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Nanotechnology in Gastro-Retentive Drug Delivery: Current Status and Future Prospects

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ABSTRACT

In the bioavailability and therapeutic efficacy of poorly absorbed drugs that require local gastric activity, GRDDS-targeted duration of drug residence in the stomach truly reflects its significance. Therefore, these strategies in nanotechnology provide a cost-effective approach to enhance the GRDDS performance by methods such as controlled release, targeted delivery, and better mucosal adhesion with the assistance of nanomaterials. This review highlights the study status of GRDDS resulting from nanotechnology application, focusing on major types of nano-formulation, including nanoparticles, nanomicelles, and nanofibers, along with the corresponding gastric retention mechanisms. In addition, advances in the field in stimuli-responsiveness and bioinspired concepts are elucidated with respect to their clinical potential and applications for gastrointestinal and systemic disorders. Moreover, regulatory and safety issues for the successful translation of these systems are discussed. The future perspectives emphasize the concepts of smart materials, artificial intelligence, and personalized medicines, all coming together to step into the next generation of gastro-retentive nanocarriers. To underscore the potentiality of nanotechnology in revolutionizing oral drug delivery, the introduction of a newer dimension with more efficacy and patient-centered drug-delivery systems via GRDDS is being represented in this review.

Keywords: nanotechnology, gastroretentive drug delivery, nanoparticles, mucoadhesion, controlled release, floating systems, smart nanocarriers, oral bioavailability, personalized medicine, and regulatory aspects.

Introduction

Oral drug delivery is considered the best and most convenient way among all possible routes of general administration for therapeutic agents due to its non-invasive nature and patient compliance. But commonly, conventional oral dosage forms are characterized by poor drug bioavailability due to narrow absorption windows or low solubility or instability in the intestinal environment. To overcome these problems, a relatively novel approach in drug delivery systems, gastro-retentive drug delivery systems (GRDDS), has come up to prolong the gastric residence time of drugs for sustained release and better absorption in the upper gastrointestinal tract [1].

Gastro-retentive systems would remain in the stomach for a long time by virtue of buoyancy, mucoadhesion, swelling, and high density, among other factors. As promising as the GRDDS appear, several physiological factors are the culprits behind their limited success; for example, gastric motility and variation in gastric emptying time with food intake, thus affecting the dynamic nature of the gastric environment [2]. Such limitations drew researchers toward novel technologies where nanotechnology has emerged as an exciting horizon to enhance the performance and function of GRDDS.

Nanotechnology helps improve the solubility, controlled release, permeation enhancement, and targeting capabilities of drug delivery. In GRDDS, nanocarriers such as nanoparticles, nanomicelles, and solid lipid nanoparticles can stick to gastric mucosa, resist gastric emptying, and ensure sustained release of the drug for maximal therapeutic efficacy [3]. Furthermore, nanoscale dimensions support deeper penetration and facilitate the interaction with the mucosal surface, which adds to retention and absorption.

Gastro-Retentive Drug Delivery: Challenges and Opportunities

The gastro-retentive drug delivery systems (GRDDS) prolong the residence time of dosage forms in the stomach for enhanced absorption of the drug in the upper gastrointestinal tract. This is beneficial particularly in the case of such drugs that have absorption windows that tend to be narrow, low solubility in intestinal fluids, or poor stability in an alkaline pH environment. Extend the time the drug is released, lessen the frequency of dosing, and improve patient adherence [4]. It may also be beneficial for local treatment of gastric diseases, such as peptic ulcers and Helicobacter pylori infections, since long-term contact with the stomach can improve therapeutic efficacy [5].

Though GRDDS offers this advantage, there are several challenges formulated related to the development of effective GRDDS from the physiological standpoint. The first limitation is hugely variable gastric emptying time, since it varies widely owing to the above factors, which include food intake, posture of the patient, and, in some cases, it happens that the presence of disease states may change these conditions. Such unpredictability would lead to the premature evacuation of the dosage form into the small intestine, thereby producing subtherapeutic drug levels [6]. In addition, acidity in the stomach environment and enzymatic activities often lead to the destruction of some drugs before absorption, thus leading to compromised bioavailability. Traditional conventional approaches such as floating systems or bioadhesives have a tendency to fail in maintaining retention under fasting or where there are conditions of gastric motility [7].

However, limitations open windows for more advanced technologies in optimizing GRDDS. New delivery platforms, such as swellable matrices, expandable systems, and very nanoscale carriers, allow possible formulations that are much more stable in the highly dynamic environments of the stomach. Nanotechnology, for example, gives avenues to improve adhesion to mucosa, solubilizes drugs better, and, primarily, targets the absorption site for delivery. These will hold the promise of having new therapeutic options that may be available against these conditions that now obstruct the controlled and localized delivery in the upper gastrointestinal tract [3].

The future of GRDDS lies in an association between conventional principles and many emerging novel technologies that can respond to physiological cues, fit individual patient needs, and furnish much more predictable retention and release profiles. This will not only address the limitation but also pave the way for the future of more efficient and personalized oral drug therapies [8].

Role of Nanotechnology in GRDDS

Nanotechnology: Revolutionizing drug delivery with its unique physicochemical properties, which would give value addition to the traditional gastro-retentive drug delivery systems (GRDDS). In such instances, by having the control over the process at the nanolevel, the absolute synergism with the design itself can have synergetic effects with respect to solubility, stability, and mucoadhesion to achieve a lot of goals that are otherwise unavailable for conventional formulations [9]. Nanoparticles could efficiently entrap poorly water-soluble drugs, shield labile molecules from the acidic destruction of the stomach, and control or target release, prolonging the retention of a drug within the stomach.

GRDDS mainly benefits from nanotechnology with the development of mucoadhesive nanocarriers designed to interact with the mucus layer in the stomach. Such nanocarriers have advantageous characteristics like small size and high surface area, which allow them to obtain more effective adhesion with gastric mucosa than conventional systems and to resist peristalsis and gastric emptying [11]. The site for incorporation of bioadhesive polymers like chitosan or alginate in the composition of nanoparticles also enhances retention capabilities for long duration of action in the stomach for the drug under consideration [12].

Yet another benefit of nanotechnology-based GRDDS is the possibility of making these systems stimuli-responsive or targeted. Engineering the smart nanoparticles to respond to the acidic pH, enzymatic activity, or temperature of the stomach would allow the drug to release precisely in the stomach and not at any other sites. Magnetofection nanoparticles and ligand-targeted systems were investigated in order to achieve site-specific retention within the gastric mucosa and to treat localized gastric disorders like ulcers or infections [13]. Such innovations are of great benefit to drug adherence to the therapeutic efficacy but also minimize the frequency of dosing and side effects, which helps in the overall patient compliance.

Nanotechnology interprets, reshapes, and reinvents the whole concept of gastro-retentive drug administration by folding itself into the design of those intelligent systems that would adapt to the changes occurring in conjunction with the very complex environment found in the stomach. It is very promising in terms of the future of oral drug therapy, especially in nanoscience integration into GRDDS designs [14].

Key Nano formulations and Mechanisms

Nanotechnology offers a plethora of formulation strategies for effective gastro-retentive delivery of drugs. Among all these, polymer nanoparticles are one of the most explored and studied systems. These carriers, which are usually prepared with the use of biodegradable polymers such as chitosan, PLGA (poly(lactic-co-glycolic acid)), or Eudragit, demonstrate controlled release of the drug from the formulation and high mucoadhesion essential for retention enhancement within the gastric environment. Their size and surface charge can also be optimized for possible interaction with the gastric mucosa, thus prolonging the retention time in the stomach and enhancing their potential for local or systemic absorption [15].

In fact, solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) are lipid-based systems that combine the advantages of glial nanoparticles and liposomes. They provide superb biocompatibility, protect labile drugs from harsh acidic degradation, and show a sustained drug release profile. SLN, when modified with mucoadhesive polymers or hydrophilic coatings, will show enhanced interaction with gastric mucus, thus improving gastro-retention properties [16]. Moreover, these lipid systems were found really promising for poorly water-soluble drugs and those localized to specific gastric conditions such as ulcers and infectious agents [17].

Another popular form is nanomicelles, which are amphiphilic block co-polymers that have developed into areas of interest for gastro-retentive application as they are small-sized (<100 nm), show very high drug-loading efficiency, and have been stabilized within acidic media. These types of structures are able to encapsulate poorly soluble drugs while being able to provide controlled release of that drug inside the stomach. In addition, it is worth mentioning

their spontaneous formation when dispersed in aqueous solutions, as well as their tendency to solubilize hydrophobic drugs, thus making them ideal candidates for improving the oral bioavailability of some therapeutic agents [18].

With respect to retention mechanisms, mucoadhesion is one of the most particularly deployed in nanoformulation ranges. The action is inevitably based on interaction between the nanoparticle surface and mucin glycoproteins present in the gastric mucus layer. The polymers, such as chitosan, carbopol, and pectin, are commonly used for enhancement of this effect [12]. Others are floating systems, which generally have densities lower than that of gastric fluids to obtain buoyancy, and swelling systems that could swell as a result of contact with gastric fluids to prevent early passage. Some others being developed involve magnetically responsive nanoparticles and bioadhesive smart systems for target-specific and time-controlled retention in the stomach [3].

Recent Advances and Applications

Amazing progress has been made in the past few years in nexus with the use of nanotechnology in gastro-retentive drug delivery systems (GRDDS) attempting to overcome the obstacles faced by a modular oral formulation. Recent emergences of surface-modified nanoparticles, multi-layered nanocarriers, and stimuli-responsive nanoplatforms have increased to an incredible extent the efficacy of these gastro-retentive systems. Consider the results reported by some researchers who fabricated chitosan-coated nanoparticles with improved mucoadhesive property and acid stability, assuring longer gastric retention and targeting the drug release at upper gastrointestinal sites [19]. Such systems are expected to function best for drugs demonstrating a narrow absorption window or degradation within the intestinal environment.

A most remarkable advancement is the floating nanocarrier, which is designed in such a way that its density is lower than that of gastric fluids, making it remain buoyant in the stomach. These types of drug carriers are polyethylene or Eudragit-formed and have been used for amoxicillin antibiotic delivery for Helicobacter pylori eradication, thus increasing its contact time with the gastric mucosa and maximizing treatment outcomes [20]. In addition, swelling-type nanoparticles have also been reported that on campus, hydration resists gastric emptying. Such systems have shown promising sustained delivery of anti-inflammatory and anti-ulcer drugs such as ranitidine and famotidine [2].

Smart nanocarriers that respond to pH, temperature, or enzymatic triggers are currently being developed for delivering site-specific and time-controlled drugs. For example, pH-sensitive polymeric nanoparticles might release their payload solely in the acidic gastric environment, making them perfectly applicable in handling alarming gastric cancers or localized bacterial infections [21]. Furthermore, magnetically guided nanoparticles have been studied to achieve on-site delivery where an external magnetic field holds the mixture at a location in the stomach, thus increasing the precision of therapy [22].

From a clinical application standpoint, nanotechnology-based GRDDS have been explored in the therapeutic domain for gastric ulcer diseases, gastric cancers, bacterial infection treatment, such as that of H. pylori, and peptic acid disorders. Such systems have also been optimized for systemic delivery and improved pharmacokinetics and treatment efficacy for drugs administered via prolonged gastric retention, such as levodopa or metformin [3].

Regulatory and Safety Aspects

Regulatory challenges represent a significant mark on nanotechnology and its therapeutic ability in gastro-retentive drug delivery systems (GRDDS). Regulatory agencies like the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have yet to develop a comprehensive guideline for GRDDS that takes into account the nature of nanoparticles. Currently, nanomedicines are being evaluated as per existing regulations laid down for conventional pharmaceuticals; however, these do not properly address the distinctive behavior and interaction of the nanocarriers with the gastrointestinal tract [23]. The heterogeneous nature of nanoscale materials and the variability presented by different formulation methods pose serious challenges for establishing uniform standard parameters for the assessment of quality, safety, and efficacy [24].

From a safety standpoint, the biocompatibility and toxicity of nanoparticles with long-standing implications remain major concerns. Nanocarriers could be expected to interact with the biological system in an unpredictable manner, especially under docking and on gastric milieu hurdles like acids and enzymes. Problems such as nanoparticle accumulation, mucosal irritation, and unforeseen immune responses should all be evaluated with extreme care. Studies have shown that surface charge, size, and composition can influence different toxicity profiles, whereby cationic nanoparticles are generally expected to induce more mucosal irritation than neutral- or anionic-charged ones [25]. Therefore, extensive preclinical testing—cytotoxicity, genotoxicity, and immunogenicity studies—will be required prior to entering into human trials [26].

In addition to biological safety, manufacturing reproducibility and scalability are key regulatory concerns. Consistency in manufacturing processes in terms of batch-to-batch consistency, nanoparticle stability, and contamination control must be strictly adhered to on the one hand, though achieving such standards has never been easy due to the highly sensitive nature of nanoformulation. The FDA's "Nanotechnology Regulatory Science Research Plan" speaks to a need for analytical tools with validated performance for characterization of nanomaterials and prediction of their behavior in vivo [27]. Moreover, post-marketing surveillance and pharmacovigilance mechanisms need to have been placed to detect delayed adverse effects due to still-poorly-understood long-term exposure of some nanomaterials [28].

Future Perspectives

Nanotechnology is going to change the direction of oral therapeutics through gastro-retentive drug delivery systems (GRDDS). It will enable sustained and selective release of drugs at the stomach site. If we analyze the prospects, therefore, the design of multifunctional nanoparticles integrating targeting, imaging, and therapeutic capabilities would likely become a hallmark of next-generation GRDDS. Such smart nanocarriers can respond to internal stimuli (like pH, redox conditions) or external triggers (magnetic fields and light) that modulate drug release in a spatiotemporally controlled manner [29].

Recent technologies such as bioinspired/biomimetic nanoparticles seem to open new avenues for overcoming traditional biological barriers. For example, mucus-penetrating nanoparticles or gastric-epithelial-targeting ligands would enhance gastric residence time and thereby local therapeutic concentration. Further, 3D printing and microfabrication could allow the customization of nanoparticle-loaded gastro-retentive platforms for personalized medicine, particularly in the management of chronic gastric conditions, such as ulcers and infections [30].

AI and machine-learning methods would also play an increasingly important role in the design and optimization of nano-GRDDS. Indeed, these could predict the behavior of nanoparticles. optimize formulation parameters, and eventually speed up preclinical development by minimizing the use of trial-and-error experimentation. Coupled with high-throughput screening, these approaches may open a faster path to identifying ideal nanocarriers based on desired release profiles and safety margins [31].

Translationally, therefore, the future looks to research directed toward gaining scalability, reproducibility, and cost-effectiveness in nanoformulation manufacturing. Adapting regulatory science parallelly to frameworks specifically suited for complex GRDDS nanostructures shall be viable. The international harmonization of protocols for nanoparticle characterization and toxicological assessment methods remains critical to linking laboratory research and clinical application [32].

Conclusion

Gastro-retentive drug delivery systems based on nanotechnology present immense potentials and new solutions to circumvent hurdles associated with conventional oral dosage forms. Nanoformulations extremely enhance therapeutic efficacy and patient compliance when enhanced mucoadhesion, prolonged gastric residence time, and controlled drug release are vital for drugs with narrow absorption windows or localized gastric activity.

Very promising prospects arise from the ongoing study on smart responsive and multifunctional nanocarriers, computational modeling, and biomimetic design, keeping in view the phenomenal strides accomplished and the challenges posed in regulatory clarity perception, large-scale manufacture, and long-term safety evaluation. Supported through interdisciplinary science and favorable regulations, ultimately, nanotechnology GRDDSs shall migrate from experimentation to therapeutics, able to reshape oral drug delivery.

REFERENCES

1. Jain, N. K., & Sharma, S. N. (2012). Gastroretentive Drug Delivery Systems: A Review. Drug Delivery, 19(6), 1-10.
2. Talukder, R., & Fassihi, R. (2004). Gastroretentive delivery systems: A mini review. Drug Development and Industrial Pharmacy, 30(10), 1019–1028.
3. Pawar, V. K., et al. (2014). Gastroretentive dosage forms: a review with a special emphasis on floating drug delivery systems. Drug Delivery, 21(6), 223–241.
4. Rouge, N., Buri, P., & Doelker, E. (1996). Drug absorption sites in the gastrointestinal tract and dosage forms for site-specific delivery. International Journal of Pharmaceutics, 136(1-2), 117–139.
5. Mojaverian, P., et al. (1985). Effect of gender, posture, and age on gastric residence time of an indigestible solid: Pharmaceutical considerations. Pharmaceutical Research, 2(2), 102–106.
6. Streubel, A., Siepmann, J., & Bodmeier, R. (2006). Gastroretentive drug delivery systems. Expert Opinion on Drug Delivery, 3(2), 217–233.
7. Bardonnet, P. L., Faivre, V., & Fuks, L. (2006). Gastroretentive dosage forms: Overview and special case of Helicobacter pylori. Journal of Controlled Release, 111(1–2), 1–18.
8. Khan, M. A., et al. (2020). Advances in gastroretentive drug delivery systems: New insights for effective oral delivery. Current Pharmaceutical Design, 26(26), 3185–3199.
9. Kaur, R., et al. (2018). Nanotechnology-based approaches for enhancing oral bioavailability of poorly soluble drugs. Drug Development and Industrial Pharmacy, 44(9), 1405–1425.
10. Jani, R. K., & Patel, M. M. (2020). Nanoparticles for gastroretentive drug delivery: An overview of current approaches and future perspectives. Current Drug Delivery, 17(7), 591–602.
11. Liu, D., et al. (2012). Mucoadhesive nanoparticles for targeted delivery to the stomach. Journal of Controlled Release, 162(1), 86–93.
12. Sogias, I. A., et al. (2008). Chitosan-based mucoadhesive nanoparticles for drug delivery. European Journal of Pharmaceutics and Biopharmaceutics, 69(1), 253–262.
13. Lopes, C. M., et al. (2016). Smart design of gastroretentive drug delivery systems: A new era in targeted therapies. International Journal of Pharmaceutics, 514(1), 88–102.

14. Ahmad, Z., et al. (2021). Recent advances in nanotechnology-based drug delivery systems for targeting gastric diseases. Journal of Drug Targeting, 29(7), 744–757.

15. Kalepu, S., & Nekkanti, V. (2015). Biopharmaceutical classification system and formulation development: A practical guide for oral drug delivery. Pharmaceutical Research, 32(2), 378–392.

16. Beloqui, A., et al. (2016). Nanostructured lipid carriers: Promising drug delivery systems for future clinics. Nanomedicine: Nanotechnology, Biology and Medicine, 12(1), 143–161.

17. Patil, S. S., et al. (2019). Gastroretentive drug delivery system: A review on recent trends. Asian Journal of Pharmaceutical Sciences, 14(3), 293–305.

18. Ramasamy, T., & Kim, J. O. (2016). Polymeric micelles for drug delivery: Clinical outlook, mechanistic insight, and future perspectives. Advanced Drug Delivery Reviews, 108, 1–2.

19. Jain, D., et al. (2013). Design and development of mucoadhesive nanoparticles for sustained delivery of ciprofloxacin hydrochloride. Drug Development and Industrial Pharmacy, 39(1), 95–104.

20. Arora, S., et al. (2005). Floating drug delivery systems: A review. AAPS PharmSciTech, 6(3), E372–E390.

21. Kharia, A. A., et al. (2021). Smart nanocarriers for gastrointestinal tract targeting: Current status and future perspectives. Expert Opinion on Drug Delivery, 18(3), 319–335.

22. Gupta, P. K., et al. (2010). Magnetic drug targeting using gastroretentive nanoparticles: A novel approach. International Journal of Pharmaceutics, 388(1–2), 245–252.

23. EMA. (2020). Reflection paper on the data requirements for intravenous liposomal products developed with reference to an innovator liposomal product. European Medicines Agency.

24. Tinkle, S., et al. (2014). Nanomedicines: Addressing the scientific and regulatory gap. Annals of the New York Academy of Sciences, 1313(1), 35–56.

25. Mukherjee, A., et al. (2019). Nanoparticle-induced toxicity in gastrointestinal tract: A review. Environmental Toxicology and Pharmacology, 69, 73–80.

26. Fadeel, B., et al. (2018). Safety assessment of nanomedicines: The role of in vitro and in vivo studies. Journal of Controlled Release, 275, 3–17.

27. FDA. (2021). Nanotechnology regulatory science research plan. U.S. Food and Drug Administration.

28. Ventola, C. L. (2012). The nanomedicine revolution: Part 2: Current and future clinical applications. P&T, 37(10), 582–591.

29. Torchilin, V. P. (2014). Multifunctional, stimuli-sensitive nanoparticulate systems for drug delivery. Nature Reviews Drug Discovery, 13(11), 813–827.

30. Zhang, L., et al. (2017). Bioinspired materials and their application in gastroretentive drug delivery systems. Advanced Drug Delivery Reviews, 118, 28–45.

31. Xu, Y., et al. (2022). Artificial intelligence in nanoparticle design for drug delivery: Opportunities and challenges. Advanced Drug Delivery Reviews, 183, 114128.

32. Park, K. (2021). Facing the truth about nanotechnology in drug delivery. ACS Nano, 15(2), 1793–1797.