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Applications of Nanoplatforms in *Helicobacter pylori* Infection: A Narrative Review

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A B S T R A C T

Objective: *Helicobacter pylori* is a spiral-shaped, Gram-negative bacterium that colonises the gastric mucosa and is recognised as the principal aetiological agent of chronic gastritis, peptic ulcer disease, mucosa-associated lymphoid tissue (MALT) lymphoma, and gastric adenocarcinoma. The increasing prevalence of antibiotic-resistant strains, declining eradication rates associated with conventional treatment regimens, and frequent recurrence of infection have created an urgent need for alternative therapeutic strategies. Nanotechnology-based drug delivery systems have emerged as promising approaches because they can selectively target the gastric mucosa, enhance drug stability, improve penetration into bacterial biofilms, and increase local antimicrobial concentrations while minimising systemic exposure. This review critically examines the therapeutic potential of nanoplatforms for the management of *H. pylori* infection and discusses their underlying mechanisms of action.

Methods: A comprehensive analytical review was conducted based on a systematic literature search of PubMed, Scopus, and Web of Science for studies published between 2010 and 2025. Medical Subject Headings (MeSH) and related keywords, including *Helicobacter pylori*, *nanoparticles*, *targeted drug delivery*, *antibacterial therapy*, and *biofilm*, were used to identify relevant publications. Eligible studies included in vitro investigations, in vivo animal studies, and relevant review articles. The retrieved evidence was synthesised using qualitative thematic analysis.

Results: The available evidence indicates that nanotechnology-based platforms offer multiple complementary strategies for combating *H. pylori*. Metallic nanoparticles, particularly silver, gold, and zinc-based nanomaterials, together with polymeric–lipid nanocarriers and chitosan-based delivery systems, demonstrated potent antibacterial activity through disruption of the bacterial cell envelope, generation of reactive oxygen species (ROS), inhibition of urease activity, and interference with biofilm formation. In addition, mucoadhesive and targeted nanoformulations encapsulating therapeutic agents such as berberine and clarithromycin enhanced gastric mucosal retention, enabled sustained drug release, increased local drug concentrations, and consequently reduced bacterial colonisation, attenuated gastric inflammation, and promoted mucosal healing. Collectively, these findings suggest that nanomedicine may represent an effective strategy for overcoming antibiotic resistance and improving eradication outcomes. Nevertheless, concerns regarding nanoparticle-associated toxicity, tissue accumulation, manufacturing scalability, and long-term biosafety remain important challenges that require further investigation.

Conclusion: Nanoparticle-based drug delivery systems represent a promising therapeutic strategy for the management of *H. pylori* infection by enhancing antibiotic penetration, disrupting bacterial biofilms, improving targeted drug delivery, and exerting direct antibacterial effects. Although preclinical findings are highly encouraging, successful clinical translation will require rigorous safety evaluation, standardised formulation strategies, and well-designed clinical trials to establish long-term efficacy and biosafety.

Keywords: *Helicobacter pylori,* Nanoparticles, Nanomedicine; Antibacterial agents

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Introduction

Helicobacter pylori is a spiral-shaped, Gram-negative bacterium that chronically colonises the gastric mucosa and remains one of the most prevalent bacterial pathogens affecting humans worldwide. Persistent infection is strongly associated with chronic gastritis, peptic ulcer disease, gastric adenocarcinoma, and mucosa-associated lymphoid tissue (MALT) lymphoma, making *H. pylori* a major global public health concern [1]. Owing to its remarkable ability to survive the highly acidic gastric environment and establish long-term colonisation within the gastric mucus layer, the bacterium infects more than half of the world's population, with the highest prevalence reported in low- and middle-income countries [2,3]. Socioeconomic conditions, inadequate sanitation, household overcrowding, contaminated food and water, and person-to-person transmission all contribute to its widespread distribution. Given its well-established role in gastrointestinal disease and gastric carcinogenesis, effective eradication of *H. pylori* remains a major objective in contemporary gastroenterology.

The pathogenesis of *H. pylori* infection is multifactorial and involves complex interactions between bacterial virulence factors, host immune responses, and disruption of gastric mucosal homeostasis [4]. A hallmark of the organism is the production of urease, which hydrolyses urea into ammonia and carbon dioxide, thereby buffering gastric acidity and creating a favourable microenvironment for bacterial survival [5]. In addition, the major virulence determinants, cytotoxin-associated gene A (CagA) and vacuolating cytotoxin A (VacA), contribute to epithelial injury, immune dysregulation, and persistent inflammation. Infection stimulates the production of numerous pro-inflammatory mediators, including interleukin (IL)-1β, IL-6, IL-8, and tumour necrosis factor-α (TNF-α), leading to chronic gastritis, oxidative stress, and progressive mucosal damage [4,5]. Furthermore, increased production of reactive oxygen species (ROS) and reactive nitrogen species (RNS) promotes DNA damage and may accelerate the progression from chronic inflammation to premalignant and malignant gastric lesions [6]. These complex pathogenic mechanisms suggest that successful eradication requires therapeutic strategies extending beyond conventional antibiotic therapy alone.

Current eradication regimens generally combine proton pump inhibitors (PPIs) with two or more antibiotics and, in many cases, bismuth-containing compounds [7]. Although these multidrug regimens remain the standard of care, their effectiveness has declined substantially in many regions because of the increasing prevalence of antibiotic-resistant *H. pylori* strains [8]. Resistance to clarithromycin, metronidazole, and levofloxacin has become one of the principal causes of treatment failure worldwide (9). Furthermore, drug degradation within the acidic gastric environment, poor local bioavailability, limited penetration through the gastric mucus layer, bacterial biofilm formation, prolonged treatment regimens, and treatment-related adverse effects all compromise therapeutic efficacy. These limitations have stimulated growing interest in innovative drug delivery systems capable of enhancing antimicrobial efficacy while reducing the development of antimicrobial resistance [8,9].

Nanotechnology has emerged as one of the most promising approaches for overcoming these therapeutic challenges. Owing to their nanoscale dimensions, high surface-area-to-volume ratio, tunable physicochemical properties, and versatile surface functionalisation, nanoparticles provide highly efficient platforms for the targeted delivery of antimicrobial agents and other therapeutic molecules [10,11)]. Nanocarriers can protect acid-sensitive compounds from degradation, prolong gastric residence time, improve drug bioavailability, and enable sustained drug release directly at the site of infection. Collectively, these properties facilitate higher local drug concentrations while minimising systemic exposure and reducing treatment-associated toxicity [11].

A broad range of nanoplatforms, including polymeric nanoparticles, lipid-based nanocarriers,

liposomes, nanoemulsions, dendrimers, metallic nanoparticles, and multifunctional nanocomposites, has been investigated for the management of *H. pylori* infection [12]. Metallic nanoparticles, particularly silver, gold, and zinc oxide nanoparticles, together with chitosan-based nanocarriers, have attracted considerable attention because of their intrinsic antibacterial activity, ability to disrupt bacterial biofilms, and potential to overcome antimicrobial resistance. In addition to functioning as drug delivery vehicles, these nanoplatforms facilitate the targeted administration of antibiotics, phytochemicals, probiotics, antimicrobial peptides, and anti-inflammatory agents while enabling controlled or stimuli-responsive drug release [13]. Experimental studies have demonstrated that mucoadhesive nanoparticles enhance retention within the gastric mucus layer, thereby increasing local drug accumulation and improving eradication efficacy. Moreover, pH-responsive nanocarriers capable of releasing their payload selectively within the acidic gastric environment represent an important advance towards precision therapy for *H. pylori* infection [12,13].

The applications of nanotechnology extend beyond antimicrobial therapy. Nanoparticle-based biosensors, nanoprobes, and theranostic platforms have enabled the rapid, sensitive, and specific detection of *H. pylori*, offering valuable opportunities for early diagnosis and treatment monitoring [14]. In addition, nanocarriers have been investigated for the delivery of vaccines, small interfering RNAs (siRNAs), antimicrobial peptides, and other nucleic acid therapeutics, highlighting the potential of nanomedicine to support targeted immunotherapy and gene-based interventions against persistent gastric infection [15]. Collectively, these emerging technologies may facilitate the development of more precise, personalised, and effective therapeutic strategies for gastrointestinal infectious diseases.

Despite these encouraging advances, several important challenges continue to limit the clinical translation of nanoparticle-based therapies. Concerns regarding long-term biocompatibility, tissue accumulation, nanoparticle-associated toxicity, unintended immune activation, environmental safety, and the lack of standardised manufacturing processes remain unresolved [16]. Moreover, the acidic gastric environment, the dynamic mucus barrier, and continuous gastrointestinal motility present substantial physiological obstacles that may reduce nanoparticle stability, gastric retention, and therapeutic efficacy. Addressing these challenges will require comprehensive investigations into the pharmacokinetics, biodistribution, biodegradability, biosafety, and long-term clinical performance of nanomaterials before their routine clinical application can be achieved [17].

Given the rapid expansion of research in nanomedicine and gastrointestinal infectious diseases, a comprehensive synthesis of the available evidence is both timely and warranted. Although numerous studies have investigated nanoparticle-based interventions against *Helicobacter pylori*, current knowledge remains fragmented regarding their mechanisms of action, therapeutic efficacy, safety profile, and translational potential. Accordingly, this review critically examines the therapeutic applications of nanoplatforms in *H. pylori* infection, with particular emphasis on the major classes of nanocarriers, their mechanisms of action, preclinical and clinical evidence, current limitations, and future perspectives for improving the management of this globally important bacterial pathogen.

Methodology

Study Design

This study was conducted as a narrative review based on a literature search to critically evaluate the therapeutic applications of nanotechnology-based platforms for the management of *Helicobacter pylori* infection, with particular emphasis on recent advances in nanomedicine, targeted drug delivery, and nanoparticle-mediated antibacterial therapies. The review methodology was designed to provide a transparent, comprehensive, and reproducible synthesis of the

available evidence. Relevant studies published between January 2010 and March 2025 were considered for inclusion.

Literature Search Strategy

A comprehensive literature search was performed using the electronic databases PubMed, Scopus, Web of Science, Google Scholar, Scientific Information Database (SID), and Islamic World Science Citation Center (ISC). The search strategy combined Medical Subject Headings (MeSH), where applicable, with free-text keywords related to *Helicobacter pylori*, nanotechnology, and targeted antibacterial therapy.

The principal search terms included Helicobacter pylori, H. pylori, Nanoparticles, Nanomedicine, Drug Delivery, Targeted Drug Delivery, Antibacterial Therapy, Nanocarriers, Gastroretentive Drug Delivery Systems, Antimicrobial Nanoparticles

These terms were combined using the Boolean operators AND and OR to maximise the sensitivity and specificity of the search. A representative search strategy was as follows:

(*Helicobacter pylori* OR *H. pylori*) AND (Nanoparticles OR Nanomedicine OR Nanocarriers) AND (Drug Delivery OR Antibacterial Therapy OR Targeted Therapy)

Eligibility Criteria

Studies published between January 2010 and March 2025 were considered eligible.

Publications were included if they met one or more of the following criteria:

Original in vitro investigations evaluating nanoparticle-based therapeutic strategies against *H. pylori*.

In vivo animal studies investigating the efficacy and/or safety of nanotechnology-based interventions.

Preclinical studies evaluating targeted drug delivery systems, antimicrobial nanomaterials, or gastroretentive nanoformulations.

High-quality narrative reviews or systematic reviews addressing the biomedical applications of nanotechnology in *H. pylori* infection.

Studies were excluded if they:

Were unrelated to nanotechnology-based management of *H. pylori* infection.

Consisted of conference abstracts, editorials, correspondence, opinion articles, or non-peer-reviewed publications.

Provided insufficient scientific evidence or lacked adequate methodological detail.

Focused exclusively on nanoparticle toxicity without evaluating therapeutic efficacy or biomedical applications.

Only full-text articles published in English were included.

Study Selection and Data Extraction

Following the database search, duplicate records were removed prior to screening. Titles and abstracts were independently assessed for relevance, after which potentially eligible articles underwent full-text evaluation according to the predefined eligibility criteria.

Relevant information was extracted using a standardised data collection framework. The extracted variables included the first author, year of publication, study design, experimental model (in vitro, animal, or other preclinical model), nanoparticle type and composition, drug delivery platform, proposed mechanism of action, therapeutic target, antibacterial and anti-biofilm activity, principal findings, and reported study limitations.

Critical Appraisal and Evidence Synthesis

The scientific relevance of the included studies was critically appraised by considering study design, methodological rigour, experimental model, sample size (where applicable), consistency of the reported findings, and overall relevance to the objectives of the present review. As this review included heterogeneous in vitro, animal, and preclinical studies with substantial methodological diversity, a formal risk-of-bias assessment and quantitative meta-analysis were not considered appropriate.

The extracted evidence was synthesised qualitatively using a thematic approach. Studies were organised according to nanoparticle class, antibacterial mechanisms, gastroretentive drug delivery strategies, anti-biofilm activity, immunomodulatory and anti-inflammatory effects, approaches for overcoming antibiotic resistance, and emerging targeted nanotherapeutic technologies. Particular attention was given to comparing the therapeutic advantages, current limitations, translational challenges, biosafety considerations, and future perspectives of nanotechnology-based interventions for *Helicobacter pylori* infection, thereby providing a comprehensive overview of the current state of the field.

Results

The evidence synthesised in this review indicates that a broad range of nanotechnology-based platforms, including metallic, polymeric, lipid-based, and biologically derived nanoparticles, exhibit considerable therapeutic potential against *Helicobacter pylori* in both in vitro and in vivo experimental models. Across the included studies, nanoparticle-mediated interventions consistently enhanced antibacterial efficacy through multiple complementary mechanisms while improving the pharmacological performance of conventional antimicrobial agents.

Several nanoplatforms demonstrated direct antibacterial activity by disrupting bacterial membrane integrity, inducing the generation of reactive oxygen species (ROS), inhibiting urease activity, and interfering with biofilm formation. These multimodal mechanisms not only suppressed bacterial growth but also reduced the persistence of *H. pylori* within the protective gastric mucus layer, thereby increasing bacterial susceptibility to antimicrobial therapy.

Compared with conventional free-drug formulations, nanoparticle-based delivery systems exhibited superior gastric mucosal penetration, prolonged gastric residence time, enhanced mucoadhesion, and sustained drug release. These characteristics resulted in higher local drug concentrations at the site of infection while reducing premature drug degradation within the acidic gastric environment. Consequently, several studies reported improved antibacterial efficacy with lower therapeutic doses, potentially reducing systemic drug exposure and minimising treatment-related adverse effects.

The reviewed evidence further suggests that targeted nanocarriers may overcome several important limitations of conventional eradication therapy. By enhancing antibiotic delivery, disrupting bacterial biofilms, improving local drug bioavailability, and facilitating sustained drug release, these systems have the potential to address one of the greatest challenges in the management of *H. pylori* infection—antibiotic resistance. In addition, several nanoplatforms exhibited anti-inflammatory and gastroprotective properties, contributing to reduced gastric mucosal injury and promoting tissue repair in experimental models.

Overall, the available evidence indicates that nanotechnology-based drug delivery systems can improve antibacterial efficacy, enhance target specificity, and optimise the pharmacokinetic performance of antimicrobial agents compared with many conventional therapeutic approaches. Nevertheless, important challenges remain, including limited clinical evidence, manufacturing scalability, regulatory standardisation, nanoparticle-associated toxicity, and long-term biosafety. Addressing these limitations will be essential before nanotechnology-based

interventions can be routinely integrated into the clinical management of *H. pylori* infection.

A comprehensive summary of the studies included in this review, together with the principal characteristics, mechanisms of action, and therapeutic outcomes of the investigated nanoplatforms, is presented in Table 1.

Table 1. Representative nanoparticle-based platforms investigated for the treatment of *Helicobacter pylori* infection

Nanoparticle / Nanoplatform	Particle Size (nm)	Experimental Model	Proposed Mechanism(s) of Action	Principal Findings	Ref.
Metallic nanoparticles (Ag, Au, Bi, ZnO, Fe_2O_3)	10–100	*In vitro* and *in vivo*	Generation of reactive oxygen species (ROS), disruption of bacterial membrane integrity, and metal ion release	Demonstrated potent antibacterial activity against *H. pylori*, with bismuth- and silver-based nanoparticles showing the greatest efficacy	[18]
Pexiganan peptide nanoparticles (PNPs)	Nanoscale	*In vitro* and animal studies	Enhanced peptide stability, prolonged gastric retention, and improved mucoadhesion	Achieved greater bacterial eradication than free pexiganan	[19]
Antibiotic-free FU/ML-LA/EB nanoparticles	Approx. 100–200	*In vitro* and *in vivo*	Biofilm disruption, urease inhibition, and activation of the AMPK signalling pathway	Effectively eradicated bacterial biofilms and intracellular *H. pylori*	[20]
Lipid–polymeric nanoparticles (RHL-PC-LPNs) loaded with amoxicillin	Approx. 200	*In vitro*	Disruption of extracellular polymeric substances (EPS), biofilm destabilisation, and sustained drug release	Reduced the minimum inhibitory concentration (MIC) of amoxicillin from 125 to 15.6 µg/mL	[21]
Chitosan/CuO nanocomposite	Nanoscale	*In vitro*	Growth inhibition, cyclooxygenase-2 (COX-2) suppression, and antibacterial activity	Completely inhibited bacterial growth at a concentration of 1.95 µg/mL	[22]
Clarithromycin-loaded lipid–polymeric nanoparticles containing rhamnolipid	Approx. 100–200	*In vitro*	Enhanced biofilm disruption, improved antibiotic penetration, and controlled drug release	Achieved complete eradication of *H. pylori* biofilms	[23]

Fucose–chitosan/heparin nanoparticles loaded with berberine	Approx. 100–200	*In vitro* and *in vivo*	Mucoadhesive targeting, controlled drug release, and enhanced gastric retention	Significantly reduced gastric bacterial colonisation and gastric mucosal inflammation	[24]
Gastric epithelial cell membrane-coated nanoparticles (AGS-NPs) loaded with clarithromycin	Approx. 100	*In vitro* and *in vivo*	Biomimetic targeting via gastric epithelial cell membrane mimicry and targeted drug delivery	Demonstrated highly specific binding to *H. pylori* and improved targeted antibiotic delivery	[25]
Copper oxide (CuO) nanoparticles	Nanoscale	Computational and *in vitro* studies	Interaction with bacterial molecular targets, catalytic antibacterial activity, and ROS generation	Exhibited potent anti-*H. pylori* activity	[26]
Chitosan nanoparticles incorporating *Aloe vera* gel	36–83	*In vitro*	Bacterial membrane disruption, antioxidant activity, and enhanced antibacterial efficacy	Reduced the MIC to 3.9 µg/mL and enhanced antibacterial activity	[27]

Discussion

Helicobacter pylori infection remains one of the leading causes of upper gastrointestinal disease and is firmly established as a major aetiological factor in chronic gastritis, peptic ulcer disease, gastric adenocarcinoma, and mucosa-associated lymphoid tissue (MALT) lymphoma [28]. Although combination regimens consisting of proton pump inhibitors (PPIs) and multiple antibiotics have substantially improved eradication rates over recent decades, their long-term effectiveness has been increasingly compromised by the emergence of antimicrobial resistance, treatment-related adverse effects, prolonged treatment regimens, and suboptimal patient adherence. Consequently, considerable attention has shifted towards innovative drug delivery strategies capable of enhancing antibacterial efficacy while overcoming the limitations of conventional pharmacotherapy.

The findings of this review indicate that nanotechnology-based drug delivery systems offer several important pharmacological advantages over conventional formulations. One of their principal strengths is the ability to protect therapeutic agents from degradation within the highly acidic gastric environment while simultaneously increasing drug retention at the site of infection [29]. Mucoadhesive nanocarriers, particularly those based on chitosan and related biopolymers, prolong gastric residence time and enhance penetration through the gastric mucus barrier, thereby improving access to bacterial colonies embedded beneath the mucus layer [30]. This localised and sustained drug delivery increases antimicrobial exposure at the site of infection and has the potential to reduce treatment failure and disease recurrence.

Beyond improving drug delivery, numerous nanomaterials possess intrinsic antibacterial activity against *H. pylori*. Metallic nanoparticles, particularly silver, gold, and zinc-based nanomaterials, have demonstrated broad-spectrum antibacterial effects through multiple complementary mechanisms [31]. These include disruption of bacterial membrane integrity, induction of oxidative stress through the generation of reactive oxygen species (ROS), interference with essential metabolic pathways, and inhibition of urease, a key enzyme required for bacterial survival within the acidic gastric environment [32]. Importantly, several studies have also demonstrated that nanoparticles interfere with biofilm formation and destabilise established biofilms. Because biofilm formation is a major mechanism contributing to antimicrobial tolerance and persistent infection, these anti-biofilm properties may enhance eradication efficacy when nanoplatforms are combined with conventional antibiotics [33].

Another important finding of this review is the capacity of nanoparticle-based systems to optimise targeted drug delivery. Polymeric and lipid-based nanocarriers have been shown to protect antibiotics such as clarithromycin, as well as bioactive compounds including berberine, from premature degradation while enabling sustained and site-specific drug release within the gastric mucosa [34]. These properties increase local drug concentrations, improve therapeutic efficacy, and may reduce the systemic doses required to achieve bacterial eradication, thereby lowering the risk of treatment-related toxicity. Furthermore, nanoformulations incorporating phytochemicals and other naturally derived bioactive compounds may provide synergistic antibacterial, antioxidant, and anti-inflammatory effects that promote mucosal healing in addition to bacterial clearance.

In addition to their antimicrobial activity, several nanoplatforms appear capable of modulating host inflammatory responses. Persistent *H. pylori* infection activates signalling pathways such as nuclear factor-kappa B (NF-κB), leading to sustained production of pro-inflammatory cytokines and progressive gastric mucosal injury. Experimental evidence suggests that selected nanoformulations can attenuate these inflammatory pathways while simultaneously suppressing bacterial growth, thereby providing complementary antibacterial and immunomodulatory effects [35]. This combination of targeted drug delivery, direct antibacterial activity, and host immune modulation distinguishes nanomedicine from conventional antibiotic therapy and represents a promising strategy for the management of chronic *H. pylori*-associated gastric inflammation.

Despite these encouraging findings, several important barriers continue to limit the clinical translation of nanoparticle-based therapies. Concerns regarding the biosafety of certain metallic nanoparticles remain particularly significant, as excessive production of reactive oxygen species may induce oxidative stress, DNA damage, and unintended cytotoxicity in healthy gastric tissues. In addition, the long-term consequences of nanoparticle accumulation within biological tissues remain incompletely understood, highlighting the need for comprehensive toxicological and pharmacokinetic evaluation before routine clinical application.

Further challenges arise from the considerable heterogeneity of currently available nanoplatforms. Variations in nanoparticle composition, synthesis methods,

particle size, surface charge, drug-loading efficiency, and release kinetics complicate direct comparisons among studies and hinder the development of standardised therapeutic protocols. Moreover, the majority of available evidence is derived from in vitro investigations and animal studies, whereas well-designed clinical trials remain limited. Consequently, successful clinical translation will require harmonised manufacturing procedures, standardised evaluation criteria, and adequately powered multicentre clinical studies that comprehensively assess therapeutic efficacy, pharmacokinetics, biodistribution, and long-term biosafety.

Conclusion

The available evidence indicates that nanotechnology-based drug delivery systems represent a promising therapeutic strategy for improving the management of *Helicobacter pylori* infection. By enhancing drug stability within the gastric environment, prolonging mucosal residence time, facilitating targeted antibiotic delivery, disrupting bacterial biofilms, and exerting direct antibacterial activity, nanoplatforms have the potential to overcome several limitations of conventional eradication therapy, including antimicrobial resistance and suboptimal drug delivery.

Nevertheless, the successful clinical implementation of these technologies will depend on further advances in nanoparticle design, rigorous biosafety evaluation, harmonised manufacturing standards, and robust clinical validation. Future research should prioritise well-designed multicentre clinical trials, comprehensive pharmacokinetic and biodistribution studies, and long-term safety assessments to establish the clinical efficacy and biosafety of these nanotherapeutic systems. Continued advances in nanomedicine are expected to facilitate the development of intelligent, targeted, and clinically translatable therapeutic platforms capable of improving eradication rates while minimising adverse effects, ultimately contributing to more effective management of *H. pylori* infection.

Author Contributions:

All study activities, including study design, data collection, analysis, interpretation, manuscript preparation, and final revision, were carried out exclusively by Mahsa Esmaeili. The author approved the final version of the manuscript.

Conflict of interests

The authors declare there are no conflicts of interest.

Ethical considerations

Authors have carefully monitored ethical issues such as text plagiarism, duplicated publication, misconduct, data fabrication, and falsification.

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