RSC Advances

REVIEW

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Cite this: *RSC Adv.*, 2025, **15**, 5558

Helicobacter pylori and gastric cancer: current insights and nanoparticle-based interventions

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Background: *H. pylori* is recognized as one of the main causes of gastric cancer, and this type of cancer is considered as one of the leading diseases causing cancer deaths all over the world. Knowledge on the interactions between *H. pylori* and gastric carcinogenesis is important for designing preventive measures. *Objective*: the objective of this review is to summarize the available literature on *H. pylori* and gastric cancer, specifically regarding the molecular mechanisms, nanoparticle-based therapy and clinical developments. *Methods*: the databases including PubMed, Google Scholar and web of science were searched as well as papers from 2010 to 2024 were considered for review. Research literature on *H. pylori*, gastric cancer, nanoparticles, nanomedicine, and therapeutic interventions was summarized for current findings and possible treatments. *Results*: the presence of *H. pylori* in gastric mucosa causes chronic inflammation and several molecular alterations such as DNA alteration, epigenetic changes and activation of oncogenic signaling pathways which causes gastric carcinogenesis. Conventional antibiotic treatments have some issues because of the constantly rising levels of antibiotic resistance. Lipid based nanoformulations, polymeric and metallic nanoparticles have been delivered in treatment of *H. pylori* to improve drug delivery and alter immunological responses. *Conclusion*: nanoparticle based interventions have been widely explored as drug delivery systems by improving the treatment strategies against *H. pylori* induced gastric cancer. Further studies and clinical trials are required to bring these findings into a clinical setting in order to possibly alter the management of *H. pylori* related gastric malignancies.

Received 5th November 2024
Accepted 7th February 2025

DOI: 10.1039/d4ra07886a

rsc.li/rsc-advances

1. Introduction

Gastric cancer is still a strong public health issue and is ranked among the most common causes of cancer deaths across the globe.[1] Even though diagnostic and therapeutic strategies have been improving, the prognosis of gastric cancer patients is still relatively grim mainly due to the advanced stage at diagnosis and lack of effective treatments.[2] According to estimates, there were 1.09 million new cases of gastric cancer and 0.77 million gastric cancer-related deaths reported worldwide in 2020. Globally, the annual incidence rates for males and women were 15.6 to 18.1 and 6.7 to 7.8 per 100 000, respectively.[3] Many cross-sectional studies have established that *H. pylori* positive people are at higher risk of developing gastric cancer in central Asia and Africa.[4] For example, Helicobacter and cancer collaborative group meta-analysis published in 2001 assert that the risk of developing gastric cancer among patients with *H. pylori* infection is 2–3-fold that of the non-infected patients.[5] The most significant risk factor for the formation of gastric cancer is the chronic infection of the stomach lining by the Gram-negative bacterium called *Helicobacter pylori* (*H. pylori*). *H. pylori* infection is very common, with 50% of the world population being infected, and the prevalence is even higher in the developing nations.[6] *H. pylori* is a group 1 carcinogen having highest risk category for cancer development as described by International Agency for Research on Cancer (IARC) and is recognized as playing a substantial role in gastric carcinogenesis. Cytotoxin associated gene A (CagA) and Vacuolating cytotoxin A (VacA) are the main virulence factors of the bacterium that play a significant role in the development of gastric adenocarcinoma.[7] These factors compromise the gastric epithelial barrier and induce chronic inflammation, which in addition to genetic and epigenetic changes, create a tumorigenic milieu.[8] The progress from *H. pylori* infection to gastric cancer is a process of chronic gastritis, atrophic gastritis, intestinal metaplasia, dysplasia, and adenocarcinoma.[9] Contemporary management of *H. pylori* infection is based on the use of antibiotics in the combination with proton pump inhibitors (PPIs). Treatment of *H. pylori* often involves triple therapy that includes clarithromycin, amoxicillin, or metronidazole.[10] But antibiotic resistance has become a major concern and it has greatly reduced the effectiveness of these treatments making it important to look for other treatment options.[11] Also, conventional treatments are inadequate to

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eliminate the infection or to hinder the occurrence of gastric cancer in those with a high risk. Nanotechnology has now been defined as a unique field in the discovery of various therapeutic interventions.[12] Nanoparticles as a result of their physicochemical characteristic possess several advantages over the conventional therapy such as site-specific release, improved absorption, and minimal side effects.[13] Antimicrobial medications, specifically antibiotics, had to be encapsulated for targeted drug delivery to combat *H. pylori*. Different categories of drug induced nanoparticles including zinc oxide nanoparticles, silver nanoparticles, chitosan based nanoparticles and liposomes are at the experimental stage to enhance the treatment outcomes of *H. pylori* and to prevent the oncogenic action of this bacterium.[14] The antimicrobial effects of antibiotic mediated nanoparticles on *H. pylori* are mediated by medication transport, biofilm destruction, immunological modulation, and possible probiotic usage. The capacity of these nanoparticles to overcome challenges including poor medication absorption and antibiotic resistance makes them an effective weapon to fight against *H. pylori* infection.[15]

In this review, our main objectives are to present the updated knowledge about the epidemiology and molecular pathways of *H. pylori*-related gastric cancer, to describe the modern treatment strategies and their drawbacks in the context of *H. pylori* infection treatment, and to introduce the recent developments and perspectives of the liposomes, polymeric, and metallic nanoparticles use for the treatment and diagnosis of *H. pylori* and gastric cancer.[16] This review particularly focuses on the kinds of nanoparticles that have shown effectiveness against *H. pylori*, as well as their modes of action and their benefits over traditional antibiotic treatments. It was also evaluated the difficulties, and potential paths forward in creating nanoparticle-based treatments for the successful elimination of *H. pylori*, tackling problems such as antibiotic resistance, bioavailability, and targeted delivery. Thus, this review highlights the significance of adopting innovative approaches in the *H. pylori* associated gastric cancer treatment and patient care based on the integration of modern data and new therapeutic approaches.

1.1 *H. pylori* and gastric carcinogenesis

H. pylori is a Gram-negative bacterium that infects the human stomach, and it is considered as a potent carcinogen for gastric cancer especially that of the non-cardia gastric adenocarcinoma.[17] The infection begins by colonization of the columnar glandular epithelium of the stomach by the bacterium *H. pylori* mostly in the pyloric area. Its action is to secrete virulence factors that results into an inflammatory process.[18] This condition can result to gastritis as well as ulcers. If the inflammation is chronic, there will be changes such as metaplasia in which the stomach cells alter their structure.[19] These metaplastic cells are capable of mutations, which results to neoplasia, the abnormal and uncontrolled growth of cells. There are two main subtypes of adenocarcinoma (the most common type of gastric cancer, accounting for about 90% of cases): intestinal which is also called well-differentiated and diffuse which is also called undifferentiated. The diffuse type is characterized by mutation in the CDH1 gene and loss of E-CADHERIN function that results in cell disorganized division and cancer.[20] The (Fig. 1;[21]) shows the sequence of events that occur in relation to the development of *Helicobacter pylori* infection to gastric cancer.

1.2 Molecular mechanisms of *H. pylori* and role of inflammatory mediators

H. pylori through several molecular pathways such as inflammation, DNA damage and epigenetic changes contributes to gastric carcinogenesis.[22] The important factors of virulence include cytotoxin-associated gene A (CagA) and vacuolating cytotoxin A (VacA) which affect the gastric epithelial cells and stimulate the oncogenic pathways.[23] Electron microscopic image of *H. pylori*, in (Fig. 2;[23]) clearly signifies the spiraling nature of the bacteria. The bacterium is mobile and has several flagella that enables it to swim in the mucus layer of the stomach lining and causes chronic infections that can culminate into serious illnesses such as gastric cancer.[24,25]

One of the critical pathways of carcinogenesis in the stomach is the chronic inflammation caused by *H. pylori*.[26,27] It activates a continuous inflammatory response that results to the synthesis of various cytokines like interleukin-1 beta, interleukin-6, and tumor necrosis factor-alpha, as well as reactive oxygen species. These inflammatory mediators are pro genotoxic, pro carcinogenic and pro angiogenic, therefore they induce DNA damage, predispose to genetic instability and create a tumorigenic stroma.[28,29] *H. pylori* infection directly caused DNA damage by producing ROS and indirectly by chronic inflammation. Also, the bacterium causes epigenetic modifications that involve DNA methylation and histone modification, leads to the down-regulation of tumor suppressor genes and up-regulation of oncogenes.[30] For instance, the gene CDH1 that codes for E-cadherin, is commonly hypermethylated in *H. pylori* infected gastric mucosa and the risk of cancer is significantly higher in such cases.[31] *H. pylori* infection is also known to cause epithelial–mesenchymal transition (EMT) which is known to increase the invasiveness and metastasizing abilities of the gastric epithelial cells.[32] The *H. pylori* virulence factors are known to activate several signaling pathways that are involved in this process such as Wnt/β-catenin, TGF-β, and NF-κB signaling pathways.[33,34]

1.3 Current therapeutic approaches

1.3.1 Conventional treatments. *H. pylori* infection is typically treated using antibiotics and with proton pump inhibitors.[35] However, the newer and more resistant *H. pylori* strains have made the administration of these regimens quite ineffective.[36] It has been reported in several researches that the eradication rates of *H. pylori* in standard triple therapy has reduced below 80% in many areas and therefore call for new treatment regimens.[37,38]

1.3.2 Novel therapies. To overcome the difficulties related to antibiotic resistance, new methods of treatment have been proposed, such as the use of probiotics, bismuth-containing

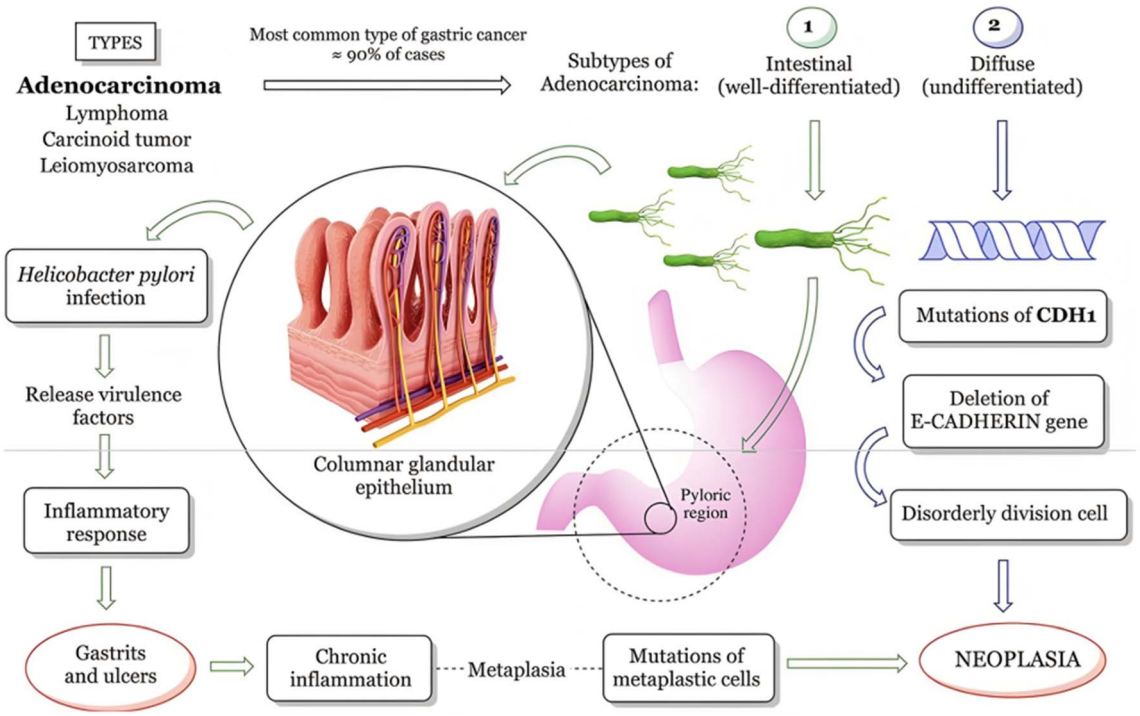

Fig. 1 Mechanism of *Helicobacter pylori* and gastric carcinogenesis.

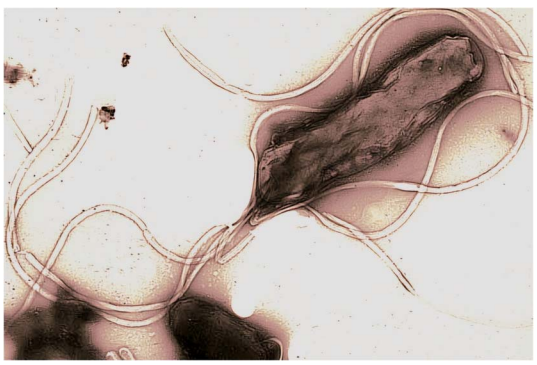

Fig. 2 Microscopic structure of *Helicobacter pylori*.

quad therapy, and sequential therapy.[39] Though these strategies have been effective in increasing the eradication rates, they are still accompanied by challenges like patient adherence to the prescribed medications, and possible side effects of the drugs.[40,41]

1.3.3 Nanoparticle-based interventions

1.3.3.1 Advantages of nanoparticles. Nanoparticles are considered to be advantageous over the conventional therapies for drug delivery as these are effective in targeted delivery, possess better bioavailability and possess low level of systemic toxicity.[42] They afford the opportunity to encapsulate and deliver a large amount of therapeutic agents to the site of infection enhancing the efficiency of treatment with minimal side effects.[43]

1.3.3.2 Types of nanoparticles. (1) Lipid-based nanoparticles: liposomes and solid lipid nanoparticles (SLNs) can encapsulate antibiotics and deliver them directly to the gastric mucosa. Studies have shown that liposomal formulations of clarithromycin significantly enhance its antibacterial activity against *H. pylori*.[44]

(2) Polymeric nanoparticles: biodegradable polymers, such as PLGA and chitosan, are used to create nanoparticles that release antibiotics in a controlled manner. For instance, there is evidence based on PLGA nanoparticles containing amoxicillin that provides prolonged antibacterial effect and higher rates of eradication in animal trial.[45]

(3) Metallic nanoparticles: the antibacterial activity of silver, gold and zinc oxide nanoparticles is high against *H. pylori*. Due to their physicochemical properties, they can compromise the bacterial membranes and affect various metabolic activities. For instance, the synthesized silver nanoparticles proved to give a good result in elimination of *H. pylori* in the stomach.[46,47]

The polymeric and metallic nanoparticles cause damage to the bacterial cell membrane, denatured bacterial proteins, and heat shock proteins are produced (Fig. 3).[1] They also suppress enzymatic activity, break down nucleic acids and produce a reactive oxygen species which leads to oxidative stress in bacteria. These individual actions cause the bacteria to enter a lethal stress response, which in turn leads to their death. This particular strategy focuses on one of the possible uses for nanoparticles and their capability to eliminate *H. pylori*, which is a factor that can lead to gastric cancer.[48]

1.4 Mechanisms of action

Nanoparticles can combat *H. pylori* through multiple mechanisms, including:

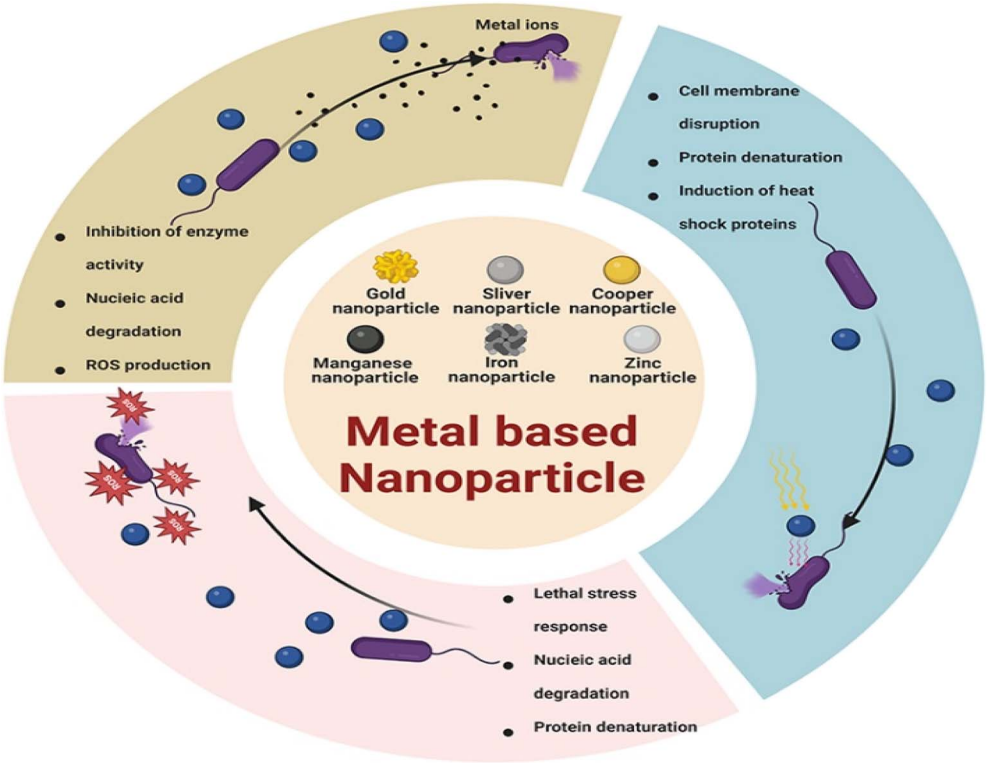

Fig. 3 Metal based nanoparticles.

• Direct antibacterial activity: metallic nanoparticles produce ROS resulting in oxidative stress and bacterial cell death. Also, nanoparticles can weaken the bacterial membranes and cause the release of cellular contents.[49]

• Enhanced drug delivery: one can use nanoparticles that can encapsulate the antibiotics and then release the drug directly to the stomach lining thus solving problems that are associated with conventional drug delivery systems.[50] This targeted delivery increases the drug concentration at the site of infection and decreases the concentration in the whole body.[51]

• Modulation of immune response: nanoparticles can be engineered to modulate the host immune response, promoting anti-inflammatory effects and reducing gastric mucosal damage.[52]

1.5 Clinical applications and future directions

1.5.1 Preclinical studies. *In vitro* studies have shown that nanoparticle-based drugs are effective in killing *H. pylori* and preventing gastric cancer.[53] For example, the preparations of clarithromycin by liposomes have reported better bactericidal effects and lesser ulcerogenic effects in animal studies. In the same way, the gold nanoparticles that are linked with antibiotics showed high bioactivity against *H. pylori*.[54]

1.5.2 Clinical trials. Although *in vitro* and *in vivo* studies show great potential for nanoparticle-mediated therapies for *H. pylori*-induced gastric cancer, their clinical application is still in its infancy.[55] Current clinical trials are being conducted to explore the side effects, effectiveness, absorption, distribution, metabolism, and excretion of nanoparticle formulations in a human body. These studies will give important information in the possibility of nanomedicine in the clinical practice.[56]

1.5.3 Challenges and opportunities. The use of nanoparticle theranostic platforms for *H. pylori* and gastric cancer has a few limitations. The synthesis of nanoparticles for large-scale applications, their use from a regulatory perspective, and the long-term toxicity of nanoparticles. Nevertheless, the growth in nanotechnology and the understanding of *H. pylori* infectivity provide the chance to overcome the mentioned difficulties and change the treatment significantly.[57,58] Tables 1 and 2 presented epidemiological studies and mechanisms of action of nanoparticles.

1.6 Immunotherapy approaches

1.6.1 Integrating immunotherapy with nanoparticles. • Vaccine delivery: substances called nanoparticles can be employed to bring vaccines that incite the immune system to identify and destroy *H. pylori*.[64] It can help to strengthen the natural defense of the body and to prevent the illness from recurring.[65]

• Immune boosters: nanoparticles can encapsulate immune-modulating agents that would boost the body's immune response against the *H. pylori*. For instance, nanoparticles can have cytokines that enhance the immune response against the particular infection incorporated in them.[66,67]

• Checkpoint inhibitors: the co-employment of immune checkpoint inhibitors and nanoparticles can assist in eradicating immune resistance hence effectively respond to *H. pylori* infected cells.[68,69]

Table 1 Summary of epidemiological studies linking *H. pylori* infection to gastric cancer

Study	Year	Population	Relative risk (RR)	Conclusion	References
Exploring the interactions between *Helicobacter pylori* (Hp) infection and other risk factors of gastric cancer. A pooled analysis in the stomach cancer pooling (StoP) project	2021	Global	2.5	*H. pylori* infection significantly increases gastric cancer risk	59
Helicobacter pylori and its role in gastric cancer	2023	Global	3.8	*H. pylori*-positive patients had a higher incidence of gastric cancer than *H. pylori*-negative patients	60

1.7 Improving adherence to nanoparticle therapies

• Convenient drug delivery: create nanoparticle formulations that can be administered by increasing the patient's compliance with the prescribed schedules.[70]

• Patient education: ensure that patient education is given to the patients on the need to adhere to their treatment schedule and how to use the new nanoparticle-based drugs.[71]

• Taste and comfort: design the oral nanoparticle drugs to be easily swallowed and with little discomfort in a bid to enhance patient's adherence to the medication.[72]

• Support systems: use the follow-up and reminder systems that can assist the patients to adhere to their prescribed treatments.[73]

1.7.1 Comparative studies

1.7.1.1 Effectiveness. In general, the nanoparticle-based treatments have been found to be effective in increasing the therapeutic efficiency of *H. pylori* against the conventional antibiotics and the new treatment modalities that include the probiotics and the bismuth containing preparations.[74] Research studies shown that nanoparticles enhance the solubility and stability of the antibiotics, decrease the frequency of administration, and decrease the propensity for the development of antibiotic resistance, thus, suggesting that they may be more effective than conventional methods.[75]

1.7.1.2 Safety. It is necessary to contrast nanoparticle treatments with standard therapies and their side effects and adverse reactions. This will also minimize the effects of the drugs on the rest of the body, hence reducing on systemic toxicity.[76] Comparing the results with other types of particles is required to find out whether there are any specific threats of nanoparticles, including long-term toxicity or other improper behaviors in biological environments.[77]

1.7.1.3 Practicality. The reality of using nanoparticles in practice is therefore measured by how affordable it is to use nanoparticles, how easy it is to access nanoparticles and how easy it is to apply nanoparticles.[78] Attributes like processes of making them, the storage conditions and the methods of administration are also gain much importance. Furthermore, the evidence evaluating patient's compliance with treatment regimens, which depends on dosing frequency and intolerance, is essential for practical application.[79]

1.8 Long-term follow-up data

1.8.1 Durability of effects. Further research of longer-term nature will help to determine the effectiveness and safety of the application of nanoparticle-based treatments.[80] This entails the evaluation of the sustainment of therapeutic benefits in the long run in order to ascertain whether the initial positive outcomes of treatment are sustained. Maintenance studies assist in finding out whether nanoparticles offer long-term protection against *H. pylori* infection and reoccurrence.[81]

1.8.2 Late-onset side effects. Monitoring the patients for signs of possible side effects that may occur due to the long-term use of nanoparticle treatments is crucial for the determination of safety in the long run.[82] The long-term monitoring of the patients and follow-up can help to identify these complications which may be rare but severe and thus prove that these therapies are safe.[83]

1.8.3 Cancer prevention. To establish whether nanoparticle treatments not only kill the *H. pylori* but also prevent the occurrence of gastric cancer, longitudinal studies are needed. They enable assessment on whether therapies based on nanoparticles can halt transition of chronic *H. pylori* infection to gastric malignancies.[84,85]

Table 2 Nanoparticle types and their mechanisms of action against *H. pylori*

Nanoparticle type	Composition	Mechanism of action	Key studies	References
Lipid-based	Liposomes, SLNs	Encapsulation of antibiotics, targeted delivery	Liposomal clarithromycin, PLGA-amoxicillin	61
Polymeric	PLGA, chitosan	Controlled drug release, sustained antimicrobial activity	PLGA nanoparticles, chitosan nanoparticles	62
Metallic	Silver, gold, zinc oxide	ROS generation, membrane disruption	Silver nanoparticles, gold nanoparticles	63

1.9 Economic analysis

1.9.1 Cost comparison. In order to compare the costs of nanoparticle-based therapies with conventional therapies one has to take into consideration direct costs such as medication and administration along with indirect costs such as decrease in number of complications. The economic approach can help to identify the costs in the case of using nanoparticle therapies compared to traditional ones.[86]

1.9.2 Value for money. Identifying the costs of nanoparticle therapies and deciding whether the potential advantages outweigh the costs is the key. This entails assessing the kind of results patients get, the side effects, and the level of adherence to the nanoparticles treatment to understand if the high costs of nanoparticles are offset by improved health and reduced costs of care.[87]

1.9.3 Accessibility. An understanding of the economic rationality of employing nanoparticle therapies in various populations, especially in developing countries, is required. Issues like cost, accessibility, and readiness for increased usage should also be taken into account to make sure those sophisticated treatments reach all the population.[88]

1.10 Personalized medicine implications

1.10.1 Genetic profiling. The need to set aside genetic and molecular markers that will help in the identification of patients most responsive to nanoparticle treatments cannot be overemphasized. The use of genetic profiles in therapy means that the therapy is adjusted to the patient's genetic makeup, which can enhance the worth of treatment therapy.[89]

1.10.2 Customized formulations. Besides, creating individual NPs for treating *H. pylori* according to the infected person's characteristics and genetic markers can increase the accuracy of the treatment. Concentrated solutions act on the infection more sensitively and the risk of side effects is minimized.[90]

1.10.3 Improved outcomes. The personalization can result in better treatments with fewer side effects and thus can enhance the general status of patients. Thus, using nanoparticles to meet the specific requirements of each patient can maximize the therapeutic efficacy and improving the patient's quality of life.[91]

1.11 Regulatory and ethical considerations

1.11.1 Regulatory approval. The procedure of getting approval for the use of nanoparticles for therapeutic purposes requires that were proven safe for use, effective and of good quality in a process that involves several trials.[92] The regulation of nanotechnology is a vital aspect that should be well understood for effective use of nanoparticle-based therapies.[93]

1.11.2 Ethical use. Some of the ethical concerns range from the fairness issue of these treatments from the rest to the danger involved in administering the treatment to the patients. Ethical decisions should revolve around inequitable distribution of the innovative treatments and equal treatment of all patients.[94]

1.11.3 Transparency. It is important that the processes of the development and use of nanoparticle therapies are made transparent. Giving enough information to the patients and the healthcare practitioners on the gains, losses, and unknowns effects of these treatments allows for proper decision making.[95]

1.12 Global health implications

1.12.1 Accessibility in low-income countries. There is a need to find ways on how nanoparticle-based treatments can be introduced in Low and Middle Income Countries (LMICs) where *H. pylori* prevalence is high. Overcoming the economic, logistic and infrastructural disadvantages guarantees these advanced therapies to be made available to the needy.[96]

1.12.2 Healthcare infrastructure. It is important to evaluate the preparedness of healthcare facilities to deliver nanoparticle treatments and educating the healthcare providers in different parts. The above analysis shows that a good infrastructure are important for the implementation of new therapeutics.[97]

1.12.3 Global collaboration. International cooperation in research and development to solve the problem of *H. pylori* and gastric cancer is vital. Multifaceted and multicultural interventions can be beneficial in the treatment of these disorders (Table 3) and increase cooperation and exchange of information.[101]

2. Methodology

2.1 Literature search

A comprehensive literature search was conducted using PubMed, Google Scholar, and other relevant databases to gather data on the relationship between *H. pylori* and gastric cancer, and recent advancements in nanoparticle-based therapeutic interventions. Keywords used included "*H. pylori*", "gastric cancer", "nanoparticles", "nanomedicine", and "therapeutic interventions". The search focused on articles published between 2010 and 2024.[102]

2.2 Inclusion and exclusion criteria

- Inclusion criteria: scientific papers including published articles, clinical trials, review papers and meta-analysis regarding the correlation between *H. pylori* and gastric cancer, nanoparticle-based treatment for *H. pylori*.[103]
- Exclusion criteria: review articles, editorials and letters, articles unrelated to *H. pylori* or gastric cancer, articles not available in English, and articles before 2010.[104]

2.3 Data extraction

Relevant data were extracted from the selected studies, including:

- *H. pylori* infection and gastric cancer risk, an epidemiological study.
- The biological relationship between *H. pylori* and the development of gastric carcinoma.
- Current therapeutic strategies and their problems.

Table 3 Summary of comparative studies and key findings

Study year	Intervention	Comparison	Outcome	Reference
2024	Nanoparticle-based therapy	Traditional antibiotics	Higher efficacy, lower resistance rates	98
2024	Silver nanoparticles with probiotics	Probiotics alone	Synergistic effect, enhanced antibacterial activity	98
2023	PLGA-amoxicillin nanoparticles	Amoxicillin	Sustained antimicrobial activity	1
2023	Nanoparticle-based vaccine	Traditional vaccine	Longer-lasting immunity, fewer doses needed	99
2022	Gold nanoparticles with antibiotics	Silver nanoparticles	Higher bioactivity, reduced colonization	61
2022	Zinc oxide nanoparticles	Conventional therapy	Effective against resistant strains	48
2022	Nanoparticle immunotherapy combination	Conventional treatment	Improved immune response, reduced side effects	48
2021	Liposomal clarithromycin	Standard clarithromycin	Enhanced antibacterial activity	59
2021	Polymeric nanoparticles with cytokines	Antibiotics alone	Enhanced immune response, better outcomes	63
2020	Chitosan nanoparticles	Standard antibiotic therapy	Improved drug delivery, lower toxicity	100

- Types of nanoparticles and their application in the management of *H. pylori* infection as well as the working mechanisms.
- Forced outputs from preclinical and clinical trials on nanoparticle-based theranostics.

2.4 Analysis

The data extracted were analyzed to give a brief on the existing knowledge of *H. pylori* in gastric carcinogenesis and the possibility of using nanoparticles for treatment.[105]

3. Results

The present review study has also shown that *H. pylori* infection increases the risk of developing gastric cancer particularly non-cardia gastric adenocarcinoma. From the epidemiological perspective, it was demonstrated that patients with *H. pylori* infection have 2–3-fold increased risk of gastric cancer compared to the population without this infection. The role of *H. pylori* in gastric carcinogenesis is well established and it occurs by altering the molecular pathways related to chronic inflammation, DNA damage and epigenetic modifications. The pathogen factors including CagA and VacA weaken the gastric epithelial cells, which triggers oncogenic pathways. Inflammation due to *H. pylori* leads to the secretion of pro-inflammatory cytokines and ROS causing DNA damage, genetic instability and thus tumorigenicity. In addition to that, *H. pylori* also results in changes in methylation pattern and histone modification through which tumor suppressor genes are deactivated and oncogenes overexpressed. Standard medications used to treat *H. pylori* using antibiotics have been made ineffective by increasing resistance to antibiotics. Such difficulties have led to the emergence of new approaches to the problem, one of which is nanoparticle-based treatments. The use of nanoparticles has multiple advantages like high selectivity for the drug delivery, enhanced bioavailability and minimal systemic side effects. Lipid based nanoparticles, polymeric and metallic nanoparticles have been found to be effective in preclinical studies. These nanoparticles can improve the antibiotics uptake, redesign immune reactions and demonstrate the bactericidal effect on *H. pylori*. However, these therapies are still in the experimental stage and in clinical trial, therefore, their safety and effectiveness for use in humans has not been ascertained. Nanoparticle based therapies have the potential in the enhancement of the treatment of gastric malignancies associated with *H. pylori*.

4. Discussion

The *H. pylori* infection is positively associated with the risk of gastric cancer. Subsequent meta-analyses and large cohorts have further affirmed the causal association between *H. pylori* and GC and in particular, the risk of developing non-cardia gastric adenocarcinoma.[106] This explains why management of *H. pylori* infection is important in order to reduce the occurrences of gastric cancer. Evaluation of the roles of *H. pylori* and other factors showed that chronic inflammation being caused by *H. pylori* is a major step in the development of gastric cancer.[107] CagA and VacA of the bacterium impair the epithelial cell function, cause DNA damage, and bring about epigenetic modifications. The following processes play a role in the initiation of gastric cancer as well as the development of the disease. Knowledge of these molecular processes forms a framework of how to reduce oncogenic properties of *H. pylori* through specific therapeutic interventions.[108] Current *H. pylori* antibiotics have many limitations because of the increased resistance to antibiotics in the world. This has diminished the efficacy of the traditional treatments and made people seek for the other method of treating the diseases.[109]

A study described that ano-amoxicillin, nano-azithromycin, and nano-metronidazole were the three nano-antibiotics with the corresponding optical density (OD) values of 0.386, 0.258, and 0.167. Each of the nano-antibiotics showed a higher percentage of inhibition than the micro-antibiotics. They were also discovered to be all non-oxidants and to be safe to employ as effective antioxidants in medical treatments. The novel antibiotic effectiveness was proportionate to its concentration, and all of the antibiotics in the nanomedicine had antibacterial properties.[110] To eradicate *H. pylori*, antimicrobial medications, specifically antibiotics, had to be encapsulated in most cases. These nanoparticles (NP) were superior to non-targeted drugs because they prevented the bacteria from adhering to gastric

cells and made it possible to administer medications inside the bacterium.[111] Nanoparticles are an efficient targeted drug delivery technique for treating *H. pylori*, according to the cellular uptake mechanism. They can also be employed as potential nano-carriers for the oral delivery of other therapeutic medications that target *H. pylori*.[112] New strategies include the use of probiotics and bismuth containing regimens that however need further confirmation and fine tuning. Therefore, nanoparticles can be considered as a new and effective strategy of *H. pylori* eradication. This increases therapeutic effectiveness and decreases the general toxicity of the antimicrobial agents employed in the treatment of bacterial infections. In the preclinical studies, different types of nanoparticles such as polymeric based and metallic based nanoparticles have shown promising results. The administrations of these nanoparticles can deliver antibiotics and have direct antibacterial actions including production of ROS or disrupting bacterial membrane.[113] *In vitro* and *in vivo* database have revealed that nanoparticle mediated formulations of the existing antibiotics can improve the efficacy of drugs, decrease gastric irritation and even delay the carcinogenic transformation in the stomach. These nanoparticle-based therapies are only in the phase I trials for determining the safety, effectiveness, and metabolism in the human body. The outcomes of these trials will define the clinical potential of nanomedicine for the *H. pylori* related diseases.[114] However, there are specific obstacles that need to be overcome in the case of nanoparticle-based therapies. These are the concerns that touch on scalability, regulatory approval, and stability over the extended period. However, more studies are required to fine-tune the nanoparticle formulations and to understand their biological behavior and response in various patients' groups. Future development in nanotechnology along with the enhanced understanding of the pathogenesis of *H. pylori* will provide the key to overcome these issues and to bring these advancements to clinics.[115]

5. Conclusion

H. pylori is one of the leading causes of gastric cancer in the global population, thus there is need to develop efficient therapeutic interventions to address this health burden. Nanoparticles have been considered as a therapeutic option against *H. pylori* infection and its carcinogenic consequences. These new approaches use the specific characteristics of nanoparticles and promote drug delivery more effectively, as well as have lesser side effects. Further scientific work and clinical studies will be required to implement these findings for clinical uses, this could transform the approach to managing *H. pylori* related gastric malignancies. The proposed approach has the potential to contribute to enhancement of outcomes in patients with gastric cancer and in general decrease the global morbidity rate of this disease.

6. Future prospectives

Nanoparticles are a promising path for future research and application in the battle against *H. pylori* because of their ability to address global health issues including antibiotic resistance and their integration with personalized medicine approaches. Ultimately, nanoparticle-based treatment for *H. pylori* infections and gastric cancer offer encouraging benefits like increased effectiveness, and decreased resistance, there are still important issues that must be resolved. Clinical trials, economic evaluations, and regulatory frameworks must be given top priority in future research in order to get nanoparticle-based medicines from the lab to the clinic.

Ethical statement

Our study requires no ethical approval as it was a review based study and all data collected from ethically approved sources of publicly available free databases and articles of PubMed, springer, BMC, nature.

Consent to participate

All authors are equally participated in writing, data collection and preparation of this article.

Consent to publish

All authors gave their consent to publish this article.

Data availability

No data generated during this review article study.

Author contributions

Conceptualization, writing original draft; Syed Ali Raza Shah, Maria Mumtaz; resources; Syed Ali Raza Shah, Sumaira Sharif; data curation, review and editing, Syed Ali Raza Shah, Iffat Nayila, and Sumaira Sharif; supervision; Syed Ali Raza Shah, Sumaira Sharif and Imtiaz Mustafa. All authors have read and agreed to the published version of the manuscript.

Conflicts of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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