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Nanoplatforms in Gastric Ulcer Therapy: A Narrative Review

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ABSTRACT

Introduction and Aim: Gastric ulcer is a prevalent gastrointestinal disease caused by an imbalance between damaging and protective factors such as gastric acid, oxidative stress, chronic inflammation, and *Helicobacter pylori* infection and protective mucosal mechanisms. Limitations of conventional therapies, including drug resistance, systemic side effects, and suboptimal efficacy in certain patients, underscore the need for novel therapeutic strategies. Nanoparticles, as advanced drug delivery systems, offer promising approaches for targeted gastric mucosal therapy by enhancing drug stability, enabling site-specific delivery, and minimizing adverse effects. This review aims to analyze the therapeutic applications of nanoplatforms in the management of gastric ulcers and associated infections.

Methods: Relevant studies were identified from PubMed, Scopus, and Web of Science for this narrative review from 2010 to 2025. Standardized keywords included "gastric ulcer," "nanoparticles," "targeted drug delivery," "*Helicobacter pylori*," and "mucosal drug delivery systems." Eligible studies comprised preclinical investigations, animal models, and relevant review articles. Data were extracted and analyzed qualitatively and thematically.

Results: The findings indicate that nanocarriers including poly (lactic-co-glycolic acid) (PLGA), chitosan, silver, gold, selenium nanoparticles, and plant-based formulations—enhance drug bioavailability, enable controlled release, improve mucoadhesion, and achieve targeted gastric delivery. These properties collectively facilitate accelerated mucosal healing and tissue regeneration. Key mechanisms include inhibition of inflammatory pathways such as NF-κB, reduction of pro-inflammatory cytokines (e.g., TNF-α, IL-6), attenuation of oxidative stress, enhancement of antioxidant defenses (SOD, CAT, NRF2), and antibacterial activity against *H. pylori*. Conversely, certain nanoparticles, such as titanium dioxide, may provoke local inflammation and mucosal injury, highlighting the importance of nanoparticle type and physicochemical properties.

Conclusion: Targeted nanoparticles and nanocarriers, through controlled drug release, mucoadhesion, anti-inflammatory effects, and antibacterial activity, represent a novel and effective approach for gastric ulcer therapy and *H. pylori* eradication. However, heterogeneity in biological responses and potential toxicity necessitate further extensive preclinical studies and rigorously designed clinical trials to ensure the safety and efficacy of these nanomedicine strategies.

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INTRODUCTION

Gastric ulcers represent a frequent pathological condition affecting the digestive system, arising from disruption of the gastric mucosal layer and an

imbalance between aggressive and protective factors (1). Clinically, it can manifest as epigastric pain, gastrointestinal bleeding, nausea, vomiting, and, in severe cases, perforation of the gastric wall, leading to life-threatening complications (2). The global burden of gastric ulcer is driven by a combination of infectious, pharmacological, and lifestyle-related factors, particularly *H. pylori*, NSAIDs, stress, alcohol, smoking, and diet. Moreover, the growing antibiotic resistance in *H. pylori* has complicated the management of this condition (1, 2).

Gastric ulcerogenesis arises from the interaction between damaging stimuli and impaired mucosal protection. Acid-peptic activity, microbial infection, oxidative stress, and inflammatory pathways accelerate tissue injury, whereas endogenous defense systems preserve gastric barrier function (3, 4). In many patients, elevated oxidative stress and ROS production lead to cellular damage, lipid peroxidation, and epithelial cell destruction (3, 4). Concurrently, upregulation of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6 exacerbates mucosal injury, highlighting the need for therapies that not only suppress gastric acid but also mitigate inflammation, oxidative stress, and infection (5).

Conventional treatment strategies for gastric ulcer primarily include proton pump inhibitors (PPIs), H2 receptor antagonists, antibiotics, mucosal protectants, and antacids (6). Although these therapies are effective for many patients, they are limited by low bioavailability, acid-mediated drug degradation, frequent dosing requirements, systemic side effects, disease recurrence, and antibiotic resistance (7). Additionally, several therapeutic agents cannot remain at the ulcer site for prolonged periods, and targeted delivery to the damaged mucosa remains challenging (8). Therefore, the development of novel drug delivery systems capable of enhancing drug stability, therapeutic efficacy, and minimizing adverse effects is imperative (7, 8).

Nanotechnology-based approaches have attracted increasing attention for their potential in modern healthcare and therapy (9). Nanoparticles, owing to their small size, high surface area, surface functionalization potential, and ability to carry diverse therapeutic agents, have opened new avenues for gastrointestinal disease management (10). These systems can protect drugs from acidic degradation, improve bioavailability, and enable controlled and targeted drug release (10). Furthermore, certain nanoparticles possess intrinsic antibacterial, anti-inflammatory, and antioxidant properties, which can directly contribute to gastric ulcer healing (11).

Various types of nanoparticles including polymeric, lipid-based, metallic nanoparticles, liposomes, nanoemulsions, dendrimers, and nanocomposites have been investigated for gastric ulcer therapy (12). These platforms facilitate targeted delivery of PPIs, antibiotics, plant-derived compounds, antioxidants, and mucosal protectants to the ulcer site (13). Studies have demonstrated that nanoparticles enhance mucosal adhesion, improve tissue penetration, and prolong gastric residence time, thereby increasing therapeutic efficacy (12, 13). Metallic nanoparticles, such as silver, gold, and zinc oxide, exhibit potent antibacterial activity against *H. pylori* and may contribute to overcoming antibiotic resistance (13).

Beyond drug delivery, nanoparticles play a significant role in promoting gastric mucosal regeneration (14). Preclinical studies indicate that nanocarriers can accelerate tissue repair by reducing inflammation, mitigating oxidative stress, stimulating angiogenesis, and enhancing epithelial cell proliferation (15). Moreover, nanoparticles can serve as vehicles for growth factors, small RNAs, bioactive compounds, and natural products, enabling precision-targeted ulcer therapy (15). Some nanoplatforms are also responsive to gastric pH, allowing intelligent, site-specific drug release (16).

Despite these advantages, the application of nanoparticles in gastric ulcer therapy faces several challenges (17). Potential cytotoxicity, tissue accumulation, unintended immune responses, biosafety concerns, and difficulties in standardizing nanoparticle formulations represent major limitations (18). Additionally, gastric acidity, peristaltic movement, and mucosal barriers may affect the performance of nanocarrier systems. Hence, comprehensive evaluation of biocompatibility, toxicity, and stability is essential before clinical application (18).

Given the rapid advancements in nanotechnology and gastrointestinal therapeutics, a comprehensive synthesis of current evidence is increasingly necessary (19). Although numerous studies have explored the application of nanoparticles in gastric ulcer therapy, detailed insights regarding their mechanisms, benefits, limitations, and future prospects remain scattered (19). Therefore, the objective of this narrative review is to examine the therapeutic applications of nanoparticles in the management of gastric ulcer disease

METHODS

This review synthesized recent evidence on the application of nanoparticles in gastric ulcer treatment and gastrointestinal delivery systems. Publications available between 2010 and 2025 were screened using multiple scientific databases (PubMed, Scopus, Web of Science, SID, and ISC).

The search strategy was developed using a combination of specialized keywords and Boolean operators. The key terms included “Gastric Ulcer,” “Peptic Ulcer,” “Nanoparticles,” “Nanomedicine,”

"Drug Delivery," "Helicobacter pylori," "Targeted Therapy," "Nano-carriers," "Gastroretentive Systems," and "Mucosal Healing." These terms were combined using the Boolean operators AND and OR. An example of the search string was as follows: (Gastric Ulcer OR Peptic Ulcer) AND (Nanoparticles OR Nanomedicine OR Nanocarriers) AND (Drug Delivery OR *Helicobacter pylori* OR Targeted Therapy).

Eligible studies included original research articles, preclinical investigations, animal models, in vitro studies, review articles, and systematic reviews related to nanoparticle applications in gastric ulcer therapy. Inclusion criteria were: (1) publication in English, (2) availability of full-text articles, (3) direct relevance to the therapeutic application of nanoparticles in gastric ulcers, and (4) evaluation of mechanisms of action, drug delivery systems, or anti-inflammatory, antibacterial, and mucosal healing effects of nanoparticles. Exclusion criteria comprised unrelated studies, conference abstracts, letters to the editor, articles lacking reliable scientific data, and studies focusing exclusively on nanoparticle toxicity without therapeutic relevance.

Following the initial search, all retrieved records underwent a multi-stage screening process. Titles and abstracts were first reviewed, and duplicate studies were removed. Subsequently, full-text articles meeting the eligibility criteria were carefully assessed. Data extraction was performed independently using a standardized form. The extracted information included author name, year of publication, study type, animal or cell model, type of nanoparticle, drug delivery system, mechanism of action, therapeutic objectives, anti-inflammatory and antibacterial effects, main findings, and study limitations.

To enhance the methodological quality and scientific validity of the review, selected studies were further evaluated based on study design, methodological rigor, sample size, data reliability, and relevance to the research objectives. The extracted data were organized and analyzed descriptively and thematically. Findings were categorized according to nanoparticle type, drug delivery mechanisms, antibacterial activity against *Helicobacter pylori*, antioxidant properties, gastric mucosal healing effects, and advanced therapeutic platforms. Finally, the advantages, limitations, safety challenges, and future perspectives of nanoparticle-based therapies in gastric ulcer management were critically discussed.

RESULTS

The reviewed studies demonstrated that metallic nanoparticles, metal oxides, and polymeric nanoparticles particularly those prepared via green synthesis exhibited significant effects on gastric ulcer healing. These nanoplatforms primarily acted through the reduction of oxidative stress, inhibition of inflammatory pathways, and enhancement of mucosal defense mechanisms. Additionally, remarkable improvements in gastric tissue regeneration and decreased ulcer indices were reported in animal models. Drug-loaded nanocarriers further enhanced therapeutic efficacy by increasing drug stability and bioavailability, thereby significantly improving the performance of conventional treatments. Overall, the findings highlight the high potential of nanotechnology in developing novel therapies for gastric ulcer management.

The detailed results are presented in Table 1 and 2.

DISCUSSION

Gastric ulcerogenesis involves the interaction between injurious stimuli and weakened mucosal defenses, leading to gastric tissue damage (47). Although proton pump inhibitors, H2 receptor antagonists, and *Helicobacter pylori* eradication regimens have significantly improved therapeutic outcomes, challenges such as antibiotic resistance, disease recurrence, drug-related adverse effects, and reduced efficacy in certain patients persist. The findings of this review indicate that nanoparticle-based drug delivery platforms can mitigate many of these limitations by enhancing mucosal targeting, improving drug bioavailability, and providing controlled release.

A major advantage of nanoparticle carriers in gastric ulcer therapy is their ability to prolong drug residence

Table 1. Nanoparticles with Table 1. Systematic review studies on the application of nanoparticles in the prevention and treatment of gastric ulcers.

Author & Year	Nanoparticle / System	Drug / Active Agent	Study Type	Key Mechanisms	Main Outcomes	Ref.
Bahramikia & Izadi (2023)	Green-synthesized nanoparticles (metallic, oxide, polymeric)	Plant extracts / phytocompounds	Systematic review	Antioxidant and anti-inflammatory activity; inhibition of *Helicobacter pylori*	Reduced gastric mucosal damage; enhanced tissue regeneration and ulcer healing	20
Yadav et al. (2025)	Green metal and metal oxide nanoparticles	Bioactive plant compounds	Review study	Free radical scavenging; anti-inflammatory and antibacterial activity	High therapeutic efficacy with improved biocompatibility and reduced toxicity	21

Table 2. Preclinical (in vitro and in vivo) studies on nanoparticle-based therapies for gastric ulcer treatment.

Author & Year	Nanoparticle / System	Drug / Active Agent	Study Model	Key Mechanisms	Main Outcomes	Ref.
Alai & Lin (2015)	PLGA and Eudragit nanoparticles	Lansoprazole	Rat	Enhanced bioavailability and targeted delivery	92–95% ulcer healing within 7 days	22
Li et al. (2023)	Bletilla polysaccharide nanoparticles	Omeprazole	Rat	Reduction of ROS, TNF-α, and IL-6	90–95% mucosal lesion recovery	23
Zewail et al. (2024)	Lecithin–chitosan nanoparticles	Famotidine	Rat	Increased mucoadhesion and antioxidant activity	~96% gastric mucosal protection	24
Wang et al. (2025)	TiO_2 nanoparticles	No drug	Rat	Pro-inflammatory activation; mast cell stimulation	Gastric mucosal injury and gastrointestinal dysfunction	25
Alai & Lin (2014)	PLGA and Eudragit nanoparticles	Lansoprazole	In vitro / in vivo	Enhanced cellular uptake and drug transport	89–92% ulcer healing improvement	26
Albalawi & Khateeb (2025)	Glycyrrhizic acid nanoparticles	Glycyrrhizic acid	Rat	NF-κB inhibition; SIRT1/FOXO pathway modulation	Significant improvement in ulcer healing	27
El-Sheikh & Hamad (2025)	Starch nanoparticles	None	Mouse	Mucosal barrier reinforcement	Reduced inflammatory and oxidative lesions	28
Huang et al. (2021)	Chitosan–bilirubin nanoparticles	Bilirubin	In vitro / in vivo	Potent antioxidant activity; ROS scavenging	Marked reduction in acute gastric ulcers	29
Abd El Hady et al. (2019)	PLGA–diosmin nanoparticles	Diosmin	Rat	NF-κB pathway inhibition	Improved histopathological parameters	30
Zhang et al. (2025)	Curcumin–oleanolic acid nanoparticles	Curcumin	Mouse	Anti-inflammatory and antioxidant effects	Reduced fibrosis, oxidative stress, and apoptosis	31
Aman et al. (2021)	CS/STPP nanoparticles	Allantoin	Rat	Mucoadhesion and tissue regeneration	Significant reduction in ulcer area	32
Salem et al. (2018)	Silver oxide nanoparticles	Silver	Rat	TNF-α and MDA reduction	Superior efficacy compared to omeprazole	33
Kumar et al. (2022)	Cellulose-based CuO nanoparticles	Copper oxide	Rat	TNF-α and IL-1β suppression	Enhanced tissue regeneration	34
Sreelakshmy et al. (2016)	Biosynthesized silver nanoparticles	Silver	In vitro (*H. pylori*)	Direct antibacterial activity	Growth inhibition of *H. pylori* (MIC ~250 µg/mL)	35
Abd El-Rady et al. (2021)	Pomegranate extract-loaded polymeric nanoparticles	Polyphenols	Rat	Increased IL-10; reduced IL-6	Enhanced efficacy vs free extract	36
Moradi et al. (2025)	Green-synthesized AgNPs (Lavandula)	Silver	Rat	Increased SOD; reduced oxidative stress	Comparable efficacy to famotidine	37
Sun et al. (2017)	Solid lipid nanoparticles (SLNs)	Sanguinarine	Mouse	NF-κB inhibition	Significant anti-ulcer activity	38
Prasad et al. (2013)	CeO_2 nanoparticles	Cerium oxide	Rat	ROS scavenging; antioxidant activity	~80% gastric mucosal protection	39
Elsisi et al. (2023)	CORM2 nanoparticles	CO donor	Rat	NRF2 and HO-1 activation	Strong anti-inflammatory and cytoprotective effects	40

Table 2. Preclinical (in vitro and in vivo) studies on nanoparticle-based therapies for gastric ulcer treatment.

Shareef et al. (2022)	Gold nanoparticles	Gold	Rat	Increased SOD and CAT activity	Reduced mucosal damage and oxidative stress	41
Perumcherry Raman et al. (2022)	Chitosan–anthocyanin nanoparticles	Anthocyanins	Rat	Immune modulation (IL-4/IFN-γ balance)	Reduced gastric inflammation	42
Fath-All et al. (2025)	Yeast-derived selenium nanoparticles	Selenium	Rat	Gut microbiota modulation; anti-inflammatory effect	Accelerated epithelial regeneration	43
Alamoudi et al. (2024)	Hesperidin nanoparticles	Hesperidin	Rat	SIRT1/PGC-1α activation; NF-κB inhibition	Strong mucosal protective effect	44
Nagarajana et al. (2015)	Chitosan–lansoprazole nanoparticles	Lansoprazole	In vitro	Controlled drug release	Sustained release up to 24 hours	45
Manivannan et al. (2023)	CS–OME–ATM nanoparticles	Omeprazole + H_2S donor	Rat	Increased NO and H_2S; improved perfusion	Enhanced mucosal healing and regeneration	46

time in the stomach and enhance contact with the injured mucosa (48). Mucoadhesive systems, such as chitosan-based nanoparticles, can adhere to the gastric epithelium, extending local drug retention. This property not only improves therapeutic efficacy but also reduces dosing frequency and stabilizes local drug concentrations, thereby optimizing clinical outcomes. In addition, protecting drugs from the acidic gastric environment and enabling sustained release further contribute to the therapeutic benefits of nanoparticles.

This review also highlights that a substantial part of the therapeutic effects of nanoparticles in gastric ulcers is mediated through modulation of inflammatory processes. Chronic mucosal inflammation is a key factor in sustained tissue damage and delayed ulcer healing (49). Several studies reported that therapeutic nanoparticles inhibit critical inflammatory pathways, including NF-κB, and reduce pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6 (50). Suppression of these pathways limits inflammatory cell infiltration, reduces oxidative damage, and provides a favorable environment for gastric epithelial regeneration (50).

ROS overproduction contributes substantially to gastric mucosal injury through oxidative damage to cellular components and compromised healing processes. Studies suggest that selenium nanoparticles and bioactive plant-based nanocomposites exert gastroprotective effects by restoring antioxidant capacity and upregulating enzymes such as SOD and CAT (51). Activation of NRF2-dependent signaling by nanoparticles further promotes resistance to oxidative stress and facilitates mucosal repair (52).

Another important observation from this review is the role of nanoparticle platforms in managing *H. pylori* infection (53). This bacterium is the most recognized risk factor for gastric ulcers and gastric cancer, and rising antibiotic resistance has compromised standard treatment efficacy (53). Nanocarriers improve the delivery of antibiotics to the infection site and provide controlled, localized drug release, ensuring therapeutically effective concentrations at the gastric mucosa. Additionally, metallic nanoparticles, such as silver and gold, exhibit intrinsic antibacterial activity against *H. pylori*, positioning nanoparticle-based therapies as promising strategies against drug-resistant infections (53).

Despite these therapeutic advantages, the review underscores the critical need to evaluate the biocompatibility and safety of nanoparticles. While many carriers demonstrate favorable biocompatibility, certain inorganic nanoparticles, such as titanium dioxide, can induce local inflammation, disrupt cellular function, and exacerbate tissue damage under specific conditions. These effects are highly dependent on physicochemical properties, including particle size, surface charge, morphology, dose, and exposure duration. Therefore, careful selection of materials and optimization of nanoparticle design are essential to maximize efficacy and minimize toxicity.

Although preclinical results are promising, the translation of nanomedicine from laboratory models to clinical applications faces several challenges. Most data are derived from animal studies, with limited information on long-term safety, pharmacokinetics, and biodistribution in humans. Moreover, the lack of standardized protocols for nanoparticle design and evaluation complicates cross-study comparisons. Consequently, well-designed, multicenter clinical trials are needed to establish the safety and efficacy of these nanoplatforms.

CONCLUSION

Current evidence indicates that nanoparticle-based drug delivery systems hold significant potential to enhance gastric ulcer therapy. These platforms can accelerate ulcer healing by improving drug bioavailability, targeting the gastric mucosa, modulating inflammation, reducing oxidative stress, and controlling *H. pylori* infection. However, successful clinical translation requires the development of safer nanocarriers, standardization of manufacturing processes, and extensive clinical evaluation. Future advances in nanomedicine and smart delivery systems are expected to enable more effective, safer, and personalized therapies for patients with gastric ulcers.

Declaration

Conflict of Interest

The authors declare no competing interests.

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Consent for Publication

The authors have given their approval for the publication of this manuscript.

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Ethical Considerations

The authors declare that the study complies with ethical publishing guidelines and adheres to principles of research integrity.

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