

FORMULATION AND EVALUATION OF COLON-TARGETED SODIUM PICOSULFATE TABLETS USING pH-SENSITIVE POLYMERIC COATING FOR SITE SPECIFIC DRUG DELIVERY

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ABSTRACT

Background: Colon-targeted oral dosage forms aim to limit drug release in the stomach and small intestine and to provide release after exposure to conditions associated with the distal gastrointestinal tract. Sodium picosulfate is a stimulant laxative activated by colonic bacteria; therefore, its delivery profile is relevant to bowel evacuation and constipation management.

Objective: To formulate sodium picosulfate core tablets by direct compression, coat the selected core with pH-sensitive Eudragit® S100 at different weight gains, and evaluate physicochemical quality, sequential in-vitro release, release kinetics, and short-term stability.

Methods: Six core formulations (F1–F6) were prepared using crospovidone XL-10, sodium starch glycolate, or croscarmellose sodium at two concentrations. The selected core was coated to produce F7, F8, and F9 with 6%, 8%, and 10% weight gain, respectively. Preformulation included solubility, loss on drying, UV calibration, and FTIR compatibility screening. Tablets were assessed for blend flow, weight, thickness, hardness, friability, drug content, and sequential dissolution. Stability was examined for three months under $30 \pm 2^\circ\text{C}/65 \pm 5\% \text{ RH}$ and $40 \pm 2^\circ\text{C}/75 \pm 5\% \text{ RH}$.

Results: F6 showed the most favourable reported blend parameters and core-tablet quality. F9 had a mean weight of $164.2 \pm 0.68 \text{ mg}$, hardness of $4.9 \pm 0.07 \text{ kg/cm}^2$, friability of 0.19%, and drug content of $99.58 \pm 0.31\%$. Cumulative release at 2 h in pH 1.2 medium was $2.18 \pm 0.16\%$; release was $24.76 \pm 0.41\%$ at 6 h and $91.48 \pm 0.72\%$ at 7 h after transfer to pH 7.2 medium. Hixson–Crowell gave the highest reported coefficient of determination ($R^2 = 0.867$). After three months, drug content was $99.01 \pm 0.37\%$ under long-term conditions and $97.03 \pm 0.52\%$ under accelerated conditions.

Conclusion: The results support further investigation of Eudragit® S100-coated sodium picosulfate tablets as a pH-triggered delivery platform. The work is limited by in-vitro evidence, three-month stability, and inconsistencies in the source dissertation's description of pH-stage timings and media. These details must be reconciled against original laboratory records before submission.

Keywords: Sodium picosulfate; colon-targeted drug delivery; Eudragit® S100; pH-sensitive coating; direct compression; dissolution; stability.

1. INTRODUCTION

Oral administration remains a preferred route for many medicines because it is familiar to patients, economical to manufacture, and generally convenient for long-term use. Conventional immediate-release products, however, commonly release their drug in the stomach or small intestine. Where the therapeutic objective or drug activation mechanism is linked to the colon, premature release may reduce site specificity and expose the active ingredient to environments that are not optimal for the intended purpose. Colon-targeted drug delivery systems are designed to postpone release until the formulation has traversed the upper gastrointestinal tract. Their performance depends on the interplay between gastrointestinal physiology, polymer properties, dosage-form design, and variability between individuals ^[1-6].

The colon is an important site for local treatment of inflammatory and infectious conditions, for delivery of compounds intended to act on colonic contents, and for selected systemic-delivery strategies. It differs from the small intestine in transit characteristics, fluid availability, microbial density, and luminal chemistry. These features can be exploited using pH-sensitive coatings, time-dependent barriers, microbiota-responsive materials, prodrugs, pressure-responsive systems, and combinations of mechanisms. No single approach is universally reliable: gastrointestinal pH and transit are variable, disease can change physiology, and polymer dissolution may not occur at a consistent anatomical position in every subject.

Sodium picosulfate is used as a stimulant laxative and is converted by bacterial enzymes in the colon to the active metabolite bis-(p-hydroxyphenyl)-pyridyl-2-methane (BHPM). This pharmacological relationship makes delivery and activation in the large intestine especially relevant to the drug's intended action. The present work explores a formulation strategy based on an Eudragit® S100 film designed to remain relatively resistant in acidic and intermediate-pH media and to dissolve at higher pH. The study is a formulation-development investigation and does not establish clinical superiority, therapeutic equivalence, or in-vivo colon targeting.

1.1 Rationale and significance

The central formulation challenge is to maintain tablet integrity and limit release during the gastric and upper-intestinal stages, while allowing release once the surrounding medium reaches the selected higher-pH trigger. A film coating can provide a barrier to wetting and drug diffusion; however, the practical performance of a pH-sensitive coating depends on coating thickness, polymer grade, plasticizer content, coating uniformity, curing, and the dissolution conditions used during evaluation. Increasing coating weight may strengthen the barrier but can also lengthen the lag phase and delay drug availability. Formulation optimization therefore requires evaluation of multiple coating levels rather than assuming that the thickest film is automatically optimal ^[11,67].

Eudragit® S100 is an anionic methacrylate copolymer widely used for pH-dependent release designs. Its ionizable carboxyl groups promote dissolution at higher pH, allowing the polymer to act as a pH-responsive barrier. The formulation concept investigated here uses 6%, 8%, and 10% coating weight gains. The resulting release profiles are compared across sequential media to determine how the coating level affects early release and later release after the pH trigger. The selected product is also assessed during three months of storage under long-term and accelerated conditions described in the dissertation with reference to ICH Q1AR2 ^[68].

1.2 Aim

To formulate and evaluate colon-targeted sodium picosulfate tablets using a pH-sensitive Eudragit® S100 coating, with emphasis on core-tablet optimization, coating-level selection, sequential in-vitro dissolution, release-kinetic modelling, and short-term stability.

1.3 Specific objectives

- Characterize sodium picosulfate by physical examination, solubility testing, loss on drying, UV-visible analysis, and FTIR compatibility screening.
- Prepare six core-tablet formulations by direct compression using three superdisintegrants at two levels.
- Compare blend flow, density, compressibility, tablet weight, thickness, hardness, friability, disintegration, and drug content.
- Apply Eudragit® S100 coating at 6%, 8%, and 10% weight gain and evaluate coated-tablet quality.
- Assess release through sequential media and compare the optimized formulation's in-vitro profile with the reported marketed comparator.
- Fit the reported release profile to common kinetic models and monitor selected quality attributes for three months.

2. COLON PHYSIOLOGY AND DESIGN CONSIDERATIONS

A colon-targeted formulation must pass through the mouth, oesophagus, stomach, and small intestine before it reaches the intended region. Gastric pH is typically acidic, while the pH rises through the small intestine and can be higher in parts of the distal gut. The colon is not a uniform compartment: pH varies with diet, microbial metabolism, transit, disease state, and local contents. Thus, pH values used in laboratory dissolution testing represent controlled test environments rather than exact anatomical markers ^[25].

Transit time is another determinant of site specificity. Gastric emptying varies with food and dosage form, and intestinal transit varies between individuals. A formulation relying only on pH can begin releasing earlier than intended in a person whose upper-intestinal pH reaches the polymer dissolution threshold, or may release later in a person whose colonic pH is lower. These sources of variation are particularly relevant when a coating is selected using a single in-vitro pH sequence. For this reason, dissolution testing should be interpreted as a screening tool for formulation behaviour, not as proof that the tablet will release exclusively in the colon ^[63].

The colon also contains a dense and metabolically active microbial population. Microbial enzymes can cleave selected polysaccharides or activate prodrugs, creating opportunities for delivery systems that respond to colonic bacteria. Such approaches may complement pH-based coatings, particularly where inter-individual pH variability is a concern. Time-dependent systems and pressure-sensitive designs offer additional mechanisms, but each has practical constraints involving lag-time variability, manufacturing complexity, reproducibility, or sensitivity to physiological conditions ^[12–14].

The present formulation uses a single pH-responsive polymer coating. This is a rational starting strategy because it can be manufactured using conventional coating equipment and evaluated with sequential dissolution. Its principal limitation is that pH responsiveness alone cannot guarantee anatomical targeting in vivo. A stronger development package would combine robust acid resistance, biorelevant upper-intestinal testing, a validated release method, and appropriate in-vivo imaging or pharmacokinetic evidence before making claims about site-specific delivery.

2.1 Approaches to colon-specific drug delivery

pH-dependent systems use polymers that resist dissolution below a defined pH and dissolve as the pH rises. They are relatively straightforward to manufacture and are compatible with tablet coating, but the trigger depends on gastrointestinal pH and the polymer's dissolution threshold. Eudragit® L grades are generally associated with lower pH thresholds than Eudragit® S100; selection should be

guided by the intended release region and the evidence from sequential dissolution rather than by polymer name alone ^[11,18].

Time-dependent systems employ a lag phase created by a coating, swelling layer, or erodible barrier. The formulation releases after a planned delay, but actual transit and hydration vary across patients. Microbial-triggered systems use polysaccharides or other substrates that are degraded by colonic microbiota. They may provide a biologically relevant trigger but can be affected by differences in microbial composition, diet, and disease ^[12].

The prodrug approach links a drug to a moiety that is cleaved by enzymes or chemical conditions in the target region. This can provide strong specificity but requires suitable chemistry, safety evaluation, and regulatory development. Pressure-controlled systems exploit the mechanical environment of the colon, though pressure profiles and device performance can be variable. Coating-based systems remain popular because they can be integrated with established oral dosage-form manufacturing, are relatively scalable, and permit tuning of the barrier through polymer grade, coat weight, plasticizer, and process settings ^[18,20].

Hybrid approaches combine two or more triggers, such as pH plus microbial degradation or pH plus time delay. These can reduce reliance on a single variable but also increase formulation and analytical complexity. In a development programme, the simplest design that meets pre-defined release criteria is often preferable, provided the test method is physiologically meaningful and the claims match the evidence. For the present study, Eudragit® S100 was evaluated as a single pH-triggered coating system; the results are best described as promising in-vitro pH-dependent release behaviour.

2.2 Eudragit® S100 and pH-sensitive coating

Eudragit® S100 is an anionic copolymer of methacrylic acid and methyl methacrylate. Its carboxylic acid groups become increasingly ionized as the environmental pH rises, promoting hydration and dissolution of the film above the polymer's nominal threshold. In dosage forms, the film may delay liquid penetration and drug release during the acidic stage and then dissolve or erode as the medium becomes more alkaline. The actual response depends on polymer grade, coat weight, film integrity, curing, plasticizer, solvent system, and the composition and ionic strength of the dissolution medium ^[18,21].

Plasticizers such as polyethylene glycol can improve film flexibility and reduce brittleness by changing polymer-chain mobility. Excessive or insufficient plasticizer may alter permeability and mechanical properties, so the formulation must balance film strength with the ability to dissolve when the trigger condition is reached. Pigments or opacifiers can affect visual appearance and may influence the coating suspension; they should be selected with compatibility and regulatory requirements in mind. Organic solvents evaporate during drying, and residual-solvent control is an important manufacturing consideration even though solvents do not contribute to final tablet weight.

Coating weight gain is a practical variable for comparing barrier thickness. At a lower weight gain, a film may contain thinner regions or be more susceptible to early penetration, potentially increasing premature release. Higher weight gain can improve resistance to the initial media but may delay release after the target pH is reached. Therefore, the optimum is not determined solely by minimizing release in acid; it should also meet a suitable release profile in later stages. The present study compared 6%, 8%, and 10% weight gains and selected F9, the 10% coating formulation, for detailed dissolution and stability testing.

The study's dissolution media included acidic conditions and multiple buffer stages. Because the dissertation describes the sequence and stage durations differently in some sections, exact

interpretation of the pH trigger requires checking the original laboratory protocol. The reported results are reproduced here with the same key time points and pH labels given in the source data, and the inconsistency is explicitly retained as a limitation.

2.3 Sodium picosulfate: pharmaceutical relevance

Sodium picosulfate is a stimulant laxative used in constipation management and bowel evacuation. It acts as a prodrug: after reaching the colon, bacterial enzymes convert it to BHPM, which promotes colonic motility and fluid secretion. The intended pharmacological activity is therefore linked to colonic metabolism, making delivery-system design relevant to where the drug becomes available [28,29]. This formulation study does not alter the active ingredient and does not demonstrate that the coated tablet will improve clinical outcomes compared with currently marketed products.

In the source dissertation, sodium picosulfate was described as a white to almost white, odourless crystalline powder with a melting/decomposition range of 170–174°C and a pH of 6.3 ± 0.1 for a 1% w/v aqueous solution. The reported solubility values were 2.4 ± 0.2 mg/mL in distilled water, 1.6 ± 0.1 mg/mL in 0.1 N HCl, 18.7 ± 0.6 mg/mL in pH 6.8 phosphate buffer, and 27.3 ± 0.8 mg/mL in pH 7.4 phosphate buffer. These are study-specific measurements and should be confirmed against the laboratory notebooks and the validated analytical method before publication.

The drug's reported solubility profile informed the choice of acidic and buffer media for testing. UV-visible quantification was performed at 266 nm using a calibration range of 2–10 µg/mL in 0.1 N HCl, with a reported regression equation of $y = 0.0676x + 0.0005$ and $R^2 = 0.9997$. The high reported coefficient of determination supports linearity over the tested range, but a complete analytical validation would also require selectivity, accuracy, precision, range, robustness, and appropriate checks for interference from the coating and excipients.

Sodium picosulfate is commonly used in bowel-preparation products in combination with other agents; the current study compares dissolution behaviour with a reported bisacodyl product. Because these contain different active ingredients, the comparison is strictly an in-vitro profile comparison and cannot establish bioequivalence, equivalent therapeutic effect, or equivalent safety.

3. MATERIALS

Sodium picosulfate was used as the active pharmaceutical ingredient. The source dissertation lists microcrystalline cellulose PH-102, lactose monohydrate, crospovidone XL-10, sodium starch glycolate, croscarmellose sodium, colloidal anhydrous silica, magnesium stearate, Eudragit® S100, polyethylene glycol 400, and titanium dioxide among the formulation materials. Isopropyl alcohol and acetone were listed as coating solvents. Analytical-grade reagents and buffers were used for preformulation and dissolution work. Supplier details should be inserted exactly as recorded in purchase documents or certificates of analysis; they should not be inferred or invented.

3.1 Functional role of excipients

Microcrystalline cellulose PH-102 serves as a directly compressible filler and contributes to compact formation. Lactose monohydrate provides additional diluent mass and influences powder packing and compaction. Crospovidone, sodium starch glycolate, and croscarmellose sodium were compared as superdisintegrants, with the objective of evaluating their effect on core-tablet disintegration. Colloidal anhydrous silica was included as a glidant, while magnesium stearate served as a lubricant. The formulation matrix was designed to maintain a 150 mg core tablet containing 10 mg sodium picosulfate.

Eudragit® S100 was the principal pH-sensitive film-forming polymer. PEG 400 was used as plasticizer, and titanium dioxide as opacifier. The source formula lists isopropyl alcohol and acetone as the coating solvent system. Because solvent selection and residual-solvent levels are important

quality attributes, a publication-ready methods section should identify the actual coating equipment, spray parameters, drying temperature, curing duration, and any residual-solvent testing that were used. These parameters are not replaced by general descriptions in this expanded manuscript.

3.2 Equipment and analytical instruments

The dissertation describes a UV-visible spectrophotometer for drug quantification, an FTIR spectrometer for compatibility screening, equipment for powder-flow and density measurements, tablet compression equipment, hardness and friability testers, a disintegration apparatus, and a USP Type II paddle dissolution apparatus. Where the exact instrument manufacturer and model are available in laboratory records, they should be added to the final manuscript. Reporting instrument identity improves reproducibility and allows readers to understand the technical context of the measurements.

All quantitative results in this manuscript are reproduced from the source dissertation and are not independently remeasured. Any unresolved discrepancy between the source text, tables, figures, or laboratory notebooks should be resolved before journal submission.

4. METHODS: PREFORMULATION AND ANALYTICAL PROCEDURES

4.1 Physical characterization and solubility

The drug was examined for appearance, odour, taste, and melting/decomposition range. The pH of a 1% w/v aqueous solution was measured as reported in the dissertation. Qualitative and quantitative solubility were assessed in distilled water, 0.1 N hydrochloric acid, phosphate buffers pH 6.8 and 7.4, methanol, and ethanol. The reported solubility values are included in the results section. Temperature, equilibration time, sample excess, filtration procedure, and replicate count should be checked against the original laboratory protocol to ensure the method is reproducible.

4.2 Loss on drying

Loss on drying was used to estimate volatile or moisture loss from sodium picosulfate and selected excipients. The source dissertation reports values of $0.34 \pm 0.05\%$ for sodium picosulfate, $4.1 \pm 0.3\%$ for microcrystalline cellulose pH-102, $4.8 \pm 0.2\%$ for lactose monohydrate, and $2.6 \pm 0.2\%$ for Eudragit® S100. These values were compared with the limits or expected ranges cited in the source. For lactose monohydrate, water of crystallization must be distinguished from excess surface moisture when interpreting the result.

4.3 UV-visible calibration

A standard calibration curve was prepared in 0.1 N HCl over 2–10 $\mu\text{g/mL}$, with absorbance measured at 266 nm. The reported mean absorbance values were 0.131, 0.279, 0.405, 0.542, and 0.675 at 2, 4, 6, 8, and 10 $\mu\text{g/mL}$, respectively; the blank absorbance was 0.000. Linear regression gave $y = 0.0676x + 0.0005$ and $R^2 = 0.9997$. The calibration was used for drug-content and dissolution measurements as described in the dissertation.

4.4 FTIR compatibility screening

FTIR spectroscopy was used to examine characteristic absorption bands of sodium picosulfate and screen for potential drug–excipient interactions. The dissertation reports no incompatibility signal that prevented formulation development. FTIR is a useful screening tool, but absence of a conspicuous band shift does not alone prove complete compatibility or long-term chemical stability; interpretation should consider peak assignment, sample preparation, spectral resolution, and whether mixtures were assessed under relevant storage conditions ^[60,61].

4.5 Preparation of core tablets

Six core formulations (F1–F6) were prepared by direct compression. Each tablet contained 10 mg sodium picosulfate and 60 mg lactose monohydrate. Microcrystalline cellulose PH-102 was adjusted between 69.50 and 73.25 mg to compensate for the superdisintegrant level. Crospovidone XL-10 was used in F1 and F2, sodium starch glycolate in F3 and F4, and croscarmellose sodium in F5 and F6. For each superdisintegrant, the lower and higher levels were 3.75 and 7.50 mg, equivalent to 2.5% and 5.0% of the 150 mg core tablet. Colloidal anhydrous silica and magnesium stearate were each included at 1.50 mg per tablet.

TABLE.1.Preparation of core tablets

Ingredient (mg/tablet)	F1	F2	F3	F4	F5	F6
Sodium picosulfate	10.00	10.00	10.00	10.00	10.00	10.00
Microcrystalline cellulose PH-102	73.25	69.50	73.25	69.50	73.25	69.50
Lactose monohydrate	60.00	60.00	60.00	60.00	60.00	60.00
Crospovidone XL-10	3.75	7.50	—	—	—	—
Sodium starch glycolate	—	—	3.75	7.50	—	—
Croscarmellose sodium	—	—	—	—	3.75	7.50
Colloidal anhydrous silica	1.50	1.50	1.50	1.50	1.50	1.50
Magnesium stearate	1.50	1.50	1.50	1.50	1.50	1.50
Total	150.00	150.00	150.00	150.00	150.00	150.00

The source dissertation describes weighing and sifting the ingredients, blending the drug with diluent and superdisintegrant, adding the glidant, and incorporating lubricant before compression. Exact blending times, sieve sizes, order of addition, compression force, and punch dimensions should be transcribed from the original batch records if they are to be reported as definitive manufacturing parameters. The core tablets were intended to provide a consistent platform for comparison before application of the pH-sensitive coating.

4.6 Preparation of coated tablets

The selected core formulation F6 was coated with Eudragit® S100 at three target weight gains: 6% (F7), 8% (F8), and 10% (F9). The coating formula reported in the dissertation included Eudragit® S100, PEG 400, titanium dioxide, isopropyl alcohol, and acetone. Target coated tablet weights were 159 mg, 162 mg, and 165 mg for F7, F8, and F9, respectively, based on a 150 mg core. The coating weight gain was used as the principal independent variable for assessing barrier performance.

TABLE.2. Preparation of coated tablets

Coating component / target	F7	F8	F9
Eudragit® S100 (mg)	7.50	9.50	11.50
PEG 400 (mg)	1.00	2.00	3.00
Titanium dioxide (mg)	0.50	0.50	0.50
Isopropyl alcohol	QS	QS	QS
Acetone	QS	QS	QS
Target weight gain (mg)	9.00	12.00	15.00
Core tablet weight (mg)	150.00	150.00	150.00
Target coated weight (mg)	159.00	162.00	165.00

The source dissertation describes preparation of a coating solution, pre-coating checks, application of the film, and drying/curing of coated tablets. The exact process parameters—including solvent ratio, polymer concentration, spray rate, atomization pressure, pan speed, inlet/outlet temperatures, and curing time—must be verified against the experimental record. These details have a direct influence on film uniformity, residual solvent, and release behaviour and should not be fabricated from typical industry practice.

4.7 Selection of optimized formulation

The core formulation was selected using a combined assessment of blend flow, weight uniformity, hardness, friability, disintegration, and drug content. Coated formulations were then compared for physical quality and sequential dissolution. F9 was selected for detailed release-kinetic and stability evaluation because it showed the lowest reported acid-stage release and the highest coating weight gain among the tested variants. This selection reflects the tested in-vitro criteria and should not be interpreted as confirmation of in-vivo targeting.

4.8 Evaluation of powder blends and tablets

Powder flow was assessed using angle of repose, bulk density, tapped density, Carr's compressibility index, and Hausner ratio. Bulk density reflects the mass of powder occupying a defined bulk volume, whereas tapped density is measured after standardized tapping. Carr's index and Hausner ratio are derived from these values and provide indirect indicators of packing and flow. These measures are useful for assessing suitability for die filling but should be interpreted alongside observed tablet weight variation and manufacturing consistency.

Compressed cores were evaluated for appearance, average weight, thickness, hardness, friability, disintegration time, and drug content. Average weight was used to assess mass uniformity; thickness and hardness were used to monitor tablet dimensions and mechanical strength. Friability provides an estimate of resistance to abrasion and handling damage. Disintegration time describes the time required for the tablet to break apart under the specified test conditions, while drug content estimates the amount of active ingredient recovered from the tested sample. The source reports the sample sizes for several parameters: weight ($n = 20$), thickness ($n = 10$), hardness and disintegration ($n = 6$), and drug content ($n = 3$). Friability was reported as a single-batch determination.

Coated tablets were assessed for appearance, average weight, thickness, hardness, friability, and drug content. Coating integrity was also assessed through disintegration/dissolution behaviour across the sequential media. An intact coating during the acid stage is a necessary screening result, but it is not sufficient by itself to prove colonic release in vivo. A robust evaluation should also examine coating defects, batch-to-batch variability, and reproducibility of the dissolution profile.

For quantitative interpretation, results are presented as mean $\pm$ standard deviation where the source provides such values. The article does not add inferential statistical claims because a complete statistical analysis plan and raw replicate-level data were not available in the extracted source. Where only one friability result was reported, it is presented as reported rather than converted into an unsupported mean $\pm$ standard deviation.

4.9 Sequential dissolution and stability protocol

The source dissertation describes dissolution testing using a USP Type II paddle apparatus, 900 mL medium, $37 \pm 0.5^\circ\text{C}$, and a paddle speed of 100 rpm. The sequential protocol included 0.1 N HCl (pH 1.2), followed by buffer media reported at pH 6.0, pH 6.8, and pH 7.2 or pH 7.4 in different parts of the dissertation. Samples were withdrawn at stated intervals and replaced with equal

volumes of fresh medium. Drug concentration was estimated by UV-visible spectrophotometry at 266 nm using the reported calibration curve.

The method description and the results section do not fully agree on the buffer pH values and duration of the individual stages. For example, some passages describe a sequence involving pH 6.8 and 7.4, whereas the tabulated dissolution results use pH 6.0, 6.8, and 7.2. This is a material methodological discrepancy. The numerical values are retained with the stage labels supplied in the corresponding source tables, but the definitive article must use one verified protocol and correct any table or figure labels accordingly.

Release data were fitted to zero-order, first-order, Higuchi, Korsmeyer–Peppas, and Hixson–Crowell models. The coefficient of determination (R^2) was used as a descriptive indicator of model fit. Kinetic models are empirical simplifications; a high R^2 does not by itself prove a unique mechanism, particularly for a coated tablet with a distinct lag phase and a sharp pH-triggered change in release. The reported model output is therefore interpreted cautiously.

The optimized formulation F9 was stored for three months under long-term conditions ($30 \pm 2^\circ\text{C}/65 \pm 5\% \text{ RH}$) and accelerated conditions ($40 \pm 2^\circ\text{C}/75 \pm 5\% \text{ RH}$). The source describes sampling at initial, one-month, two-month, and three-month intervals. Appearance, hardness, friability, drug content, and dissolution behaviour were monitored. The three-month study is a preliminary stability assessment and is insufficient by itself to assign a commercial shelf life.

5. RESULTS: PREFORMULATION AND ANALYTICAL PERFORMANCE

5.1 Physical characteristics and solubility

TABLE.3. Parameter and results

Parameter	Reported result
Appearance	White to almost white crystalline powder
Odour	Odourless
Taste	Slightly bitter
Melting/decomposition range	170–174°C
pH of 1% w/v aqueous solution	6.3 ± 0.1
Distilled-water solubility	$2.4 \pm 0.2 \text{ mg/mL}$
0.1 N HCl, pH 1.2	$1.6 \pm 0.1 \text{ mg/mL}$
Phosphate buffer pH 6.8	$18.7 \pm 0.6 \text{ mg/mL}$
Phosphate buffer pH 7.4	$27.3 \pm 0.8 \text{ mg/mL}$
Methanol	$12.1 \pm 0.4 \text{ mg/mL}$
Ethanol	$6.8 \pm 0.3 \text{ mg/mL}$

The source reports a marked difference between acidic and phosphate-buffer solubility. The measured value in pH 7.4 buffer was more than an order of magnitude greater than the value in 0.1 N HCl. This pattern supports the use of pH-dependent media for analytical evaluation, although it should not be assumed that solubility alone predicts the release rate from a coated tablet. Film dissolution, medium penetration, tablet disintegration, and drug dissolution can all contribute to the observed profile.

5.2 Moisture and compatibility screening

TABLE.4. Moisture and compatibility screening

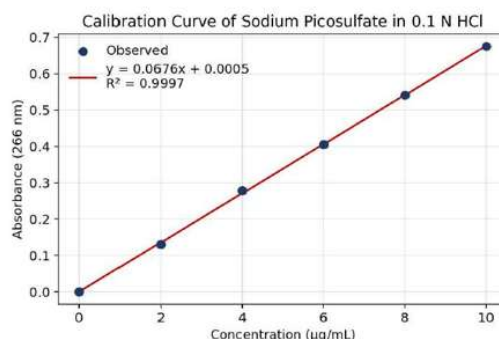
Material	Loss on drying (% w/w)	Source-reported limit/range
Sodium picosulfate	0.34 ± 0.05	NMT 1.0%
Microcrystalline cellulose PH-102	4.1 ± 0.3	NMT 5.0%
Lactose monohydrate	4.8 ± 0.2	4.5–5.5% water of crystallization
Eudragit® S100	2.6 ± 0.2	NMT 5.0%

The reported loss-on-drying values were within the limits or expected ranges stated in the dissertation. FTIR screening was reported as not indicating a major drug–excipient incompatibility that prevented formulation. The result is supportive but preliminary: further confirmation could include differential scanning calorimetry, chromatographic impurity assessment, and stability-indicating assay where justified by the product-development stage.

5.3 UV calibration and powder-flow properties

TABLE.5. Concentration and Absorbance

Concentration (µg/mL)	Absorbance (mean ± SD, n=3)
0	0.000 ± 0.000
2	0.131 ± 0.002
4	0.279 ± 0.003
6	0.405 ± 0.003
8	0.542 ± 0.004
10	0.675 ± 0.004



The reported calibration equation was $y = 0.0676x + 0.0005$ with $R^2 = 0.9997$. This indicates a strong linear relationship over the studied concentration range. Because the same UV method was used for drug content and dissolution, the suitability of the assay depends on the absence of interference from excipients, coating components, or degradation products. The source does not provide a full validation package; the reported calibration should therefore be described as a linearity assessment rather than a complete analytical validation.

5.4 Pre-compression results

TABLE.6. Pre-compression results of formulations

Formulation	Angle of repose (°)	Bulk density (g/mL)	Tapped density (g/mL)	Carr's index (%)	Hausner ratio
F1	30.42	0.426	0.502	15.14	1.18
F2	29.65	0.431	0.501	13.97	1.16
F3	28.94	0.438	0.503	12.92	1.15
F4	27.86	0.445	0.505	11.88	1.13
F5	26.92	0.452	0.506	10.67	1.12
F6	25.74	0.462	0.508	9.06	1.10

Angle of repose ranged from 25.74° to 30.42°, Carr's index from 9.06% to 15.14%, and Hausner ratio from 1.10 to 1.18. F6 showed the lowest angle of repose, Carr's index, and Hausner ratio, as well as the highest bulk density among the reported blends. The data suggest that F6 had the most favourable measured flow and packing characteristics in this formulation set. The source also reports a progressive improvement across F1–F6; because several formulation variables change together, this trend should not be interpreted as an isolated causal effect of superdisintegrant chemistry alone.

5.5 Core-tablet evaluation

TABLE.7. Core-tablet evaluation of formulations

Code	Weight (mg)	Thickness (mm)	Hardness (kg/cm ²)	Friability (%)	Disintegration (min)	Drug content (%)
F1	149.6 ± 1.12	3.38 ± 0.03	3.4 ± 0.12	0.68	8.45 ± 0.31	97.86
F2	150.2 ± 1.08	3.39 ± 0.04	3.6 ± 0.10	0.61	7.20 ± 0.28	98.24
F3	149.8 ± 1.15	3.41 ± 0.03	3.7 ± 0.14	0.56	6.58 ± 0.25	98.65
F4	150.4 ± 1.04	3.42 ± 0.04	3.9 ± 0.11	0.49	5.42 ± 0.22	99.12
F5	149.9 ± 0.96	3.40 ± 0.03	4.1 ± 0.09	0.42	4.38 ± 0.18	99.48
F6	150.1 ± 0.89	3.41 ± 0.02	4.3 ± 0.08	0.31	3.26 ± 0.15	99.82

The mean weights of F1–F6 ranged from 149.6 to 150.4 mg, close to the 150 mg target. Thickness values were tightly grouped between 3.38 and 3.42 mm. Hardness increased from 3.4 ± 0.12 kg/cm² in F1 to 4.3 ± 0.08 kg/cm² in F6, while friability decreased from 0.68% to 0.31%. All reported friability values were below 1.0%. Drug content ranged from 97.86% to 99.82%, with F6 showing the highest reported value.

Disintegration time decreased across the series, from 8.45 ± 0.31 min in F1 to 3.26 ± 0.15 min in F6. F6 contained croscarmellose sodium at 5% w/w. The results are consistent with selection of F6 as the optimized core because it combined the shortest reported disintegration time with favourable mechanical properties and drug content. The disintegration time of 3.26 min is not an immediate-release orodispersible-tablet performance claim; it is the result reported for this colon-targeted core formulation and its specified test method.

The data support the choice of F6 as the core used in subsequent coating experiments. However, a formal optimization claim would be stronger if the study used a factorial or response-surface design, with predefined responses and statistical analysis, rather than selecting a formulation based on sequential comparisons among six batches.

5.6 Coated-tablet quality and coating optimization

TABLE.8. Coated-tablet quality and coating optimization

Code	Coating gain	Weight (mg)	Thickness (mm)	Hardness (kg/cm ²)	Friability (%)	Drug content (%)
F7	6%	158.1 ± 0.84	3.52 ± 0.03	4.5 ± 0.10	0.28	98.76 ± 0.42
F8	8%	161.6 ± 0.76	3.58 ± 0.02	4.7 ± 0.08	0.24	99.21 ± 0.36
F9	10%	164.2 ± 0.68	3.64 ± 0.02	4.9 ± 0.07	0.19	99.58 ± 0.31

Average weight, thickness, and hardness increased with coating level. F9 had the highest reported weight (164.2 ± 0.68 mg), thickness (3.64 ± 0.02 mm), and hardness (4.9 ± 0.07 kg/cm²). Friability declined from 0.28% for F7 to 0.19% for F9, while drug content increased from $98.76 \pm 0.42\%$ to $99.58 \pm 0.31\%$. The observed coated weights were close to the target values, suggesting reasonably consistent deposition under the conditions used.

Coating weight gain had a pronounced effect on release behaviour. The 6% coat allowed the highest release at the end of the acidic stage, whereas the 10% coat showed the lowest. The thicker coating also restrained release during the pH 6.0 and pH 6.8 stages. This supports the selection of F9 when the primary criterion is minimizing premature release in the reported upper-GI simulation. However, the release response after transfer to the highest-pH stage was not simply proportional to coating level; the abrupt increase suggests a trigger-related change in polymer behaviour and underlines the importance of using a verified, reproducible sequential method.

The 10% coating level should be described as the best-performing of the three tested levels under the reported in-vitro conditions, not as a universally optimized coating weight. The optimum could change with polymer grade, solvent composition, film curing, batch scale, or a different dissolution protocol. Additional coating weight-gain levels and replicate batches would be required to define a robust design space.

5.7 Sequential dissolution of coated formulations

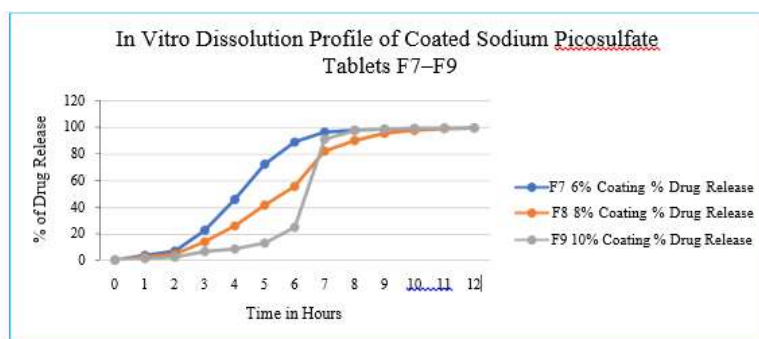
TABLE.9. Sequential dissolution of coated formulations

Time (h)	Reported stage medium	F7 release (%)	F8 release (%)	F9 release (%)
2	0.1 N HCl, pH 1.2	6.78 ± 0.24	4.36 ± 0.21	2.18 ± 0.16
4	Buffer, pH 6.0	45.82 ± 0.52	25.76 ± 0.43	8.36 ± 0.28
6	Buffer, pH 6.8	89.24 ± 0.73	55.68 ± 0.61	24.76 ± 0.41
7	Buffer, pH 7.2	96.84 ± 0.76	82.45 ± 0.69	91.48 ± 0.72
12	Buffer, pH 7.2	100.00 ± 0.82	99.86 ± 0.79	100.00 ± 0.80

At 2 h in pH 1.2 medium, F9 showed the lowest cumulative release ($2.18 \pm 0.16\%$), followed by F8 ($4.36 \pm 0.21\%$) and F7 ($6.78 \pm 0.24\%$). At 4 h, the reported release in pH 6.0 buffer was $8.36 \pm 0.28\%$ for F9, compared with $25.76 \pm 0.43\%$ for F8 and $45.82 \pm 0.52\%$ for F7. At 6 h, cumulative release was $24.76 \pm 0.41\%$ for F9, $55.68 \pm 0.61\%$ for F8, and $89.24 \pm 0.73\%$ for F7. These values indicate that increasing coating weight gain reduced release through the earlier stages of the reported test.

After transfer to pH 7.2 medium, F9 release increased to $91.48 \pm 0.72\%$ at 7 h and reached $100.00 \pm 0.80\%$ at 12 h. F7 and F8 also approached complete release by 12 h. F9 therefore demonstrated a more pronounced early lag followed by substantial release in the higher-pH stage. This is consistent with the intended pH-triggered design, but the stage labels and time sequence must be verified because the source dissertation uses different pH-stage descriptions in its methods, summary tables, and results text.

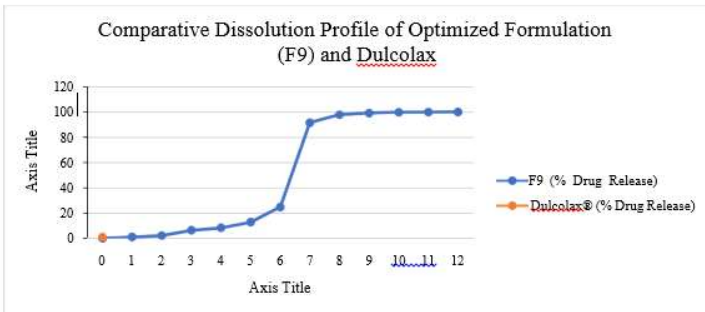
A complete dissolution report should include the full time-course data, individual replicate values, sampling correction, sink-condition justification, medium composition, apparatus details, and the validated UV method. The selected points shown here summarize the source data but do not replace the full release profile needed for regulatory-quality assessment.



5.8 Comparator study and release kinetics

The source dissertation compared F9 with a marketed Dulcolax® (bisacodyl 5 mg) product. At 2 h, the reported release was $2.18 \pm 0.16\%$ for F9 and $3.54 \pm 0.12\%$ for Dulcolax®. At 4 h, release was $8.36 \pm 0.28\%$ and $15.84 \pm 0.24\%$, respectively. At 6 h, F9 reached $24.76 \pm 0.41\%$, whereas the comparator reached $85.54 \pm 0.39\%$. At 7 h, the reported values were $91.48 \pm 0.72\%$ for F9 and $94.24 \pm 0.66\%$ for the comparator; both approached complete release by 12 h.

Because sodium picosulfate and bisacodyl are different active pharmaceutical ingredients, their dissolution profiles cannot establish bioequivalence or therapeutic interchangeability. Differences may reflect drug properties, dosage form, label strength, and assay conditions as well as coating performance. The comparator results are therefore descriptive only and should be reported without terms such as “equivalent,” “superior therapeutic performance,” or “bioequivalent.”

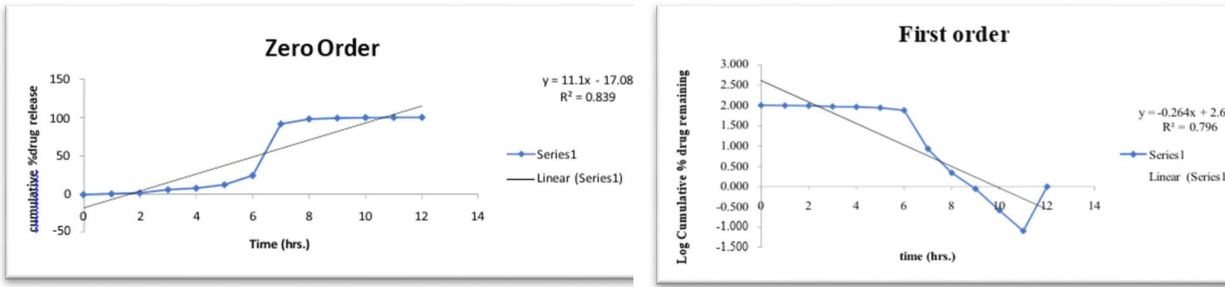


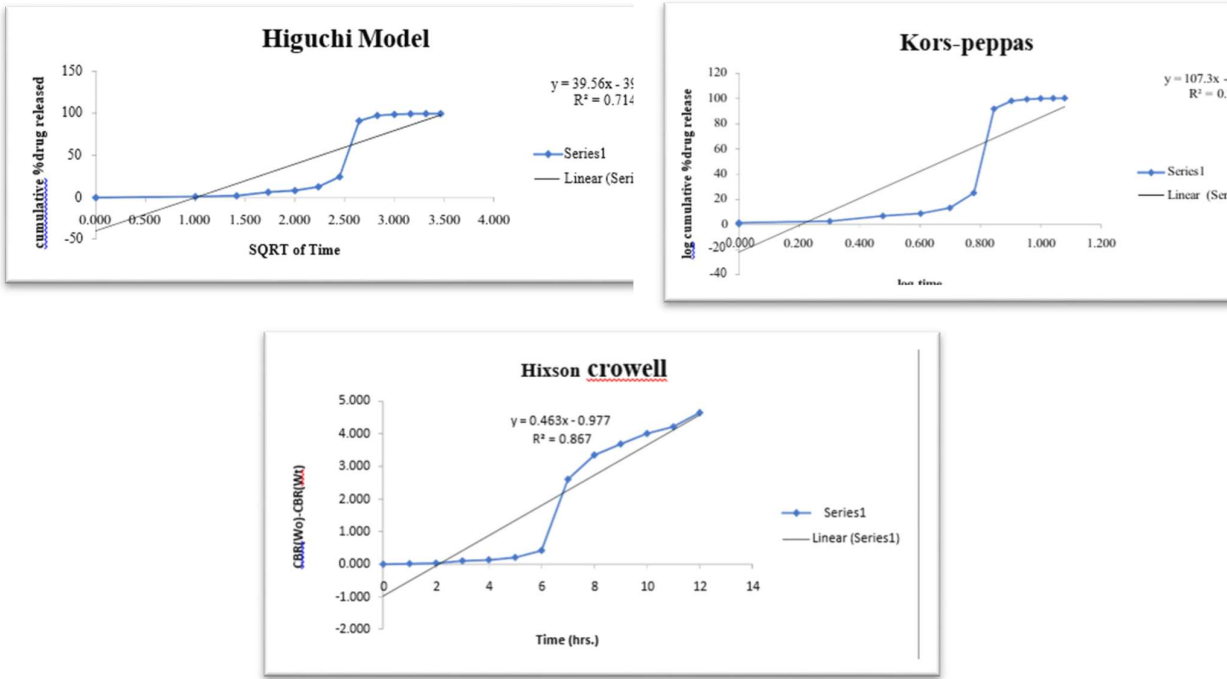
5.8.1 Release-kinetic modeling

TABLE.10. Release-kinetic modeling

Model	Reported R ²	Interpretive note in source
Zero-order	0.839	Moderate fit
First-order	0.796	Moderate fit
Higuchi	0.714	Poor diffusion fit
Korsmeyer–Peppas	0.720	Moderate fit
Hixson–Crowell	0.867	Highest reported fit

Hixson–Crowell provided the highest reported R² (0.867), followed by zero-order (0.839), first-order (0.796), Korsmeyer–Peppas (0.720), and Higuchi (0.714). The source table also associates a reported exponent of 1.66 with the best-fitting Hixson–Crowell result; technically, an exponent is usually associated with the Korsmeyer–Peppas model, not Hixson–Crowell. This apparent reporting or table-label inconsistency should be checked against the original regression calculations before publication. Given the pH-triggered lag phase and sharp increase in release, fitting the entire profile to a single model may be intrinsically limited.

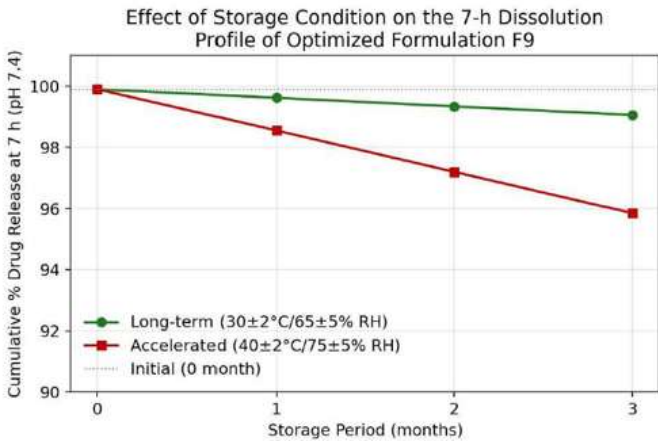




5.9 Stability evaluation

TABLE.11. Stability evaluation

Parameter	Initial	3 months long-term	3 months accelerated
Appearance	Smooth, uniform coating	No significant change	Slight dullness; no cracks
Hardness (kg/cm²)	4.90 ± 0.07	4.77 ± 0.08	4.48 ± 0.12
Friability (%)	0.19	0.25	0.38
Drug content (%)	99.58 ± 0.31	99.01 ± 0.37	97.03 ± 0.52
Release at 7 h (%)	99.90 ± 0.06	99.06 ± 0.09	95.85 ± 0.17



After three months at 30 ± 2°C/65 ± 5% RH, F9 showed no significant visible change. Hardness decreased from 4.90 ± 0.07 to 4.77 ± 0.08 kg/cm², friability increased from 0.19% to 0.25%, drug content decreased from 99.58 ± 0.31% to 99.01 ± 0.37%, and 7-hour release changed from 99.90 ± 0.06% to 99.06 ± 0.09%. These changes were modest in the reported dataset.

Under accelerated conditions (40 ± 2°C/75 ± 5% RH), slight dullness was observed by the later sampling period, although no cracks were reported. Hardness declined to 4.48 ± 0.12 kg/cm², friability increased to 0.38%, drug content decreased to 97.03 ± 0.52%, and 7-hour release was 95.85 ± 0.17%. The acid-stage release was also reported to increase from 2.20 ± 0.08% initially to

$3.46 \pm 0.15\%$ after three months under accelerated conditions; release up to the pH 6.8 stage increased from $10.40 \pm 0.10\%$ to $12.56 \pm 0.18\%$.

The reported results indicate retention of many physical and chemical quality attributes during the three-month study, with larger changes under accelerated storage. The data are preliminary and do not justify a shelf-life assignment. Longer-term stability, stability-indicating assay, packaging justification, and validated dissolution testing would be needed for a more complete assessment. The source's reported stage-time and pH inconsistencies should also be resolved before stability dissolution results are interpreted definitively.

6. DISCUSSION

This study evaluated a conventional direct-compression core followed by a pH-sensitive Eudragit® S100 film. The design is practical because it separates two formulation tasks: first, producing a mechanically acceptable core; second, adding a barrier intended to delay release until exposure to higher-pH media. F6 was selected as the core based on the combined pattern of blend flow, hardness, friability, disintegration, and drug content. F9 was selected among the coated formulations because it minimized the reported early release while still reaching extensive release after transfer to the higher-pH stage.

The pre-compression measurements indicate acceptable flow and packing for all six blends, with F6 showing the most favourable numerical values. The core-tablet data suggest that formulation differences coincided with improved mechanical strength and lower friability and disintegration time. Nevertheless, because the formulations differ in superdisintegrant type and concentration and the diluent quantity was adjusted, the experiment does not isolate one variable completely. A factorial design could determine whether the observed effects arise from superdisintegrant identity, concentration, or interactions with the rest of the formulation.

The coating results show the expected relationship between weight gain and early release: F9, with the highest coating level, had the lowest acid-stage release and the lowest release by 6 h. After exposure to the higher-pH stage, F9 showed a sharp rise in cumulative release. This pattern is compatible with a pH-responsive barrier, although a laboratory pH shift is not identical to passage through the human gastrointestinal tract. Interindividual differences in pH, transit, fluid volume, food, and disease state can affect the location and timing of polymer dissolution.

The stability data suggest that F9 retained acceptable appearance, drug content, and release characteristics over three months, especially under the long-term condition. The greater changes under accelerated storage are consistent with the need to optimize film composition, curing, and packaging. Because the source provides a limited duration and does not provide raw replicate-level data, no inferential statistical conclusions or shelf-life predictions are made here.

6.1 Study limitations, implications, and future work

Several limitations should be acknowledged. First, the evidence is entirely *in vitro*; no animal or human study is presented to establish the anatomical site of release or the pharmacological effect of the coated tablets. Second, the dissertation contains discrepancies in the pH values and durations assigned to sequential dissolution stages. These differences could materially affect the interpretation of the release profile and must be reconciled against laboratory records before submission. Third, the reported kinetic table appears to associate a release exponent with the Hixson–Crowell model; the regression calculations and labels require verification. Fourth, the comparator product contains bisacodyl rather than sodium picosulfate, so the comparison cannot demonstrate bioequivalence or therapeutic equivalence.

The study also has a short stability period, limited reported batches, and incomplete analytical-validation details. Supplier information, exact manufacturing settings, coating-process parameters, full dissolution time courses, and raw replicate values should be provided wherever available. The UV method should be validated for specificity, accuracy, precision, linearity, range, and robustness. The coating should be characterized for uniformity, adhesion, and residual solvent where relevant. A design-of-experiments approach could establish the relationship between coat weight, plasticizer level, curing conditions, acid resistance, and release after the pH trigger.

Further work should use a harmonized sequential dissolution method with a scientifically justified sequence of gastric, small-intestinal, and colonic conditions. The method should include appropriate sink-condition assessment and media that reflect physiological ionic strength. Testing across multiple batches would help establish reproducibility. Biorelevant dissolution, imaging or transit studies, and suitable in-vivo pharmacokinetic or pharmacodynamic studies would be required to establish whether the formulation truly targets the colon and whether the release profile offers a clinically meaningful advantage. A combined pH- and microbiota-triggered design may be explored if pH variability proves to be a major limitation, but this would require additional formulation and validation work.

7. CONCLUSION

Sodium picosulfate core tablets were prepared by direct compression and coated with Eudragit® S100 at 6%, 8%, and 10% weight gains. Among the core batches, F6 showed the most favourable reported combination of blend properties, tablet mechanical characteristics, disintegration time, and drug content. Among coated batches, F9 (10% weight gain) showed the lowest release in the acidic stage ($2.18 \pm 0.16\%$ at 2 h) and lower cumulative release through the reported pH 6.8 stage ($24.76 \pm 0.41\%$ at 6 h), followed by $91.48 \pm 0.72\%$ release at 7 h after transfer to pH 7.2 medium and complete release by 12 h. Hixson–Crowell had the highest reported R^2 (0.867), although the model labelling requires verification. F9 retained most measured quality attributes over three months, with greater changes under accelerated conditions. The findings support further investigation of this pH-sensitive coating strategy but do not establish in-vivo colon targeting or clinical superiority. Before journal submission, the dissolution protocol, kinetic-model labelling, source references, and raw data should be checked against the original experimental records.

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