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Design and Evaluation of Mesalamine-Loaded Nanospheres for Site-Specific Drug Delivery in Ulcerative Colitis Treatment

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Abstract

Colon-specific drug delivery systems (CSDDS) have gained significant attention due to their therapeutic advantages in treating local colonic diseases such as inflammatory bowel disease (IBD), ulcerative colitis (UC), Crohn's disease, and colorectal cancer. Conventional drug delivery systems fail to provide targeted release at the colon, leading to systemic side effects and reduced therapeutic efficacy. This study aimed to develop and evaluate colon-targeted nanosphere formulations of mesalamine (5-aminosalicylic acid) using Eudragit RS and Eudragit L polymers for site-specific delivery to the colon. Nanospheres were prepared by the nanoprecipitation method, characterized for particle size, zeta potential, drug entrapment efficiency, morphology, and in-vitro drug release. The nanospheres were subsequently compressed into tablets and coated with cellulose acetate phthalate. Preformulation studies, FTIR compatibility studies, DSC thermal analysis, and XRD were conducted. In-vivo evaluation was performed using DSS-induced colitis model in BALB/c mice. The optimized formulation F2 (Eudragit RS, 500 mg polymer) demonstrated 96% drug entrapment efficiency and released 96.24% drug within 15 hours under simulated colonic conditions. Tablet formulation F3 exhibited maximum drug release of 96.58% at 17 hours. Stability studies at accelerated conditions confirmed formulation stability over three months. In-vivo results showed significant reduction in disease activity index (DAI), CRP, ESR, and WBC levels, with histopathological studies confirming near-complete mucosal recovery. These findings suggest mesalamine nanosphere tablets as a promising colon-targeted drug delivery platform.

Keywords: Colon-specific drug delivery, Mesalamine, Nanospheres, Eudragit, Ulcerative colitis, Inflammatory bowel disease, Nanoprecipitation.

1. Introduction

Drug delivery systems aim to regulate the location, timing, and rate of drug release within the body to improve efficacy and safety. Among various administration routes, the oral drug delivery system has been the most practical, widely recognized, and preferred method for administering therapeutic drugs over several decades. Modern pharmaceutical science has focused on developing cost-effective, safe, and efficacious formulations to promote human health and well-being. The optimal dosage schedule for pharmacological therapy is one that instantly reaches the targeted therapeutic concentration of the drug in plasma and maintains it throughout the treatment period [1,2].

Conventional dosage forms often fail to sustain medication plasma levels within the therapeutic range. Repeated drug administration at fixed dose intervals results in saw-tooth kinetics, characterized by significant peaks and troughs in drug concentration over time. This unpredictability represents a fundamental pharmacokinetic limitation of traditional formulations [3]. Controlled drug delivery systems address this challenge by administering the medication at a predefined rate for a predetermined time period, either locally or systemically. Modified release features of oral dosage forms have been described by various terms: controlled release, prolonged release, sustained release, delayed release, and repeated action release [4].

The fundamental principle behind a controlled drug delivery system involves optimizing a drug's biopharmaceutical, pharmacokinetic, and pharmacodynamic qualities to minimize side effects while maximizing efficacy using the least drug quantity. Most controlled release systems for oral use rely on diffusion, dissolution, or a combination of both to regulate the rate of drug release. Such systems may be categorized as continuous release systems, delayed transit systems, or delayed release systems based on the mechanism and site of drug release [5,6].

When localized colonic drug delivery is necessary, physiological differences in pH, motility, and enzyme activity among the stomach, small intestine, and large intestine create significant challenges. Targeted drug delivery into the colon is particularly desirable for the local treatment of conditions including ulcerative colitis, inflammatory bowel disease, amoebiasis, colonic cancer, Crohn's disease, and for systemic distribution of protein and peptide medicines [7]. The colon-specific drug delivery system (CDDS) should protect the drug during transit through the upper gastrointestinal tract, ensuring that neither the drug nor the bioactive agent is degraded before reaching the colon [8].

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CDDS protects peptide drugs from hydrolysis and enzymatic degradation in the duodenum and jejunum, releasing the drug into the ileum or colon to increase systemic bioavailability. The colon is considered a suitable absorption site for peptides and protein drugs due to: (i) less diversity and intensity of digestive enzymes; (ii) significantly lower comparative proteolytic activity than the small intestine; and (iii) high susceptibility to absorption enhancers with a lengthy residence time of up to five days [9,10].

2. Anatomy and Physiology of the Colon

The gastrointestinal tract (GIT) comprises the stomach, small intestine, and large intestine. The large intestine runs from the ileocecal junction to the anus and is divided into three major sections: the colon, rectum, and anal canal. The colon—the last part of the digestive system in most vertebrates—consists of four portions: ascending, transverse, descending, and sigmoid colons. The proximal (right) colon extends from the cecum to the splenic flexure, while the remaining portion constitutes the distal (left) colon. Arterial supply is provided by branches of the superior and inferior mesenteric arteries [11].

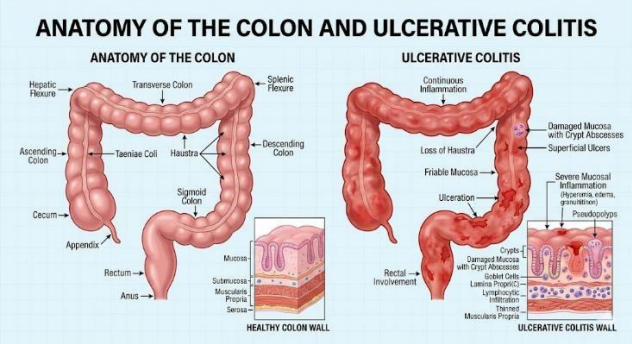

Figure 1: Diagram illustrating anatomy of colon and ulcerative colitis.

The proximal and distal colons differ physiologically in ways relevant to drug absorption. Luminal contents change from liquid in the cecum to semisolid in the distal colon. The colon receives approximately 1.5 liters of water daily, reabsorbing water and salt from solid wastes before excretion. The average adult human male colon is approximately 166 cm in length. The colon's pH ranges from approximately 5.5 to 7.0, varying from the ascending (pH 5.7) to the descending and sigmoid colons (pH 7.0) [12].

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S. No.	Part of Large Intestine	Length (cm)	pH
1	Ascending colon	20-25	5.7
2	Transverse colon	40-45	6.6
3	Descending colon	10-15	7.0
4	Sigmoid colon	35-40	7.0
5	Rectum	12	7.0-7.5
6	Anal canal	3	—

Table 1: Parts of Colon

The colon hosts more than 400 different bacterial species, with a potential population of up to 10^10 bacteria per gram of colonic content. These gut microbes perform a variety of metabolic processes, including azoreduction and enzymatic cleavage, which produce glycosides and other metabolites. These metabolic pathways can be exploited for colon-targeted drug delivery [13].

3. Colonic Diseases and IBD

3.1 Inflammatory Bowel Disease (IBD)

Inflammatory bowel disease (IBD) is an idiopathic inflammatory condition affecting the colon's mucosa and submucosa. Although IBD is limited to the GIT, it can manifest with wide-ranging extraintestinal symptoms. Crohn's disease (CD) and ulcerative colitis (UC) are the two most prevalent types in humans. Both are histologically distinct and clinically similar chronic intestinal inflammations characterized by sporadic acute episodes [14].

Ulcerative colitis (UC), first described by Wilks in 1859, is characterized by chronic inflammation in a continuous and confluent pattern, primarily affecting the colon and rectum. Approximately 80% of children with UC suffer from pancolitis. Endoscopic characteristics include ulcers, erythema, lack of vascular pattern, friability, spontaneous bleeding, and pseudopolyps. Histologically, UC inflammation is limited to the mucosa, with goblet cell depletion, crypt deformation, and crypt abscesses [15].

Crohn's disease (CD), first described in 1932, is characterized by segmental, patchy inflammation spanning any part of the GIT. Approximately 35-40% of CD patients have only colonic involvement, 30-40% have only small intestine disease, and 15-25% have ileum and cecum disease. Unlike UC, CD inflammation affects all intestinal layers. Complications include intestinal neoplasia, obstruction, fistulae, and abscesses [16].

3.2 Colorectal Cancer and Diverticulosis

Colonic tumors arise from the inner wall of the large intestine and may be benign (polyps) or malignant. Colon and rectal cancer are the third most common cancer in men and fourth in women. The incidence has increased due to

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dietary adaptations to western diets. Diverticulosis refers to the development of diverticula—pouches of the colon's mucosal layer—occurring in approximately 20% of cases with diverticulitis. Symptoms include tenesmus, rectal bleeding, fever, and painful urination [17].

4. Strategies for Colon-Targeted Drug Delivery

4.1 pH-Dependent Drug Delivery

The pH gradient along the GIT provides a rational basis for colon targeting. The stomach exhibits pH 1.2, the proximal small intestine pH 6.6, and the distal small intestine approximately pH 7.5. pH-sensitive enteric coatings protect formulations in the stomach but dissolve at higher pH values encountered in the intestine and colon. Methacrylic acid copolymers such as Eudragit L (dissolves at pH 6) and Eudragit S (dissolves at pH 7) are the most widely utilized polymers. The copolymer Eudragit FS dissolves at the higher threshold pH of 7 to 7.5, addressing the issue of premature drug release [18].

4.2 Time-Dependent Drug Delivery

Time-dependent systems release the drug after a predefined lag time equivalent to the GIT transit time to the colon. A lag period of 5-6 hours is generally considered adequate for colon targeting. Polymers used include polyvinyl acetate, hydroxypropyl methyl cellulose (HPMC), HPMC phthalate, cellulose acetate trimelitate, methacrylic acid copolymers, and shellac. The PulsincapTM system was the first formulation designed using this approach, utilizing a hydrogel plug that releases after a specific time interval [19]

4.3 Microbially Triggered Drug Delivery

The colon is rich in microorganisms, primarily anaerobic bacteria such as Bacteroides and Bifidobacterium, which produce specific enzymes capable of degrading biodegradable polymers. Dosage forms coated with natural polysaccharides such as guar gum, pectin, chitosan, and amylose are degraded by colonic microflora, releasing the drug load in the colonic region. The intestinal microbes leave the dosage form intact in the stomach and small intestine where insufficient microbial activity prevents polymer cleavage [20].

4.4 Prodrug Approach

Prodrugs are pharmacologically inactive derivatives of parent drugs that require enzymatic or spontaneous transformation in vivo to release the active drug. The prodrug undergoes minimal hydrolysis in the upper GIT but is enzymatically cleaved in the colon by the resident microflora. Sulfasalazine is a classic prodrug that is broken down by bacterial azoreductase in the colon to release mesalamine and sulfapyridine. Various linkages sensitive to bacterial hydrolysis include

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amino acids, glycosides, glucuronic acids, glucose, galactose, and cellulose [21]

4.5 Polysaccharide-Based Drug Delivery

Naturally occurring polysaccharides—including pectin, chitosan, guar gum, xanthan gum, alginate, dextran, amylose, and inulin—are widely used for colon targeting due to their abundance, biocompatibility, non-toxicity, hydrophilicity, gel-forming capability, and biodegradability. Multiple bacterial enzymes in the colon such as β-D-galactosidase, amylase, pectinase, β-D-glucosidase, and dextranase can hydrolyze their glycosidic bonds. These polysaccharides remain intact in the stomach and small intestine, ensuring colon-specific release [22].

5. Drug and Excipient Profile

5.1 Mesalamine (Drug Profile)

Mesalamine (5-aminosalicylic acid, 5-ASA) is an anti-inflammatory agent with the chemical name 5-Amino-2-hydroxybenzoic acid. Its molecular formula is C7H7NO3 with a molecular weight of 153.135 g/mol and a melting point of 283°C. It is slightly soluble in water (0.84 g/L at 20°C), more soluble in hot water and hydrochloric acid, and practically insoluble in ethanol. The Log P is 1.2. Routes of administration include oral and rectal. Brands include Asacol, Canasa, Lialda, Pentasa, and Rowasa.[23-27]

Mechanism of action: Those with inflammatory bowel illness have higher mucosal synthesis of arachidonic acid metabolites via the lipoxygenase and cyclooxygenase pathways. Mesalamine reduces inflammation by inhibiting cyclooxygenase and lipoxygenase, thereby lowering synthesis of prostaglandins, leukotrienes, and hydroxyeicosatetraenoic acids (HETEs). Approximately 20-30% is absorbed after oral dosing; the remainder acts topically to reduce stomach pain, diarrhea, rectal bleeding, and bowel inflammation. Metabolism occurs in the liver to form N-Acetyl 5-aminosalicylic acid. After oral administration, 20% is eliminated as metabolites in the urine, with a half-life of 12 hours for delayed-release tablets.[28-30]

6. Aim and Objectives

The goal of the current work was to formulate and assess techniques for colon-targeted drug delivery based on nano-formulation of mesalamine.

Specific objectives included:

- Reduction of particle size to improve the drug's low solubility.
- Achieving extended and close contact between the absorbing membrane and the drug delivery device to optimize the rate and extent of drug absorption.

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- Maintaining a steady blood drug concentration to improve patient compliance.
- Lowering the frequency of doses to increase patient compliance.
- Defending the drug against environmental factors such as moisture, light, heat, and oxidation.
- Manufacturing drugs with controlled and sustained release profiles.
- Lessening variation in the drug's plasma levels and improving its therapeutic efficacy.
- Increasing bioavailability and reducing adverse effects.
- Disguising taste and odor.

7. Materials and Methods

7.1 Materials

Mesalamine was obtained from Akums Pharma Ltd., Mumbai. Eudragit L and Eudragit RS were sourced from Evonik Industries and FMC Biopolymer, Mumbai, respectively. Other excipients included magnesium stearate, talc, lactose (Merck Corporation, Germany), dextrose (Signet Corporation, Mumbai), methanol, sodium hydroxide, isopropyl alcohol, and hydrochloric acid from their respective suppliers. All chemicals were of analytical or pharmaceutical grade.

7.2 Preformulation Studies

Preformulation studies were conducted to determine the physicochemical characteristics of mesalamine prior to formulation development. Parameters evaluated included organoleptic characterization (color, taste, odor), solubility profile in various solvents, melting point determination by fused capillary method, FTIR spectroscopy for drug identification and functional group analysis, UV spectrophotometric determination of analytical wavelength, standard calibration curve preparation in 0.1 N HCl and phosphate buffer pH 6.8, partition coefficient determination using n-octanol and phosphate buffer pH 7.4, X-ray diffraction (XRD), differential scanning calorimetry (DSC), and micromeritic properties.

Mesalamine was identified as a white to off-white amorphous powder with a characteristic odor and slight bitter taste. Solubility studies demonstrated that the drug was soluble in 0.1 N HCl (10.23 mg/mL), phosphate buffers of varying pH (6.8: 23.1 mg/mL; 7.4: 23.7 mg/mL), and DMSO (30.21 mg/mL), while being slightly soluble in water (1.21 mg/mL) and insoluble in methanol (0.65 mg/mL). The melting point was determined to be 283°C (range 283–284°C), consistent with the standard value of 283–285°C. FTIR analysis confirmed characteristic peaks at 1600–1400 cm^{-1} (C=C aromatic), 1750–1730 cm^{-1} (C=O ester), 1725–1700 cm^{-1} (C=O carboxylic acid),

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1300–1000 cm^{-1} (C-O), and 3300–2500 cm^{-1} (O-H carboxylic acid). The UV λmax was determined to be 232 nm in phosphate buffer pH 7.4.

The standard calibration curve in phosphate buffer pH 6.8 showed linearity (R^2 = 0.9933) in the concentration range of 10–60 µg/mL with the equation: Absorbance (y) = 0.0169x – 0.0051. In 0.1 N HCl, the calibration curve showed R^2 = 0.9947 with the equation: Absorbance (y) = 0.0159x – 0.0445. The partition coefficient (Log P) was observed as 0.98 against the reported value of 1.1. DSC analysis showed a melting endotherm peak at 283.25°C (onset 279.76°C, end set 285.84°C), confirming drug purity. XRD diffraction peaks at 2θ values of 5.86°, 10.56°, 22.26°, 27.38°, and 32.89° confirmed the crystalline nature of mesalamine.

7.3 Preparation of Nanospheres

Mesalamine nanospheres were prepared using the nanoprecipitation method. Briefly, 200 mg of polymer (Eudragit RS or Eudragit L) was dissolved in 50 mL of water, and the drug was dissolved in 20 mL of methanol. Both solutions were combined and stirred for 30 minutes. Methanol and water were evaporated under reduced pressure using a rotary flash evaporator until 10 mL of solution remained. The resulting suspension was centrifuged at 15,000 rpm for 30 minutes at 40°C. The supernatant was discarded, the residue was washed with distilled water, and the nanospheres were dried overnight at 60°C and stored in desiccators.

Formulation	Mesalamine (mg)	Eudragit RS (mg)	Eudragit L (mg)	Tween 80 (mL)	Methanol (mL)	Water (mL)
F-1	500	250	—	0.2	20	100
F-2	500	500	—	0.2	20	100
F-3	500	—	250	0.2	20	100
F-4	500	—	500	0.2	20	100

Table 2: Different Formulations

7.4 Preparation of Nanosphere Tablets

After passing through #40 sieves, the mesalamine nanosphere was compacted into tablets using a rotary tablet punching machine with talc and magnesium stearate as lubricant. Film coating was applied using a 6% w/v solution of cellulose acetate phthalate in isopropyl alcohol with 2% Tween-80 as plasticizer in a coating pan. A minimum of 100 tablets were prepared for each formulation batch. Six formulation batches (F1–F6) were prepared with varying concentrations of Eudragit RS (F1–F3: 25, 50, 75 mg) and Eudragit L (F4–F6: 25, 50, 75 mg), with corresponding amounts of lactose and dextrose as diluents.

7.5 Evaluation of Nanospheres and Tablets

Nanospheres were evaluated for shape and surface morphology by scanning electron microscopy (SEM), particle size and size distribution by photon correlation spectroscopy

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(Zetasizer), zeta potential by laser Doppler anemometry, drug entrapment efficiency (DEE) by UV spectrophotometry at 232 nm, and FTIR analysis for polymer-drug compatibility. In-vitro drug release studies were conducted using dialysis tubes in simulated GI fluids: 0.1 N HCl for the first 3 hours followed by phosphate buffer pH 6.8. Samples were withdrawn at specified intervals and drug content analyzed at 232 nm.

Tablet formulations were evaluated for pre-compression parameters (angle of repose, bulk density, tapped density, Carr's index, Hausner's ratio) and post-compression parameters (weight variation, hardness, friability, thickness, drug content, and disintegration time). In-vitro drug release was studied using USP Dissolution Apparatus Type II at 75 rpm in 900 mL of 0.1 N HCl for 3 hours followed by phosphate buffer pH 6.8 for the remaining study period.

8. Results and Discussion

8.1 Nanosphere Characterization

SEM analysis confirmed that the drug-loaded, polymer-coated nanospheres were distinct, spherical to oval, with a slightly rough surface. No significant shape change was observed between drug-loaded and polymer-coated nanospheres. Aspect ratio analysis demonstrated values close to 1.0 for all batches: F1 (1.038), F2 (1.040), F3 (1.076), F4 (1.024), confirming good spherical geometry.

Particle size analysis showed that polymer-coated nanospheres were in the size range of 9.14 ± 0.96 to 11.61 ± 0.5 µm, appropriate for reaching the afflicted colitis site (8–15 µm). The polydispersity index (PDI) of 0.245 and 0.267 confirmed uniform, homogeneous distribution. Zeta potential values of –26.78 ± 4.66 mV and –29.36 ± 3.36 mV for uncoated and coated nanospheres, respectively, indicated adequate stability of the formulations through electrostatic repulsion.

Drug entrapment efficiency ranged from 92% to 96% across batches. Formulation F2 demonstrated the highest entrapment efficiency of 96%, making it the optimal nanosphere formulation. Percentage assay and content uniformity results confirmed that F2 had the most consistent drug content (99.8% assay, 100.2% CU) with 98.75% yield.

Formulation	% Entrapment	% Assay	% CU	% Yield
F1	94	93.1	95.8	97.96
F2	96	99.8	100.2	98.75
F3	92	101.8	102.8	98.43
F4	93	100.2	102.2	98.13

Table 3: Nanoparticle Characterization table

8.2 In-Vitro Drug Release from Nanospheres

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In-vitro dissolution studies were conducted in simulated gastrointestinal fluids. During the first 4 hours (acid phase), approximately 7% drug release was observed for all coated nanosphere batches. At 6 hours, approximately 25–28% of the drug had been released following removal of the pH-sensitive coating. By 11 hours, approximately 70–73% drug release was recorded. At pH 7.4 (simulated colonic conditions), approximately 93–96% of the drug was released within 15 hours. Formulation F2 demonstrated the highest drug release of 96.24% at 15 hours, exhibiting the most favorable release profile for colon targeting.

8.3 Pre- and Post-Compression Parameters of Tablets

Pre-compression studies of all nanosphere formulations (F1–F6) showed angles of repose between 20.18° and 22.16°, indicating good flow behavior. Bulk density ranged from 0.352 to 0.376 g/mL and tapped density from 0.423 to 0.442 g/mL. Carr's index values between 12.92 and 15.55% and Hausner's ratios between 1.114 and 1.235 confirmed acceptable flowability and compressibility for all batches.

Post-compression evaluations revealed average tablet weights between 607 and 613 mg, with weight variation within the acceptable limit of ±5%. Thickness ranged from 5.11 to 5.18 mm. Hardness was 5.1 to 5.5 kg/cm². Friability was 0.31 to 0.35% w/w, within the acceptable range of <1%. Drug content ranged from 92.58% (F4) to 97.75% (F3), all within acceptable limits.

8.4 In-Vitro Drug Release from Tablets

In-vitro dissolution studies were performed using USP Dissolution Apparatus Type II. The drug release from all formulations in phosphate buffer pH 6.8 (acceptance criteria: NLT 80%) ranged from 87.92% (F4) to 96.58% (F3) at 17 hours. Formulation F3 showed the maximum drug release of 96.58%, while F2 showed 94.89% release. All formulations met the acceptance criteria. The release kinetics data confirmed that the Higuchi model best described the drug release mechanism for formulation F4 (R^2 = 0.994), indicating diffusion-controlled release. First-order kinetics provided the best fit for F5 (R^2 = 0.997). Similarity factor (f2) analysis demonstrated f2 > 50 for all formulations compared to the innovator, with F4 showing f2 = 65.4 and F3 showing f2 = 48.99.

9. In-Vivo Evaluation (DSS-Induced Colitis Model)

An institutional animal ethics committee-approved in-vivo study was conducted using BALB/c male mice (20–25 g). Acute colitis was induced by administering 4% DSS in drinking water for 7 days. Eight groups (n=10 per group) were evaluated: normal control (vehicle), disease control (DSS alone), and six treatment groups

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receiving formulations F1–F6 at 100 mg/kg via oral gavage for 15 days.

Body weight assessment: The DSS-induced disease control group showed significant weight loss (mean: 200.20 g Day 1 to 169.60 g Day 15), while all formulation-treated groups maintained or gained body weight by Day 15. The formulation F2 group at 20 mg/kg showed mean body weight increasing from 194.40 g (Day 1) to 229.80 g (Day 15). Statistical analysis showed all formulation groups were significant ($p<0.001$) compared to disease control at Day 15.

Macroscopic scores: The disease control group scored 4.0 for all parameters (weight loss, stool consistency, lesion score, macroscopic score). Formulation F2 at 20 mg/kg and plain mesalamine at 30 mg/kg both achieved scores of 1.0 for all parameters, demonstrating near-normal recovery. WBC levels normalized ($10.1 \times 10^3/\mu L$ for F2 at 20 mg/kg vs. $14.9 \times 10^3/\mu L$ for disease control), CRP decreased from 10.1 mg/dL (disease control) to 5.7 mg/dL, and ESR reduced from 23.2 mm/hr to 8.8 mm/hr with optimal treatment.

Histopathological examination of colonic sections (H&E stain) confirmed that the disease control group exhibited extensive mucosal ulceration with inflammatory cellular infiltration, neutrophil and eosinophil infiltration, crypt abscesses, and fibrinoid-like necrosis across all colonic wall layers. The formulation F2 group at 20 mg/kg demonstrated near-complete healing of the colonic mucosa with restoration of mucosal lining glands, closely comparable to the plain mesalamine group at 30 mg/kg. These results confirm the efficacy of nanosphere formulation in delivering mesalamine specifically to the colonic site of inflammation.

10. Stability Study

Stability studies were conducted on the optimized formulation F2 in accordance with ICH guidelines under accelerated conditions (40°C ± 2°C / 75% RH ± 5% RH) for 3 months. The formulation showed no significant changes in physical appearance (color), drug content, or dissolution profile. Drug release after 3 months was 93.94% at 16 hours compared to 96.57% initially, a difference within acceptable limits. The stability results confirm that formulation F2 is stable under accelerated storage conditions and maintains its colon-targeting characteristics.

11. Conclusion

Ulcerative colitis is a chronic idiopathic recurrent disease characterized by colonic mucosal inflammation that can progress to colon cancer in severe cases. Mesalamine, a first-line anti-inflammatory agent for UC treatment, suffers from non-specific systemic distribution and rapid absorption from the small intestine when administered conventionally, resulting in hepatotoxicity, headaches, nausea, and other

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adverse effects. Current standard drug delivery techniques are insufficient for targeted delivery to the afflicted inflammatory site in the colon.

This study successfully developed and evaluated mesalamine nanosphere formulations and tablets using Eudragit RS and Eudragit L polymers for colon-targeted delivery. The nanoprecipitation method produced spherical, uniform nanospheres in the 9–12 µm range with high drug entrapment efficiency (up to 96%). The optimized formulation F2 demonstrated excellent physicochemical properties, acceptable stability, and superior in-vitro drug release (96.24% at 15 hours) under simulated colonic conditions. Tablet formulation F3 showed the highest drug release (96.58% at 17 hours).

In-vivo studies in a DSS-induced colitis mouse model confirmed the therapeutic superiority of nanosphere formulations over conventional delivery. Significant reductions in DAI scores, CRP, ESR, and WBC levels were observed, with histopathology confirming near-complete mucosal recovery comparable to standard mesalamine treatment. Stability studies confirmed formulation integrity over three months under accelerated conditions.

These findings establish mesalamine nanosphere tablets as a promising, effective, and stable colon-targeted drug delivery system. The Eudragit polymer-based nanosphere approach offers a viable strategy to improve therapeutic outcomes, reduce systemic side effects, and enhance patient compliance in the management of inflammatory bowel diseases and other colonic disorders. Further clinical studies are warranted to confirm these promising results in human subjects.

Declaration

Conflicts of Interest

The authors declare that there are no conflicts of interest related to this study. The research was conducted independently, and the findings represent the unbiased results and interpretations of the authors.

Financial Support

This study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request. The data will be made available to qualified researchers for non-commercial purposes only, subject to ethical and privacy considerations. Due to privacy restrictions, participant data cannot be publicly shared, but can be accessed by contacting the corresponding author.

Protection of humans and animals.

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The authors declare that no experiments involving humans or animals were conducted for this research.

Declaration on the use of artificial intelligence.

The authors declare that no generative artificial intelligence was used in the writing of this manuscript

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