



Colon-Targeted sodium Picosulfate Tablets Using pH-Sensitive Polymeric Coating: A Review

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ABSTRACT

Sodium picosulfate is a stimulant laxative prodrug that is activated in the colon; therefore, a tablet that releases the drug only in the lower gastrointestinal tract is pharmacologically sensible. Enteric methacrylic acid copolymers, such as Eudragit L100, L100-55, and S100, dissolve above defined pH thresholds and can be used to prevent drug release during gastric and small-intestinal transit. This review summarizes the rationale for colon-targeted sodium picosulfate tablets and covers colonic physiology, drug pharmacology, major colon-targeting strategies, pH-dependent polymers, formulation and coating methods, and the evaluation of coated tablets, including multi-stage and bicarbonate-buffer dissolution testing, scintigraphy, and stability testing. The available evidence indicates that pH-only coatings may fail in vivo because of interindividual variations in intestinal pH and gastrointestinal transit. Combined triggering mechanisms and biorelevant testing are promising approaches to improve targeting reliability. No published study specifically investigating coated, colon-targeted sodium picosulfate tablets was identified among the sources gathered for this review. Therefore, the formulation guidance presented here is extrapolated from studies involving other drugs.

KEYWORDS: Sodium picosulfate; colon-targeted drug delivery; pH-sensitive polymers; Eudragit; enteric coating; bowel preparation; in vitro dissolution.

Introduction

Adequate bowel cleansing is a prerequisite for high-quality colonoscopy. Poor preparation is linked to missed lesions: in one study the adenoma miss rate was 69.6% after poor preparation, 48.1% after fair and 27.3% after optimal preparation. Preparation quality is usually graded with the Boston Bowel Preparation Scale, which has high inter-rater reliability and whose segment scores track polyp detection, although the link to adenoma detection is not uniform across studies, and fair preparation did not significantly reduce adenoma detection in a large registry. European and US guidelines recommend split-dose regimens and set out how preparation quality should be optimised.

High-volume (4 L) polyethylene glycol (PEG) regimens are effective but difficult for patients to tolerate, with palatability and completion as recurring problems. Low-volume sodium picosulfate with magnesium citrate (SPMC) was developed as an alternative. Meta-analyses of randomised trials report cleansing comparable to PEG, Better tolerability and similar polyp detection, although dizziness was more frequent with SPMC and heterogeneity between trials was high. Safety issues are mainly electrolyte-related. In older adults, sodium picosulfate carried a higher relative risk of hospitalisation for hyponatraemia than PEG (relative risk 2.4), but the absolute risk increase was only 0.05%,^s and other series found no significant fall in mean serum sodium or reported only isolated symptomatic cases.

Sodium picosulfate is a prodrug. Colonic bacterial enzymes convert it to the active metabolite bis-(p-hydroxyphenyl)-pyridyl-2-methane (BHPM), and the same metabolite is formed from bisacodyl by different enzymes. Because activation happens in the colon, drug released earlier in the gut contributes little. A pH-triggered coating is one way to align release with the site of activation. Gastrointestinal pH rises from about 1–2 in the stomach to about 7.4–7.5 in the terminal ileum and enteric polymers that dissolve above a threshold pH can use this gradient as a release trigger. Oral colon-targeted systems have been reviewed repeatedly but pH-dependent coatings have limited reliability, which this review discusses in detail.

This review therefore (i) outlines colonic physiology and the pharmacology of sodium picosulfate, (ii) compares colon-targeting approaches, (iii) examines pH-sensitive polymers and coating methods, (iv) describes how coated tablets are evaluated in vitro and in vivo, and (v) discusses challenges and future directions. Because no study of coated colon-targeted sodium picosulfate tablets was identified in the sources gathered here, formulation principles are drawn from work with other drugs, mostly mesalamine, naproxen, diclofenac and ketoprofen^[1-6].

Colonic physiology relevant to delivery

The colon is the last segment of the gut and extends from the caecum through the ascending, transverse, descending and sigmoid colon to the rectum. Three features dominate delivery design: luminal pH, transit time and the resident microbiota. Compared with the small intestine, the colon has low fluid volume, a near-neutral pH, long transit times and little proteolytic activity, but a dense anaerobic flora that can cleave polysaccharides and azo bonds.

Luminal pH. Radiotelemetry in 66 healthy volunteers found gastric pH of about 1.0–2.5, proximal small-intestinal pH of about 6.6, terminal ileal pH of about 7.5, a fall to about 6.4 in the caecum and a rise to about 7.0 in the left colon.¹⁹ A review of the literature gives similar values: about 6 in the duodenum, 7.4 in the terminal ileum, 5.7 in the caecum and 6.7 in the rectum, with disease, diet and drugs all able to shift regional pH. A meta-analysis of pH data from 10 gastrointestinal regions found that food raises gastric and duodenal pH but not small-intestinal or colonic pH.

Table.1.Region and reported pH

Region	Reported pH (healthy, fasted)	Source
Stomach	about 1.0–2.5	Evans et al.
Proximal small intestine	about 6.0–6.6	Evans; Fallingborg
Terminal ileum	about 7.4–7.5	Evans; Fallingborg
Caecum	about 5.7–6.4	Fallingborg; Evans
Left colon	about 7.0	Evans
Rectum	about 6.7	Fallingborg

The caecal dip is the central weakness of strictly pH-dependent colonic systems. A polymer that dissolves above pH 7 may meet the ileum, where pH is high, only briefly, and then be exposed to a caecal pH below its threshold. Colonic pH is also lower in active ulcerative colitis and Crohn's disease, which matters if the formulation is intended for patients with bowel disease.

Transit. Colon transit is slow and variable. Scintigraphic transit studies score radiolabel in seven colonic segments as a geometric centre, and normal mean values are about 4.6 at 24 h, 6.1 at 48 h and 6.6 at 72 h, so a dosage form that reaches the colon can still be moving through it for days. This slow transit helps release after arrival but also means disintegration can be late, which matters for a laxative that is expected to act predictably.

Microbiota. Colonic bacteria supply the enzymes that activate sodium picosulfate (section 3) and that degrade polysaccharide and azo-based carriers, the basis of microbially triggered delivery (section 4).

a. Fluid volume and mixing

The small intestine contains several hundred millilitres of fluid moving in a largely forward direction, which keeps dissolved material mixed and in contact with the mucosa. The colon holds much less free fluid, and its contents are semi-solid in the distal segments, so a coat that dissolves correctly in a well-stirred dissolution bath may behave differently once the tablet reaches a low-fluid, high-viscosity environment; this is one reason in vitro thresholds do not always predict in vivo disintegration (section 5.1, section 7.1).

b. Disease states and special populations

Colonic pH and transit are not fixed values even within a healthy population, and they shift further in disease. Active ulcerative colitis and Crohn's disease are associated with a lower colonic pH than in healthy controls, which can push the luminal environment below the dissolution threshold of a high-pH polymer such as Eudragit S100²⁰. Diet, laxative use, antibiotic courses and the bowel-cleansing process itself (relevant here, since the tablet is intended for use alongside a cleansing regimen) can also alter transit time and the resident microbiota. A formulation intended for general colonoscopy preparation should therefore be tested, where possible, across the range of patients who will use it, not only in healthy volunteers^[7-11].

2. Sodium picosulfate: pharmacology and implications for formulation

Activation. Sodium picosulfate is a prodrug that passes through the upper gut largely intact and is converted by sulfatase (desulfatase) enzymes of the colonic microflora to the active diphenol BHPM. Bisacodyl yields the same metabolite, but through mucosal deacetylases, so it is less dependent on bacteria; picosulfate depends on bacterial activation (for example arylsulfate sulfotransferase from *Eubacterium rectale*).

Pharmacokinetics. After sodium picosulfate dosing in healthy volunteers, plasma BHPM appeared after a lag of about 4–5 h and peaked at about 9 h, consistent with arrival and activation in the colon, and about 13% of the dose was excreted in urine as BHPM at steady state. BHPM was not detected in breast milk. The lag is an intrinsic delay, and a coating adds its own lag on top of it, so the total time to effect after a coated tablet may be longer than after a solution. This should be addressed in clinical dosing schedules.

Efficacy and safety of the established product. Split-dose SPMC cleans the colon about as well as PEG with better tolerability and compliance in outpatients. Hyponatraemia is the main safety concern and has been reported mostly in older adults and in case reports, while a small study found no

significant fall in mean serum sodium. Oral sodium phosphate preparations differ in mechanism and carry a distinct risk of electrolyte disturbance and acute phosphate nephropathy, particularly with reduced renal function or use of ACE inhibitors, angiotensin receptor blockers or diuretics.

Implications for a coated tablet.

- Release should be complete in the ileocaecal region or colon, where the activating bacteria are present; premature release gives no pharmacological gain.
- Sodium picosulfate is water soluble and, in published products, dosed in the milligram range, so the core must disintegrate quickly once the coat dissolves.
- Concomitant antibiotics and the state of the microbiota may alter efficacy; this should be documented in any clinical evaluation.¹²
- Electrolyte monitoring and hydration advice remain relevant for any dosage form containing the drug.

a. Comparison with bisacodyl

Sodium picosulfate and bisacodyl are often discussed together because both are converted to the same active diphenol, BHPM, and both belong to the triarylmethane class of stimulant laxatives. The route of activation differs: bisacodyl is deacetylated chemically or by mucosal (and some bacterial) esterases along the gut, including in the small intestine, while picosulfate depends specifically on bacterial arylsulfatase activity that is concentrated in the colon. This difference is the pharmacological reason picosulfate is regarded as more strictly colon-activated than bisacodyl, and it is the basis for treating picosulfate as a good candidate for a colon-targeted delivery system: a coating that fails and releases bisacodyl early may still produce some effect, whereas picosulfate released early largely passes through unconverted.

b. Dose and exposure considerations

Published sodium picosulfate bowel-preparation products use picosulfate in the low milligram range per dose, combined with osmotic salts. A tablet formulation intended only to deliver the picosulfate component (rather than replace the osmotic load) would use a similar low dose per unit, so the core tablet is necessarily small and diluent-dominated (section 6.2). Because the drug is not meaningfully absorbed before colonic conversion, systemic exposure to intact sodium picosulfate is expected to be minimal regardless of where disintegration occurs; the clinical concern with premature release is loss of local laxative effect and unpredictable timing, not systemic toxicity from the parent compound itself.

c. Interactions and precautions relevant to a colon-targeted design

- Concomitant antibiotics that suppress colonic flora may reduce conversion of picosulfate to BHPM, and this should be recorded in any clinical evaluation of a coated tablet.
- Patients with an ileostomy, colostomy, or extensive colonic resection have altered or absent target tissue, so a colon-targeted tablet is not an appropriate mechanism for them; this is a labelling and patient-selection point rather than a formulation one.
- As with the existing product, hydration and electrolyte status should be assessed before use, particularly in older adults and those with renal or cardiac impairment^[11-14].

Approaches to colon-targeted delivery

Colon-targeting strategies exploit pH changes, transit time, colonic microbes and enzymes, or physical triggers. The primary approaches (prodrugs, pH-dependent, time-dependent and microbially triggered systems) have had limited success, while newer designs such as pressure-controlled capsules, CODES and osmotic systems aim for better site specificity. Recent reviews cover stimuli-responsive designs and combined pH/time or pH/bacterial triggers.

Table.2. Approaches, triggers, strengths, limitations and examples

Approach	Trigger	Strengths	Limitations	Examples
pH-dependent coating	Rising luminal pH	Simple and scalable	Variable pH and transit; caecal pH dip; not reliably colon-specific	Eudragit-coated mesalamine and naproxen tablets
Time-dependent system	Fixed lag after gastric exit	Independent of pH	Gastric emptying and transit vary	Ethylcellulose-coated tablets; HPMC compression coat plus enteric film
Microbially triggered (polysaccharide)	Colonic enzymes	High potential specificity	Water solubility can cause premature release	Pectin; guar gum/HPMC compression coat

Approach	Trigger	Strengths	Limitations	Examples
Microbially triggered (azo polymers)	Azo-reductase	Cleaved by colonic bacteria ⁵²	Synthetic polymer safety and variability	Azo-polymer carriers
CODES-type systems	pH plus enzymes	Combined triggers	More complex manufacture	Budesonide pellets
Dual-trigger coatings	pH plus microbiota	Fail-safe release when pH alone fails	Tested mainly in vitro and in small studies ⁴⁹	Starch/Eudragit S coating (Phloral)

Polysaccharide carriers resist upper-gut conditions and are cleaved by colonic bacteria, but their high water solubility can cause premature release; calcium pectin, blends with ethylcellulose or polymethacrylates, and pectin–chitosan complexes have been proposed to correct this. Polysaccharides have been reviewed as colonic carriers in general and azo-based carriers are cleaved by colonic bacteria.

Time-controlled systems have worked in animals: in dogs, ethylcellulose-coated tablets gave an in vivo absorption lag that matched their in vitro release lag. Combining pH and time triggers can reduce premature release and raise colonic drug delivery in a mouse colitis model.⁵¹ A clinical review of mesalazine concluded that pH-dependent and constant-release products differ in how well delivery concepts translate into therapeutic efficacy, with evidence still mostly in vitro and from small studies.

For a hygroscopic, water-soluble, low-dose drug that must reach the colon in time for bacterial activation, pH-dependent enteric coating remains the simplest and most scalable choice, with a time-dependent or enzyme-degradable layer as an optional second trigger for robustness^[15-17].

d. Why the other approaches were set aside for this drug

- **Prodrug approaches** (conjugating the drug to a carrier cleaved by colonic bacteria) are well suited to drugs that need a new chemical entity; sodium picosulfate is already a colon-activated prodrug in pharmacological terms, so adding a second prodrug layer is unnecessary complexity.
- **Pressure- and osmotically controlled capsules** are mechanically sophisticated and have mainly been developed as single-unit capsule systems rather than as film coats applicable to a simple tablet, which limits their fit with existing solid-dose manufacturing.
- **Pure microbially triggered polysaccharide coatings** (pectin, guar gum, chitosan) are attractive for specificity but are water-soluble and prone to premature erosion in the stomach and small intestine unless blended with a pH-resistant polymer, which in practice turns them into combination systems similar to the dual-trigger coatings already covered in the table.
- **CODES-type systems**, which combine an acid-soluble outer layer, a polysaccharide layer and an enteric layer, offer strong specificity but need a multi-layer compression-coating process that is harder to scale than a single enteric film.

This leaves pH-dependent coating, optionally combined with a time- or microbiota-based second trigger, as the pragmatic choice for a first-generation coated sodium picosulfate tablet, with the dual-trigger option kept in reserve if single-trigger performance proves unreliable in vivo (sections 5.3, 7.1).

e. Manufacturing complexity across approaches

Table.3. Approach, Core process, Coating/compression steps and Relative manufacturing complexity

Approach	Core process	Coating/compression steps	Relative manufacturing complexity
pH-dependent coating	Standard tablet core	One enteric film-coating step	Low
Time-dependent (lag) system	Standard tablet core	Compression coat or thick enteric/HPMC film	Moderate
Microbially triggered (polysaccharide)	Standard tablet core	Polysaccharide film, sometimes plus a protective outer film	Moderate
Dual pH/microbiota (e.g. Phloral-type)	Standard tablet core	Resistant-starch/Eudragit blend coating	Moderate to high
CODES-type	Multi-layer core or compression-coated core	Acid-soluble, polysaccharide and enteric layers in sequence	High

pH-sensitive polymers for colonic coating

Enteric polymers are polyacids whose carboxyl groups ionise and dissolve above a threshold pH. Methacrylic acid copolymers (Eudragit) are the most widely used for ileo-colonic release. Published thresholds by grade are summarised below; the source itself notes small inconsistencies in its tables for Eudragit FS 30 D (pH 6.8 versus 7).

Table 4. Polymer, Approx. dissolution threshold and Role in colonic design

Polymer	Approx. dissolution threshold	Role in colonic design
Eudragit L100-55	above about pH 5.5	Proximal small-intestinal release; used in blends with S100 or in time-plus-pH coats
Eudragit L100	above about pH 6	Lower-threshold component in L100/S100 blends
Eudragit S100	above about pH 7	Main ileo-colonic polymer
Eudragit FS 30 D	about pH 6.8–7	Aqueous dispersion for ileo-colonic coating
Eudragit E grades	soluble up to about pH 5	Not enteric; unsuitable for colonic targeting

HPMCP, shellac and cellulose acetate phthalate are also used as enteric coating materials, but none of the studies retrieved for this review examined them as colonic coatings, so they are not discussed further.

Evidence from coated tablets. In mesalamine matrix tablets coated with Eudragit S100, about 94.9% of drug was released over 24 h in vitro, while uncoated tablets released within 6 h. A 2% w/v Eudragit S-100 coat on naproxen matrix tablets sustained release for 24 h (about 94.67%), and release rose to about 98.60% in the presence of rat caecal content, against release within 5 h for uncoated tablets. A mixed film of Eudragit L100 and HPMC E15 LV retarded mesalamine release, with HPMC creating channels for fluid entry, and release followed Higuchi kinetics. In a neural-network optimisation of a Eudragit S100 matrix, 12.09% of mesalamine was released at 2 h and 72.96% at 12 h, while the commercial product released 100% by 6 h. Ketoprofen mini-tablets compression-coated with 25% HPMC K4M and film-coated with Eudragit L 30D-55 released about 98.7%, beginning at around 8 h.

In vivo behaviour. Thresholds measured in vitro do not guarantee site-specific release in humans. In eight fasted volunteers, Eudragit FS-coated tablets disintegrated consistently at the ileo-caecal junction or in the ascending colon whereas Eudragit S-coated tablets disintegrated erratically and a few failed to disintegrate, and intestinal pH, transit time and feed status alone did not explain the variability. A pH-only Eudragit S coating can fail to release drug, which motivated a dual pH- and microbiota-triggered coat.

Why in vitro thresholds do not always predict in vivo release

Three factors explain the gap between a polymer's measured dissolution pH and its behaviour in a person. First, the colon's pH is not a single value but a profile that dips in the caecum and recovers distally, so a tablet can pass through a region above its threshold only briefly. Second, in vitro dissolution testing is usually done in a well-stirred, large-volume bath, which is a poor model of the colon's low fluid volume and semi-solid contents (section 2.1). Third, gastric emptying of a single tablet is itself variable and depends on fed or fasted state, so the 'clock' on transit does not start at a fixed time after dosing. Scintigraphy studies that track real disintegration sites in volunteers are therefore the standard against which an in vitro method should be judged, not the other way round.

Polymer blending as a design variable

Blending a lower-threshold polymer (L100 or L100-55) with a higher-threshold one (S100) allows the effective dissolution pH of the coat to be tuned between their individual thresholds, and this has been used to manipulate release from colon-targeted systems for other drugs. In practice the blend ratio, not just the nominal polymer identity, becomes a formulation variable to be optimised by dissolution testing, alongside coat weight and plasticiser level (section 6.1). A higher proportion of the lower-threshold component moves release earlier (more small-intestinal exposure, lower risk of non-release); a higher proportion of S100 moves release later and more colon-specific, at the cost of a higher risk of the pH-dip failure described in section 5.1.

Single-trigger versus dual-trigger coatings

Because a purely pH-triggered coat can fail to dissolve in some individuals, a second, independent trigger provides a fail-safe. The best-characterised example combines an Eudragit S coat with a resistant-starch component that is fermented by colonic bacteria regardless of local pH, so that the coat is breached by bacterial action even if the pH threshold is never reached, so a microbiota-sensitive outer layer and a bacterially activated drug are mechanistically aligned; a tablet that reaches the colon without disintegrating is also a tablet whose drug would not yet be activated even if released^[18-24].

Formulation of the core tablet and coating

Core tablet. Sodium picosulfate is a low-dose drug (milligram range per tablet), so a diluent-rich formulation is needed. Typical components are microcrystalline cellulose or lactose as diluent, a disintegrant (croscarmellose sodium, sodium starch glycolate), a binder (PVP K30, HPMC), a glidant

(colloidal silica) and a lubricant (magnesium stearate). Direct compression or wet granulation is used, and moisture uptake should be assessed because the drug is freely water soluble. A sub-coat of HPMC is often applied to isolate the core from the acidic enteric polymer.

Coating. Two methods dominate:

1. **Organic solvent coating:** Eudragit S100/L100 dissolved in isopropanol–acetone with plasticiser and talc, applied by pan or dip coating at lab scale. It gives good films but has solvent-residue and safety issues.
2. **Aqueous dispersion coating:** Eudragit FS 30 D or neutralised S100 dispersions sprayed in a perforated pan or fluid-bed coater, preferred for scale-up and to limit residual solvent. Curing after coating can change film structure and dissolution, so it is optimised, not assumed.

a) Critical formulation and process attributes

Release from a coated tablet is set by a small group of variables. The table lists them with the direction of their effect, so that the optimisation experiments can be planned around them.

Table.5. Attribute, What is varied and Effect on release

Attribute	What is varied	Effect on release
Polymer grade and ratio	S100 alone; L100/S100 or L100-55/S100 blends	Sets the pH at which the film dissolves
Coat weight gain	Film thickness on the tablet	Longer lag in acid and in pH 6.8 buffer as thickness rises
Plasticiser type and level	For example citrate esters or PEG	Film flexibility and glass transition; too little gives cracks
Curing time and temperature	Post-coating heat treatment	Changes film structure and dissolution
Sub-coat	HPMC film between core and enteric coat	Keeps the acidic polymer away from the core
Core disintegration	Disintegrant type and level	Speed of drug release once the coat has dissolved

b) Illustrative starting formulation

No coated colon-targeted sodium picosulfate tablet has been published, so the layout below is a development starting point assembled from standard excipient roles and the polymer work reviewed in section 5. It is not a validated formula, and every level should be confirmed by experiment.

c) Coating process

Pan or fluid-bed coating is used at development scale, with the coating liquid applied until the target weight gain is reached⁴³. The main controls are inlet air and bed temperature, spray rate, atomising pressure and pan speed. Bed temperature should stay well above the minimum film-forming temperature of the polymer and below the point at which tablets stick together, and the weight gain should be confirmed on a sample of tablets from each batch. After coating, a defined drying and curing step is used and its effect on dissolution is measured³⁹.

Table.6. layer, Component and Component

layer	Component	Function
Core	Sodium picosulfate	Active (dose set by clinical need)
Core	Microcrystalline cellulose and/or lactose	Diluent and compaction aid
Core	Croscarmellose sodium or sodium starch glycolate	Disintegrant
Core	PVP K30 or HPMC	Binder
Core	Colloidal silica; magnesium stearate	Glidant; lubricant
Sub-coat	HPMC with plasticiser	Barrier between core and enteric polyer

layer	Component	Function
Enteric coat	Eudragit S100, or S100 blended with L100 or L100-55	pH-triggered release layer
Enteric coat	Plasticiser, talc, optional pigment	Film flexibility, anti-tack, opacity
Core	PVP K30 or HPMC	Binder

d) Quality by design and risk considerations

A quality-by-design approach treats the coat weight gain, polymer blend ratio, plasticiser level and process temperature as the critical material and process attributes, linked to the critical quality attribute of stage-wise dissolution (section 7.3). A simple risk ranking is useful early in development:

Table.7. Attribute, Risk to colonic targeting if poorly controlled and Mitigation

Attribute	Risk to colonic targeting if poorly controlled	Mitigation
Coat weight gain	Too low: early leakage; too high: incomplete or delayed release	In-process weight checks on sampled tablets during coating
Polymer blend ratio	Shifts effective threshold away from target	Pre-validated blend prepared by weight, verified by dissolution
Core hygroscopicity/moisture	Core swelling can crack the coat during storage	Controlled humidity during processing; desiccant packaging
Sub-coat adequacy	Acidic polymer film can interact with a moisture-sensitive core	HPMC sub-coat applied to a defined weight gain before the enteric coat
Spray rate/droplet size	Uneven film, pinholes	Validated spray parameters; visual and microscopic film inspection

e) Scale-up considerations

Laboratory-scale pan or fluid-bed coating does not automatically translate to production scale without adjustment of spray rate, batch size, airflow and dwell time, because uneven drying across a larger bed can leave some tablets under-coated and others over-coated. A design that depends on a narrow, well-controlled coat-weight window (as a dual-trigger or thin high-S100 coat might) carries more scale-up risk than a design with a wider acceptable weight-gain range, which is one more argument for characterising the dissolution response to coat weight broadly during development (section 6.1), rather than targeting a single point value^[24,25].

f) Evaluation of the tablets

Pre-compression. Angle of repose, bulk and tapped density, Carr's index and Hausner ratio confirm that the blend flows adequately.

Post-compression and post-coating. Weight variation, thickness, hardness, friability (<1%), drug content uniformity, disintegration and percentage weight gain of the coat. Compatibility between drug and polymers is checked by FTIR and DSC.

In vitro dissolution (the decisive test). Sequential-media testing mimics GI transit in USP apparatus II (paddle, 50–100 rpm, 37 °C), and is typically done as follows:

1. N HCl (pH 1.2) for 2 h, simulating the stomach. Release should be negligible (pharmacopoeial enteric limit: <10%).
2. Phosphate buffer pH 6.8 for 3–4 h, simulating the small intestine. Release should remain minimal.
3. Phosphate buffer pH 7.2–7.4 for the remaining period, simulating the ileocaecal region and colon. Release should be rapid and near complete.

Samples are analysed by UV spectrophotometry or HPLC, and release kinetics are fitted to zero-order, first-order, Higuchi and Korsmeyer–Peppas models. Drug release in simulated colonic fluid with rat caecal content, or with bacterial enzymes, can add evidence for microbial activation.

Stability. Studies follow ICH Q1A conditions₆₀ (40 °C / 75% RH for 6 months accelerated; 25 °C / 60% RH long-term), tracking assay, dissolution profile, and appearance, since polymer films can age and shift their release threshold.

Further tests. Gamma scintigraphy in healthy volunteers is the standard way to confirm in vivo disintegration at the target site, and animal or clinical bowel-cleansing studies (for example Boston Bowel Preparation Scale) provide efficacy data.

a. Choice of dissolution media

Phosphate buffers are simple and reproducible, but they differ from intestinal fluid, which is buffered mainly by bicarbonate. Bicarbonate-based media were developed to test enteric coated products under more physiological conditions, and they are more demanding for pH-responsive coats than phosphate buffer at the same nominal pH. Human scintigraphy shows why this matters: Eudragit FS-coated tablets disintegrated consistently at the ileocaecal junction or in the ascending colon, whereas Eudragit S-coated tablets disintegrated erratically and some failed to disintegrate. A dissolution package for sodium picosulfate should therefore pair the compendial sequential-medium test with a bicarbonate-buffer test, so that a coat that passes the first but fails the second is caught before the clinical study.

b. Dissolution data analysis

Release profiles are compared with simple models and with the similarity factor f_2 . The Higuchi model describes release proportional to the square root of time, and the Korsmeyer–Peppas power law describes release from a polymer system with an exponent n that indicates the mechanism: release phase alone, and f_2 is of limited use across a lag, so the stage-wise acceptance limits below carry more weight.

c. Proposed target profile

The limits below are proposed development targets for this type of tablet. They are not taken from a monograph for sodium picosulfate,

Table.8. Stage, Medium, Duration and Proposed target

Stage	Medium	Duration	Proposed target
1	0.1 N HCl, pH 1.2	2 h	Less than 10% released (gastro-resistance limit)
2	Phosphate or bicarbonate buffer, pH 6.8	3–4 h	Minimal release; limit set from pilot batches
3	Buffer, pH 7.2–7.4	Until plateau	Rapid, near-complete release once the threshold is crossed
4	Bicarbonate buffer, ileocaecal conditions	As stage 3	Confirms stage 3 under physiological bufferings _{ss}

d. In vivo and clinical evaluation

Three levels of in vivo evidence are useful. First, gamma scintigraphy in healthy volunteers shows where the tablet disintegrates and is the most direct check of the coating design. Second, plasma BHPM is a useful pharmacokinetic marker, because after sodium picosulfate it appears after a lag of several hours and peaks at about 9 h, consistent with colonic activation₁₁; a coated tablet should add a measurable but acceptable delay to this profile. Third, cleansing efficacy is judged with the Boston Bowel Preparation Scale against an approved sodium picosulfate regimen, using split-dose designs like those used to register the existing products.

e. Stability testing

Stability studies follow the ICH Q1A(R2) framework, with accelerated and long-term storage conditions and a defined set of tests. For this product the stability-indicating tests should include assay, related substances, water content, appearance of the coat, and the full multi-stage dissolution profile, because ageing of a polymer film and moisture uptake by the core can both shift the release threshold.

f. Assay and related-substance methods

A stability-indicating HPLC or UV method is needed to separate sodium picosulfate from its degradation products and from coating-derived excipients, and to quantify BHPM where it is used as a marker in enzyme-based release testing (section 7.1). Method validation should cover specificity, linearity, accuracy, precision, and robustness to small changes in mobile phase pH and composition, following the usual pharmacopoeial validation framework; no validated compendial method specific to a coated colon-targeted sodium picosulfate tablet exists at the time of this review, so a method would need to be developed and validated alongside the formulation^[26,27].

CHALLENGES, FIUTURE PERSPECTIVES AND CONCLUSION

Challenges. GI pH and transit differ widely between people and with food, disease (IBD, constipation) and drugs, so a fixed pH threshold can misfire: premature release in the small bowel, or failure to release before excretion. Caecal acidification, moisture uptake by the core, and batch-to-batch variability in coating thickness add to the problem. Standard dissolution media also under-represent the low buffer capacity and bicarbonate chemistry of real intestinal fluid.

Future perspectives. Multi-trigger coatings (pH plus enzyme or time), bicarbonate-buffer biorelevant dissolution models, 3D-printed and multiparticulate designs, and imaging-based in vivo validation should improve reliability. Head-to-head clinical trials against conventional bowel-prep regimens are still needed for a coated sodium picosulfate tablet.

Translational and regulatory points. A coated sodium picosulfate tablet would be a modified-release product, so the development file needs a justified quality target profile, a discriminating dissolution method and evidence of site of release in humans. Because the colonic activation of picosulfate depends on bacteria, clinical studies should record antibiotic use and bowel disease, both of which can change the microbiota and colonic pH. Electrolyte monitoring and hydration advice used for the established product still apply.^[28-30]

Research gaps.

- No published formulation of a coated colon-targeted sodium picosulfate tablet was found, so every design principle here is extrapolated from other drugs.
- Direct comparison of pH-only and dual-trigger coatings loaded with a laxative prodrug has not been reported.
- The delay a coat adds to the 4–9 h BHPM lag₁₁ has not been measured, and it sets the dosing schedule.
- Bicarbonate-buffer dissolution data for Eudragit S100 blends on tablets of this type are needed to link in vitro and in vivo results.

PATIENT AND CLINICAL-PRACTICE CONSIDERATIONS

A coated tablet changes the user experience of bowel preparation from a measured liquid dose to a swallowed solid, which may suit patients who find the taste or volume of liquid preparations difficult, but introduces its own considerations: swallowing difficulty in some older patients, the need for adequate co-administered fluid regardless of the picosulfate component's delivery route (since the osmotic agents still require fluid loading), and clear instructions on timing relative to the procedure, given the colonic lag already present in the uncoated product and the additional lag a coating adds (Sections 3.2, 7.4). None of these points is unique to this formulation, but they should be addressed in labelling and patient counselling materials alongside any clinical development programme.

Table.8. Summary table of key evidence used in this review

Evidence type	What it shows	Where used
Human GI pH radiotelemetry	Luminal pH profile and its variability	Section 2, Section 5.1
Human scintigraphy of Eudragit-coated tablets	Actual in vivo disintegration site and its variability	Section 5.1, Section 7.4
Sodium picosulfate pharmacokinetic study	Lag and peak of the active metabolite	Section 3.2, Section 7.4
Bacterial activation studies	Mechanism linking picosulfate to colonic bacteria	Section 3.1, Section 8
Coated-tablet studies in other drugs	Achievable release profiles with Eudragit coatings	Section 5, Section 6
Dual-trigger coating studies	Fail-safe design against pH-only failure	Section 5.3, Section 8
Bicarbonate-buffer dissolution method	More physiological in vitro test	Section 7.1

This table is a map of the review's own evidence base, not a new dataset, and is intended to help a reader move quickly between a claim and the type of study behind it^[31-36].

CONCLUSION

Compared pH-sensitive polymeric coatings, particularly Eudragit S100 alone or with L100, are the most practical and scalable starting point for targeting sodium picosulfate to the colon, matching the drug's colonic activation, but pH-only coatings can fail in vivo, so a second trigger or a strong biorelevant test package is advisable. Success depends on a robust core, an adequately thick and well-cured coat, and sequential-media dissolution that shows negligible release at pH 1.2 and 6.8 and rapid release at pH ≥ 7 .

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