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# Preliminary Study on the Composition of Nanoparticles for the Treatment of Peptic Ulcer

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## ABSTRACT

One of the most frequent gastrointestinal issues is a gastric ulcer. Throughout their lives, peptic ulcer disease affects more than 10% of the adult population in Western countries. The pathogenesis of peptic ulcer disease is based on an imbalance between mucosal defense factors (bicarbonate, mucin, prostaglandin, nitric oxide, and other peptides and growth factors) and hazardous chemicals (acid and pepsin). Certain acid-related illnesses can be addressed and prevented by lowering gastric acidity or improving mucosal protection. In the treatment of stomach ulcers, nanoparticles are being developed for antiulcer drug delivery. Other treatments, such as nanotechnology, are gaining prominence as a result of the challenges in treating peptic ulcers. Different types of nanoparticles have strong antibacterial properties, polymeric nanoparticles have advantages in drug delivery and drug protection and membrane-coated nanoparticles have prominent properties of indirect targeting, demonstrating the importance of nanotechnology in the development of new peptic ulcer treatments. The pharmacokinetic performance and ulcer healing response of an antiulcer medicine in the form of nanoparticles were evaluated in Wistar rats with produced ulcers during characterization. The size distribution of the drug-filled particles was limited, with a size of approximately 200 nm.

**Key Words:** Proton Pump Inhibitor, Peptic Ulcers Disease, Gastro-intestinal track, Nanoparticles, Nonsteroidal Anti-inflammatory Drug, Nano- Materials

## INTRODUCTION

Acids and pepsin cause ulcers on the lining of the duodenum and stomach, causing peptic ulcers (PUD). PUD is caused by an imbalance between protective factors such as prostaglandins, blood flow, and cell regeneration and aggressive factors such as alcohol abuse, smoking, *Helicobacter pylori* colonization, and the use of nonsteroidal anti-inflammatory drugs.<sup>1</sup>

Peptic ulcer (PUD) is a term used to describe a wound in the gastrointestinal tract (GIT) that reaches the inner, submucosal, and possibly outer muscle layers, causing perforation and death. Organ wall lead. The disease affects a significant portion of the world's population and increases public health costs. Ulcers are a common condition that affects people around the world. Symptomatic treatment of ulcers hurts health due to unpleasant side effects. Many herbs and secondary metabolites are currently used to treat ulcers.<sup>2</sup>

Traditional oral treatments are well known. However, drug degradation in the gastrointestinal environment, reduced

oral bioavailability and lack of drug delivery to the target site can reduce the effectiveness of this treatment. After this approach, it becomes attractive to use tactics to improve the effectiveness of these traditional medicines.<sup>1</sup> For better effect, the particle size of the formulation in the nanometer range is preferred for high penetration efficiency. Therefore, the composite material is prioritized over the nanoparticles formed. Nanomaterials are gaining importance in innovation due to their adjustable physical, chemical, and biological properties, and their superior performance compared to bulk materials. The size, composition, shape, and origin of nanomaterials are all factors that need to be considered.<sup>3</sup>

### Role of nanoparticles in peptic ulcer

Nanoscale devices less than 50 nanometres in diameter can easily penetrate most cells, while devices less than 20 nanometres in diameter can easily exit the blood arteries as they circulate through the body. Due to their small size, nanoscale devices can easily interact with biomolecules both on the

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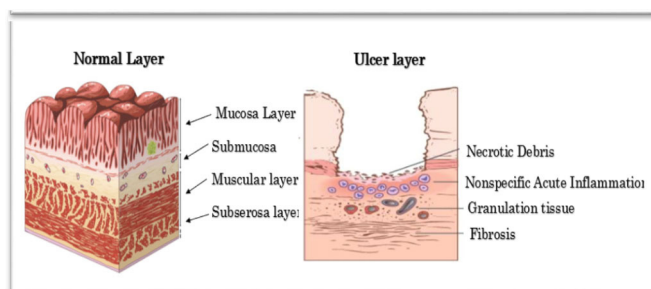
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surface and inside the cell. As a result, it is made of high molecular weight nanoparticles that can be used to treat ulcers.<sup>4</sup> The production of high molecular weight nanoparticles by high-speed homogenizer and ultrasonic technology increases the solubility and absorption of the drug, increasing its availability at the action site and the therapeutic index.<sup>5</sup> In peptic ulcers, sucralfate is a topically active chemical that combines with hydrochloric acid in the stomach in an acidic environment to produce a pasty, viscous crosslinker capable of serving as an acid buffer for up to 6 to 8 hours after a single dose in an acidic environment<sup>6</sup>. This project creates polymeric nanoparticles, reducing the available particle size and increasing treatment efficiency<sup>7</sup>. Due to the formation of a polymeric coating, the absorption rate is also increased in the stomach and intestine.<sup>8</sup> Using an ultrasonic homogenizer is very efficient in reducing soft and hard particles. Homogeneity is based on cavitation<sup>9</sup>. When a liquid undergoes intensive sonication, the sound waves propagate through the liquid, causing alternating high-pressure and low-pressure cycles (approximately 20,000 cycles/sec).<sup>10</sup>

The epithelium of the small and large intestines is in intimate contact with ingested material to absorb nutrients. Disaccharides, peptides, fatty acids, and monoglycerides are produced in the small intestine, then converted and absorbed in the villi. Due to electrostatic repulsion and trapping means, charged particles such as carboxylate polystyrene nanoparticles or those made from positively charged polymers have limited oral bioavailability<sup>11</sup>. The smaller the diameter of the particles, the faster they can pass through the mucus and reach the colon cells; a Diameter of 14 nm penetrates in 2 min, the diameter of 415 nm penetrates in 4 min. particles look 30 min while 1000 nm particles cannot shift this barrier.<sup>12</sup>

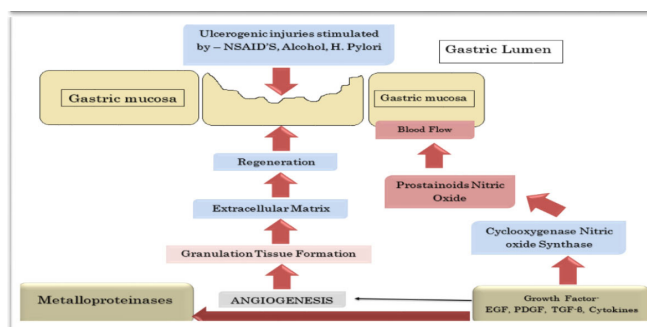
## Ulcer Anatomy & Pathophysiology

An ulcer is a continuous rupture of the covering epithelium, whether it is the skin or the mucosa, due to molecular death. An ulcer is a rupture or rupture of the inner lining of the body that prevents a membrane-bound organ from continuing to function normally. An imbalance between protective and destructive factors in the gastrointestinal tract lining causes



**Figure 1:** Representative diag. of different barriers targeted by nanoparticles for peptic ulcer recovery<sup>12</sup>.

peptic ulcer disease. duodenum (PUD). Risk factors for PUD include *H. pylori* infection, NSAID use, first-degree relative



**Figure 2:** The main mechanism involved in the healing of gastric ulcers. EGF: epidermal growth factor; PDGF: platelet-derived growth factor; TGF $\beta$ : transforming growth factor  $\beta$ <sup>14, 15</sup>.

with PUD, migration from developed countries, and African-American/Hispanic ethnicity. A mucosal defect extending to the muscular mucosa is common with peptic ulcers. The inner layers are susceptible to acid when the mucous membrane that protects the surface is damaged. The ability of mucosal cells to release bicarbonate is also impaired. *H. pylori* is known to localize and inflame the gastric mucosa. *H. pylori* also inhibits bicarbonate release, promotes metabolism, and increases gastric acidity.<sup>12</sup>

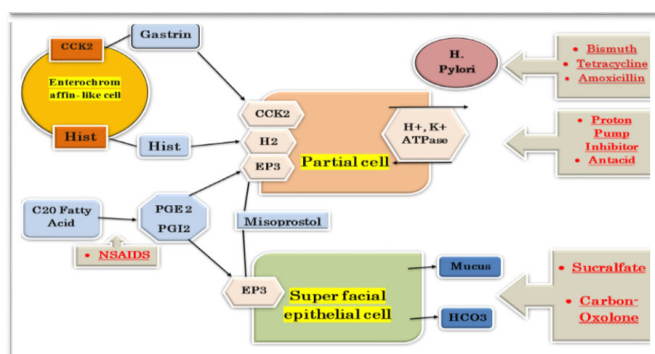
## Preliminary test for peptic ulcer

### Stool monoclonal antigen tests

When using a laboratory-certified monoclonal test, fecal antigen screening uses a monoclonal antibody that is as accurate as of the urea breath test<sup>16</sup>. The urea breath test is more expensive and requires more equipment. Similar to how a urea breath test only detects an existing infection, a stool antigen test can be used as a curative test. PPIs should avoid for two weeks before testing, but stool antigen testing is not as affected as urea breath tests using PPIs.<sup>17</sup>

### Mechanism of Action of drug

Finally, PPIs work by reducing gastric acid secretion. These drugs are absorbed near the small intestine and then released into the circulation, where they affect the stomach's parietal cells.<sup>18</sup> The enzyme H<sup>+</sup>/K<sup>+</sup> ATPase, or proton pump, is found in parietal cells and is blocked by PPIs. The penultimate stage in gastric acid secretion is this enzyme. PPIs are active precursors in the acid-secreting tubules of parietal cells only after acid-catalyzed cleavage. PPIs are broken down by the liver enzyme P450.<sup>19</sup> Though there are slight differences in which the P450 enzyme predominates in breaking down some PPIs, CYP2C19 is the most common.<sup>14</sup> Understanding how PPIs are metabolized can help us understand why certain PPIs work better for some people than others. For example, people of Asian descent have higher bioavailability of



**Figure 3:** Schematic representation of the major pathophysiological mechanisms involved in the pathogenesis of peptic ulcer disease and the sites of action of the most commonly used pharmacological treatment options for peptic ulcer disease. CCK2 = cholecystikinin receptor; PGE2 = prostaglandin E2; PGI2 = prostaglandin I2; EP3 = prostaglandin E3 receptor; HIST = histamine.<sup>21</sup>

PPIs and should start at a lower dose. The bioavailability of PPIs increases with age. Therefore, the dosage in the elderly should be checked frequently and changed as necessary. PPIs are the most effective drugs to reduce acid production in the stomach.<sup>15</sup>

### Role of additives for nanoparticles drug targeting-

#### Organic Solvent

Organic solvents recognized as neurotoxins include hexane, tetrachlorethylene, and toluene. Fatty and aromatic hydrocarbons, amines, esters, ethers, ketones, and nitrated or chlorinated hydrocarbons are all examples of organic solvents.<sup>16</sup>

#### Polymer

Allows the modification of ligand surfaces for stealth and drug delivery, ensuring the stability of labile molecules. e.g. Gelatine, lecithin, albumin<sup>17</sup>.

#### Surfactant

Surfactants reduce the average particle size by changing the surface energy of the particles. As a result, the surface tension decreases, and the Kelvin barrier changes, allowing more particles to avoid agglomeration<sup>18</sup>.

#### Aq. Solvent

The aq. Solvents are used to dissolve the surfactant and form a solution<sup>19</sup>.

### Production technique used in particles

#### Solvent Evaporation Method

Solvent evaporation was the original approach to producing macromolecular NPs from a prefabricated polymer. The

production of an oil-in-water (o/e) emulsion is required for this process, which leads to the synthesis of nanoparticles<sup>25</sup>. The whole process is described, to begin with, an organic phase is produced using a polar organic solvent, in which the polymer is dissolved and the active ingredient (eg a drug) is decomposed. canopy. Both chloroform and dichloromethane have been used extensively in the past, but more often in the past. Due to their toxicity, they have been replaced by ethyl acetate, which is more toxic and therefore more suitable for biomedical applications<sup>20</sup>. Aqueous phases containing surfactants (eg polyvinyl acetate; PVA) were also frequently produced. The organic solution is emulsified in the aqueous phase with a detergent and processed into a nanodroplet dispersion using high-speed homogenization or ultrasonic waves. Evaporation of the polymeric solvent that can diffuse into the continuous phase of the emulsion results in a suspension of NP. The solvent is expelled either by continuous magnetic stirrer at room temperature (for more polar solvents) or constant depressurization (as for dichloromethane and chloroform). The cured nanoparticles can then be washed and collected by centrifugation, and after the solvent has evaporated, they can be lyophilized for long-term storage<sup>21</sup>.

#### Emulsions - Diffusion Method

This is due to Leroux et al. The patented approach is a modified version of the salting-out process. The polymer was dissolved in a water-miscible solvent (propylene carbonate, benzyl alcohol) and then the solution was saturated with water<sup>28</sup>. The solvent phase saturated with polymer water is emulsified into an aqueous solution containing stabilizers<sup>29</sup>. Then the solvent is removed by evaporation or filtration<sup>30</sup>. The advantages of this approach are excellent encapsulation efficiency (typically 70%), minimal homogenization requirements, high batch-to-batch reproducibility, easy scaling, simplicity, and limited size distribution<sup>31</sup>. The leakage of water-soluble drugs into the saturated aqueous outer phase during emulsification reduces encapsulation efficiency, which is a drawback of this approach<sup>32</sup>.



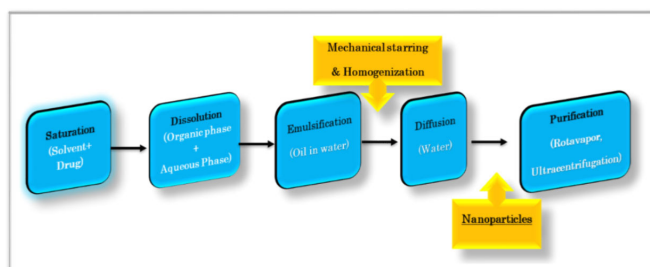
**Figure 4:** Schematic representation of the solvent evaporation method<sup>27</sup>.

### Characterization of nanoparticles

#### Morphology

Scanning and transmission electron microscopes (SEM and TEM) are widely used to learn more about the shape and

size of polymer NPs. To analyse the morphology of NP, NP is often used in combination with cryofracture technology. Electron microscopy (TEM) is often used to distinguish between nano capsules and nanospheres and to measure the wall thickness of nano-capsules. Nanospheres have a spherical, solid polymer structure, while nano-capsules have an oily core surrounded by a thin polymer shell (about 5 nm). Atomic force microscopy is another approach that has been used to analyse the surface morphology of macromolecular NPs (AFMs)<sup>33</sup>.



**Figure 5:** Representation of the emulsification-diffusion technique<sup>31, 32</sup>

### Particle size and size distribution

Microspheres were suspended in liquid paraffin and observed with an optical microscope. The size distribution of the microsphere was investigated using laser diffraction technology (Malvern Instruments Ltd., Malvern, UK). Average particle size was calculated and reported in micro-meters using cyclohexane as a dispersant<sup>34</sup>.

### The yield of Nanoparticles

The total weight of the nanoparticles produced was compared to the total weight of the copolymer and the drug to calculate the nanoparticle yield.<sup>35</sup>

$$\text{Percentage yield} = \frac{\text{amount of nano-particles}}{\text{amount of drug + polymer}} \times 100$$

### Entrapment efficiency

The nanoparticles were separated from the dispersion by centrifugation at 22,000 rpm for 25 min. The supernatant obtained after centrifugation was appropriately diluted and analysed for free diazepam by UV-Visible spectrophotometer at specific nanometres. The trap effectiveness percentage is calculated as follows<sup>36</sup>.

$$\text{Percentage Entrapment efficiency} = \frac{[\text{Drug}]_{\text{total}} - [\text{Drug}]_{\text{supernatant}}}{[\text{Drug}]_{\text{total}}} \times 100$$

### Drug Content analysis

Properly weigh 10 mg of microspheres into a clean 100 ml volumetric flask, dissolve in approximately 2 ml of acetone, adjust the volume with a pH 7.4 buffer, then increase the volume with a pH 7.4 buffer for marking. Rice field. completely. After filtration and dilution, samples were analysed spectrophotometrically to estimate drug concentrations in microspheres. The drug content of each sample was averaged

in three separate tests. The containment efficiency of microspheres was estimated by dividing the actual drug content by the theoretical drug content of microspheres<sup>37</sup>

### Stability of Nanoparticles

The storage of optimal formulations at 4°C 1°C and 30°C 2°C in a stabilization chamber for 90 days determines the stability of the resulting nanoparticles. Samples were examined for drug content, drug release rate (t50%), and any changes in appearance after some time, such as 0, 1, 2, and 3 months<sup>38</sup>

### Drug-Excipients Compatibility Studies

Excipients are essential components of almost all pharmaceutical dosage forms, so it is essential to investigate any physical or chemical interactions between the drug and the excipients, as excipients can change in drug bioavailability and stability. To create a product that is stable, effective, attractive, easy to use, and safe, drugs and excipients must be compatible. Compatibility studies are especially important if the excipients are new and have never been used in formulations containing the active ingredient. To test drug compatibility with different excipients used, DSC and FTIR techniques have been widely used<sup>39</sup>

### Pharmacokinetic study

We generated three groups of four Wistar rats (250-300 g) with ulcers. Drugs with NaHCO<sub>3</sub> solution (5 mg/kg) or drug formulation (5 mg/kg) were administered to Wistar rats. Blood samples were obtained from the tail vein of each rat before drug treatment and at levels of 0.5, 1, 1.5, 2, 3, 4, 5, 6, 8, 10, 12, and 24 h after dosing. The supernatant was collected after centrifugation of the blood sample at 12,000 rpm for 10 min at 4 °C. Using acetonitrile and centrifugation, the drug formulation of each sample was extracted. The supernatant was collected, dried, and reconstituted using the mobile phase for HPLC analysis. The number of drug formulations that can be recovered from serum samples has been calculated. Using a non-inhibitory pharmacokinetic analysis model, pharmacokinetic parameters were calculated.<sup>40</sup>

### Pharmacodynamic study

Wistar rats with ulcer-induced ulcers were divided into four groups (n = 4) and received saline (control group), drug solution, or capsule containing the drug formulation. For 7 days, the formulations were administered orally once daily. After 24 h, the mice were dead. The stomach was sectioned along the greatest curvature and its mucosal surface was cleaned with saline solution<sup>40</sup>. The total mucosal area and ulcerated area were measured using Axio Vision software after imaging the gastric mucosa. The equation used to determine ulcer index (IU)

$$\text{Ulcer index (UI)} = \frac{\text{The ulcerated area}}{\text{Total mucosal area}} \times 100$$

**Table 1: The following is a list of drugs available in nanoparticle dose forms with various polymers for a variety of uses**

Sr. No	Drug name	Category	Polymer	Particle size	Method of preparation	Reference
1	ketoprofen	Pain Relieve	Acrylic	50-100 nm.	Solvent evaporation	[43]
2	Ketoprofen	Pain Relieve	Eudragit E 100,	5-10 um	Emulsion evaporation	44]
3	Repaglinide	Diabetes mellitus type 2. I	Chitosan	48-100 nm	Solvent evaporation	[45]
4	Gamma-oryzanol	Hypolipidemic Agents	Ethyl Cellulose (EC)	2495.5 nm	Nanoprecipitation technique	[46]
5	Lansoprazole	Proton Pump Inhibitor (PPI)	Eudragit RS100, poly (lactic-co-glycolic acid)	200nm	Solvent evaporation	[39]
6	Diazepam	Use in abnormal overactivity in the brain.	Poly (lactic-co-glycolic acid)	250 nm	Solvent evaporation	[29]
7	Sodium polystyrene sulfonate	Increased amounts of potassium in the body	Poly (lactic-co-glycolic acid)	200nm	Solvent evaporation	[47]
8	zinc	Use Alzheimer disease	2-hydroxyethyl methacrylat	1um	Solvent evaporation	[48]
9	Ethambutol	Antimycobacterial antibiotics	Eudragit RS-100	136.1 nm	Diffusion technique.	[49]
10	Lansoprazole	Antiulcer	Chitosan	360 nm	Ionotropic gelation technique	[50]
11	Cetuximab	Monoclonal antibodies	PLGA [Poly (lactic-co-glycolic acid)]	200 nm	Diffusion technique.	[51]
12	Simvastatin	HMG-CoA reductase inhibitors	Eudragit	148.8 nm	Nanoprecipitation	[52]
13	Ivermectin	anthelmintics	Poly (Lactic/ Glycolic) Acid (PLGA)	200 nm	Nanoprecipitation	[[53]
14	Diosmin	Use in hemorrhoids	Poly (Lactic/ Glycolic) Acid (PLGA), chitosan	200 nm	Solvent evaporation	[54]
15.	Passiflora serrato-digitata L. Extracts	Antiulcerogenic	poly(epsilon-caprolactone)	200 nm	Solvent evaporation	[55]

### **Biodistribution of nanoparticles in stomach tissue-**

Male Wistar rats weighing 250-300 gms were used in this investigation, and they were obtained from the local Laboratory Animal Center. All animal experiments followed the National Institutes of Health Guidelines for the Care and Use of Laboratory Animals, and all procedures were reviewed by the Animal Research Ethics Board. During the night, the rats were fasted but were given free water. Oral doses of 100% ethanol (5 ml/kg) cause gastric ulcers. The ulcer-induced mice were divided into three groups, with four mice each (one control and two treatment groups). The treatment groups received ready-to-use drugs, while

the control groups received only physiological saline. Formulas were used orally 1 h after ethanol administration<sup>40</sup> Four after receiving the dose, the rats were slaughtered. The stomach is opened longitudinally and saline solution is rubbed. Stomach tissue was divided into ulcerated and non-ulcerative sections, and freshly removed tissue was frozen using Tissue Tek. A CM3050 S cryostat was used to segment the molded tissue sample, which was then examined under a fluorescence microscope with an integrated digital microscopy system.<sup>41</sup> Hematoxylin and eosin were also stained with hematoxylin and eosin to show healthy and ulcerated tissue morphology. The total mucosal area and ulcerated area were measured using Axio Vision software for

**Table 2: The many aspects of a unique medication delivery system for the treatment of peptic ulcers are summarized in this table**

Sr. No	Technique use	Category	Drug Name	Remark	Reference
1	Coated (Polymeric) nanoparticle	Antibiotics	clarithromycin	Membrane coated (Polymeric) nanoparticles could be used to construct nanocarrier systems for the treatment of H. Pylori. Only one study has used AGS cell membrane coated PLGA nanoparticles with clarithromycin antibiotic in the treatment of Helicobacter pylori.	[56]
2	Nano-lipobeads	Antibiotic	Polyvinyl alcohol	Experiments showed that nano-lipobeads formulations could be effective in the treatment of peptic ulcers caused by H. pylori. These drug delivery methods have the potential to not only reduce or eliminate the drawbacks of traditional dosage forms, but also to exert a "plug and seal effect," which could improve medication targetability in the area of H. pylori.	[57]
3	floating tablets	Antibiotics & PPI	Esomeprazole and Roxithromycin	There are few oral dose forms that include both an antibiotic and a proton pump inhibitor. According to the literature reviewed, floating drug delivery has a number of potential benefits for drugs with low bioavailability because absorption is limited to the upper gastrointestinal tract (GIT) and they can be delivered efficiently, maximising absorption and increasing absolute bioavailability.	[58]
4	Novel floating tablets	Treat stomach and esophagus problems	Esomeprazole magnesium trihydrate	The enteric coating of esomeprazole magnesium trihydrate tablets with Acryl EZE prevents the medicine from degrading in the stomach and allows it to reach the proximal region of the small intestine.	[59]
5	Mucoadhesive microballons	H <sub>2</sub> antagonist	Nizatidine	The delivery methods ensure that drug content is accessible at the assimilation site for the desired amount of time. The effects of several factors such as polymer (PAA-PVP) concentration, drug concentration, internal phase/external phase ratio.	[60]
6	Nano-capsule	Treat stomach and esophagus problems	Passiflora serratodigitata L. Extracts	The dried crude extract (DCE), ethylacetate fraction (EAF), and residual water fraction of Passiflora serratodigitata L. demonstrate potential antiulcerogenic efficacy, according to this study. Surprisingly, the polymeric nanocapsule containing EAF had ten times the activity of free EAF.	[61]
7	Mucoadhesive Nanosuspension	prevent and treat heartburn due to acid indigestion	Famotidine	The desirability function and the Box-Behnken design were used to demonstrate the quality of famotidine loaded nanosuspension. In vitro mucoadhesion and drug release experiments revealed that the produced formulation had sufficient adherence and could prolong drug release for up to 8 hour. When compared to nanosuspension, mucoadhesive nanosuspension had a greater ex-vivo retention.	[62]
8	Microspheres	prevent and treat heartburn due to acid indigestion	Famotidine	To lengthen gastric residence time and target stomach ulcers, construct and characterise a multiple-unit-type oral floating microsphere of famotidine. Based on the findings, such dosage forms could be a promising choice for stomach targeting and could be administered in hard gelatin capsules.	[63]

Table 2: (Continued)

Sr. No	Technique use	Category	Drug Name	Remark	Reference
9	Self-Nanoemulsion	Antiinflammatory, and antipyretic activity	Thymoquinone	A TQ-loaded self-nanoemulsifying drug delivery system was developed to increase the water solubility of thymoquinone (TQ), a significant ingredient of <i>Nigella sativa</i> seed oil. The globule size ranged from 65 to 320 nm, according to the findings. Furthermore, the system estimation and the experimental globule size values were found to be in good agreement.	[64]
10	mucoadhesive tablet	Treat stomach and esophagus problems	Aloe vera powder	Mucoadhesive tablet are promising dosage form that adhere to the mucosa and deliver the drug through it, which present several advantages. The study was designed to develop mucoadhesive tablet of aloe vera powder using chitosan, guar gum and hyaluronic acid as mucoadhesive polymer. Mucoadhesive tablet of aloe vera powder prepared by wet granulation technique	[65]
11	Gastro-retentive Drug Delivery System	Improve the treatment of peptic ulcer	Turmeric Extract Solid Dispersion	The use of alginate beads containing a solid dispersion of turmeric extract was found to be useful in the treatment of stomach ulcers. There was a statistically significant difference in efficacy, Turmeric solid dispersion alginate beads were somewhat more efficient than turmeric extract alginate beads, although the difference was not statistically significant.	[66]
12	Mucoadhesive Bilayer Tablet	PPI	Pantoprazole	The peppas model with a non-fickian diffusion mechanism was observed as the feasible order and drug release mechanisms for the optimised mucoadhesive bilayer tablets of pantoprazole. The final optimised formulations' expedited stability testing revealed no significant differences in drug content or in vitro drug release rates. To achieve optimal absorption and therapeutic efficacy, a stable and safe mucoadhesive bilayer pill of pantoprazole can be developed.	[67]
13	Mucoadhesive Bilayer Tablet	Reduces the amount of acid	Esomeprazole and melatonin	The combination was found to be beneficial in treating peptic ulcers synergistically, as it greatly increased the antiulcer impact when compared to the other treatment groups. Based on the findings, it was determined that the combination is synergistic.	[68]
14	Resin-based combination drug-delivery system	PPI	Ranitidine HCl	Using ion exchange resins, the researchers will prepare and characterise a combination tablet containing ranitidine in immediate release. Ranitidine reduces acid secretion, while domperidone released over time enhances stomach motility, proving the efficacy of this combination in the treatment of gastroesophageal reflux disease (GERD).	[68]

quantitative determination. Ulcerated and non-ulcerative tissues were lyophilized separately in the dark. Each tissue sample was sonicated for 15 min after immersion in acetone. The supernatant was obtained after centrifugation of those tissue samples for 5 min at 2000 pm. Three times the extraction process was performed. Finally, the supernatant was diluted with acetone and examined with a fluorescence spectrometer at 430 nm and 490 nm. The absorption ratio of

nanoparticles per cm<sup>2</sup> of gastric tissue, whether ulcerated or not, was used to calculate the absorption of nanoparticles.<sup>42</sup>

## DISCUSSION

According to evaluations of multiple papers, reducing the particle size of the dosage form increases porosity and per-

meability, which increases bioavailability and therapeutic efficacy, and this phenomenon is useful for treating peptic ulcers. Proton pump inhibitors are the best category of the drug in polymeric nanoparticle form, according to the review, and produce better results than other drug categories. When standard dose forms are compared to novel drug delivery systems (NDDS) dosage forms, we discover that NDDS is more effective and patient compliance is higher.

## CONCLUSION

We can treat PU with high drug potency, bioavailability and efficacy by using formulations containing NPs, resulting in reduced dosing frequency. A lot of research has been done to better understand how nanoparticles heal peptic ulcers, but one of the 4,444 hardest parts of characterizing is their microscopic size. The charge carriers are about 200 nm in size and narrow in size distribution. Nano-sized devices with a diameter of fewer than 50 nanometres can easily enter most cells, while those with a diameter of fewer than 20 nanometres can easily exit blood arteries as they travel in the body. Nanoscale devices can easily interact with biomolecules both on the surface and inside cells due to their small size.

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## Author Contribution-

All authors contributed equally towards the data collection, data analysis & compilations.

## REFERENCES

- Spósito L, Fortunato GC, Furquim de Camargo BA, Dos Santos MA, de Souza PMC, Meneguim AB, et al. Exploiting drug delivery systems for an oral route in the peptic ulcer disease treatment," *J. Drug Target.*, vol. 0, no. 0, pp. 1–19, 2021, doi: 10.1080/1061186X.2021.1904249.
- Singh AK, Singh SK, Singh PP, Srivastava AK, Pandey KD, Kumar A, et al. "Biotechnological aspects of plants metabolites in the treatment of ulcer: A new perspective," *Biotechnol. Reports*, vol. 18, p. e00256, 2018, doi: 10.1016/j.btre.2018.e00256.
- Chaubey P, Mishra B, "Mannose-conjugated chitosan nanoparticles loaded with rifampicin for the treatment of visceral leishmaniasis," *Carbohydr. Polym.*, vol. 101, no. 1, pp. 1101–1108, 2014, doi: 10.1016/j.carbpol.2013.10.044.
- El-Bialy T, *Nanotechnology in Orthodontics-2: Facts and Possible Future Applications*. Elsevier Inc., 2012.
- Guardia P, Batle-Brugal B, Roca AG, Iglesias O, Morales MP, Serna CJ et al., "Surfactant effects in magnetite nanoparticles of controlled size," *J. Magn. Magn. Mater.*, vol. 316, no. 2 SPEC. ISS., pp. 756–759, 2007, doi: 10.1016/j.jmmm.2007.03.085.
- Lv Q, Zhang B, Xing X, Zhao Y, Cai R, Wang W et al., "Bio-synthesis of copper nanoparticles using *Shewanella lochia* PV-4 with antibacterial activity: Novel approach and mechanisms investigation," *J. Hazard. Mater.*, vol. 347, no. 2010, pp. 141–149, 2018, doi: 10.1016/j.jhazmat.2017.12.070.
- Wang Y, Li P, Tran TTD, Zhang J, Kong L. "Manufacturing techniques and surface engineering of polymer-based nanoparticles for targeted drug delivery to cancer," *Nanomaterials*, vol. 6, no. 2, 2016, doi: 10.3390/nano6020026.
- Zielinska A, Carreiro F, Oliveira AM, Neves A, Pires B, Nagaswamy Venkatesh D, et al. "Polymeric Nanoparticles: Production, Characterization, Toxicology and Ecotoxicology," *Molecules*, vol. 25, no. 16, 2020, doi: 10.3390/molecules25163731.
- Kang Y, Huang Y, Yang R, Zhang C. "Synthesis and properties of core-shell structured Fe(CO)<sub>5</sub>/SiO<sub>2</sub> composites," *J. Magn. Magn. Mater.*, vol. 399, pp. 149–154, 2016, doi: 10.1016/j.jmmm.2015.09.061.
- Nassif M, Elaskary FS. "Nanotechnology and Nanoparticles in Contemporary Dental Adhesives," *Nanobiomaterials Clin. Dent.*, pp. 131–164, 2012, doi: 10.1016/B978-1-4557-3127-5.00007-6.
- Brooks FP, "The pathophysiology of peptic ulcer disease," *Dig. Dis. Sci.*, vol. 30, no. 11 Supplement, pp. 15–29, 1985, doi: 10.1007/BF01309381.
- Hasnath Siddique DRA, "Prevalence of Peptic Ulcer Disease among the Patients with Abdominal Pain Attending the Department Of Medicine in Dhaka Medical College Hospital, Bangladesh et al.," *IOSR J. Dent. Med. Sci.*, vol. 13, no. 1, pp. 05–20, 2014, doi: 10.9790/0853-13190520.
- Kron J, "Peptic ulcer disease," *J. Complement. Med.*, vol. 7, no. 1, pp. 12–19, 2008, doi: 10.1300/j100v01n03\_04.
- Ivanova N, Gugleva V, Dobрева M, Pehlivanov I, Stefanov S, Andonova V, et al. Pathophysiology of Gastric Ulcer Development and Healing: Molecular Mechanisms and Novel Therapeutic Options," *Intech*, vol. I, no. tourism, pp. 114–142, 2016.
- Snowden FM, "Emerging and reemerging diseases: a historical perspective. (Special Issue: Immunology of emerging infections)," *Immunol. Rev.*, vol. 225, pp. 9–26, 2008.
- Low VHS. "Peptic ulcer disease," *Abdom. Imaging*, vol. 9783642133, pp. 383–390, 2013, doi: 10.1007/978-3-642-13327-5\_18.
- Fisher J, Gitu AC. Diagnosis and treatment of peptic ulcer disease and *H. pylori* infection," *Am. Fam. Physician*, vol. 91, no. 4, pp. 236–242, 2015.
- Moayyedi P, Talley NJ, Fennerty MB, Vakil N, et al., "Can the clinical history distinguish between organic and functional dyspepsia?" *J. Am. Med. Assoc.*, vol. 295, no. 13, pp. 1566–1576, 2006, doi: 10.1001/jama.295.13.1566.
- T. Chatila, M. Bilal, and P. Guturu, et al., "Evaluation and management of acute pancreatitis," *World J. Clin. Cases*, vol. 7, no. 9, pp. 1006–1020, 2019, doi: 10.12998/wjcc.v7.i9.1006.
- Gomes CA, Junior CS, Di Saverio S, Gomes CC, Sartelli M, Kelly MD et al. "Acute calculous cholecystitis: Review of current best practices," *World J. Gastrointest. Surg.*, vol. 9, no. 5, p. 118, 2017, doi: 10.4240/wjgs.v9.i5.118.
- G. R. Lichtenstein, Proton pump inhibitors," *Gastroenterol. Hepatol.*, vol. 14, no. 3, p. 135, 2018.
- El Rouby N, Lima JJ, Johnson JA, et al. "Proton pump inhibitors: from CYP2C19 pharmacogenetics to precision medicine,"



- Expert Opin. Drug Metab. Toxicol., vol. 14, no. 4, pp. 447–460, 2018, doi: 10.1080/17425255.2018.1461835.
23. Taheri PA, Mahdianzadeh F, Shariat M, Sadeghi M. “Combined therapy in gastroesophageal reflux disease of term neonates resistant to conservative therapy and monotherapy: A clinical trial,” *J. Pediatr. Neonatal Individ. Med.*, vol. 7, no. 2, pp. 1–8, 2018, doi: 10.7363/070201.
  24. E. E. Guidelines “Entitlement Eligibility Guidelines Peptic Ulcer Disease,” no. February 2005.
  25. Boselli I, Lopez H, Zhang W, Cai Q, Giannone VA, Li J et al., “Classification and biological identity of complex nano shapes,” *Commun. Mater.*, vol. 1, no. 1, pp. 1–12, 2020, doi: 10.1038/s43246-020-0033-2.
  26. Smitha KT, Nisha N, Maya S, Biswas R, Jayakumar R. “Delivery of rifampicin-chitin nanoparticles into the intracellular compartment of polymorphonuclear leukocytes,” *Int. J. Biol. Macromol.*, vol. 74, pp. 36–43, 2015, doi: 10.1016/j.ijbiomac.2014.11.006.
  27. Tiwari AD, Mishra AK, Mishra SB, Kuvarega AT, Mamba BB. “Stabilisation of silver and copper nanoparticles in a chemically modified chitosan matrix,” *Carbohydr. Polym.*, vol. 92, no. 2, pp. 1402–1407, 2013, doi: 10.1016/j.carbpol.2012.10.008.
  28. Yadi M, Mostafavi E, Saleh B, Davaran S, Aliyeva I, Khalilov R, et al. “Current developments in green synthesis of metallic nanoparticles using plant extracts: a review,” *Artif. Cells, Nanomedicine Biotechnol.*, vol. 46, no. sup3, pp. S336–S343, 2018, doi: 10.1080/21691401.2018.1492931.
  29. Bohrey S, Chourasiya V, Pandey A. “Polymeric nanoparticles containing diazepam: Preparation, optimization, characterization, in-vitro drug release and release kinetic study,” *Nano Converg.*, vol. 3, no. 1, pp. 3–9, 2016, doi: 10.1186/s40580-016-0061-2.
  30. Arnaud Mayence. Design and characterization of nanoparticles and their assemblies. 2016.
  31. Pal SL, Jana U, Manna PK, Mohanta GP, Manavalan R. “Nanoparticle: An overview of preparation and characterization,” *J. Appl. Pharm. Sci.*, vol. 1, no. 6, pp. 228–234, 2011.
  32. Lohat SK, Kumar S, Gaba P. “An Overview: Preparation Characterization and Applications of Nanoparticles,” *J. Drug Deliv. Ther.*, vol. 10, no. 6-s, pp. 159–167, 2020, doi: 10.22270/jddt.v10i6-s.4398.
  33. Krukemeyer MG, Kren V, Huebner F, Wagner W, Resch R. “History and Possible Uses of Nanomedicine Based on Nanoparticles and Nanotechnological Progress,” *J. Nanomed. Nanotechnol.*, vol. 06, no. 06, 2015, doi: 10.4172/2157-7439.1000336.
  34. Harrison ME, Anderson MA, Appalaneni V, Banerjee S, Ben-Menachem T, Cash BD et al., “The role of endoscopy in the management of patients with known and suspected colonic obstruction and pseudo-obstruction,” *Gastrointest. Endosc.*, vol. 71, no. 4, pp. 669–679, 2010, doi: 10.1016/j.gie.2009.11.027.
  35. Betala S, Varma MM, Abbulu K. Formulation and Evaluation of Sustained Release Microspheres of Metoprolol,” *Int. Res. J. Pharm.*, vol. 8, no. 11, pp. 103–108, 2017, doi: 10.7897/2230-8407.0811226.
  36. Tiruwa R. “A review on nanoparticles – preparation and evaluation parameters,” *Indian J. Pharm. Biol. Res.*, vol. 4, no. 2, pp. 27–31, 2016, doi: 10.30750/ijpbr.4.2.4.
  37. Datta N, Pal M, Roy U, Mitra R, Pradhan A. “WJPR,” *Infection*, vol. 13, no. 10, p. 15, 2014, doi: 10.20959/wjpr201810-12383.
  38. Ito Y, Arai H, Uchino K, Iwasaki K, Shibata N, Takada K, et al., “Effect of adsorbents on the absorption of lansoprazole with surfactant,” *Int. J. Pharm.*, vol. 289, no. 1–2, pp. 69–77, 2005, doi: 10.1016/j.ijpharm.2004.10.010.
  39. Alai M. “Application of nanoparticles for oral delivery of acid-labile lansoprazole in the treatment of gastric ulcer: In vitro and in vivo evaluations,” *Int. J. Nanomedicine*, vol. 10, no. 2, pp. 4029–4041, 2015, doi: 10.2147/IJN.S82366.
  40. Payab S, Davaran S, Tanhaei A, Fayyazi B, Jahangiri A, Farzaneh A et al. “Triamcinolone acetonide-Eudragit® RS100 nanofibers and nanobeads: Morphological and physicochemical characterization,” *Artif. Cells, Nanomedicine Biotechnol.*, vol. 44, no. 1, pp. 362–369, 2016, doi: 10.3109/21691401.2014.953250.
  41. Kuna L, Jakab J, Smolic R, Raguz-Lucic N, Vcev A, Smolic M, et al., “Peptic ulcer disease: A brief review of conventional therapy and herbal treatment options,” *J. Clin. Med.*, vol. 8, no. 2, 2019, doi: 10.3390/jcm8020179.
  42. Comoglu T, Gonul N, Dogan A, Basci N. “Development and in vitro evaluation of pantoprazole-loaded microspheres,” *Drug Deliv.*, vol. 15, no. 5, pp. 295–302, 2008, doi: 10.1080/10717540802006864.
  43. Hoa LTM, Chi NT, Nguyen LH, Chien DM. “Preparation and characterization of nanoparticles containing ketoprofen and acrylic polymers prepared by emulsion solvent evaporation method,” *J. Exp. Nanosci.*, vol. 7, no. 2, pp. 189–197, 2012, doi: 10.1080/17458080.2010.515247.
  44. Hoa LTM, Chi NT, Triet NM, Nhan LNT, Chien DM. “Preparation of drug nanoparticles by an emulsion evaporation method,” *J. Phys. Conf. Ser.*, vol. 187, pp. 1–4, 2009, doi: 10.1088/1742-6596/187/1/012047.
  45. Poovi G. “Preparation and characterization of Rapaglinide Loaded Chitosan Polymeric Nanoparticles,” *IEEE Nanotechnol. Mag.*, vol. 5, no. 1, p. 3, 2011, doi: 10.1109/MNA-NO.2010.939835.
  46. Ghaderi S, Ghanbarzadeh S, Hamishehkar H “Evaluation of different methods for preparing nanoparticle containing gamma oryzanol for potential use in food fortification,” *Pharm. Sci.*, vol. 20, no. 4, pp. 130–134, 2015, doi: 10.5681/PS.2015.001.
  47. Guo S, Liang Y, Liu L, Yin M, Wang A, Sun K et al. “Research on the fate of polymeric nanoparticles in the process of the intestinal absorption based on model nanoparticles with various characteristics: size, surface charge and pro-hydrophobics,” *J. Nanobiotechnology*, vol. 19, no. 1, pp. 1–21, 2021, doi: 10.1186/s12951-021-00770-2.
  48. Osorio R, Alfonso-Rodríguez CA, Medina-Castillo AL, Alaminos M, Toledano M. “Bioactive polymeric nanoparticles for periodontal therapy,” *PLoS One*, vol. 11, no. 11, pp. 1–18, 2016, doi: 10.1371/journal.pone.0166217.
  49. Hussain M. “Formulation and evaluation of Ethambutol polymeric Nanoparticles,” *Int. J. Appl. Pharm.*, vol. 12, no. 4, pp. 207–217, 2020.
  50. Nagarajan E, Shanmugasundaram P, Ravichandiran V, Vijayalakshmi A, Senthilnathan B, Masilamani K, et al. “Development and evaluation of chitosan-based polymeric nanoparticles of an antiulcer drug Lansoprazole,” *J. Appl. Pharm. Sci.*, vol. 5, no. 4, pp. 20–25, 2015, doi: 10.7324/JAPS.2015.50404.
  51. Kaushik A, Sharma HK. “FORMULATION AND EVALUATION OF CETUXIMAB LOADED POLYMERIC NANOPARTICLES,” *IJPSR*, vol. 10, no. 1, pp. 1–23, 2016, doi: 10.13040/IJPSR.0975-8232.10(1).266-71.
  52. Rodrigues DF, Do Couto RO, Sinisterra RD, de Jensen CE. “Novel eudragit-based polymeric nanoparticles for sustained release of simvastatin,” *Brazilian J. Pharm. Sci.*, vol. 56, pp. 1–12, 2020, doi: 10.1590/s2175-97902019000418363.
  53. Tavares EJM, De Araújo DR, Fraceto LF. “Ivermectin-loaded polymeric nanoparticles: Screening the effects of polymers, methods, and the usefulness of mathematical models,” *J. Na-*

- nosci. Nanotechnol., vol. 17, no. 6, pp. 4218–4234, 2017, doi: 10.1166/jnn.2017.13111.
54. El Hady WEA, Mohamed EA, El-Aazeem Soliman OA, El-Sabagh HM. “In vitro-in vivo evaluation of chitosan-PLGA nanoparticles for potentiated gastric retention and anti-ulcer activity of diosmin,” *Int. J. Nanomedicine*, vol. 14, pp. 7191–7213, 2019, doi: 10.2147/IJN.S213836.
  55. Safarov T, Kiran B, Bagirova M, Allahverdiyev AM, Abamor ES. “An overview of nanotechnology-based treatment approaches against *Helicobacter Pylori*,” *Expert Rev. Anti. Infect. Ther.*, vol. 17, no. 10, pp. 829–840, 2019, doi: 10.1080/14787210.2019.1677464.
  56. Jain AK, Jain SK. “Development and characterization of nanolipobeads-based dual drug delivery system for *H. Pylori* targeting,” vol. 2330, no. 6, pp. 593–603, 2013, doi: 10.3109/1061186X.2013.784978.
  57. Ramesh KD, Amol K, Jaydeep P. “Formulation and in-vitro Evaluation of floating tablets of Antibiotics used in the treatment of Peptic ulcer,” vol. 11, no. 1, pp. 1–7, 2021, doi: 10.5958/2231-5713.2021.00004.0.
  58. Kumar PR, Dodddayya H, Reddy SR. “Design and evaluation studies on novel floating tablets for peptic ulcer treatment,” *J. Adv. Pharm. Educ. Res.* 2, vol. 176, no. 2, pp. 159–176, 2011.
  59. Jain S, Jain N, Kor ML, Kumar UK, Jain AK. “Development and optimization of mucoadhesive microballons of nizatidine for management of peptic ulcer,” *Pharm. Sci. Dev. Res.*, vol. 6, pp. 21–29, 2020.
  60. Strasser M, Noriega P, Löbenberg R, Bou-Chacra N, Bacchi EM. “Antiulcerogenic potential activity of free and nanoencapsulation *Passiflora serratodigitata L.* extracts,” *Biomed Res. Int.*, vol. 2014, 2014, doi: 10.1155/2014/434067.
  61. Patel DJ, Patel JK. “Design and Evaluation of Famotidine Mucoadhesive Nanoparticles for Aspirin Induced Ulcer Treatment,” no. June 2014, 2013, doi: 10.1590/S1516-89132013000200007.
  62. Gupta R, Prajapati SK, Pattnaik S, Bhardwaj P. “Formulation and evaluation of novel stomach specific floating microspheres bearing famotidine for treatment of gastric ulcer and their radiographic study,” *Asian Pac. J. Trop. Biomed.*, vol. 4, no. 9, pp. 729–735, 2014, doi: 10.12980/APJTB.4.201414B73.
  63. Radwan MF, El-moselhy MA, Alarif WM, Orif M, Alruwaili NK, Alhakamy NA. “Optimization of Thymoquinone-Loaded Self-Nanoemulsion for Management of Indomethacin-Induced Ulcer,” *Dose-Response An Int. Journal*, vol. 1, no. June, pp. 1–9, 2021, doi: 10.1177/15593258211013655.
  64. H. Journals, Formulation and Evaluation of Novel Drug Delivery System for Treatment of Peptic Ulcer,” no. 1, 2017.
  65. Bangun H. “Anti-ulcer effect of gastroretentive Drug Delivery system of Alginate Beads Containing Turmeric Extract Solid Dispersion,” *Mathcad J Med Sci*, vol. 05, no. Jan, pp. 19–27, 2021.
  66. Chaudhary R, Basavaraj BV, Bharath S, Deveswaran R. “Extended-Release Gastro Retentive Mucoadhesive Bilayer Tablet of an Anti-Ulcer Drug,” *MSRUAS-SASTech Journal*, vol. 15, no. 1, pp. 41–44.
  67. Mahurkar N, Sayeed SM. “Synergistic Antiulcer Effect of Melatonin and Esomeprazole Combination in Pylorus Ligation, Ethanol, Aspirin-induced Peptic Ulcers,” *Asian J. Pharm. Res.*, vol. 5, no. 1, pp. 10–14, 2015, doi: 10.5958/2231-5691.2015.00002.7.
  68. Bhalekar MR, Kadam NM, Patil NH, Gawale NS, Madgulkar A. Novel ion-exchange resin-based combination drug-delivery system for treatment of gastroesophageal reflux diseases, *Braz J. Pharm Sci.* 46 (2) June 2010.