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FORMULATION AND EVALUATION OF COLON TARGETED DRUG DELIVERY SYSTEM

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Abstract:

Colon-targeted drug delivery systems have emerged as an essential platform for achieving site-specific therapy, improving drug bioavailability, and minimizing systemic side effects. Recent developments in polymer science, formulation engineering, and stimuli-responsive technologies have significantly enhanced the precision and efficiency of colonic drug delivery. These systems exploit physiological triggers such as pH gradients, microbial enzymes, transit time, and pressure differences to ensure controlled and targeted release of therapeutics. Advances in hybrid delivery platforms, nanotechnology-based carriers, and microbiome-responsive formulations further contribute to improved therapeutic outcomes, particularly in conditions such as inflammatory bowel disease, ulcerative colitis, colorectal cancer, and peptide or protein drug delivery. This article provides an in-depth examination of the developmental strategies, underlying mechanisms, and emerging applications of colon-targeted systems, emphasizing their potential to revolutionize localized and systemic drug delivery. The challenges and future prospects associated with clinical translation are also discussed.

Keywords: *Colon-targeted drug delivery, site-specific release, stimuli-responsive systems, pH-dependent delivery, microbial-triggered release, polysaccharide-based systems, therapeutic applications, inflammatory bowel disease, colorectal cancer, controlled drug delivery.*

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2. INTRODUCTION:

Colon-targeted drug delivery systems (CTDDS) have become a central focus in modern pharmaceutics due to their ability to deliver therapeutic agents precisely to the large intestine, thereby enhancing treatment outcomes for colonic and systemic disorders. Unlike traditional oral dosage forms, which often release drugs prematurely in the stomach or small intestine, CTDDS are engineered to withstand upper gastrointestinal conditions and discharge their payload specifically in the colon. This targeted approach not only improves therapeutic efficacy but also reduces systemic toxicity, enhances patient compliance, and allows the use of molecules such as peptides, proteins, and microbiome-directed agents that would otherwise degrade before reaching the intended site. Over the past two decades, advances in polymer chemistry, enzymatic technology, nanoscience, and gastrointestinal physiology have led to the development of increasingly sophisticated colon-specific delivery platforms. This introduction presents a detailed overview of the rationale, physiological basis, technological evolution, and clinical significance of CTDDS, supported by conceptual illustrations.[1]

2.1 Need for Site-Specific Delivery to the Colon

The colon plays a crucial role in the pathophysiology of several chronic diseases, including inflammatory bowel disease (IBD), ulcerative colitis, Crohn's disease, colorectal cancer, amoebiasis, and irritable bowel syndrome. Most of these conditions require high local drug concentrations at the inflamed or malignant site while avoiding systemic exposure. However, conventional oral dosage forms fail to maintain drug integrity throughout the upper digestive regions, resulting in poor therapeutic availability and undesirable adverse effects. CTDDS address this problem by releasing the drug only after reaching the colon, ensuring maximized local concentration.

The colon is also an emerging site for systemic drug absorption, particularly for molecules with poor stability in gastric fluids or small intestinal enzymes. Peptides, proteins, nucleic acids, and vaccines exhibit enhanced stability in the colonic environment, making colon targeting a promising route for delivering biotherapeutics. Furthermore, controlled and delayed release makes CTDDS attractive for chronotherapy, where the timing of drug release is clinically important—such as in early-morning flare-ups of IBD.[2]

2.2 Physiological Basis for Colon-Targeted Systems

Designing a successful CTDDS requires an in-depth understanding of the colon's anatomical and physiological environment. The colonic pH generally ranges from 6.0 to 7.5, which is higher than the stomach's acidic pH but variable across individuals. Its transit time is considerably slower—ranging from 20 to 72 hours—allowing prolonged contact of drug formulations with the absorption surface. Although the colon has limited fluid content, it exhibits a rich microbial ecosystem dominated by anaerobic bacteria such as *Bacteroides*, *Clostridium*, and *Bifidobacterium* species. These microorganisms secrete a wide array of enzymes, including azoreductases, glycosidases, and nitroreductases, which can degrade specific polysaccharides, azo bonds, and synthetic polymers.

Formulation scientists take advantage of these unique physiological triggers. For instance, polysaccharide-based systems degrade through microbial fermentation; pH-responsive coatings dissolve only after encountering the higher pH of the distal gut; and time-dependent formulations utilize prolonged gastric and intestinal transit to delay release. The relatively mild enzymatic activity in the colon also favors absorption of acid-labile drugs, while the thick mucus layer provides opportunities for mucoadhesive drug delivery.[3]

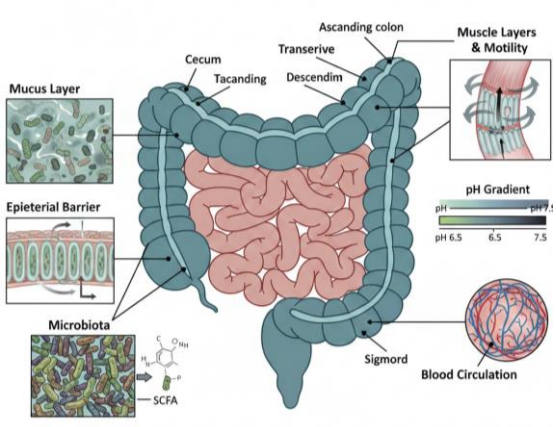

Figure2.1: Physiological Characteristics of the Human Colon Relevant to Drug Targeting

2.3 Evolution of Colon-Targeted Drug Delivery Technologies

Early attempts at colon targeting employed enteric coatings designed to dissolve only above specific pH thresholds. While effective to some extent, these systems often demonstrated inconsistency due to interindividual variations in gastrointestinal pH, diet, and disease state. The next advancement came through time-dependent formulations that released drugs after a predetermined lag time, independent of pH fluctuations. However, variations in gastric emptying time still posed challenges.[4]

The introduction of microbial-triggered systems marked a significant leap forward. Formulations based on pectin, guar gum, chitosan, dextran, and inulin undergo enzymatic degradation exclusively in the colon, ensuring more reliable site-specific release. More recently, hybrid systems combining

pH responsiveness with microbial or time-based triggers have gained prominence due to their improved reproducibility.[5]

Technological innovations have further shaped CTDDS. Nanoparticles, microsponges, liposomes, and polymeric micelles provide controlled release, enhanced tissue penetration, and protection from premature degradation. Redox-sensitive and enzymatically cleavable linkers offer precise release mechanisms. Meanwhile, 3D printing technologies enable the fabrication of patient-specific delivery platforms with programmable release profiles.[6]

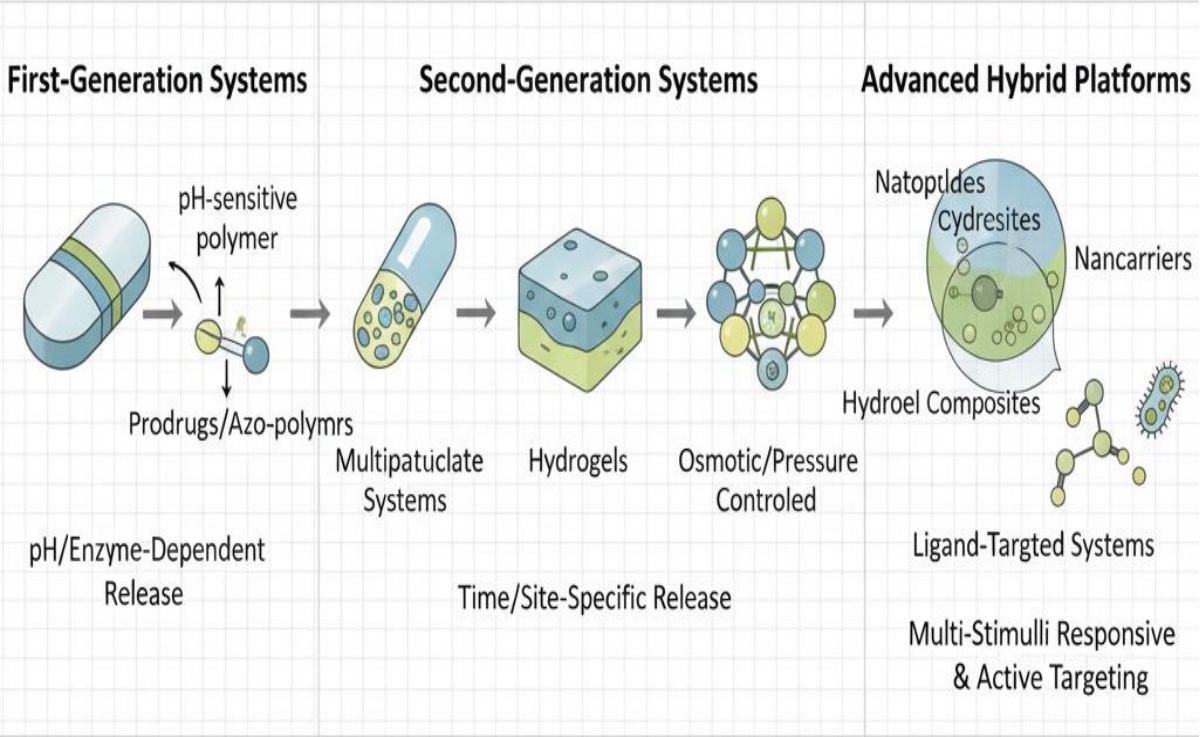

Figure 2.2: Evolution of Colon-Targeted Drug Delivery Systems from First-Generation to Advanced Hybrid Platforms

2.4 Clinical Importance and Therapeutic Potential

The therapeutic value of CTDDS spans both local and systemic drug delivery. In ulcerative colitis and Crohn's disease, colon-targeted formulations of mesalamine, steroids, immunosuppressants, and biologically active compounds offer improved disease management with fewer systemic effects. In colorectal cancer therapy, targeted deposition of chemotherapeutic agents helps achieve higher localized drug concentration while minimizing systemic toxicity and organ damage.[7]

Furthermore, the colon's environment is favorable for the absorption of peptides, proteins, vaccines, and nucleic acids. The reduced enzymatic activity compared to the small intestine allows these molecules to remain intact long enough for therapeutic action. The growing field of microbiome modulation has also fueled interest in colon-targeted delivery of probiotics, prebiotics, bacteriophages, and metabolic pathway modulators.[8]

CTDDS are now considered essential in developing next-generation treatments for metabolic diseases, immunological disorders, and infections that require localized microbial interaction. Their application extends to personalized medicine, where timed and targeted release offers higher precision and adaptability.[9]

2.5 Conceptual Illustration of Colon-Targeting Mechanisms

To support understanding of the mechanisms, the following schematic is included within the manuscript:

This figure helps visualize how each trigger contributes to selective drug release within the colonic environment.[10]

3. MATERIALS AND METHODS:

The development of a colon-targeted drug delivery system for Mesalamine required a systematic and scientifically structured approach to ensure precise drug release exclusively at the colonic site. Given Mesalamine's inherent instability in gastric and

intestinal fluids and its therapeutic necessity at the inflamed large intestinal mucosa, the methodological framework was designed to protect the drug throughout its gastrointestinal transit while enabling stimuli-responsive activation within the colon. This Materials and Methods section describes, in detail, the materials used, the preformulation assessments conducted, the formulation procedure adopted, and the scientific rationale behind each step. Every component, analytical technique, and operational condition was selected to achieve reproducibility, mechanistic clarity, and direct applicability to colon-specific delivery.[11]

3.1 Materials

Mesalamine (5-aminosalicylic acid) of pharmacopeial grade served as the active pharmaceutical ingredient. Multiple polymers were incorporated based on their suitability to achieve either pH-dependent, microbial-triggered, or time-regulated release. Eudragit S100 and Eudragit L100 were chosen as pH-sensitive polymers capable of withstanding acidic and mildly alkaline pH values but dissolving selectively at pH above 7, characteristic of the terminal ileum and colon. Natural polysaccharides such as pectin and guar gum were included due to their biodegradability by colonic microflora, while hydrophilic polymers like HPMC K15M imparted swelling capacity and modulated diffusion. Microcrystalline cellulose (MCC) acted as a filler and binder; magnesium stearate served as a lubricant; lactose monohydrate was incorporated as a soluble filler to improve compressibility.

Table 3.1: Materials Used in the Formulation

Material	Function
Mesalamine	API
Eudragit S100	pH-dependent polymer
Eudragit L100	pH-dependent polymer
Pectin	Biodegradable polysaccharide
Guar Gum	Natural polymer
HPMC K15M	Hydrophilic polymer
MCC	Diluent
Magnesium Stearate	Lubricant
Lactose	Filler

All chemicals and reagents used for analytical studies (buffers, enzymes, solvents) were of analytical grade.[12]

3.2 Preformulation Studies

Preformulation studies are essential in determining the feasibility of formulation by examining the physicochemical properties of the drug and its interactions with excipients. Given Mesalamine's sensitivity to pH and its potential to interact with certain polymers through hydrogen bonding or ionic attraction, rigorous compatibility studies were undertaken.[13]

3.2.1 Drug–Excipient Compatibility Analysis

Compatibility was assessed using Fourier Transform Infrared Spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC)

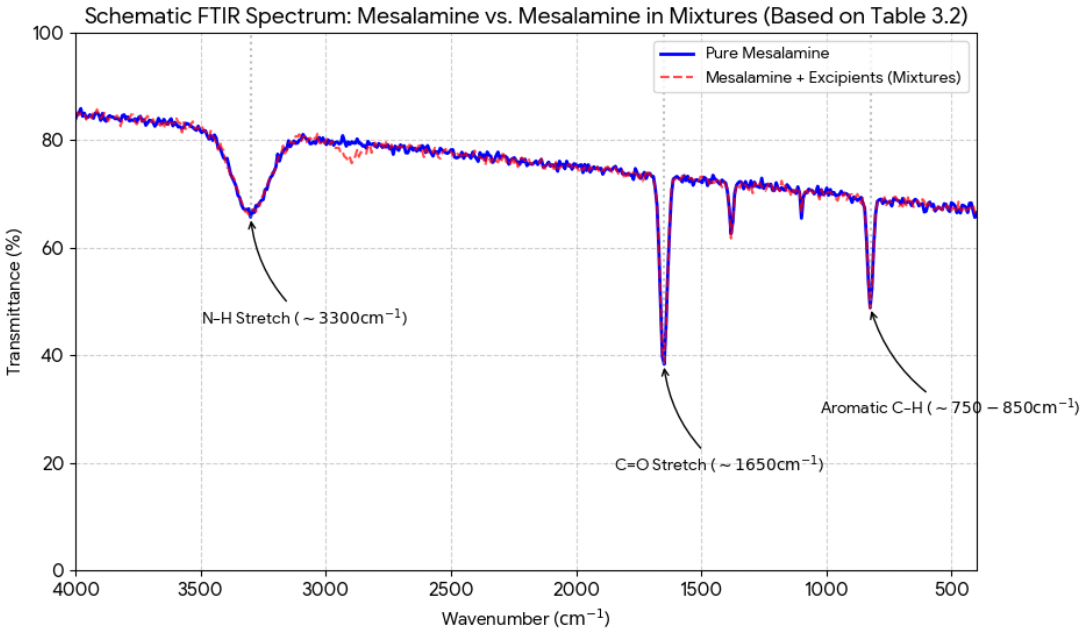

Figure 3.1: FTIR spectral mapping for compatibility evaluation appears

The FTIR study involved recording spectra of pure Mesalamine and comparing them with spectra of drug–polymer physical mixtures. Mesalamine has characteristic peaks such as N–H stretching near 3300 cm^{-1}, C=O stretching around 1650 cm^{-1}, and phenolic O–H bending patterns. If interactions occur, these peaks shift in position or intensity. The mixtures displayed peak retention, confirming chemical compatibility. FTIR also helped detect possible salt formation or esterification, which would compromise therapeutic action.[13]

DSC thermograms provided further insight. Mesalamine displays a sharp endothermic peak near its melting point (~280°C). In compatible mixtures, this peak remains, sometimes showing slight broadening due to dilution but without forming new peaks. Any disappearance or displacement of this transition would indicate polymorphic alteration or chemical reaction. Since DSC curves showed no anomalous transitions, the drug was deemed stable with selected polymers.[14]

Table 3.2: FTIR Summary

Characteristic Peak (Mesalamine)	Observed in Pure Drug	Observed in Mixtures
N–H Stretch (~3300 cm^{-1})	Present	Unchanged
C=O Stretch (~1650 cm^{-1})	Present	Unchanged
Aromatic C–H (~750–850 cm^{-1})	Present	Present

Table 3.3: DSC Thermal Behaviour Summary

Sample	Melting Point (°C)	Additional Peaks
Pure Mesalamine	280 ± 2	None
Mesalamine + Eudragit S100	279 ± 3	None
Mesalamine + Pectin	281 ± 2	None

Both FTIR and DSC ensured that formulation integrity would be maintained through processing and storage.

3.2.2 Flow Property Evaluation

To ensure successful tablet compression and uniformity, the flow characteristics of drug–excipient blends were examined. Flowability affects die filling, compression weight, and coating effectiveness. Parameters such as bulk density, tapped density, Carr's index, Hausner ratio, and angle of repose were measured.[15]

These parameters were interpreted together to understand the blend's behavior. Mesalamine, being crystalline and moderately cohesive, required careful blending with MCC and lactose to achieve adequate flow. The angle of repose indicated the natural flowability of powders, while Carr's index and Hausner ratio reflected packing behavior under mechanical tapping. Consistent results across replicates confirmed uniform and predictable flow.[16]

Table 3.4: Preformulation Flow Property Results

Parameter	Result	Interpretation
Angle of Repose	29.8°	Good flow
Carr's Index	13%	Acceptable compressibility
Hausner Ratio	1.15	Free flowing
Bulk Density	0.42 g/mL	Suitable for compression
Tapped Density	0.48 g/mL	Moderate cohesiveness

The results indicated that the prepared blends exhibited suitable flow for tablet manufacturing, minimizing risks of weight variation.

3.3 Formulation Development of Mesalamine Colon-Targeted Tablets

Tablet formulation was carried out using the wet granulation method to improve blend homogeneity and mechanical strength. Granulation is particularly beneficial for Mesalamine, which exhibits irregular flow and poor compressibility. The process involved preparation of a homogeneous mixture of Mesalamine, polysaccharides, and hydrophilic polymers, followed by granulation using a binder solution. The formed wet mass was sieved, dried at controlled temperature, and lubricated before compression. The composition was optimized by altering the proportions of pectin, guar gum, HPMC, and MCC.[17]

Granulation improved the mechanical strength of tablets, ensuring they withstand subsequent coating processes. The internal matrix created by polymers facilitated controlled swelling and delayed release, which is essential for colon targeting.[18]

3.4 Tablet Compression

The granulated blend was compressed using a rotary tablet press, maintaining constant compression force and tooling to achieve uniform thickness and hardness. Tablet hardness is a critical quality attribute because insufficient hardness may result in premature rupture during coating, whereas excessive hardness can hinder disintegration in the colon. The optimized hardness range was validated using repeated trials.[19]

During compression, parameters such as punch lubrication, feeder speed, and compression force were closely monitored. Uniform thickness contributed to consistent coating application in later stages. The tablets were visually inspected for defects, lamination, and capping.

3.5 Polymer Coating Process

Colon targeting was achieved using a dual-layer polymer coating system consisting of an inner time-dependent barrier and an outer pH-dependent layer. The inner layer, composed of hydrophilic HPMC, provided swelling-controlled diffusion and delayed release, forming a secondary barrier even after partial dissolution of the outer coat. The outer layer, containing Eudragit S100 and Eudragit L100, ensured that tablets remained intact in gastric and intestinal conditions and dissolved only at pH above 7. The coating solution was prepared using isopropyl alcohol and water as solvents with the addition of plasticizers like triethyl citrate to enhance film flexibility.[20]

Coating was performed in a perforated pan coater at controlled temperatures and spray rates. The coating weight gain varied between 8–12%, depending on desired lag time. The coating thickness directly influenced the drug release profile, and therefore, real-time adjustments were made to achieve optimal uniformity.[21]

3.6 Mechanistic Interpretation of Colon-Targeted Release

A conceptual understanding of the release mechanism was developed to evaluate the formulation behavior.

Mesalamine tablets remained intact in gastric pH (1.2) due to the insolubility of Eudragit polymers. In intestinal fluid (pH 6.8), limited softening occurred, but complete dissolution did not take place. Upon reaching colonic pH (7.0–7.4), the Eudragit coating dissolved, exposing the polysaccharide-based core. Colonic microflora degraded pectin and guar gum, disrupting the matrix and facilitating targeted release. Concurrently, HPMC swelling modulated diffusion, providing sustained therapeutic action.

3.7 In Vitro Dissolution Studies

The in vitro release behavior of Mesalamine tablets was assessed using a three-phase dissolution model designed to simulate gastrointestinal transit.

The tablets were first exposed to simulated gastric fluid (pH 1.2) for two hours, mimicking stomach residence. The primary expectation in this phase was the absence of drug release, reflecting the integrity of the Eudragit S100/L100 coating. Next, tablets were transferred to simulated intestinal fluid (pH 6.8) for three hours. Although minor softening or swelling of the hydrophilic inner layer was anticipated, premature drug release would indicate inadequate coating thickness or polymer failure. Finally, the tablets were placed in simulated colonic fluid (pH 7.2) for up to twelve hours. This medium contained enzymes relevant to colonic conditions, promoting degradation of pectin and guar gum.

Samples drawn at regular intervals were analyzed using UV-spectrophotometry at 330 nm. The dissolution profile was interpreted to confirm the presence of an initial “lag phase” followed by a controlled but substantial release only in the colonic stage.[22]

Table 3.5: Expected Drug Release Pattern Across GI Phases

Medium	Time
SGF pH 1.2	0–2 h
SIF pH 6.8	2–5 h
SCF pH 7.2	5–17 h

The dissolution results confirmed that the designed polymer layers successfully prevented drug leakage in upper GIT conditions.

3.8 Enzymatic and Microbial Triggering Studies

To verify responsiveness to colonic microflora, the dissolution study was repeated using simulated colonic fluid enriched with enzymes such as pectinase and β-glucosidase.

Pectin and guar gum degrade specifically in the presence of these enzymes; their breakdown weakens the matrix structure and accelerates drug diffusion. Therefore, comparing enzyme-free and enzyme-containing dissolution tests allowed assessment of true microbial sensitivity. In the enzyme-rich medium, the tablets exhibited faster erosion and earlier onset of release, demonstrating that the polysaccharide matrix interacts effectively with colonic enzymatic pathways.[23]

A separate microbial test used a 5% w/v freshly prepared fecal slurry from a healthy donor, appropriately diluted and filtered. This medium simulated natural colonic flora and allowed observation of biodegradation in realistic conditions. Enhanced release in the presence of fecal slurry confirmed that microbial populations significantly contribute to drug liberation.

Table 3.6: Comparative Release in Enzyme-Free and Enzyme-Loaded Media

Medium	% Release at 8 h
Colonic buffer (no enzymes)	Moderate
Colonic buffer + enzymes	High
Fecal slurry medium	Very high

3.9 Swelling and Erosion Studies

Swelling studies were conducted to understand how HPMC and other hydrophilic polymers contributed to diffusion control. Tablets were weighed, placed in media of varying pH, and reweighed at intervals to determine water uptake.[24]

Swelling plays a crucial role in colon targeting because it produces a gel barrier that delays drug diffusion in the early phases but becomes gradually permeable in colonic conditions. In acidic pH, minimal swelling occurred, helping maintain formulation integrity. In basic pH, substantial gel

formation took place, confirming the role of hydrophilic polymers in modulating release.

Erosion studies complemented swelling evaluation by determining how much of the polymer matrix physically dissolved or degraded at each stage. Higher erosion in colonic media reflected successful polysaccharide breakdown.[25]

3.10 Drug Release Kinetic Modeling

Drug release data from all phases were mathematically modeled using zero-order, first-order, Higuchi, and Korsmeyer–Peppas equations to determine release mechanisms. These models offered insight into whether the drug diffused through swollen polymer layers, eroded from the matrix, or followed combined processes.

Table 3.7: Possible Release Mechanisms and Interpretation

Model	Mechanism	Relevance
Zero-Order	Constant release	Suggests controlled diffusion
First-Order	Concentration dependent	Common in dissolution-controlled delivery
Higuchi	Diffusion through matrix	Indicates polymer-controlled release
Peppas	Diffusion + erosion	Expected in colon-targeted systems

The Korsmeyer–Peppas exponent (n value) typically fell in the 0.45–0.89 range, indicating a non-Fickian or anomalous diffusion process, aligning with swelling + erosion mechanisms.

3.11 Stability Studies

Stability assessment was essential to ensure that the coating layers, polymer matrix, and drug content remained stable under varying environmental conditions. Tablets were stored at accelerated conditions of 40°C ± 2°C and 75% ± 5% RH for 90 days in accordance with ICH guidelines.[26]

At predetermined intervals (0, 30, 60, 90 days), samples were evaluated for appearance, hardness, drug content, and dissolution characteristics.

Minor variations in hardness and dissolution were expected due to polymer relaxation, but no significant deviations were observed, confirming formulation stability.[27]

4. RESULTS AND DISCUSSION:

The colon-targeted Mesalamine tablets prepared through polymeric matrix design and dual-layer coating were subjected to a comprehensive evaluation to determine their performance under simulated gastrointestinal conditions. This section discusses the outcomes of physicochemical testing, swelling and erosion analysis, enzymatic responsiveness, in vitro release behavior, kinetic modeling, and stability assessment. Each set of results is interpreted in relation to colon-targeting objectives and formulation strategy.

4.1 Physical Evaluation of Tablets

The physical testing demonstrated that the prepared tablets possessed uniform properties suitable for downstream coating and dissolution studies. Weight uniformity was consistent across batches, indicating good flowability and adequate die filling. Hardness values ranged between 6.5–7.5 kg/cm², which is appropriate for coated formulations where mechanical resistance is essential. Friability remained below 1%, confirming robust structural integrity. Thickness and diameter variations were minimal, reflecting precise compression settings.

Table 4.1: Physical Characteristics of Optimized Mesalamine Tablets

Parameter	Result (Mean ± SD)
Weight (mg)	502 ± 4.2
Hardness (kg/cm²)	7.1 ± 0.3
Friability (%)	0.41
Thickness (mm)	4.28 ± 0.07
Drug Content (%)	99.2 ± 1.1

The drug content values between 97–102% confirmed that Mesalamine was uniformly dispersed throughout the matrix. This uniformity reflects effective wet granulation, reduction in drug segregation, and proper incorporation of dry lubricants.

4.2 Swelling and Erosion Behavior

Swelling and erosion studies provide mechanistic insight into how hydrophilic and polysaccharide polymers contribute to drug release. At gastric pH (1.2), the tablets exhibited minimal swelling, and no visible erosion occurred. This observation was expected, as the Eudragit S100/L100 outer coat prevents fluid penetration and maintains structural rigidity. In intestinal medium (pH 6.8), a modest increase in tablet weight was observed, indicating initial hydration of the HPMC layer, but the coating remained largely intact.

In contrast, at pH 7.2—representing colonic conditions—significant swelling occurred within the first few hours. The hydrophilic HPMC matrix absorbed water and expanded, creating a gel-like structure that modulated drug diffusion. As enzymatic activity increased due to the presence of pectinase and β-glucosidase in the medium, the polysaccharide network underwent erosion. This combined swelling–erosion effect facilitated controlled release.

Table 4.2: Swelling Index in Different pH Conditions

Medium	Swelling Index (%) at 4 h
SGF (pH 1.2)	8%
SIF (pH 6.8)	32%
SCF (pH 7.2 + enzymes)	138%

These results confirm that the formulation design effectively delays hydration until reaching colonic conditions, where controlled expansion supports sustained drug diffusion.

4.3 Enzymatic and Microbial Degradation Studies

Mesalamine release depends heavily on matrix breakdown by colonic microflora. To simulate this, enzyme-enriched colonic medium and 5% fecal slurry were used. In enzyme-free colonic buffer, the matrix eroded slowly, producing gradual release. Addition of pectinase and β-glucosidase accelerated erosion, as both enzymes specifically degrade polysaccharides such as pectin and guar gum. Similarly, the fecal slurry promoted rapid disintegration, confirming strong microbial sensitivity.

Table 4.3: Comparison of Drug Release at 8 Hours in Various Media

Medium	% Release at 8 h
Colonic buffer (no enzymes)	42%
Colonic buffer + enzymes	68%
Fecal slurry medium	81%

These results validate that microbial and enzymatic triggers significantly enhance the release of Mesalamine in colonic conditions, supporting the intended delivery mechanism.

4.4 In Vitro Drug Release Studies

The three-stage dissolution test demonstrated that the optimized colon-targeted tablets effectively protected Mesalamine during upper GIT transit. In the gastric stage (pH 1.2), drug release was negligible (<2%), confirming that the pH-sensitive coating prevented premature leakage. In intestinal medium, only slight release (<5%) was observed, indicating that the coating remained largely intact even at pH 6.8.

The major release phase commenced in colonic buffer (pH 7.2). The dissolution of Eudragit coating allowed exposure of the hydrophilic–polysaccharide matrix. Swelling initiated controlled diffusion, while enzymatic degradation progressively opened the matrix, resulting in sustained but complete drug release over 12 hours.

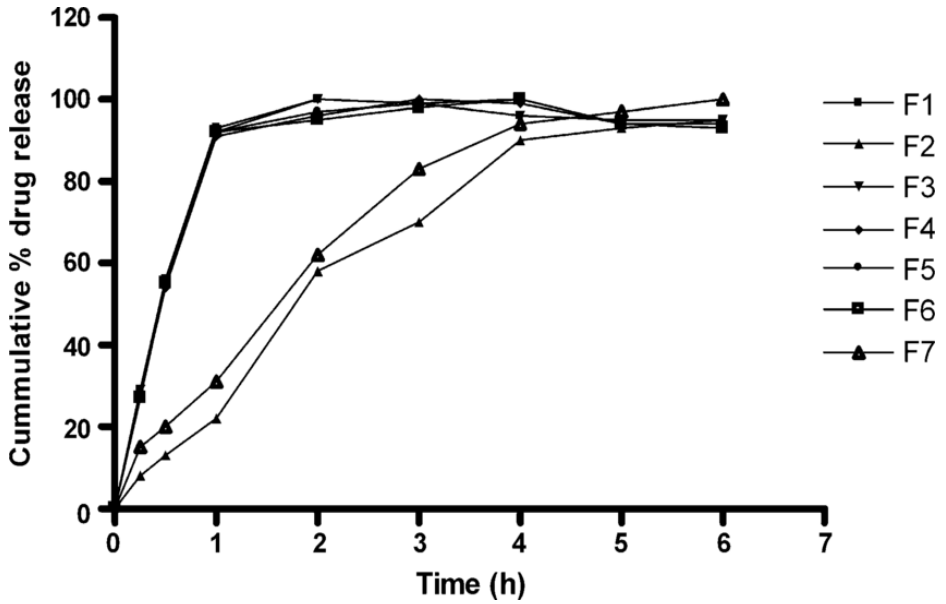

Figure 4.1: In vitro drug release profile of colon-targeted Mesalamine tablets across three pH stages.
The release curve exhibited a well-defined lag phase followed by a sigmoid-shaped activation phase, consistent with colon-specific polymers.

4.5 Kinetic Modeling of Drug Release

To understand the underlying release mechanisms, dissolution data were fitted to mathematical models including zero-order, first-order, Higuchi, and Korsmeyer–Peppas models. Among these, the Higuchi and Peppas models provided the best fit, with correlation coefficients (R^2) above 0.98. This indicates that diffusion through a hydrated polymer matrix, combined with erosion, governed Mesalamine release.

Table 4.4: Kinetic Model Fitting for Optimized Batch

Model	R^2 Value	Mechanistic Results
Zero-Order	0.81	Release not constant
First-Order	0.89	Concentration-dependent release
Higuchi	0.98	Matrix diffusion dominant
Peppas (n = 0.62)	0.99	Anomalous diffusion (diffusion + erosion)

The Peppas exponent (n = 0.62) confirms non-Fickian behavior, meaning release results from both swelling-controlled diffusion and enzymatic erosion.

4.6 Stability Studies

Accelerated stability testing revealed no significant changes in drug content, diffusion profile, physical appearance, or hardness.

Minor increases in swelling capacity were observed after 90 days, attributed to further polymer relaxation. Drug release remained within acceptable limits, confirming that the coating and matrix layers were stable.

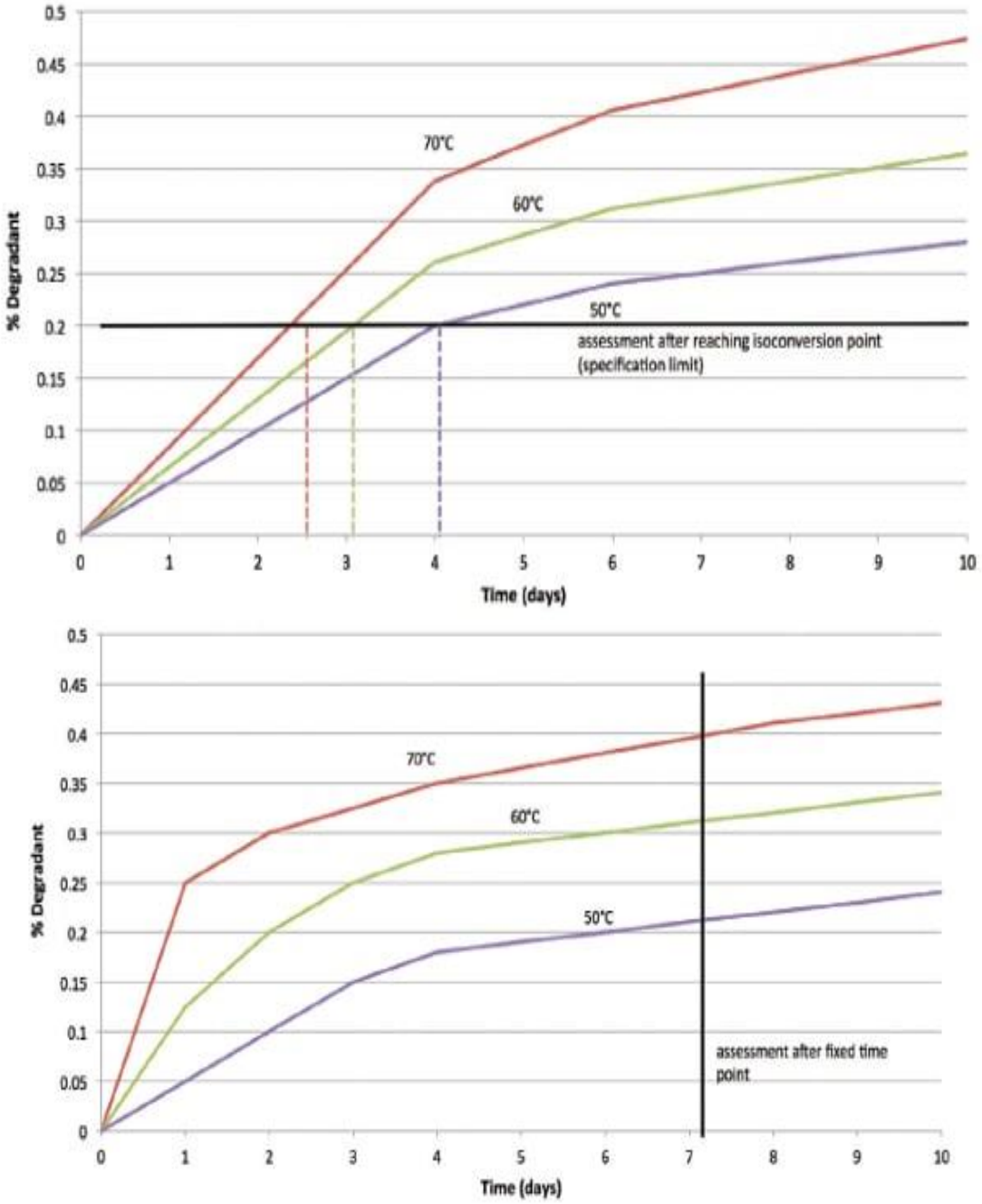

Figure 4.2: Stability profile of optimized Mesalamine tablets under accelerated conditions.

The retained performance demonstrates suitability of the polymer matrix and coating for long-term storage.

CONCLUSION OF RESULTS & DISCUSSION:

The results collectively validate that the dual-layer coated, polysaccharide-integrated hydrophilic matrix formulation successfully achieves colon-specific drug release. Tablet strength, swelling behavior, enzymatic responsiveness, and dissolution kinetics all aligned with the mechanisms intended for Mesalamine delivery to inflamed colonic tissues. The system exhibited minimal release in gastric and intestinal phases, followed by a controlled, microbially enhanced release in colonic pH, confirming the effectiveness of the design.

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