RESEARCH PAPER

Colon-Targeted Delivery of Mesalamine: Formulation, Optimization, In Vitro Evaluation and Roentgenography Using Carboxymethyl Tamarind Gum

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ABSTRACT

Background: Mesalamine, BCS Class IV drug, exhibits poor solubility and requires site-specific delivery to colon for effective management of inflammatory bowel disease. Natural polymers such as Carboxymethyl tamarind (CMT) gum, in combination with pH-sensitive Eudragit S100, can provide controlled and targeted drug release.

Objectives: This study aimed to formulate and optimize colon-targeted mesalamine tablets using CMT gum and Eudragit S100 coating, employing response surface methodology (RSM) for systematic evaluation.

Methods: Solid dispersion (SD) of mesalamine with Kollicoat-IR was prepared by solvent evaporation to enhance solubility. Tablets were formulated by wet granulation using varying concentrations of CMT gum (75, 100, 125 mg) and coated with Eudragit S100 at different levels (2.5%, 5%, 7.5%). Two-factor, three-level factorial design (RSM) was applied with amount of gum (X_1) and coating level (X_2) as independent variables, while % Cumulative drug release (CDR) at 2 h, 5 h, and 8 h were considered as dependent responses. Tablet evaluation and in vitro drug release studies were performed in simulated gastrointestinal fluids.

Results: Factorial design demonstrated that both polymer concentration and coating level significantly influenced mesalamine release. The optimized formulation exhibited minimal release in acidic pH (≤2% at 2 h), controlled release in intestinal pH (≈16–20% at 5 h), and maximum release in colonic pH (≥90% at 8 h). Experimental results were in close agreement with RSM-predicted values, confirming reliability of the optimization model.

Conclusion: Colon-targeted mesalamine tablets using CMT and Eudragit S100 were successfully formulated and optimized. The developed system effectively prevented drug release in upper GIT and provided sustained, site-specific release in colon, making it promising approach for targeted therapy in inflammatory bowel disease.

Keywords: *Carboxymethyl Tamarind Gum, Colon Targeting, Eudragit S100, Mesalamine, Response Surface Methodology, Solid Dispersion*

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1. INTRODUCTION

Poor aqueous solubility of drugs is significant challenge in pharmaceutical development, as it directly limits dissolution, oral absorption, and overall bioavailability.[1,2] SD technology has been widely explored to overcome these limitations. Chiou and Riegelman (1971) first defined SDs as "dispersion of one or more Active pharmaceutical ingredients (APIs) in inert carrier in a solid state." Since then, this technique has been extensively investigated due to its simplicity, reproducibility, and versatility in enhancing the dissolution of poorly soluble drugs.[3,4] The mechanisms underlying SDs include reduction of drug particle size to the molecular level, improved wettability, prevention of drug aggregation, solubilizing effects of the carrier, and possible drug-polymer complexation. Together, these factors improve drug dissolution, enhance gastrointestinal absorption, and consequently increase bioavailability.[5,6]

Mesalamine (5-aminosalicylic acid, 5-ASA) is first-line therapeutic agent widely prescribed for the treatment and maintenance of remission in Inflammatory bowel diseases (IBD), particularly ulcerative colitis.[7–9] It acts locally in the colon by inhibiting cyclooxygenase and lipoxygenase pathways, thereby reducing synthesis of pro-inflammatory mediators such as prostaglandins and leukotrienes.[10] Clinically, mesalamine is considered an effective and well-tolerated alternative in patients who are intolerant or hypersensitive to sulfasalazine. However, its therapeutic

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potential is restricted by its poor aqueous solubility and low permeability. According to Biopharmaceutics Classification System (BCS), mesalamine is classified as Class IV drug, characterized by both low solubility and poor permeability.[9,11] Its absorption from the gastrointestinal tract is reported to be only 20–30% following oral administration. The crystalline nature, limited solubility, and poor flow properties of mesalamine make it a suitable candidate for the development of SDs.

Low solubility not only delays the onset of therapeutic action but also contributes to unpredictable and incomplete absorption of BCS Class II and IV drugs. Dissolution becomes the rate-limiting step in drug absorption, which often translates into variable bioavailability and therapeutic inefficiency. Consequently, formulation strategies aimed at enhancing solubility and dissolution are of utmost importance to achieve consistent plasma drug levels and therapeutic outcomes.

In addition to solubility enhancement, site-specific delivery of mesalamine is critical for therapeutic efficacy in ulcerative colitis and related conditions. Colon-targeted delivery offers several advantages, including localized action at the disease site, reduced systemic side effects, improved patient compliance, and lower dosing frequency.[12] Furthermore, the colon provides a relatively stable environment with near-neutral pH and low enzymatic activity, making it a favourable site for delivery of both conventional small molecules and macromolecules. Colon-targeted systems are also being explored for treatment of other disorders, including Crohn's disease, colorectal cancer, bowel infections, and chronic constipation.[13,14]

To achieve colon-specific drug delivery, two strategies are often combined: the use of natural polysaccharide-based carriers and pH-sensitive coating polymers.[15–17] CMT gum, a modified natural polysaccharide, has gained attention due to its biocompatibility, biodegradability, and ability to undergo microbial degradation in the colon.[18–20] Its high swelling capacity and gel-forming nature make it an excellent matrix-forming agent for sustained release formulations.[21,22] On the other hand, Eudragit S100, methacrylic acid copolymer soluble at pH > 7, has been widely used as a colon-specific coating polymer to prevent premature drug release in acidic environment.[23,24] Thus, a combination of CMT gum and Eudragit S100 offers a dual mechanism for colon targeting-enzyme-triggered degradation and pH-sensitive dissolution.[25,26]

In parallel, polymer selection for SD preparation plays a critical role in solubility enhancement. Traditional hydrophilic polymers such as PEG-6000 and Polyvinylpyrrolidone K30 (PVP K30) have been widely used to improve dissolution but suffer from limitations like recrystallization or incomplete dissolution enhancement.[27,28] Kollicoat-IR, a novel non-ionic, hydrophilic, and mildly surface-active polymer, exhibits excellent aqueous solubility throughout the gastrointestinal tract.[29,30] Its ability to maintain drug supersaturation makes it a promising carrier for poorly soluble drugs such as mesalamine. Combination of conventional and novel polymers in SD preparation may overcome the limitations of individual carriers and provide synergistic solubility enhancement.

In this context, present investigation was designed to improve aqueous solubility and colon-specific delivery of mesalamine. Mesalamine SD were prepared using a combination of conventional polymers (PEG-6000, PVP K30) and a new graft copolymer, Kollicoat-IR, by solvent evaporation. The optimized SDs were incorporated into tablets using CMT gum as a natural matrix polymer, and tablets were coated with Eudragit S100 to achieve pH-triggered colon targeting.

2. MATERIALS AND METHODS:

Mesalamine was purchased from Yarrow Chem Products, Mumbai. Kollicoat IR, PEG-6000, and PVP-K30 were received as gift samples from Alkem Laboratories, Mumbai. Methanol and hydrochloric acid (HCl) were purchased from Loba Chem Pvt. Ltd, Mumbai. Disodium hydrogen phosphate and potassium dihydrogen phosphate were obtained from SD Fine Chem Limited, Mumbai.

2.1 SDs preparation by solvent evaporation[31]

SD of mesalamine was developed by employing methanol as a solvent. Drug and polymers were weighed precisely in multiple proportions and placed in a porcelain dish with enough methanol for them to dissolve. At 40 °C, methanol was evaporated through a heating mantle. The resultant SDs were stored in desiccators (24 hours) after pulverizing. After passing through filter number 100, the dispersions were finally kept in airtight containers until their further processing. SD were assessed for practical yield, drug content, Solubility, FTIR, DSC, PXRD, SEM, in vitro dissolution, and stability assessment.

2.2 Formulation of core tablet using wet granulation

Core tablets were prepared by wet granulation technique. Mesalamine SD equivalent to 600 mg mesalamine was accurately weighed and blended with varying concentrations of CMT (75, 100, and 125 mg) along with lactose as a diluent, and it was passed through #10 sieve. The blend was dried at 60 °C for 2 hours. Polyvinylpyrrolidone K30 (PVP K30) was employed as the binder, while talc and magnesium stearate were used as glidant and lubricant, respectively. Dry blend was granulated using an appropriate quantity of binder solution, passed through sieve, and the wet mass was dried at a controlled temperature. The dried granules were further sieved, lubricated with talc and magnesium stearate, and compressed using a 13 mm punch into core tablets employing a single-punch tablet compression machine.[32,33]

2.2.1 Preparation of different batches using 3^2 full factorial designs

Two-factor, three-level full factorial design (3^2) based on RSM was used to optimize core tablet formulation for colonic delivery using Design-Expert® version 11.0

software. Independent variables were amount of CMT gum (X_1 75, 100, and 125 mg) and the percentage weight gain of Eudragit S100 coating (X_2 2.5, 5.0, and 7.5% w/w of tablet weight), while the dependent variables were the percentage cumulative drug release at 2 h (Y_1), 5 h (Y_2), and 8 h (Y_3). A quadratic polynomial model was fitted to evaluate the effects of main factors, their interactions, and quadratic terms on drug release. ANOVA was employed to assess model significance, adequacy, and fitness, with model validity confirmed through regression coefficients (R^2, adjusted R^2, and predicted R^2) and lack-of-fit tests. Response surface and contour plots were generated to visualize factor–response relationships, while a desirability function was employed to determine the optimal formulation with minimal drug release at 2 h, controlled release at 5 h, and maximum release at 8 h.[34,35]

Table 1: Translation of codes in the actual unit for 3^2 factorial design

Variable levels	Low (-1)	Medium (0)	High (+1)
X_1=quantity of CMT (mg)	75	100	125
X_2 = Concentration of Eudragit S100	2.5	5.0	7.5

Table 2: Variable levels and actual composition of different formulations according 3^2 factorial design

Batch Code	SD containing drug (mg)	Variable levels		Composition of different formulations	
		X_1	X_2	Quantity of CMT (mg)	Concentration of Eudragit S100
F1	600	-1	+1	75	7.5
F2	600	0	-1	100	1.46
F3	600	0	0	100	5
F4	600	0	+1	100	8.5
F5	600	+1	-1	125	2.5
F6	600	+1	+1	125	7.5
F7	600	0	0	100	5
F8	600	+1	0	135.35	5
F9	600	0	0	100	5
F10	600	0	0	100	5
F11	600	-1	-1	75	2.5
F12	600	-1	0	64.64	5
F13	600	0	0	100	5

2.3 Coating with Eudragit S100

The compressed core tablets were coated with Eudragit S100 as the enteric polymer to provide pH-dependent release. The coating solution was prepared by dissolving Eudragit S100 (5 g/100 ml) in organic solvent system consisting of acetone and isopropyl alcohol (50:50, v/v). Triethyl citrate (0.625 g/100 ml) was incorporated as a plasticizer to improve film flexibility. Talc (1%) and titanium dioxide (0.5%) were dispersed into the coating solution, while suitable coloring agents were added in a quantity sufficient to achieve the desired appearance. The coating dispersion was applied to the pre-warmed tablets using a conventional pan coater under controlled process conditions, including inlet temperature 50-55 °C, pan speed 35 -400, spray rate 2, gun bed distance 30 cm, and atomization air pressure 2. Coating was performed until the desired weight gain levels of 2.5%, 5.0%, and 7.5% of the tablet weight were achieved. The coated tablets were then dried adequately to remove residual solvents and stored in airtight containers for further evaluation.[36,37]

2.4 Tablet evaluation

2.4.1 General Appearance: Tablets were examined visually for color, surface texture, shape, and uniformity.

2.4.2 Thickness and diameter: Measured using digital Vernier caliper to ensure uniformity of size.

2.4.3. Weight Variation: Twenty tablets were randomly selected and weighed individually and collectively; % weight variation was calculated and compared with pharmacopeial limits.

2.4.4. Hardness (crushing strength): Determined using a Monsanto or Pfizer hardness tester.

2.4.5 Friability: Evaluated by Roche Fribilator at 25 rpm for 4 min (100 revolutions). A maximum weight loss of not more than 1% was considered acceptable.

2.4.6 Drug content uniformity: Ten tablets were randomly powdered, and an accurately weighed portion equivalent to one tablet was dissolved in suitable solvent and analysed spectrophotometrically/ chromatographically to determine drug content.

2.4.7 In vitro drug release

USP type II (paddle method) dissolution apparatus maintained at 37±0.5 °C was employed for this study. Three-stage sequential dissolution medium was employed to simulate the gastrointestinal environment. Initially, tablets were introduced for 2 h in 900 mL 0.1N HCl (pH 1.2) to mimic gastric conditions, followed by transfer for 3 h to Phosphate buffer solution (PBS), pH 6.8, to represent

intestinal fluid, and finally into PBS (pH 7.4) for the remaining time up to 8–12 h to simulate colonic conditions. The paddle speed was maintained at 50–100 rpm, depending on optimization requirements. At predetermined time intervals, 5 mL aliquots were removed and replaced with identical amount of fresh prewarmed medium, filtered, suitably diluted, and analysed spectrophotometrically at the λmax of mesalamine (≈330 nm) to record percentage drug release. Drug release profiles were fitted to several kinetic models, including zero-order, first-order, Higuchi, and Korsmeyer-Peppas, to clarify the release process. The dissolution data were also utilized to assess the impact of formulation variables. [36–38]

2.4.8 Coating uniformity and weight gain (for coated tablets): The percentage weight gain was calculated to ensure achievement of targeted coating levels (2.5%, 5.0%, and 7.5% w/w). Visual inspection and thickness measurement were carried out to confirm coating integrity.

2.4.10 Surface response study

Design-Expert® software was used to statistically assess the impact of variables on response variables. To find out the response surface curvature, assessment of the design was performed with an equation.

$$Y = b_0 + b_1X_1 + b_2X_2 + b_3X_1X_2 + b_4X_1^2 + b_5X_2^2 \quad \text{Equation 1}$$

Where Y is response variable,

b_0 constant,

$b_1, b_2, \ldots b_5$ the regression coefficient,

X_1, X_2 main effect,

X_1X_2 interaction terms.

2.4.9 In-vivo study (Roentgenography study)

In-vivo roentgenography studies are carried out to evaluate the gastrointestinal transit, disintegration, and site of release of oral dosage forms on White New Zealand rabbits weighing between 1.5-2.5 kg.The subjects are fasted entire night prior administration of tablet formulation. The tablet was rendered radio-opaque by incorporating a suitable material such as barium sulfate, without affecting its performance characteristics. The tablet was gently placed in larynx employing forceps, and 10-15 ml water was administered to aid its passage int oesophagus. Following oral administration of the formulation with a fixed quantity of water, sequential X-ray images are taken at predetermined time (e.g., 0, 1, 2, 4, 6, 8, 12, and 24 hours) using a roentgenographic unit. The obtained images are carefully analysed to determine parameters such as gastric residence time, intestinal transit time, disintegration or fragmentation pattern, and the site of drug release. This non-invasive method allows tracking of dosage form within gastrointestinal tract and provides valuable information on its behaviour under physiological conditions.[39,40]

3 RESULTS AND DISCUSSION

3.1 Characterization of SD

Percentage yield was found to be in the range of 86-99% and drug content was 89-98% of theoretical content, which adheres to the limit of official monographs of the mesalamine formulations in British Pharmacopeia. This assesses how well the drug is loaded in the formulation and uniformly distributed in the physical mixture. Solubility of Kollicoat-IR>PVPK-30>PEG-6000 was the outcome of solubility assessment by polymers in their greatest ratio (1:3). FTIR result revealed that there was no considerable change in principal peaks of the drug, and they were found unchanged in the final formulation of SDs. There were no peaks formed, and no shifting of peaks. DSC confirmed that the drug and polymers were compatible with each other. PXRD diffractogram revealed a lowering of intensity and number of typical diffraction peaks of mesalamine. SD X-ray diffractogram suggested the reduction in crystallinity of the drug and its partial conversion to an amorphous state. SEM photographs of SDs illustrated a reduction in drug particle size with spherical shape that might be attributed to amelioration in dissolution. Surface in SD appeared more porous in nature. Significantly higher dissolution rate was obtained from SDs owing to the absence of aggregation with crystalline drug, water-soluble carrier, which raised wettability, good dispersibility, and drug conversion to amorphous form. It was revealed that SDs were stable even when exposed to temperature and relative humidity stress conditions.

3.2 Characterization of colon-targeted mesalamine tablet

3.2.1 General appearance: The general appearance was a purple, tan, round-shaped tablet

3.2.2 Thickness and diameter

Tablet thickness is measured using a Vernier calliper or digital micrometre to assess dimensional uniformity. Consistent thickness is critical for packaging and coating processes. Thickness values ranged between 4.11 and 4.34 mm, indicating good uniformity across all batches**.** Diameter was 12 mm.

3.2.3 Weight variation

Weight variation is essential quality attribute that ensures uniformity of dosage units and was performed by weighing 20 individual tablets from each batch followed by comparing their individual weights with the average weight. A batch is considered to pass if the weight variation falls within pharmacopeial limits (±5% for tablets weighing more than 250 mg). All formulations (F1–F13) complied with the specified limits, confirming uniformity of fill during compression.

3.2.4 Hardness (Crushing strength)

The mechanical strength of tablets that is, their capacity to endure handling, packing, and transit without shattering is

assessed through hardness testing. It is measured in kg/cm² using a Monsanto or Pfizer hardness tester. The formulations exhibited hardness (Table 3) in the range of 4.1–4.6 kg/cm², which is within the acceptable range for uncoated tablets, ensuring adequate strength while not hindering disintegration.

3.2.5 Friability

It is determined using a friabilator (e.g., Roche friabilator), where pre-weighed tablets are subjected to standardized tumbling and dropping. The friability of all formulations (0.52–0.76%) complied with pharmacopeial specifications, indicating good mechanical resistance. Table 3 presents the results.

3.2.6 Drug content uniformity

This ensures each tablet contains the intended amount of API within the acceptable range (typically 85-115% of the label claim, with RSD ≤6%). The formulations demonstrated drug content values between 91.78% and 99.78%, confirming uniform distribution of drug within the tablet matrix (Table 3).

Table 3: Thickness, hardness, friability, drug content of Batch F1-F13

Batch	Thickness	Hardness	Friability	Drug content	% weight gain
F1	4.11	4.3	0.58	95.23	7.5
F2	4.13	4.4	0.63	94.20	1.46
F3	411	4.4	0.55	93.20	5
F4	4.12	4.1	0.52	97.23	8.5
F5	4.34	4.2	0.66	96.50	2.5
F6	4.16	4.3	0.69	96.13	7.5
F7	4.15	4.6	0.53	96.18	5
F8	4.17	4.5	0.63	95.21	5
F9	4.21	4.1	0.71	91.78	5
F10	4.13	4.2	0.76	97.10	5
F11	4.12	4.5	0.72	99.78	2.5
F12	4.16	4.3	0.70	94.66	5
F13	4.18	4.3	0.66	96.30	5

3.2.7 In Vitro Drug Release

Cumulative drug release (F1 to F13) was evaluated in three different dissolution media: 0.1N HCl, PBS (pH 7.4), and PBS (pH 6.8) over 10 hours. The release studies demonstrated that, for all formulations, drug release in the acidic medium (0.1N HCl) during the initial 2 hours was minimal, with values generally below 2.5%. Upon transition to a PBS at pH 7.4, modest rise in drug release was noted between 2nd and 4th hour, but the cumulative percentages remained under 8%, indicating limited drug diffusion in this environment. A marked acceleration in drug release occurred once the medium was changed to PBS (pH 6.8) at the 5th hour. Most formulations demonstrated a rapid increase in cumulative release, reaching or exceeding 90% by 9th hour for several formulations, which indicates near-complete drug delivery. Notably, formulations F4, F10, and F11 surpassed 98% cumulative release at 9 hours, while F6 and F9 exceeded 99%, highlighting the efficiency of these formulations in the simulated intestinal environment. The progressive and controlled release behaviour, characterized by low release in acidic conditions and accelerated release at near-neutral pH, suggests that these formulations are suitable for targeted intestinal drug delivery, minimizing premature gastric release and maximizing drug availability where it is most therapeutically relevant.

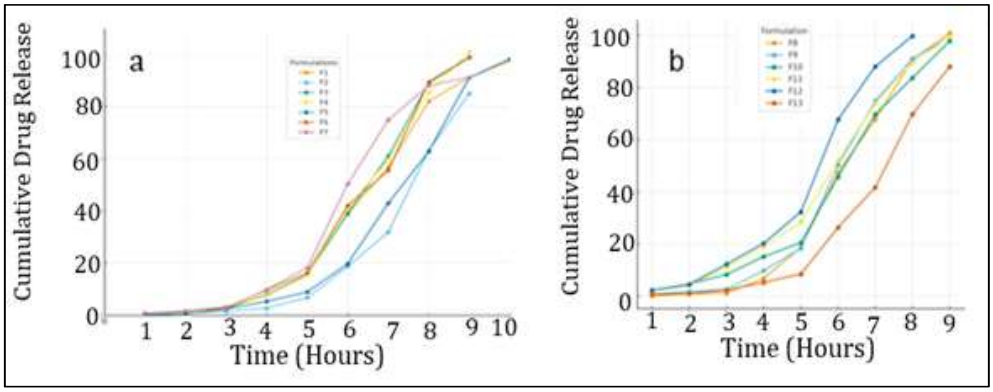

Figure 1: Cumulative drug release a) CDR of batch F1-F7 b) CDR of batch F8-F13

3.2.8 Coating uniformity and weight gain (for coated tablets)

A total of thirteen formulations (F1-F13) prepared by varying concentrations of CMT as the polymer and lactose as the diluent, while keeping the drug load (500 mg), binder (PVP K30, 10 mg), talc (3 mg), and magnesium stearate (2 mg) constant in all batches. The concentration of CMT was systematically varied from 64.64 mg to 1383 mg in order to study its effect on matrix formation and drug release, whereas lactose was adjusted accordingly to maintain uniform tablet weight. After compression, the core tablets were coated with Eudragit S100 to offer enteric protection, and the percentage weight gain due to coating ranged between 2.5% and 14.6%. Formulations with lower coating levels (2.5-5%) were expected to exhibit relatively faster release in the intestinal environment, whereas those with higher coating levels (7.5–14.6%) were designed to provide stronger resistance to gastric conditions and delayed release in the colon. This design allowed systematic evaluation of the influence of polymer loading and coating thickness.

3.2.9 Surface response study

a) Effect of factor on CDR at 2 h (Y_1)

The quadratic model for response Y_1 (drug release at 2 h) was found to be significant F (21.72) ($p<0.05$). All factors X_1 and X_2 were significant and factorial equation for the response Y_1 was,

$Y_1 = 1.60 - 0.1151\ X_1 - 1.55\ X_2 - 0.175 X_1 X_2 + 0.0509 X_{1^2} + 0.7034 X_{2^2}$ ..... Equation 2

The quadratic model developed for % CDR after 2 h showed a good fit with an R^2 of 0.9395 and an adjusted R^2 of 0.8962, indicating that the selected variables could explain more than 89% of the variability in drug release. The coefficient estimates indicate that the intercept (1.60) represents the average release across all formulations. Among the factors studied, the % weight gain due to coating (X_2) exerted the most pronounced negative influence on drug release (coefficient = –1.55, $p < 0.0001$), confirming that higher coating thickness substantially reduces early drug release. The amount of gum (X_1) had a comparatively minor and statistically insignificant effect (coefficient = –0.1151, $p = 0.5004$). The quadratic term of coating (X_{2^2}, coefficient = +0.7034, $p = 0.0049$) was also significant, highlighting that beyond a certain level, the effect of coating thickness becomes nonlinear. The interaction term ($X_1 X_2$) and quadratic term of gum (X_{1^2}) were not statistically significant, indicating minimal synergistic or curvature effects from gum concentration. Overall, the model confirms that early drug release (2 h) is governed primarily by the extent of coating, while the effect of polymer concentration is less critical at this stage.

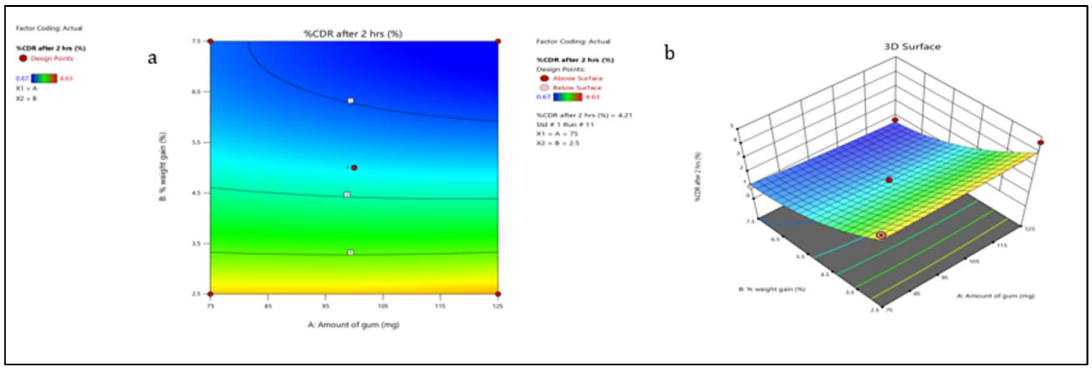

Figure 2: Surface response graphs for (Y_1) including A) Counter plot B) 3D surface response plot

b) Effect of factor on CDR at 5 h (Y_2)

The linear model for response Y_2 (drug release at 2 h) was found to be significant F (28.15) ($p<0.005$). X_1 and X_2 were significant, and the factorial equation for Y_2 was,

$Y_2 = 17.24 - 3.98\ X_1 - 7.22\ X_2$ ..... Equation 3

The regression equation shows that the intercept (17.24) represents the mean percentage drug release across all formulations at 5 h. Both formulation variables, amount of gum (X_1) and percent weight gain (X_2), had statistically significant negative coefficients (–3.98 and –7.22, respectively), confirming that increasing either gum concentration or coating thickness reduces the drug release at this time point. Among the two, coating weight gain exhibited a stronger inhibitory effect, as reflected by its larger coefficient magnitude and higher F-value (43.17, $p < 0.0001$) compared to gum (13.13, $p = 0.0047$). The model demonstrated good predictive power with an R^2 of 0.8492, an adjusted R^2 of 0.8190, and a predicted R^2 of 0.6848, which were in reasonable agreement. Adequate precision (15.004) further confirmed a strong signal-to-noise ratio, supporting reliability of model. Overall, the analysis indicates that both polymer content and coating thickness play crucial roles in controlling release at 5 h, with coating weight gain being the dominant factor governing drug retardation

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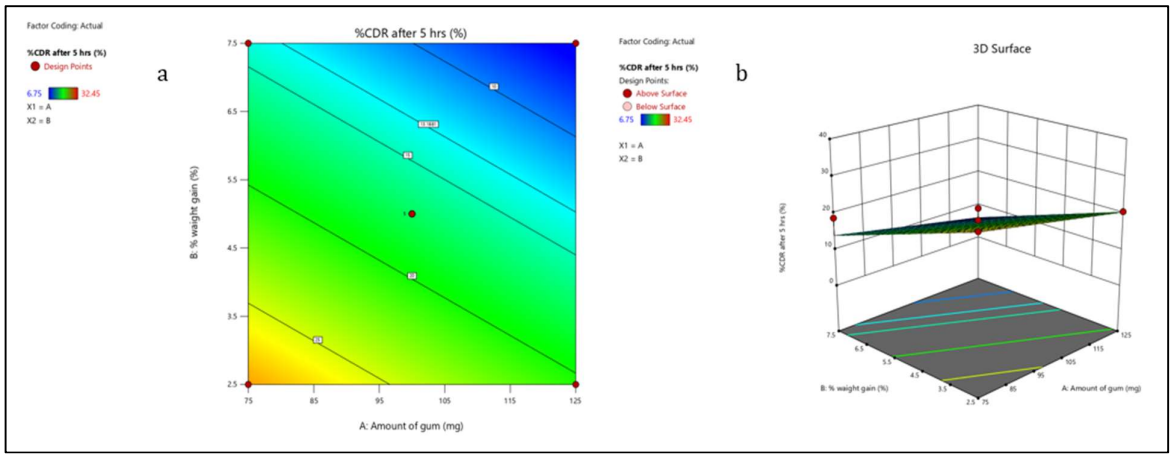


Figure 3: Surface response graphs for (Y_2) A) Counter plot B) 3D surface response plot

c) Effect of factor on CDR at 8 h (Y_3)

The quadratic model for response Y_3 (drug release at 8 h) was found significant F (13.49) ($p<0.005$). X_1 and X_2 found significant and factorial equation for response Y_3 was,

$Y_3 = 91.24 - 8.01X_1 - 8.97X_2 - 5.54X_1X_2 - 5.11X_1^2 - 4.61X_2^2$ …… Equation 4

The regression equation shows that the intercept (91.24) represents the average drug release at 8 h across all runs. Both the amount of gum (X_1) and coating weight gain (X_2) had significant negative coefficients (–8.01 and –8.97, respectively), indicating that increasing either variable reduced drug release at this time point. Among these, coating weight gain exhibited a slightly greater effect compared to gum concentration. The quadratic terms (X_1^2 and X_2^2) were also significant ($p < 0.05$), suggesting a nonlinear relationship, where excessively high levels of gum or coating further suppress release. The interaction term (X_1X_2) showed a negative but less significant influence ($p = 0.0552$), implying only a marginal synergistic effect between gum and coating. The model demonstrated good fit with $R^2 = 0.9060$ and adjusted $R^2 = 0.8388$, though the predicted R^2 (0.4347) was lower, possibly due to variability or block effects. Adequate precision (10.88) confirmed a strong signal-to-noise ratio. Overall, the analysis indicates that at 8 h, drug release is jointly governed by both polymer concentration and coating thickness, with nonlinear effects becoming more pronounced, thereby ensuring sustained release characteristics.

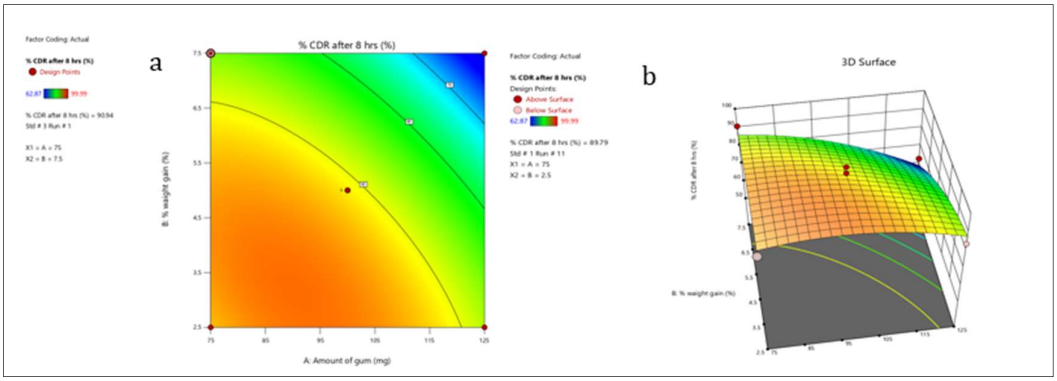
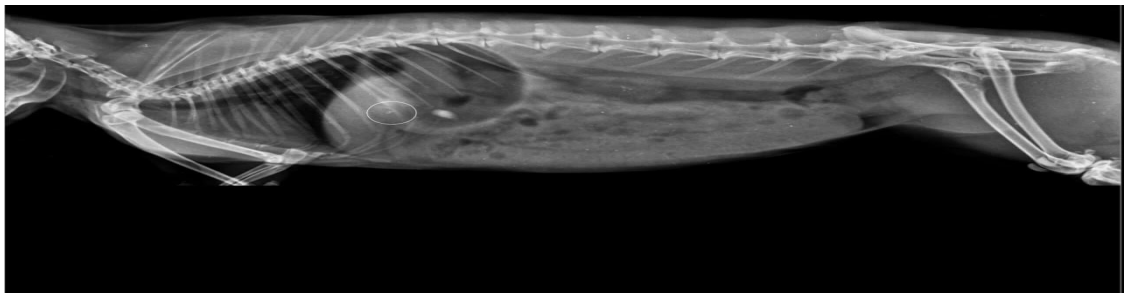


Figure 4: Surface response graphs for (Y_3) A) Counter plot B) 3D surface response plot

3.2.10 In-vivo study (Roentgenography study)

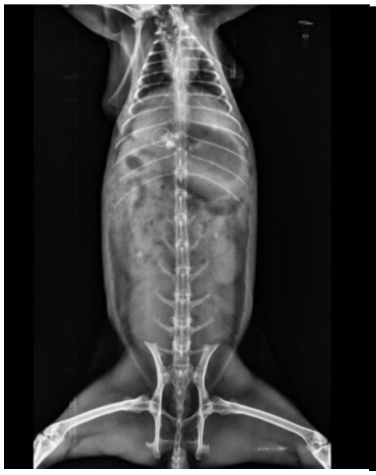
The figure 5 Serial radiographic imaging demonstrated progressive gastrointestinal transit of the radiopaque tablet following oral administration in rabbits. The tablet was initially visualized within the gastric lumen, followed by movement through the pyloric region and small intestine. At approximately 5–6 hours post-administration, the tablet was clearly localized in the right ventral abdominal quadrant corresponding to the cecal region, indicating entry into the large intestine. Subsequent radiographs taken after 6 hours failed to demonstrate the intact tablet, suggesting complete disintegration/dissolution at the cecal site. These findings confirm successful colon-targeted delivery, with dissolution occurring upon entry into the large intestine.



1. Earliest – Gastric Phase

Location: Cranial abdomen, just caudal to diaphragm

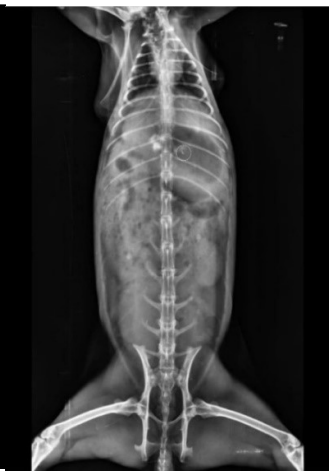
Time: - 30 min



1. Early Gastric

Location: Left cranial abdomen

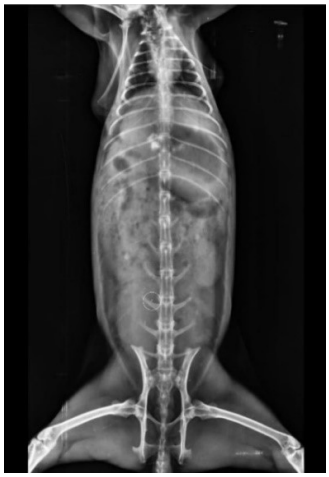
Time-1 hour



Pyloric Region

Location: Near liver shadow

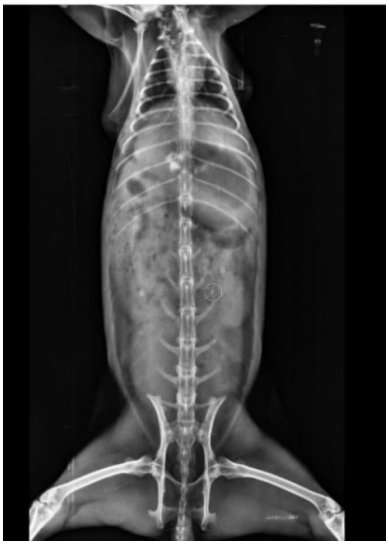
Time- 2hour



Small Intestine Phase

Location: Central abdomen

Time - 4 hour



Cecal Entry (Large Intestine Begins)

Location: Right lateral abdomen

Time- 7 hours

CONCLUSION

The present investigation successfully demonstrated formulation and optimization of colon-targeted mesalamine tablets using solid dispersion technology, natural polymer (carboxymethyl tamarind gum), and a pH-sensitive coating (Eudragit S100). Solid dispersion of mesalamine with Kollicoat-IR improved solubility and dissolution characteristics, as confirmed through physicochemical characterization. Application of response surface methodology (RSM) revealed that both polymer concentration and coating weight gain significantly influenced drug release at different stages of gastrointestinal transit. Minimal release in acidic medium (≤2% at 2 h), controlled release in intestinal pH (≈16–20% at 5 h), and maximum release in colonic pH (≥90% at 8 h) were achieved with the optimized formulation, closely matching predicted values and validating the statistical model. In-vivo roentgenography further confirmed that the coated tablets withstood gastric conditions and released the drug specifically in the colon. Thus, the developed system provided an effective, reproducible, and promising strategy for colon-targeted delivery of mesalamine, ensuring localized therapeutic action with reduced systemic side effects for management of inflammatory bowel disease.

Abbreviation	Meaning
SD	Solid dispersion
APIs	Active pharmaceutical ingredients
IBD	Inflammatory bowel diseases
BCS	Biopharmaceutics Classification System
CMT	Carboxymethyl tamarind
CDR	Cumulative drug release
(HCl)	hydrochloric acid
PVPK30	Polyvinylpyrrolidone K30
RSM	Response Surface Methodology
ANOVA	Analysis of variance
PBS	Phosphate buffer solution

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