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FORMULATION, DEVELOPMENT AND IN VITRO EVALUATION OF LAFUTIDINE AND ALOIN-LOADED NANOPARTICLES FOR ENHANCING GASTROPROTECTIVE THERAPY
OR
RECENT ADVANCES IN LAFUTIDINE AND ALOIN-LOADED NANOPARTICLES FOR GASTROPROTECTIVE DRUG DELIVERY: A REVIEW

ABSTRACT

Peptic ulcer sickness and different gastric issues stay fundamental fitness worries global because of growing occurrence related to stress, Helicobacter pylori infection, immoderate alcohol intake, smoking, and extended use of non-steroidal anti inflammatory drugs (NSAIDs). Conventional antiulcer cures frequently be afflicted by barriers inclusive of quick gastric house time, terrible bioavailability , common dosing, and systemic facet results. Nanotechnology-primarily based totally drug shipping structures have emerged as promising techniques for enhancing the healing efficacy of gastroprotective sellers via superior balance, sustained launch, stepped forward mucosal adhesion, and centered drug shipping. Lafutidine, a second-technology histamine H2 receptor antagonist, reveals amazing acid-suppressive and mucosal shielding properties, while Aloin, a herbal anthraquinone glycoside acquired from Aloe species, possesses antioxidant, anti inflammatory, cytoprotective, and wound restoration activities. The mixture of those sellers in nanoparticle structures may also offer synergistic gastroprotective results through concurrently decreasing gastric acid secretion and improving mucosal defence mechanisms. This evaluate discusses the formula strategies, coaching methods, characterization parameters, and in vitro assessment of Lafutidine and Aloin-loaded nanoparticles. Different nanoparticle structures which include polymeric, lipid-primarily based totally, and mucoadhesive nanoparticles are reviewed with emphasis on their packages in gastroprotective therapy. The evaluate additionally highlights the significance of physicochemical characterization, drug launch studies, balance assessment, and destiny views of nanoparticle-primarily based totally gastroprotective formulations. Overall, Lafutidine and Aloin-loaded nanoparticles constitute a promising method for enhancing ulcer restoration and improving the effectiveness of gastroprotective therapy.

Keywords: Lafutidine, Aloin, nanoparticles, gastroprotective therapy, gastric ulcer, nanotechnology, managed launch, mucoadhesive drug shipping

1. INTRODUCTION

Peptic ulcer disease (PUD) is characterised via way of means of discontinuation withinside the internal lining of the gastrointestinal (GI) tract due to gastric acid secretion or pepsin. It extends into the muscularis propria layer of the gastric epithelium. It normally happens withinside the belly and proximal duodenum. It can also additionally contain the decrease esophagus, distal duodenum, or jejunum. Epigastric ache normally happens inside 15-half-hour following a meal in sufferers with a gastric ulcer; on the alternative hand, the ache with a duodenal ulcer has a tendency to arise 2-three hours after a meal. Today, trying out for Helicobacter pylori is suggested in all sufferers with peptic ulcer disease. Endoscopy can be required in a few sufferers to affirm the diagnosis, mainly in the ones sufferers with sinister symptoms. Today,

maximum sufferers may be controlled with a proton pump inhibitor (PPI) primarily based totally triple-drug therapy **(Jaiswal *et al.*, 2021).**

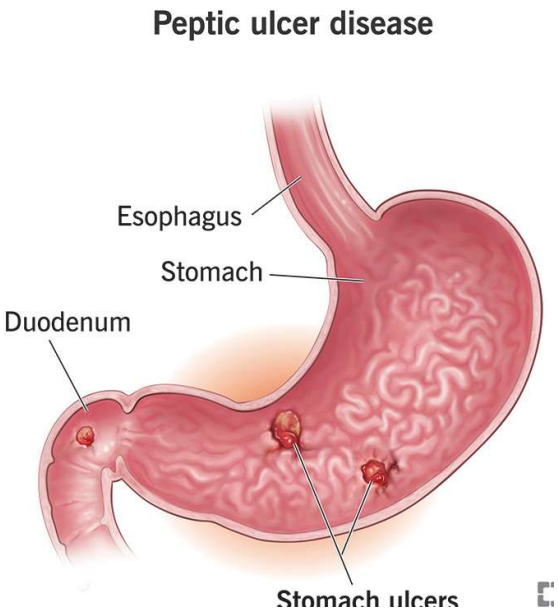

Figure 1: Peptic ulcer disease

2. Etiology and Risk Factors

Several etiological factors contribute to the development of peptic ulcers. The most common causes include Helicobacter pylori infection and prolonged use of non-steroidal anti-inflammatory drugs (NSAIDs). Other contributing factors include stress, alcohol consumption, smoking, spicy food intake, genetic predisposition, and certain chronic illnesses **(Vakil, 2024).**

2.1 *Helicobacter pylori* Infection

Helicobacter pylori is a gram-negative spiral bacterium that colonizes the gastric mucosa and plays a major role in the pathogenesis of peptic ulcer disease. The bacterium damages the mucosal lining by producing urease, cytotoxins, and inflammatory mediators. These substances weaken mucosal defenses, increase acid secretion, and promote inflammation, ultimately leading to ulcer formation. H. pylori infection is highly prevalent worldwide, especially in developing countries where poor sanitation and overcrowded living conditions facilitate transmission. Persistent infection can also lead to chronic gastritis, mucosal atrophy, and gastric carcinoma **(Reshetnyak and Reshetnyak 2017).**

2.2 Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

NSAIDs such as aspirin, ibuprofen, diclofenac, and naproxen are widely used for pain relief and inflammation management. However, long-term or excessive use of these drugs significantly increases the risk of gastric ulceration. NSAIDs inhibit cyclooxygenase (COX) enzymes responsible for prostaglandin synthesis. Prostaglandins play a vital role in maintaining gastric mucosal protection by stimulating mucus and bicarbonate secretion, maintaining blood flow, and promoting epithelial repair. Reduction of prostaglandin levels weakens the mucosal barrier and makes the stomach more susceptible to acid-induced injury **(Fokunang *et al.*, 2018).**

3. Pathophysiology

3.1 Aggressive Factors

Aggressive factors play a major role in the development of peptic ulcer disease by damaging the gastric mucosa and disrupting the balance between mucosal protection and acid secretion. These factors include gastric acid (hydrochloric acid), pepsin, Helicobacter pylori infection, non-steroidal anti-inflammatory drugs (NSAIDs), reactive oxygen species (ROS), bile salts, and ethanol. Under normal physiological conditions, gastric acid and pepsin are essential for digestion and help in the breakdown of food proteins. However, excessive secretion of hydrochloric acid or increased pepsin activity can erode the gastric mucosal lining, especially when the protective mucus barrier is weakened. Continuous exposure of the mucosa to these acidic secretions may result in inflammation, erosion, and ulcer formation **(Jaiswal *et al.*, 2021).**

Helicobacter pylori is any other vital competitive component related to peptic ulcer disease. This bacterium colonizes the gastric mucosa and produces enzymes and pollution that harm epithelial cells, growth inflammation, and stimulate gastric acid secretion. Long-time period contamination weakens mucosal protection mechanisms and considerably will increase the danger of gastric and duodenal ulcers. Similarly, extended use of NSAIDs together with aspirin and ibuprofen inhibits prostagland in synthesis via way of means of blocking off cyclooxygenase enzymes. Since prostaglandins are vital for retaining mucus secretion, bicarbonate production, and mucosal blood flow, their inhibition makes the belly lining greater liable to acid-**(Sobhani, and Cortes 2023).**

Reactive oxygen species generated during inflammation and cellular stress also contribute to gastric mucosal damage. These free radicals induce oxidative stress and damage cellular proteins, lipids, and DNA, thereby worsening inflammation and delaying ulcer healing. In addition, bile salts and ethanol can directly irritate the gastric epithelium and disrupt the mucosal barrier. Ethanol particularly causes dehydration and necrosis of gastric mucosal cells, leading to increased permeability and ulcer formation. Collectively, these aggressive factors compromise the integrity of the gastric mucosa and play a crucial role in the pathogenesis of peptic ulcer disease **(Patlevič *et al.*, 2016).**

3.2 Defensive Mechanisms

The gastric mucosa possesses several important defensive mechanisms that protect the stomach lining from acid-induced injury and maintain the integrity of the gastrointestinal tract. These protective factors include the mucus-bicarbonate barrier, prostaglandin secretion, adequate mucosal blood flow, tight epithelial junctions, cellular regeneration, and antioxidant enzymes. Under normal physiological conditions, these mechanisms work together to counteract the harmful effects of gastric acid, pepsin, and other aggressive factors, thereby preventing mucosal damage and ulcer formation **(de Lima et al., 2022).**

The mucus-bicarbonate barrier serves as the first line of defense for the gastric mucosa. The mucus layer forms a thick protective coating over the epithelial surface and prevents direct contact between gastric acid and mucosal cells. Bicarbonate ions secreted into the mucus neutralize hydrogen ions near the mucosal surface and help maintain a near-neutral pH environment, thereby protecting epithelial tissues from acid injury. Prostaglandins also play a crucial role in mucosal defense by stimulating mucus and bicarbonate secretion, maintaining adequate mucosal blood flow, and promoting repair of damaged tissues. Adequate blood circulation supplies oxygen and nutrients to gastric tissues and removes toxic metabolites,

which is essential for maintaining mucosal integrity and facilitating healing processes **(Galura *et al.*, 2019).**

Tight epithelial junctions between gastric mucosal cells act as a barrier that prevents back diffusion of hydrogen ions and other harmful substances into deeper tissues. In addition, rapid cellular regeneration and replacement of damaged epithelial cells help maintain the continuity of the mucosal lining. Antioxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase further protect the gastric mucosa by scavenging reactive oxygen species and reducing oxidative stress. Any impairment or disruption of these protective mechanisms weakens the mucosal defense system and increases susceptibility to inflammation, erosion, and peptic ulcer formation **(Liu *et al.*, 2025).**

4. Differential diagnosis

The following conditions can present with symptoms similar to peptic ulcer disease and it is important to be familiar with their clinical presentation in order to make the correct diagnosis.

- Gastritis - an inflammatory process of the gastric mucosa from immune-mediated or infectious etiology presenting with upper abdominal pain and nausea. Clinical presentation is very similar to that of peptic ulcer disease **(Choi *et al.*, 2024).**
- Gastroesophageal reflux disease (GERD) - patients usually describe a burning sensation in the epigastrium and lower retrosternal area, excessive salivation, or intermittent regurgitation of food material.
- Gastric cancer - apart from abdominal pain, patients usually describe alarm symptoms like weight loss, melena, recurrent vomiting, or evidence of malignancy elsewhere in case of metastasis.
- Pancreatitis - epigastric or right upper quadrant pain that is more persistent and severe, worse in the supine position, and patients usually have a history of alcoholism or gallstones. Elevated serum amylase and lipase are useful in the diagnosis **(Avegno and Carlisle, 2016).**
- Biliary colic - intermittent, severe deep pain in the right upper quadrant or epigastrium precipitated by fatty meals.
- Cholecystitis - right upper quadrant or epigastric pain that usually lasts for hours, is exacerbated by fatty meals, and is associated with nausea and vomiting. Fever, tachycardia, positive Murphy sign, leukocytosis, and abnormal liver functions help further distinguish this from biliary colic **(Grigorian *et al.*, 2026).**

5. Conventional Gastroprotective Therapy

The primary objectives of gastroprotective therapy are:

5.1 Proton Pump Inhibitors (PPIs)

Proton pump inhibitors such as omeprazole, pantoprazole, rabeprazole, and lansoprazole are widely prescribed for peptic ulcer disease. These drugs inhibit the H+/K+ ATPase enzyme located in gastric parietal cells and effectively suppress acid secretion **(Müller, 2024).**

Although highly effective, prolonged use of PPIs may produce adverse effects such as:

- Nutrient malabsorption
- Osteoporosis
- Kidney disorders
- Increased infection risk

- Rebound acid hypersecretion

5.2 H2 Receptor Antagonists

H2 receptor antagonists such as ranitidine, famotidine, and Lafutidine reduce gastric acid secretion by blocking histamine H2 receptors on parietal cells. Lafutidine is considered a second-generation H2 blocker with additional gastroprotective effects including stimulation of mucus secretion and enhancement of mucosal defense **(Sano *et al.*, 2017).**

5.3 Antacids

Antacids neutralize gastric acid and provide symptomatic relief from acidity and heartburn. Common antacids include magnesium hydroxide, aluminum hydroxide, and calcium carbonate. However, their short duration of action and frequent dosing limit long-term effectiveness **(Shetty and Vishwanath, 2022).**

5.4 Cytoprotective Agents

Drugs such as sucralfate and misoprostol enhance mucosal protection and promote ulcer healing. Misoprostol is particularly effective in preventing NSAID-induced ulcers but may cause abdominal cramps and diarrhea **(Kak, 2025).**

5.5 Antibiotic Therapy

Combination antibiotic therapy is used to eradicate H. pylori infection. Common regimens include clarithromycin, amoxicillin, and metronidazole combined with proton pump inhibitors. Antibiotic resistance and incomplete eradication remain significant challenges **(Rocha *et al.*, 2025).**

6. Nanotechnology in Drug Delivery

Nanoparticles are submicron colloidal structures usually ranging in length from 1 to a thousand nm and may be organized the use of a number of biodegradable and biocompatible substances along with polymers, lipids, proteins, surfactants, and herbal biomaterials. Depending at the technique of instruction and composition, nanoparticles might also additionally exist in distinct bureaucracy together with polymeric nanoparticles, strong lipid nanoparticles, nanocapsules, nanospheres, liposomes, dendrimers, and nanoemulsions. These structures are especially designed to encapsulate, adsorb, or dissolve healing retailers and supply them to the favored webweb page in a managed and centered manner. One of the predominant blessings of nanoparticle-primarily based totally drug shipping structures is their cappotential to enhance the solubility of poorly water-soluble tablets. Many traditional tablets showcase low aqueous solubility, ensuing in negative dissolution and decreased bioavailability after oral administration. Nanoparticles own a completely huge floor vicinity to quantity ratio, which substantially complements drug dissolution and absorption. In addition, nanoparticles can defend touchy tablets from chemical degradation, enzymatic metabolism, and vicious gastrointestinal conditions, thereby enhancing drug balance and healing performance (Bhatia, 2016).

Nanoparticle structures additionally offer managed and sustained drug launch, which enables keep healing drug concentrations for extended periods. Controlled launch minimizes fluctuations in plasma drug levels, reduces dosing frequency, and improves affected person compliance. Furthermore, sustained drug shipping reduces the chance of dose-associated toxicity and unfavourable consequences usually related to traditional dosage bureaucracy. Another crucial characteristic of nanotechnology-primarily based totally drug shipping is webweb page-precise concentrated on. Nanoparticles may be engineered to selectively gather

on the goal webweb page via passive or energetic concentrated on mechanisms. Passive concentrated on is performed via better permeability and retention consequences, while energetic concentrated on includes the usage of ligands, antibodies, or receptors at the nanoparticle floor for selective shipping to diseased tissues. Such centered shipping improves healing efficacy even as minimizing systemic publicity and facet consequences
(Bai *et al.,* 2022).

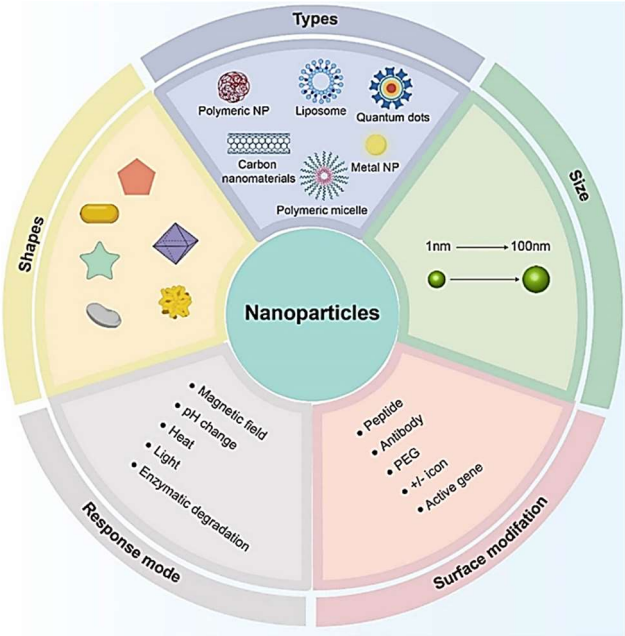

Figure 2: Nanoparticles

In gastroprotective therapy, nanotechnology offers several unique advantages for the treatment of gastric ulcers and other gastrointestinal disorders. Oral drug delivery often faces challenges such as rapid gastric emptying, degradation of drugs in acidic conditions, poor mucosal penetration, and low bioavailability. Nanoparticles help overcome these limitations by improving gastric retention time, enhancing mucosal adhesion, and delivering drugs directly to ulcerated tissues. Mucoadhesive nanoparticles can adhere strongly to the gastric mucosa, thereby prolonging contact time and increasing local drug concentration at the site of injury. This localized and sustained release of therapeutic agents accelerates ulcer healing and enhances gastroprotective effects **(Watchorn et al., 2022).**

Overall, nanotechnology-based drug delivery systems represent a significant advancement in modern pharmaceutical research. Their ability to improve drug solubility, stability, targeted delivery, and sustained release makes them highly suitable for gastroprotective therapy and various other biomedical applications. The development of biodegradable and biocompatible nanoparticles loaded with therapeutic agents offers enormous potential for enhancing treatment outcomes in gastrointestinal disorders and improving patient quality of life **(Li et al., 2023).**

Lafutidine

Lafutidine is a second-generation histamine H2 receptor antagonist widely used in the treatment and management of acid-related gastrointestinal disorders such as gastric ulcers, duodenal ulcers, gastritis, gastroesophageal reflux disease (GERD), and dyspepsia. It is considered an advanced antiulcer agent because, in addition to suppressing gastric acid secretion, it possesses strong gastroprotective and mucosal defensive properties. Compared

with conventional H2 receptor antagonists such as ranitidine, cimetidine, and famotidine, Lafutidine exhibits enhanced cytoprotective activity and improved ulcer healing capability **(Kou et al., 2024).**

Chemically, Lafutidine belongs to the class of substituted guanidine derivatives and selectively inhibits histamine H2 receptors present on gastric parietal cells. Histamine is one of the major stimulators of gastric acid secretion, and its interaction with H2 receptors activates adenylate cyclase and cyclic AMP pathways, leading to increased hydrochloric acid production. By blocking these receptors, Lafutidine effectively suppresses basal as well as stimulated gastric acid secretion and reduces gastric acidity. A unique characteristic of Lafutidine is its dual mechanism of action involving both antisecretory and mucosal protective effects. Unlike many conventional H2 blockers that mainly reduce acid secretion, Lafutidine also enhances mucosal defence mechanisms. It stimulates capsaicin-sensitive sensory neurons in the gastric mucosa, resulting in increased release of calcitonin gene-related peptide (CGRP), which improves gastric mucosal blood flow and promotes mucus secretion. Enhanced mucus production forms a protective barrier over the gastric epithelium and helps prevent acid-induced mucosal injury **(Arin et al., 2017).**

Clinically, Lafutidine is effective in treating both acute and chronic gastric lesions and is particularly useful in managing NSAID-induced gastric injury and stress-related mucosal damage. It demonstrates rapid onset of action and prolonged antisecretory activity, making it beneficial for patients suffering from acid peptic disorders. Furthermore, Lafutidine has shown good tolerability and a comparatively lower incidence of adverse effects during therapy **(Pai *et al.*, 2025).**

7.1 Mechanism of Action of Lafutidine

Lafutidine exerts its antiulcer and gastroprotective effects through multiple pharmacological mechanisms that collectively contribute to acid suppression, mucosal protection, ulcer healing, and prevention of gastric injury. This multifunctional mode of action distinguishes Lafutidine from conventional H2 receptor antagonists and makes it a highly effective gastroprotective agent. The primary mechanism of Lafutidine involves selective inhibition of histamine H2 receptors located on gastric parietal cells. Histamine normally binds to these receptors and stimulates secretion of hydrochloric acid through activation of adenylate cyclase and cyclic AMP-mediated signaling pathways. Lafutidine competitively blocks histamine binding and suppresses gastric acid secretion, thereby reducing gastric acidity and minimizing acid-induced mucosal damage **(Zhu et al., 2023).**

In addition to its antisecretory action, Lafutidine significantly enhances gastric mucus production. The mucus layer serves as an important protective barrier that shields epithelial cells from corrosive gastric acid and digestive enzymes. Increased mucus secretion improves mucosal defense and accelerates healing of ulcerated tissues. Lafutidine also stimulates bicarbonate secretion, which helps neutralize acid near the mucosal surface and maintains a favorable pH environment for tissue repair. Lafutidine also exhibits antioxidant activity by reducing oxidative stress within gastric tissues. Reactive oxygen species generated during inflammation can damage cellular proteins, lipids, and DNA, worsening mucosal injury. Lafutidine helps neutralize these free radicals and protects gastric epithelial cells from oxidative damage. This antioxidant effect contributes significantly to its cytoprotective and antiulcer properties **:**

Furthermore, Lafutidine possesses anti-inflammatory activity that helps suppress inflammatory responses associated with gastric ulceration. It reduces infiltration of inflammatory cells and decreases the production of inflammatory mediators responsible for mucosal injury. By controlling inflammation and oxidative stress simultaneously, Lafutidine promotes faster healing of gastric lesions and reduces the risk of recurrent ulceration. The combined effects of acid suppression, mucus enhancement, improved blood flow, antioxidant protection, and anti-inflammatory activity make Lafutidine highly effective in preventing and treating gastric ulcers. Its multifactorial mechanism of action provides comprehensive protection to the gastric mucosa and contributes to superior gastroprotective efficacy compared with conventional H2 receptor antagonists **(Zhang *et al.*, 2022).**

7. Introduction to Aloin

Aloin is a obviously happening anthraquinone glycoside predominantly acquired from Aloe species inclusive of Aloe vera, Aloe ferox, and Aloe barbadensis. It is one of the primary bioactive parts gift withinside the latex or exudate of Aloe leaves and is mostly liable for the various healing and medicinal residences related to Aloe plants. Chemically, Aloin exists as a yellow-brown crystalline compound and is commonly labeled into stereoisomeric bureaucracy, specifically aloin A (barbaloin) and aloin B (isobarbaloin). Among those, barbaloin is the maximum substantially studied for its pharmacological sports. Recent clinical investigations have established that Aloin possesses sizeable pharmacological ability withinside the control of gastric ulcers and gastrointestinal inflammation. It reveals robust antioxidant, anti inflammatory, cytoprotective, antimicrobial, and wound recuperation residences, all of which make a contribution to its gastroprotective activity. Gastric ulcer formation is regularly related to oxidative pressure, inflammation, immoderate acid secretion, and mucosal damage. Aloin facilitates counteract those pathological techniques through strengthening mucosal protection mechanisms and lowering oxidative harm inside gastric tissues (Otieno, 2022).

One of the maximum critical healing residences of Aloin is its antioxidant activity. Oxidative pressure resulting from reactive oxygen species performs a vital position in gastric mucosal harm and ulcer progression. Aloin facilitates neutralize unfastened radicals and forestalls lipid peroxidation, thereby defensive gastric epithelial cells from oxidative damage. Additionally, Aloin reveals anti inflammatory results through suppressing inflammatory mediators and lowering infiltration of inflammatory cells on the web website online of tissue harm. Aloin has additionally been said to stimulate epithelial regeneration and boost up wound recuperation techniques. It promotes tissue restore through improving collagen synthesis, enhancing blood circulation, and helping cell regeneration inside broken gastric mucosa. These results together make a contribution to quicker recuperation of ulcerated tissues and healing of regular gastric function (Luo et al., 2018).

Because of its a couple of healing moves and herbal origin, Aloin has emerged as a promising phytoconstituent for gastroprotective therapy. However, its medical software via traditional dosage bureaucracy stays restricted due to bad balance and coffee bioavailability. Therefore, incorporation of Aloin into superior nanoparticle-primarily based totally drug transport structures has attracted sizeable studies hobby for enhancing its healing effectiveness and centered transport in gastrointestinal issues (Bawankar and Zawar, 2025).

8.1 Pharmacological Activities of Aloin

Aloin reveals a extensive variety of pharmacological sports that make a contribution substantially to its healing ability withinside the remedy of gastrointestinal issues and gastric ulcers. These sports encompass antioxidant, anti inflammatory, cytoprotective, wound recuperation, unfastened radical scavenging, antimicrobial, and gastroprotective results. The multifaceted organic moves of Aloin make it a treasured herbal compound for superior gastroprotective formulations

8.1 Pharmacological Activities of Aloin

Aloin exhibits a wide range of pharmacological activities that contribute significantly to its therapeutic potential in the treatment of gastrointestinal disorders and gastric ulcers. These activities include antioxidant, anti-inflammatory, cytoprotective, wound healing, free radical scavenging, antimicrobial, and gastroprotective effects. The multifaceted biological actions of Aloin make it a valuable natural compound for advanced gastroprotective formulations (Xiao et al., 2022).

8.1.1 Antioxidant acticity

One of the most important pharmacological properties of Aloin is its potent antioxidant activity. Gastric ulcer formation is closely associated with oxidative stress generated by excessive production of reactive oxygen species such as superoxide radicals, hydroxyl radicals, and hydrogen peroxide. These free radicals damage cellular proteins, lipids, and DNA, leading to inflammation, tissue injury, and delayed ulcer healing. Aloin acts as an effective antioxidant by scavenging reactive oxygen species and reducing oxidative stress within gastric tissues. It also inhibits lipid peroxidation and protects cellular membranes from free radical-induced damage (Sah et al., 2023).

8.1.2 Anti-inflammatory properties

In addition to its antioxidant activity, Aloin possesses strong anti-inflammatory properties. Inflammation is an important pathological factor involved in gastric mucosal injury and ulcer progression. Aloin suppresses the release of inflammatory mediators such as cytokines, prostaglandins, and nitric oxide, thereby reducing inflammatory responses in damaged tissues. It also decreases infiltration of inflammatory cells and helps maintain mucosal integrity. Through its anti-inflammatory action, Aloin minimizes tissue destruction and accelerates ulcer healing (Luo et al., 2018).

8.1.3 Cytoprotective activity

Aloin further exhibits cytoprotective activity by strengthening the natural defence mechanisms of the gastric mucosa. It enhances mucus secretion and helps maintain the protective mucus-bicarbonate barrier that shields epithelial cells from acid and pepsin-induced injury. Improved mucosal protection reduces erosion of the gastric lining and prevents progression of ulcerative lesions (Jiang et al., 2022).

8.1.4 Wound healing

Another significant pharmacological activity of Aloin is its wound healing potential. Aloin promotes regeneration of epithelial cells, enhances collagen synthesis, and stimulates tissue repair processes within damaged mucosa. Improved cellular regeneration and angiogenesis contribute to faster healing of gastric ulcers and restoration of mucosal architecture. Aloin also improves local blood circulation, which supplies oxygen and nutrients necessary for tissue recovery

(Tarnawski and Ahluwalia 2021).

8.1.5 Antimicrobial activity

Aloin has additionally demonstrated antimicrobial activity against various pathogenic microorganisms. Some studies indicate that Aloe-derived compounds may inhibit the growth of Helicobacter pylori, a bacterium strongly associated with peptic ulcer disease and chronic gastritis. This antimicrobial effect may further support its gastroprotective and ulcer healing properties **(Donkor *et al.*, 2020).**

8. Types of Nanoparticles Used in Gastroprotective Therapy

Various nanoparticle-based drug delivery systems have been extensively explored for gastroprotective therapy because of their ability to improve gastric retention, enhance drug stability, provide controlled release, and increase therapeutic efficacy at the site of ulceration.

9.1 Polymeric Nanoparticles

Polymeric nanoparticles are one of the most commonly used nanosystems in pharmaceutical drug delivery because of their excellent biocompatibility, biodegradability, controlled release properties, and versatility in encapsulating therapeutic agents. These nanoparticles are generally prepared using natural or synthetic biodegradable polymers such as chitosan, poly lactic-co-glycolic acid (PLGA), alginate, gelatin, polycaprolactone, cellulose derivatives, and polymethacrylates (Geszke-Moritz and Moritz, 2024).

Polymeric nanoparticles are broadly classified into nanospheres and nanocapsules. In nanospheres, the drug is uniformly dispersed throughout the polymeric matrix, whereas in nanocapsules, the drug is enclosed within a polymeric shell surrounding an oily or aqueous core. These systems can encapsulate both hydrophilic and hydrophobic drugs and protect them from chemical degradation and enzymatic metabolism (Mehandole et al., 2023).

9.2 Lipid Nanoparticles

Lipid-based nanoparticles are another important class of nanocarriers extensively used in gastroprotective therapy because of their excellent biocompatibility, enhanced drug loading capacity, and ability to improve oral bioavailability of poorly soluble drugs. Lipid nanoparticles are mainly classified into solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs). Solid lipid nanoparticles are submicron colloidal systems composed of physiologically compatible solid lipids stabilized by surfactants. In these systems, the lipid matrix remains solid at both room and body temperatures, allowing controlled encapsulation and sustained release of drugs. SLNs offer several advantages including improved drug stability, protection from chemical degradation, controlled release, reduced toxicity, and enhanced bioavailability (Subramanian, 2021).

9.3 Mucoadhesive Nanoparticles

Mucoadhesive nanoparticles are specially designed nanosystems capable of adhering strongly to the mucus layer covering the gastrointestinal mucosa. These nanoparticles play a crucial role in gastroprotective therapy because they prolong the residence time of drugs within the stomach and enhance localized therapeutic action at ulcerated tissues. The gastric mucosa is continuously exposed to mucus turnover and rapid gastric emptying, which can limit the effectiveness of conventional oral dosage forms. Mucoadhesive nanoparticles overcome this limitation by establishing close contact with the mucosal surface through electrostatic

interactions, hydrogen bonding, van der Waals forces, or polymer chain interpenetration (Bayer, I2022).

Formulation Development of Lafutidine and Aloin-Loaded Nanoparticles

The formulation development of Lafutidine and Aloin-loaded nanoparticles represents an advanced pharmaceutical approach aimed at enhancing gastroprotective therapy through improved drug delivery, sustained release, enhanced bioavailability, and prolonged gastric retention. Combination therapy involving Lafutidine, a potent H2 receptor antagonist with gastroprotective properties, and Aloin, a natural bioactive compound possessing antioxidant and anti-inflammatory activities, offers synergistic therapeutic benefits for the treatment of gastric ulcers and gastrointestinal disorders. However, both compounds possess certain limitations such as instability, poor bioavailability, limited gastric residence time, and variable absorption, which may reduce their clinical effectiveness when administered through conventional dosage forms (Bhandare and Nannor, 2024).

10.Selection of Formulation Components

The development of nanoparticles requires appropriate selection of polymers, stabilizers, solvents, surfactants, and other excipients that influence particle formation, drug encapsulation, stability, and release characteristics.

11.1 Selection of Polymers

Polymers play a critical role in nanoparticle formulation because they determine particle size, drug release behavior, mucoadhesion, stability, and biodegradability. Biodegradable and biocompatible polymers are generally preferred for oral gastroprotective formulations to ensure safety and sustained therapeutic action **(Idrees *et al.*, 2020).**

Commonly used polymers for Lafutidine and Aloin-loaded nanoparticles include:

- Chitosan
- Poly lactic-co-glycolic acid (PLGA)
- Alginate
- Gelatin
- Polycaprolacton

11.1.1 Selection of Stabilizers and Surfactants

Stabilizers and surfactants are incorporated into nanoparticle formulations to prevent particle aggregation, improve stability, and maintain uniform particle distribution. These agents reduce surface tension during nanoparticle formation and help produce smaller and more stable particles **(Sultana *et al.*, 2020).**

Common stabilizers used include:

- Polyvinyl alcohol (PVA)
- Tween 80
- Poloxamers
- Lecithin
- Sodium lauryl sulfate

11.1.2 Selection of Solvents

Organic solvents are often used for dissolving polymers and drugs during nanoparticle preparation. Common solvents include:

- Ethanol

- Acetone
- Dichloromethane
- Methanol
- Ethyl acetate

11.2 Methods of Preparation of Nanoparticles

Several formulation techniques are employed for preparing Lafutidine and Aloin-loaded nanoparticles. The selection of an appropriate method depends on drug properties, polymer characteristics, desired particle size, and release profile.

11.2.1 Solvent Evaporation Method

The solvent evaporation method is one of the most commonly used techniques for preparing polymeric nanoparticles. In this method, the drug and polymer are dissolved in a volatile organic solvent to form the organic phase. This phase is then emulsified into an aqueous phase containing a stabilizer under continuous stirring or homogenization. After formation of the emulsion, the organic solvent is evaporated either by magnetic stirring or reduced pressure, resulting in precipitation of nanoparticles. The nanoparticles are then collected by centrifugation, washed, and dried **(Chaudhary *et al.*, 2021).**

11.2.2 Nanoprecipitation Method

Nanoprecipitation, also known as solvent displacement method, is a simple and rapid technique for preparing nanoparticles. In this method, the drug and polymer are dissolved in a water-miscible organic solvent and added dropwise into an aqueous phase containing stabilizers under constant stirring. Rapid diffusion of solvent into the aqueous phase causes supersaturation and precipitation of nanoparticles. The solvent is subsequently removed to obtain stable nanoparticles **(Miladi *et al.*, 2017).**

11.2.3 Ionic Gelation Method

The ionic gelation method is commonly employed for preparing chitosan-based nanoparticles. This technique involves electrostatic interaction between positively charged polymers and negatively charged cross-linking agents. Typically, chitosan is dissolved in acidic solution and mixed with a cross-linking agent such as sodium tripolyphosphate (TPP). Upon mixing, ionic interactions result in spontaneous formation of nanoparticles **(Desai, 2016).**

11.2.4 Emulsification Solvent Diffusion Method

In this technique, the polymer and drug are dissolved in a partially water-miscible solvent and emulsified into an aqueous phase containing surfactants. Diffusion of solvent into the external aqueous phase results in precipitation of nanoparticles **(Sarfraz *et al.*, 2017).**

11.2.5 Spray Drying Method

Spray drying is a scalable technique used for converting nanoparticle suspensions into dry powder form. In this process, the nanoparticle dispersion is atomized into a heated chamber, resulting in rapid solvent evaporation and formation of dry nanoparticles **(Malamatari *et al.*, 2020).**

11.3 Critical Formulation Parameters

Several physicochemical parameters are evaluated during formulation development to ensure the quality, stability, and effectiveness of nanoparticles.

11.3.1 Particle Size

Particle size is one of the most important parameters affecting drug release, absorption, stability, and mucosal penetration. Smaller particles provide larger surface area, improved dissolution, and better interaction with gastric mucosa. Nanoparticles intended for gastroprotective therapy generally range between 100–500 nm to achieve enhanced gastric retention and absorption **(Subramanian *et al.*, 2022).**

11.3.2 Surface Charge (Zeta Potential)

Zeta potential indicates the surface charge and stability of nanoparticles. Adequate surface charge prevents aggregation of particles and improves formulation stability. Positive zeta potential enhances interaction with negatively charged gastric mucosa and increases mucoadhesion **(Karmakar, 2019).**

11.3.3 Drug Loading Efficiency

Drug loading efficiency represents the amount of drug incorporated into nanoparticles relative to the total weight of nanoparticles. High drug loading is desirable for improving therapeutic effectiveness and reducing formulation volume **(Liu *et al.*, 2020).**

11.3.4 Entrapment Efficiency

Entrapment efficiency refers to the percentage of drug successfully encapsulated within nanoparticles. High entrapment efficiency ensures sustained release and minimizes drug loss during preparation. Entrapment efficiency depends on factors such as polymer type, drug solubility, and preparation method **(Gooneh-Farahani *et al.*, 2020).**

11.3.5 Morphology

Morphological characteristics such as shape and surface texture are examined using scanning electron microscopy (SEM) or transmission electron microscopy (TEM). Spherical and smooth-surfaced nanoparticles are generally preferred because they exhibit better stability and controlled release behaviour **(Inkson, 2016).**

11.3.6 Stability

Stability studies evaluate the physical and chemical integrity of nanoparticles during storage. Parameters such as particle size, drug content, and zeta potential are monitored under different temperature and humidity conditions **(Danaei *et al.*, 2018).**

11.3.7 *In Vitro* Drug Release Profile

In vitro drug release studies are performed to evaluate the release behavior of Lafutidine and Aloin from nanoparticles in simulated gastric conditions **(Sindhoor *et al.*, 2018).**

Conclusion

Lafutidine and Aloin-loaded nanoparticles represent a promising approach for enhancing gastroprotective therapy through sustained release, improved bioavailability, prolonged gastric retention, and enhanced mucosal protection. Nanoparticle-based systems effectively overcome the limitations associated with conventional oral dosage forms and provide synergistic therapeutic benefits through combined antisecretory, antioxidant, anti-inflammatory, and cytoprotective actions. Various nanoparticle preparation techniques such as solvent evaporation, nanoprecipitation, ionic gelation, and emulsification solvent diffusion have demonstrated significant potential in developing stable and effective gastroprotective formulations. Proper characterization and in vitro evaluation of nanoparticles are essential for optimizing therapeutic performance and ensuring formulation stability.

Overall, the integration of nanotechnology with synthetic antiulcer drugs and natural bioactive compounds offers a novel and highly effective strategy for the management of gastric ulcers and related gastrointestinal disorders.

REFERENCES

1. Jaiswal, F., Rai, A. K., Wal, P., Wal, A., & Singh, S. P. (2021). Peptic ulcer: a review on etiology, pathogenesis and treatment. *Asian Journal of Pharmaceutical Education and Research*, *10*(4), 1.
2. Vakil, N. (2024). Peptic ulcer disease: a review. *Jama*, *332*(21), 1832-1842.
3. Reshetnyak, V. I., & Reshetnyak, T. M. (2017). Significance of dormant forms of Helicobacter pylori in ulcerogenesis. *World journal of gastroenterology*, *23*(27), 4867.
4. Fokunang, C., Fokunang, E. T., Frederick, K., Ngameni, B., & Ngadjui, B. (2018). Overview of non-steroidal anti-inflammatory drugs (nsaids) in resource limited countries. *Moj Toxicol*, *4*(1), 5-13.
5. Jaiswal, F., Rai, A. K., Wal, P., Wal, A., & Singh, S. P. (2021). Peptic ulcer: a review on etiology, pathogenesis and treatment. *Asian Journal of Pharmaceutical Education and Research*, *10*(4), 1.
6. Sobhani, K., Li, J., & Cortes, M. (2023). Nonsteroidal anti-inflammatory drugs (NSAIDs). In *First aid perioperative ultrasound: Acute pain manual for surgical procedures* (pp. 127-138). Cham: Springer International Publishing.
7. Patlevič, P., Vašková, J., Švorc Jr, P., Vaško, L., & Švorc, P. (2016). Reactive oxygen species and antioxidant defense in human gastrointestinal diseases. *Integrative medicine research*, *5*(4), 250-258.
8. de Lima, C. A. A., de Lima, R. S., de Souza, J. B., de Souza Graça, A., Thomazzi, S. M., Batista, J. S., & Estevam, C. D. S. (2022). Gastroprotective mechanisms. *Peptic ulcer disease-what's new*.
9. Galura, G. M., Chavez, L. O., Robles, A., & McCallum, R. (2019). Gastroduodenal injury: role of protective factors. *Current gastroenterology reports*, *21*(8), 34.
10. Liu, Z., Wang, S., Yang, S., Liu, W., Huo, N., Xu, J., ... & Liu, H. (2025). Bridging Gaps in Oral Mucosa Regeneration: Advances and Challenges. *Tissue Engineering Part B: Reviews*, 19373368251405708.
11. Choi, W. T., Lauwers, G. Y., & Slavik, T. (2024). Inflammatory disorders of the stomach. *Morson and Dawson's Gastrointestinal Pathology*, 135-194.
12. Avegno, J., & Carlisle, M. (2016). Evaluating the patient with right upper quadrant abdominal pain. *Emergency Medicine Clinics*, *34*(2), 211-228.
13. Grigorian, A., Lin, M. Y., & de Virgilio, C. (2026). Right Upper Quadrant Pain, Fever, Nausea, and Vomiting. In *Surgery: A Case-Based Clinical Review* (pp. 271-279). Cham: Springer Nature Switzerland.
14. Müller, A. L. E. (2024). *Evaluation of the frequency and necessity of proton-pump-inhibitor therapy in geriatric patients* (Doctoral dissertation, Sveučilište u Splitu, Sveučilište u Splitu, Medicinski fakultet).
15. Sano, T., Utsumi, D., Amagase, K., Matsumoto, K., Tominaga, M., Higuchi, K., & Kato, S. (2017). Lafutidine, a histamine H2 receptor antagonist with mucosal protective properties, attenuates 5-fluorouracil-induced intestinal mucositis in mice through activation of extrinsic primary afferent neurons. *J Physiol Pharmacol*, *68*(1), 79-90.

16. Shetty, B., & Vishwanath, M. K. (2022). An expert opinion on antacids: A review of its pharmacological properties and therapeutic efficacy. *F1000Research*, *11*, 1057.

17. Kak, M. (2025). Rebamipide in gastric mucosal protection and healing: An Asian perspective. *World Journal of Gastrointestinal Pharmacology and Therapeutics*, *16*(1), 101753.

18. Rocha, G. R., Lemos, F. F. B., de Oliveira Silva, L. G., Luz, M. S., Santos, G. L. C., Pinheiro, S. L. R., & de Melo, (2025). Overcoming antibiotic-resistant Helicobacter pylori infection: Current challenges and emerging approaches. *World Journal of Gastroenterology*, *31*(10), 102289.

19. Bhatia, S. (2016). Nanoparticles types, classification, characterization, fabrication methods and drug delivery applications. In *Natural polymer drug delivery systems: Nanoparticles, plants, and algae* (pp. 33-93). Cham: Springer International Publishing.

20. Bai, X., Smith, Z. L., Wang, Y., Butterworth, S., & Tirella, A. (2022). Sustained drug release from smart nanoparticles in cancer therapy: a comprehensive review. *Micromachines*, *13*(10), 1623.

21. Watchorn, J., Clasky, A. J., Prakash, G., Johnston, I. A., Chen, P. Z., & Gu, F. X. (2022). Untangling mucosal drug delivery: engineering, designing, and testing nanoparticles to overcome the mucus barrier. *ACS biomaterials science & engineering*, *8*(4), 1396-1426.

22. Li, M., Liu, Y., & Weigmann, B. (2023). Biodegradable polymeric nanoparticles loaded with flavonoids: A promising therapy for inflammatory bowel disease. *International Journal of Molecular Sciences*, *24*(5), 4454.

23. Kou, E., Zhang, X., Dong, B., Wang, B., & Zhu, Y. (2024). Combination of H1 and H2 histamine receptor antagonists: current knowledge and perspectives of a classic treatment strategy. *Life*, *14*(2), 164.

24. Arin, R. M., Gorostidi, A., Navarro-Imaz, H., Rueda, Y., Fresnedo, O., & Ochoa, B. (2017). Adenosine: direct and indirect actions on gastric acid secretion. *Frontiers in Physiology*, *8*, 737.

25. Pai, U. A., Ravishankar, A. V., Bharadia, L., HR, S., Wadhwa, A., Prajapati, B., & SOANS, S. T. (2025). Evidence-based review by a multidisciplinary team of pediatricians on the use of gastric acid-reducing medications in children: Indian perspectives. *Cureus*, *17*(5).

26. Zhu, L., Guo, J., Liu, Q., Luo, Y., Zhao, J., Zhong, W., & Chen, X. (2023). Lafutidine ameliorates indomethacin-induced small intestinal damage in rats by modifying the intestinal mucosal barrier, inflammation, and microbiota. *Pharmacology*, *108*(3), 286-300.

27. Brahmeswari, P., Sultana, M., & Reddy, C. M. (2022). Formulation and Optimization of Raft Forming Chewable Tablet Containing Lafutidine. *Indo-American Journal of Pharma and Bio Sciences*, *20*(4), 126-134.

28. Zhang, J., Wang, T. X., & Wei, R. N. (2022). Clinical study on Xiaojianzhong capsules combined with lafutidine in treatment of gastric ulcer.

29. Otieno, P. O. (2022). A review on antiplasmodial potential and quantification of aloin and aloe-emodin in aloe vera.

30. Luo, X., Zhang, H., Wei, X., Shi, M., Fan, P., Xie, W., & Xu, N. (2018). Aloin suppresses lipopolysaccharide-induced inflammatory response and apoptosis by inhibiting the activation of NF-κB. *Molecules*, *23*(3), 517.

31. Bawankar, A., & Zawar, L. (2025). Recent advances in phytochemical-based nanoparticles for colon-specific drug delivery. *Cellulose chemistry and technology*, *59*(9-10), 1045-1066.

32. Xiao, J., Chen, S., Chen, Y., & Su, J. (2022). The potential health benefits of aloin from genus Aloe. *Phytotherapy Research*, *36*(2), 873-890.

33. Sah, D. K., Arjunan, A., Lee, B., & Jung, Y. D. (2023). Reactive oxygen species and H. pylori infection: a comprehensive review of their roles in gastric cancer development. *Antioxidants*, *12*(9), 1712.

34. Luo, X., Zhang, H., Wei, X., Shi, M., Fan, P., Xie, W., & Xu, N. (2018). Aloin suppresses lipopolysaccharide-induced inflammatory response and apoptosis by inhibiting the activation of NF-κB. *Molecules*, *23*(3), 517.

35. Jiang, H., Shi, G. F., Fang, Y. X., Liu, Y. Q., Wang, Q., Zheng, X., & Yin, Z. Q. (2022). Aloin A prevents ulcerative colitis in mice by enhancing the intestinal barrier function via suppressing the Notch signaling pathway. *Phytomedicine*, *106*, 154403.

36. Tarnawski, A. S., & Ahluwalia, A. (2021). The critical role of growth factors in gastric ulcer healing: the cellular and molecular mechanisms and potential clinical implications. *Cells*, *10*(8), 1964.

37. Donkor, A. M., Donkor, M. N., & Kuubabongnaa, N. (2020). Evaluation of anti-infective potencies of formulated aloin A ointment and aloin A isolated from Aloe barbadensis Miller. *BMC chemistry*, *14*(1), 8.

38. Geszke-Moritz, M., & Moritz, M. (2024). Biodegradable polymeric nanoparticle-based drug delivery systems: comprehensive overview, perspectives and challenges. *Polymers*, *16*(17), 2536.

39. Mehandole, A., Walke, N., Mahajan, S., Aalhate, M., Maji, I., Gupta, U., & Singh, P. K. (2023). Core–shell type lipidic and polymeric nanocapsules: the transformative multifaceted delivery systems. *Aaps Pharmscitech*, *24*(1), 50.

40. Subramanian, P. (2021). Lipid-based nanocarrier system for the effective delivery of nutraceuticals. *Molecules*, *26*(18), 5510.

41. Bayer, I. S. (2022). Recent advances in mucoadhesive interface materials, mucoadhesion characterization, and technologies. *Advanced Materials Interfaces*, *9*(18), 2200211.

42. Bhandare, A., & Nannor, K. M. (2024). Bioavailability in drug design and development: A comprehensive review. *World Journal of Pharmaceutical Research*, *13*(17), 145-168.

43. Idrees, H., Zaidi, S. Z. J., Sabir, A., Khan, R. U., Zhang, X., & Hassan, S. U. (2020). A review of biodegradable natural polymer-based nanoparticles for drug delivery applications. *Nanomaterials*, *10*(10), 1970.

44. Sultana, S., Alzahrani, N., Alzahrani, R., Alshamrani, W., Aloufi, W., Ali, A., & Siddiqui, N. A. (2020). Stability issues and approaches to stabilised nanoparticles-based drug delivery system. *Journal of drug targeting*, *28*(5), 468-486.

45. Chaudhary, S. A., Patel, D. M., Patel, J. K., & Patel, D. H. (2021). Solvent emulsification evaporation and solvent emulsification diffusion techniques for nanoparticles. In *Emerging technologies for nanoparticle manufacturing* (pp. 287-300). Cham: Springer International Publishing.

46. Miladi, K., Sfar, S., Fessi, H., & Elaissari, A. (2017). Nanoprecipitation process: from particle preparation to in vivo applications. In *Polymer Nanoparticles for Nanomedicines:*

A Guide for their Design, Preparation and Development (pp. 17-53). Cham: Springer International Publishing.

47. Desai, K. G. (2016). Chitosan nanoparticles prepared by ionotropic gelation: An overview of recent advances. *Critical Reviews™ in Therapeutic Drug Carrier Systems*, *33*(2).

48. Sarfraz, R. M., Bashir, S., Mahmood, A., Ahsan, H., Riaz, H., Raza, H., & Yasmeen, T. (2017). Application of various polymers and polymers-based techniques used to improve solubility of poorly water-soluble drugs: A review. *Acta Pol. Pharm*, *74*, 347-356.

49. Malamatari, M., Charisi, A., Malamataris, S., Kachrimanis, K., & Nikolakakis, I. (2020). Spray drying for the preparation of nanoparticle-based drug formulations as dry powders for inhalation. *Processes*, *8*(7), 788.

50. Subramanian, D. A., Langer, R., & Traverso, G. (2022). Mucus interaction to improve gastrointestinal retention and pharmacokinetics of orally administered nano-drug delivery systems. *Journal of nanobiotechnology*, *20*(1), 362.

51. Karmakar, S. A. N. A. T. (2019). Particle size distribution and zeta potential based on dynamic light scattering: Techniques to characterize stability and surface charge distribution of charged colloids. *Recent Trends Mater. Phys. Chem*, *28*, 117-159.

52. Liu, Y., Yang, G., Jin, S., Xu, L., & Zhao, C. X. (2020). Development of high-drug-loading nanoparticles. *Chem Plus Chem*, *85*(9), 2143-2157.

53. Gooneh-Farahani, S., Naghib, S. M., & Naimi-Jamal, M. R. (2020). A novel and inexpensive method based on modified ionic gelation for pH-responsive controlled drug release of homogeneously distributed chitosan nanoparticles with a high encapsulation efficiency. *Fibers and Polymers*, *21*(9), 1917-1926.

54. Inkson, B. J. (2016). Scanning electron microscopy (SEM) and transmission electron microscopy (TEM) for materials characterization. In *Materials characterization using nondestructive evaluation (NDE) methods* (pp. 17-43). Woodhead publishing.

55. Danaei, M., Kalantari, M., Raji, M., Fekri, H. S., Saber, R., Asnani, G. P., & Taheriazam, A. (2018). Probing nanoliposomes using single particle analytical techniques: Effect of excipients, solvents, phase transition and zeta potential. *Heliyon*, *4*(12).

56. Sindhoor, S. M., Priya, S., & Maxwell, (2018). Formulation and evaluation of novel in situ gel of lafutidine for gastroprotective drug delivery. *Asian J Pharm Clin Res*, *11*(8), 88-94.