diameter exceeding 20 mm within 15 minutes, thereby potentially preventing premature clearance from the gastric environment (Streubel *et al.*, 2006).

Magnetic Systems

Systems that contain a small internal magnet and thus have potential for drug delivery include those with an external magnet placed at a suitable point on the body and those situated in the stomach that retained proximal to the magnet (Tripathi *et al.*, 2019). The idea of magnetic drug delivery to the stomach has been evaluated using a magnet embedded in a floating alginate system. *In vivo* studies using dogs showed that when an electromagnet

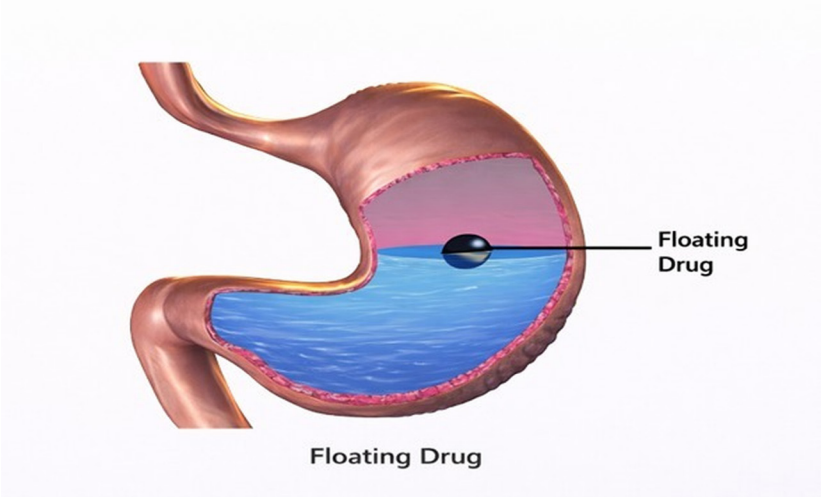

Figure 1: Discussion of floating dosage forms.

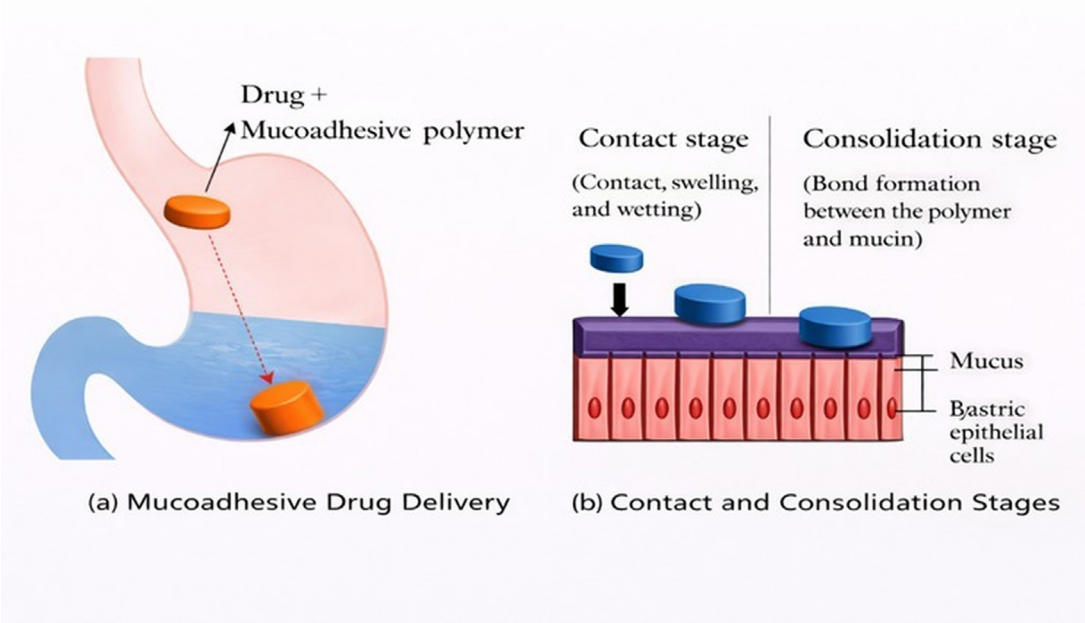

Figure 2: Discussion on Mucoadhesion.

was placed outside the abdomen, the floating was preserved for longer periods, but there was no evidence of an attraction of the dosage form to the region under the magnet. Also, the magnetic system did not show any noticeable advantage over nonmagnetic dosage forms with regard to *in vivo* gastric retention (Mishra *et al.*, 2024).

Interest has also centered on particulate drug delivery systems possessing magnetic properties. Gamma-ferric oxide magnetic particles have been used to prepare magnetic microspheres containing antioxidants with antitumor activity. Scintigraphic studies in humans demonstrated the ability to hold such particles in the stomach by the application of an external magnet situated on the abdomen shown in Figure 4. Better localization was obtained in the antrum when the magnet was held at the lower part of the abdomen (Rodrigues *et al.*, 2024). Cytotoxicity tests in mice using doxorubicin-loaded magnetic microspheres demonstrated that much smaller doses of doxorubicin were required when it was delivered using the magnetic particles (Souza *et al.*, 2021).

The Role of AI in Drug Delivery

AI is a broad branch of computer science concerned with building smart machines capable of performing tasks that typically require human intelligence. Machine learning, a subset of AI, trains computers to perform desired tasks by generalizing patterns from historical training data (Hassanzadeh *et al.*, 2019). Artificial Neural Networks (ANNs) constitute interconnected processors that simulate biological neurons and learn highly complex, nonlinear functions of underlying data. Natural Language Processing (NLP) enables computers to interpret and extract meaning from human language (Visan *et al.*, 2024). AI has afforded significant advances in numerous fields, including healthcare. It has played an increasing role in health monitoring and medical image analysis, as well as the diagnosis and treatment of diseases. More specifically, AI is being applied to improve drug delivery effectiveness and efficiency (Vora *et al.*, 2023).

AI Techniques Used In Drug Delivery Systems

Machine learning also profoundly influences drug delivery. Defined broadly, machine learning enables computer systems to learn autonomously from past data and experiences. Numerous algorithms cater to diverse applications (Tripathi *et al.*, 2019). The extensive data generated within the drug-delivery sector can be scrutinized through machine learning to extract meaningful trends and patterns. Natural-language processing tools, capable of interpreting and analyzing human languages, further augment patient-specific drug-delivery systems (Shahiwala *et al.*, 2023). Neural networks, substantially modelled on the human brain's architecture, comprise interconnected layers of input and output nodes. These systems excel in identifying underlying models and decision-making patterns from complex datasets. Convolutional neural networks, a specialized category, are designed for processing visual-content data (Gao *et al.*, 2023; Kapoor *et al.*, 2024).

Machine Learning Algorithms

Machine learning, a subset of artificial intelligence, enables computers to extract meaningful information from data without direct programming on the desired solutions. It has been applied in gastroretentive drug delivery systems by aiding in the evaluation of dosage form characteristics like size, density, and drug release properties, assisting in determining critical quality attributes for product development (Jiang *et al.*, 2022). Multiple machine learning algorithms-including linear regression, decision trees, k-Nearest Neighbors (KNN), random forest, XGBoost, Light

GBM, and Support Vector Machine (SVM)-are employed to model and predict drug delivery performance.

Linear regression is a supervised-learning technique that establishes relationships between input variables and continuous output values. Decision trees and random forests function by partitioning data based on feature thresholds to classify or predict outcomes (Staniszewska *et al.*, 2023). KNN estimates the target variable by considering the values of the nearest data points in the input space. XGBoost and LightGBM implement gradient boosting frameworks that combine multiple weak predictive models to improve accuracy and often reduce training time. SVM finds the hyperplane that best separates different classes in the feature space. Algorithm selection depends on factors such as complexity, prediction efficiency, and data set characteristics (Jawale *et al.*, 2024).

Deep learning-a specialized area within machine learning-utilizes artificial neural networks with multiple layers to model complex patterns in large datasets. Architectures such as multilayer perceptrons, Convolutional Neural Networks (CNNs), and Recurrent Neural Networks (RNNs) have been applied to pharmaceutical problems. Deep learning facilitates tasks including defect detection in tablets, prediction of storage stability, assessment of particle flowability, and modeling drug dissolution profiles. Implementation commonly involves languages like Python, with platforms such as TensorFlow or IBM Watson providing development environments. Overall, machine learning algorithms have become powerful tools for simulating and optimizing gastroretentive drug delivery systems, informing decision-making throughout design and production (Asediya *et al.*, 2025; Saleem *et al.*, 2025).

Neural Networks

ANNs constitute a class of interconnected nodes simulating simplified models of brain activity (Chaibva *et al.*, 2010). An ANN also comprises a method for analyzing data or information by their natural ability to find relationships between raw input. They consist of multiple interconnected nodes (neurons), each processing certain information and communicating the results to other connected nodes. ANNs are widely used in modeling, design, and optimization of drug delivery systems, offering tools for pharmaceutical product development and preformulation design. The application of multilayer ANNs has notably been applied to gastroretentive drug delivery, serving as an effective tool to design sustained-release formulations (Ali *et al.*, 2024).

Natural Language Processing

Natural Language Processing (NLP) plays a fundamental role in developing gastroretentive drug delivery systems. The digital age has witnessed a significant increase in unstructured medical data, including clinical discharge summaries, hospital medical records, physicians' notes, research publications, and other textual reports, presenting a prime health-related present-day challenge (Nehme *et al.*, 2021) The prospects for the application of NLP in gastroretentive discussions are extremely broad; NLP supports linguistic article analysis and reviews of gastroretentive drug delivery systems and offers a first step in the automated processing of drug delivery texts. Optimal pharmacokinetic and pharmacodynamic behavior can be ensured by associating the drugs' physicochemical properties with the drug delivery system (Pratama *et al.*, 2025).

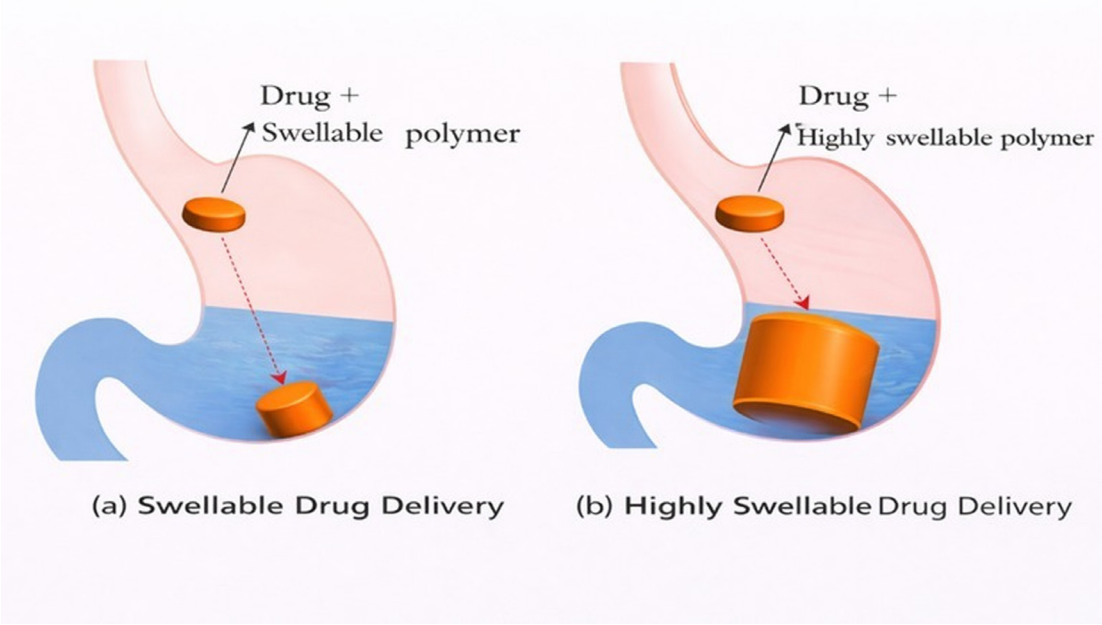

Figure 3: Discussion of expandable systems.

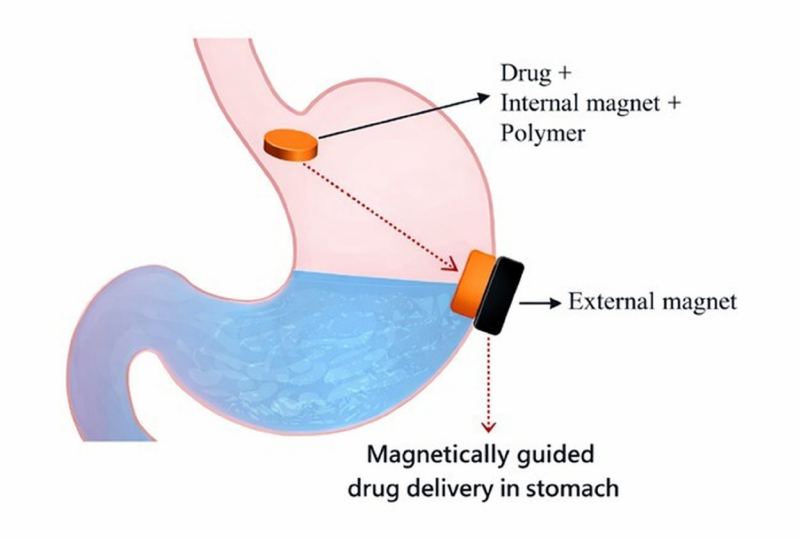

Figure 4: Discussion of magnetic systems.

Modeling Gastroretentive Systems with AI

Accurate modeling holds paramount significance in drug discovery and development, necessitating precise prediction of target properties and system behavior under specific conditions. Advances in machine learning have elevated computational power, facilitating detailed understanding of regulatory factors and the efficacy, safety, and analytical attributes of compound. Configurable models support simulation of system performance according to specified release kinetics, physical dimensions, and initial drug-load distribution, enabling comprehensive evaluation through analytical and numerical methods (Jiménez-Jiménez *et al.*, 2025). This approach assists in studying the influence of various parameters and guides optimization processes. Simulation platforms simultaneously assess multiple formulation variables and release profiles to identify optimal designs and appropriate release kinetics. Overall, computer-aided oral drug delivery offers a cost-effective, rapid, and less laborious avenue for formulation development, guiding projections for *in vitro* and *in vivo* evaluation, with wider-ranging applications in pharmaceutical industries and subsequent research (Malviya *et al.*, 2021).

Predictive Modeling

Predictive models are used to estimate drug release profiles, identify defects, or optimise manufacturing parameters for gastroretentive drug delivery systems. *In vitro* drug release studies typically involve evaluating powdered sample material in a dissolution bath with the aid of supporting equipment, and are time-consuming and require specialised facilities. Computational machine learning techniques can use critical material attributes and processing parameters to forecast important outcomes such as dissolution and disintegration times. Various algorithms achieve good results but artificial neural networks often facilitate the most accurate predictions. Particle size distribution is commonly identified as an important variable that has a significant effect on drug release rates (Cranmer *et al.*, 2017). Predictive capabilities aid in the efficient design, optimisation, and control of manufacturing processes by reducing the need for extensive physical testing. These approaches assist pharmaceutical scientists in comprehending and improving system performance, minimizing development periods, and elevating product quality (Paliwal *et al.*, 2024).

Simulation Techniques

Simulation refers to the use of models to imitate or reproduce the behaviour of a system under specified conditions and over time. In the drug delivery system, simulation refers to the production of virtual images that closely resemble the actual performance of the system. Simulation can be employed to study the flow behaviour of the system and predictions about the gastroretentive property of the system can be done (Dixit *et al.*, 2024).

The drug delivery system undergoes several processes such as the release process, transit process, and absorption process. Simulation techniques are able to predict the drug delivery system's behaviour by simulating these processes. Though the drug delivery mechanisms cannot be predicted using these techniques, the movement of the system in the GIT can be simulated and predicted (Jain *et al.*, 2019).

Challenges in Implementing AI in Drug Delivery

Despite the significant potential of AI technology in developing new candidates for gastroretentive drug delivery, AI-based drug delivery platforms remain in the initial stages of clinical development, necessitating further exploration of potential benefits in personalized treatment. Amid emerging technology adoption, concerns about data privacy and increased risk of hazardous errors highlight the need for further research into law, regulations, and cyber-security protocols. Moreover, investigating AI integration strategies within hospital infrastructures is crucial

for successful implementation in medical practice (Garg *et al.*, 2008; Malheiro *et al.*, 2023).

Data Privacy Concerns

AI-driven Gastro-Retentive Drug Delivery (GRDD) systems are at increased risk of cyberattacks because they hold vast stores of sensitive health data. Regulations such as the EU's General Data Protection Regulation (GDPR) and the US Health Insurance Portability and Accountability Act (HIPAA) therefore control the use of personal information, placing strict restrictions on data access and storage. Existing encryption systems can be difficult to implement and vulnerable to attack, so AI researchers are investigating alternative approaches based on biometric authentication (Ali *et al.*, 2024).

Integration with Existing Systems

Existing pharmaceutical equipment and computational systems facilitate the introduction of Artificial Intelligence (AI) into gastroretentive drug-delivery scenarios. Such computational and hardware systems sustain the continued industrial revolution by integrating AI as well as other Information and communication Technologies (At present, AI techniques enable the development of models that can simulate the behaviour of different systems. Nevertheless, practical data stemming from real-time experiments offer the most dependable information. Nonetheless, in the absence of such data, modelling constitutes the primary means of acquiring information (Mitta *et al.*, 2024).

To enhance the reliability of an AI model, a sufficient quantity of data that adequately represents the complete spectrum of the phenomenon under investigation is necessary. Advances in computing have augmented the efficiency of AI models, promoting their use in systems where streamlined, straightforward processes are inadequate. Additionally, numerous AI models can be appended to each other or to conventional models. AI-information-processing systems, when parallelized, sustain significant expansion. Integration of AI methods with traditional computational tools also represents a notable research direction (Mishra *et al.*, 2025).

Future Trends in AI and GRDDS

Today, gastroretentive systems spanning physiochemical, technological, and biological techniques address a growing demand for safer, therapeutic approaches that prolong gastric retention, enhance drug solubility and bioavailability, and enable more controlled pharmacokinetics. AI streamlines their development by reducing timelines and automating complex processes, substituting traditional trial-and-error procedures with in silico design. A combination of diverse AI techniques machine learning, neural networks, natural language processing, and more analyze various types of drug delivery data. The application of AI in gastroretentive delivery systems has already shaped the future of pharmaceutical innovation and will continue to do so in the

Table 1: Future Trends in AI and GRDDS.

Future Trend	An Explanation and its Implications
ML and hybrid mechanistic models	Improve the prediction of release habits and buoyancy under various stomach circumstances by using machine learning with mechanistic PK/PD and transport models. decreases the need for data and overfitting (Fu *et al.*, 2022; Corral-Acero *et al.*, 2020).
GRDDS with digital twins for customization	GI tract pathophysiology virtual models tailored to each patient to replicate *in silico* GRDDS performance for customized treatment and dosage (Harmsen *et al.*, 2022; Gómez-Bombarelli *et al.*, 2018).
Designing formulations with generative AI	Propose excipient/polymer mixes based on target release and buoyancy profiles using deep generative models (VAEs, GANs, and diffusion models (Sanchez-Lengeling *et al.*, 2018; Lundberg *et al.*, 2017).
Explainable AI (XAI)	To help with scientific understanding and regulatory acceptability, use interpretability approaches (SHAP, LIME) to pinpoint important formula factors (Yang *et al.*, 2019).
Federated learning for formulation data	Without exchanging raw data, train models on dispersed datasets from several laboratories, protecting intellectual property and privacy while boosting data variety (Sheller *et al.,* 2019).
Computer vision and multimodal sensor fusion	Integrate sensor logs, image (SEM), video, and dissolution data to improve GRDDS performance prediction and automated quality control (Aishwarya *et al.*, 2021).
Smart GRDDS and edge ML powered by IoT	Utilize wearable technology, ingestible sensors, and low-power machine learning to facilitate variable release and detect stomach retention in real time (Kalantar-Zadeh *et al.*, 2019).
Automated testing and active learning	Combine robotics and 3D printing with ML-guided experimental selection to accelerate GRDDS optimization and development (Häse *et al.*, 2019; Doshi *et al.*, 2022).
Dataset standardization and benchmarking	To enhance model comparability and repeatability, create carefully selected, publicly available datasets containing dissolving curves, floating times, and formulation data (European Medicines Agency 2021).
Workflows for ML with regulatory awareness	To satisfy regulatory criteria for model-based formula choices, construct machine learning pipelines that include simplicity, certainty measurement, and validation (Akbar *et al.*, 2024).

Table 2: Applications of AI in GRDDS.

AI/ML Algorithm	Application in GRDDS Modeling	Strengths	Limitations
Artificial Neural Networks (ANN)	Using formulation factors, predict drug release profiles, swelling index, and floating lag time.	Manages adaptive learning and nonlinear interactions.	Large datasets are needed, and overfitting is a possibility (Kakuk *et al.*, 2024).
Support Vector Machines (SVM)	Organize formulations into "optimal" versus "non-optimal" buoyancy/drug release performance.	Excellent for small-to-medium-sized datasets, with a good classification accuracy.	Kernel selection is crucial and less interpretable (Yadav *et al.*,2025).
Random Forest (RF)	Evaluation of feature relevance for variables influencing drug release and buoyant duration.	Manages a variety of data types and is noise-resistant.	Big growth can be computationally costly (Zane *et al.*,2019).
Decision Trees (DT)	Predictions based on norms for successful formulation.	Minimal cost and simple interpretation.	If not cleaned it may overfit (Ozturk Kiyak *et al.*, 2023).
k-Nearest Neighbors (k-NN)	Determine the dissolution rate or floating lag time by comparing it to established formulas.	Easy, no training stage.	High memory consumption and sensitivity to unimportant aspects (Yadav *et al.*, 2025).
Partial Least Squares Regression (PLSR)	Connect composition with releasing and floating parameters.	Interpretable and effective with multiple linearity.	Assumes linear relationships (Barmpalexis *et al.*, 2011).
Genetic Algorithms (GA)	Optimize the excipient content and polymer ratio to achieve the optimal buoyancy/release profile.	The capacity to search globally is beneficial for optimization.	Requires adjusting and is computationally demanding (Mundhe *et al.*, 2024).
Adaptive Neuro-Fuzzy Inference System (ANFIS)	Estimate nonlinear correlations between composition and release of drugs or floating.	Integrates learning and human-like thinking.	The complexity of the model can rise rapidly (Arav *et al.*, 2024).
Gradient Boosting Machines (GBM/XGBoost)	Estimate the rate of dissolution and the influence of the excipient.	High precision and suitability for a variety of data types.	Less interpretable and requires adjustments to parameters (Shahiwala *et al.*, 2023).

years ahead: it directly informs experimentation and modeling, enhances data analysis and patient monitoring, and guides regulatory issues and collaborative efforts. Such trends will enable smarter integration of gastroretentive delivery systems into the digital age and accelerate their advance toward improved patient safety (Raina *et al.,* 2023). Future trends in AI and GRDDS and their consequences are explained in Table 1.

Collaborative Efforts in Research

Collaboration across industry and academia plays an essential role in advancing artificial intelligence applications within the field of GRDDS. The development of innovative gastroretentive solutions and their technological investigation require an intensive exchange of knowledge and expertise in multiple disciplines like industry partnerships and academic collaborations (Zhang *et al.*, 2021).

Applications of AI in GRDDS

Image processing techniques play a significant role in AI development. Deep learning algorithms such as Graph Convolutional Networks (GCNs), Generative Adversarial Networks (GANs), and Convolutional Neural Networks (CNNs) showcase the impact of image processing concepts in pharmaceutical formulation development, expanding their application beyond binary to ternary systems. These advances coincide with growing industry interest in developing gastrointestinal retention drug delivery systems (Talevi *et al.*, 2020). GRDDSs extend residence time within the gastrointestinal tract and exhibit controlled drug-release behavior; they are pivotal in oral delivery, with the potential to enhance therapeutic action by prolonging the duration of release and increasing bioavailability. Examples of GRDDSs include floating, high-density, expandable, superporous hydrogel, magnetic, raft, and ion-exchange resin systems. Although numerous reports highlight their advantages, the mass manufacturing and packaging of such sustained-release, controlled-release, and targeted-release dosage forms present a major obstacle to the promotion of GRDDSs in pharmaceutical sciences. Recent efforts aim to overcome these challenges through the application of AI methodologies (Patel *et al.*, 2013). Applications are given below in Table 2.

CONCLUSION

GRDDS represent a strategic approach to oral controlled-release formulations, allowing extended gastric residency to enable complete drug release within gastric fluids. Such systems enhance the therapeutic efficacy of drugs by improving their absorption

and reducing fluctuations in plasma concentration, thereby minimizing side effects. The AI methods within the development and optimization of gastroretentive drug delivery constitutes an emerging avenue for further improving managed oral delivery approaches. AI techniques can accelerate formulation development by predicting critical quality attributes and drug concentrations early in the development cycle, guiding design decisions and identifying failures prior to product manufacturing. Therefore, comprehensive reviews that address AI applications in gastroretentive drug delivery systems are essential to support ongoing research and to highlight future directions for enhancing controlled release and improving patient compliance, ultimately facilitating the formulation of superior dosage forms.

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ABBREVIATIONS

AI: Artificial Intelligence; **ANFIS:** Adaptive Neuro-Fuzzy Inference System; **ANNs:** Artificial Neural Networks; **CNNs:** Convolutional Neural Networks; **DT:** Decision Trees; **FDDS:** Floating Drug Delivery Systems; **GA:** Genetic Algorithms; **GANs:** Generative Adversarial Networks; **GBM:** Gradient Boosting Machines; **GDPR:** General Data Protection Regulation; **GCNs:** Graph Convolutional Networks; **GRDDS:** Gastroretentive Drug Delivery Systems; **HIPAA:** Health Insurance Portability and Accountability Act; **HPMC:** Hydroxypropyl Methylcellulose; **ICTs:** Information and Communication Technologies; **KNN:** k-Nearest Neighbors; **ML:** Machine Learning; **NLP:** Natural Language Processing; **PEO:** Polyethylene Oxide; **PLSR:** Partial Least Squares Regression; **RF:** Random Forest; **RNNs:** Recurrent Neural Networks; **SVM:** Support Vector Machine; **PK:** Pharmacokinetics; **PD:** Pharmacodynamics; **GIT:** Gastrointestinal Tract; **VAEs:** Variational Autoencoders; **SHAP:** SHapley Additive exPlanations; **LIME:** Local Interpretable Model-agnostic Explanations; **IoT:** Internet of Things; **SEM:** Scanning Electron Microscopy.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

Murali Krishna: Writing, review, and editing; resources; investigation; formal analysis; data management; conceptualization. Chandra Sekhar Patro: Supervision CH. Taraka Ramarao: Editing

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