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Swellable hydrophilic matrix tablets for oral drug delivery: Mechanisms, polymer systems, formulation design and future directions

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Abstract

Swellable hydrophilic matrix tablets represent one of the most extensively validated platforms for oral controlled drug delivery, with a track record spanning several decades of clinical and commercial application. The mechanism by which these systems operate is, in principle, straightforward: upon contact with gastrointestinal fluid, the polymer at the tablet surface hydrates, undergoes a glassy-to-rubbery phase transition, and forms a gel layer that envelops the core. The properties of this gel layer — its thickness, its viscosity, and its resistance to erosion — govern the rate at which drug molecules diffuse outward and, consequently, the overall release profile. A formulation in which the gel layer is appropriately characterised is one in which the release kinetics largely take care of themselves; conversely, deficiencies at this stage are rarely correctable through subsequent formulation adjustments.

This review synthesises both foundational and contemporary literature to examine swellable matrix systems from several complementary perspectives. The discussion begins with the underlying mechanistic principles before proceeding to classification schemes, commonly employed polymers and excipients, manufacturing considerations, and the in vitro evaluation methods used during formulation development. Particular emphasis is placed on the relationship between polymer concentration and viscosity grade, a focus that reflects both its prominence in the existing literature and its status as the parameter formulators are most directly able to control. A survey of drug-specific studies across multiple therapeutic categories is also presented, illustrating the breadth of clinical application this platform has achieved. The review concludes with an examination of persistent challenges in the field — most notably, the difficulty of predicting in vivo performance from in vitro dissolution data — and identifies areas of active innovation, including gastroretentive matrix designs, hybrid natural-synthetic polymer systems, and stimuli-responsive release architectures.

Keywords: Hydrophilic polymer; HPMC; Controlled drug release; Gel layer; Oral sustained release; Gastroretentive systems

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1. Introduction

The oral route has held its dominant position in drug delivery for a long time, and the reasons are straightforward: patients accept tablets and capsules without difficulty, the risk associated with injections is absent, and tablet manufacturing at commercial scale is well understood. That said, oral delivery is not without pharmacokinetic complications. A drug administered as a conventional immediate-release tablet produces a plasma concentration peak shortly after ingestion, followed by a fall toward a trough before the next dose is taken. For agents with narrow therapeutic windows, this oscillating pattern creates recurring clinical problems — concentrations that are too high at peak and potentially sub-therapeutic in the trough period [1].

Oral formulations designed for sustained and controlled release address this problem by spreading drug delivery over several hours, often between six and twenty-four. Matrix tablets — in which drug is mixed throughout a solid polymer network rather than enclosed in a membrane — have attracted consistent attention from formulation scientists for both practical and technical reasons. They require no coating equipment, no membrane integrity monitoring, and no plasticizer optimization during processing. The same compression machinery used for immediate-release tablets serves for matrix tablets as well. Polymer raw materials are generally affordable and carry established regulatory acceptance across major markets [2].

Within the broader matrix tablet category, swellable hydrophilic systems have a distinctive feature: the polymer is not a passive scaffold. It takes an active part in drug release by absorbing water, forming a gel, and then slowly dissolving away at the surface. The combination of these three processes — water penetration, gel formation, and surface erosion — gives the formulation scientist a set of controls that neither purely diffusion-controlled nor membrane-controlled systems can match. Release from these systems reflects the contributions of at least three concurrent phenomena: fluid entry into the polymer network, outward movement of dissolved drug across the gel, and progressive loss of the outermost swollen polymer into the surrounding medium [3].

This review is organized as a structured account of current knowledge on swellable matrix systems for oral use. The discussion moves from mechanism to materials, then to formulation strategy and evaluation methods, before closing with an honest assessment of remaining limitations and the directions where useful innovation appears most likely. Tables covering polymer properties, release models, evaluation criteria, and recent formulation findings are provided throughout to support comparison and reference.

2. Mechanism of drug release from swellable matrix system

2.1. Water Entry and the Glass-to-Rubber Transition

Everything begins at the moment the tablet surface meets the dissolution medium. Water molecules enter the polymer layer by a combination of capillary action and diffusion, and the first consequence is plasticization of the outermost polymer chains. In their original dry state, hydrophilic polymers such as hydroxypropyl methylcellulose (HPMC) are in a glassy phase — their molecular chains have limited mobility and sit in tightly packed configurations. As water enters, the glass transition temperature falls rapidly — eventually dropping below the ambient temperature — and the material passes into a rubbery phase where chain movement is far less restricted. This shift is visible in the tablet as an advancing front that separates the hydrated outer zone from the still-dry inner core [4].

The hydrated polymer chains continue to absorb water and extend outward, building a three-dimensional gel network of measurable thickness. The rheological behaviour of this gel — particularly its viscosity and mechanical integrity — is one of the most important determinants of drug release rate. A gel that is strong and viscous slows the outward movement of drug and can sustain release over many hours. If the gel is too weak — typically because polymer concentration is too low or the viscosity grade too light — it loses structural coherence, and both erosion and drug release become unpredictable. There is a polymer concentration threshold below which useful controlled release behaviour is difficult to maintain consistently [5].

2.2. Release Fronts and Drug Transport

The geometry of drug release in a swelling tablet is more complex than a simple dissolving sphere. At least three distinct moving boundaries exist simultaneously within the tablet during dissolution. The innermost is the swelling front, which marks the boundary between the glassy undisturbed core and the hydrated rubbery zone. Further outward lies the diffusion front — the interface between regions containing undissolved drug and regions where drug has fully dissolved

within the gel. The outermost boundary is the erosion front, where the most hydrated and structurally weakened polymer gradually dissolves into the surrounding medium [6].

Drug exits the tablet through one of two routes, and in most practical systems both operate simultaneously. In diffusion-controlled release, dissolved drug molecules move down a concentration gradient from the gel interior toward the outer erosion surface; how fast this happens depends on gel thickness and on the size and mobility of the drug molecule within the network. In erosion-controlled release, surface polymer chains carrying associated drug molecules are progressively shed as the outer gel collapses into solution. Which mechanism dominates depends heavily on drug solubility. Freely water-soluble drugs establish steep concentration gradients that drive diffusion. Poorly soluble drugs depend more on surface erosion because dissolution within the gel is slow and diffusion cannot be the rate-limiting step [3].

3. Classification of swellable matrix system

Swellable matrix systems can be classified along two separate axes: the chemical character of the matrix-forming polymer, and the temporal pattern of drug release the system produces. In practice, these two criteria are closely connected — polymer selection directly shapes release kinetics — but separating them is useful for systematic discussion.

3.1. Classification by Polymer Type

Table 1 compares the four major matrix types encountered in oral dosage form development, organized by polymer character, typical polymers, release mechanism, and principal attributes.

Table 1 Classification of Oral Controlled-Release Matrix Systems by Polymer Type

Matrix Type	Typical Polymers	Release Mechanism	Drug Suitability	Key Attribute
Hydrophilic	HPMC, Carbopol, Xanthan gum, PEO	Water absorption → gel formation → diffusion + erosion	Hydrophilic and hydrophobic drugs	Most widely used; release tuneable through polymer grade
Hydrophobic	Ethylcellulose, Glyceryl behenate, Carnauba wax	Diffusion through water-filled pore channels	Highly water-soluble drugs	Limits burst release; minimal swelling
Inert	Polyvinyl chloride, Polyethylene	Tortuous diffusion through rigid scaffold	Varied solubility range	Mechanically stable; limited release modulation
Biodegradable	PLA, PGA, PLGA copolymers	Enzymatic or hydrolytic chain cleavage	Colon-targeted drugs	Preferred for implantables and colon delivery

3.1.1. Hydrophilic Matrix Systems

Hydrophilic matrices are the most widely studied and commercially deployed category. The thing that separates hydrophilic matrices from other controlled-release designs is what happens almost immediately after the tablet meets fluid. Swelling begins quickly, a gel layer builds at the surface, and from that point onward it is the gel — not the tablet core — that governs drug release. Most of the polymers used here are cellulose derivatives, and within that group, hydroxypropyl methylcellulose occupies a dominant position that has proved remarkably durable. HPMC gels reliably, it is available from multiple suppliers, and its regulatory history is long and well-documented [7]. Formulators can shift the release rate considerably just by changing the viscosity grade or combining two grades, which gives this material a degree of design flexibility that alternatives have struggled to match.

3.1.2. Hydrophobic Matrix Systems

Hydrophobic matrices use water-insoluble materials — waxy substances such as glyceryl behenate or polymers like ethyl cellulose — that do not swell but form a tortuous network of water-filled channels through which drug moves slowly. These systems work well for water-soluble drugs where an initial burst release needs to be controlled. Because

swelling does not occur, performance is less sensitive to processing variation, but the absence of gel formation also removes a key lever for adjusting the release profile [8].

3.1.3. Inert and Biodegradable Matrix Systems

Inert matrices are built from polymers that remain structurally intact — no water uptake, no erosion, no change of any kind during transit through the gut. Drug diffuses outward through a fixed porous scaffold. Because nothing changes structurally, mechanical behaviour is predictable and reproducible. The practical limitation is significant, though: release rate is set during compression and cannot meaningfully be adjusted after that point. The polymer is chosen because it will degrade — hydrolysis, enzymatic cleavage, or both — and that degradation is what drives release over time. As the structure breaks down, the drug is progressively freed. Polylactic acid–glycolic acid copolymers are the most established examples. Although their primary use has been in parenteral implants, biodegradable oral matrices are being investigated for colon-targeted delivery, where delayed polymer breakdown coincides usefully with intestinal transit time [9].

3.2. Classification by Drug Release Kinetics

Swellable systems can also be grouped by how drug release changes over time. Zero-order profiles — where the release rate stays constant regardless of the amount of drug remaining — are clinically attractive for agents requiring steady plasma levels. First-order profiles show a declining release rate as drug inventory falls; this pattern is more common in practice but pharmacokinetically less ideal. Many swellable HPMC matrices exhibit anomalous or non-Fickian transport, a combination of diffusion and polymer chain relaxation that produces a power-law release pattern with an exponent between the Fickian and the swelling-controlled limits. Mathematical characterisation of these kinetic patterns is discussed in Section 6 [6].

4. Polymer used in swellable matrix tablets

The polymer is the most consequential single ingredient in a swellable matrix formulation. It determines swelling rate, gel strength, erosion behaviour, and ultimately the drug release profile. Table 2 summarises the principal polymers currently in use, along with their key physicochemical characteristics and formulation notes.

Table 2 Comparative Overview of Principal Polymers Used in Swellable Matrix Tablets

Polymer	Chemical Class	Commercial Grades	Gel Viscosity	pH Sensitivity	Formulation Notes
HPMC	Cellulose ether (semi-synthetic)	K4M, K15M, K100M	Low–Very High	pH-independent	Broadest regulatory acceptance; default matrix polymer
Carbopol 934P	Cross-linked polyacrylic acid	934P, 971P, 974P	Very High (pH-dependent)	Swells more at neutral–alkaline pH	Bioadhesive; pH-responsive; useful for gastroretentive systems
Xanthan Gum	Microbial anionic polysaccharide	Standard & Xantural 75	High	pH-independent	Pseudoplastic gels; stable across physiological pH range
Guar Gum	Galactomannan (plant-derived)	Purified grades	Moderate–High	Mild ionic sensitivity	Cost-effective; colonic fermentation limits upper GI use
Sodium Alginate	Anionic marine polysaccharide	LF, MF, HF grades	Moderate	Gels with Ca^{2+} ions	Ionic cross-linking possible; pH-sensitive in acid media
PEO	Synthetic water-soluble oxide	WSR 303, Coagulant	High–Very High	pH-independent	Near zero-order release at high MW; suitable for high-dose drugs

4.1. Hydroxypropyl Methylcellulose (HPMC)

No polymer has accumulated a longer or more consistent record in hydrophilic matrix tablets than HPMC. Several factors explain its default status in early formulation work. It forms gels rapidly and uniformly upon contact with water. Its viscosity can be varied across several orders of magnitude simply by selecting a different commercial grade. Few pharmaceutical excipients come with the regulatory track record that HPMC has accumulated. It has been approved for oral use across virtually all major markets. It processes on conventional tablet equipment without modification. Viscosity grades are defined by solution viscosity at 2% concentration — K4M being the lower end, K100M the markedly more viscous counterpart. Blending grades to reach an intermediate release rate is entirely routine and appears throughout the formulation literature. [4, 5].

Higher HPMC concentration generally means a thicker gel, slower diffusion, and slower erosion at the tablet surface. The relationship has been reproduced across a wide range of compounds and does hold reasonably well — up to a point. At higher concentrations, additional polymer produces diminishing returns, and the curve flattens. This matters practically when formulating high-dose products, where polymer levels may already be pushing toward that plateau. Above a certain level, adding more polymer produces diminishing returns in release retardation, and tablet size along with patient acceptability must be weighed alongside any gain in release control.

4.2. Carbopol and Carbomer Polymers

Carbopol polymers — synthetic, cross-linked polyacrylic acid derivatives — bring pH-responsiveness that is practically useful in matrix design. Their swelling increases markedly as pH rises from gastric to intestinal values. This behaviour can be deliberately used to achieve region-selective drug delivery within the gastrointestinal tract. When combined with HPMC in a binary matrix, Carbopol also contributes bioadhesive properties that extend tablet residence time at the absorption site — a feature of interest in gastric retentive and mucoadhesive applications [10].

4.3. Natural Polysaccharide Gums

The appeal of xanthan gum, guar gum, and sodium alginate in swellable matrix research comes from their biological origin, good safety records, and cost advantages over purely synthetic alternatives. Xanthan gum — produced by bacterial fermentation — forms thick, pseudoplastic gels and has one property that makes it particularly attractive for oral formulation work: it is largely indifferent to the pH and ionic conditions it encounters in the gastrointestinal tract. [11]. Conditions that would destabilise many other hydrocolloids barely register with xanthan, and that stability simplifies the relationship between in vitro and in vivo behaviour. Guar gum derives from the endosperm of guar seeds and belongs to the galactomannan polysaccharides. How much water it takes up depends on molecular weight and on the extent of galactose substitution along the mannose backbone — both of which vary with the source material and processing conditions. Contact with divalent cations, calcium in particular, triggers rapid ionic cross-linking, and the resulting gel network is mechanically robust without any requirement for elevated temperature. Two- and three-component blends with HPMC are common precisely because combining materials often gives a more favourable release curve than any single polymer would produce, and each component can be used at a lower concentration than would otherwise be necessary [1].

4.4. Polyethylene Oxide (PEO)

Polyethylene oxide occupies a distinct technical niche. Available at molecular weights from approximately 100,000 to several million daltons, PEO produces gel layers whose strength scales with chain length in ways that broadly parallel HPMC behaviour, though the two polymers are not interchangeable. At high molecular weights, PEO matrices can deliver near zero-order release profiles for certain drug types, and the polymer has been used successfully in high-dose formulations where compressing a drug-polymer blend into a tablet of acceptable dimensions would be impractical with HPMC alone. Regulatory acceptance of PEO in oral dosage forms has grown steadily over the past two decades, and several currently approved products rely on it as the primary matrix-forming agent [7].

5. Formulation and manufacturing considaration

5.1. Manufacturing Approaches

Three manufacturing pathways account for most swellable matrix tablets produced at industrial scale: direct compression, wet granulation, and dry granulation by roller compaction. The choice among them is governed mainly by the flow and compressibility characteristics of the drug-polymer blend, the drug's sensitivity to moisture, and available processing equipment.

Direct compression is the simplest and least expensive route. Drug, polymer, and excipients are blended and compressed without any prior granulation step. For this to work reliably, both the drug and the matrix polymer must flow and compact adequately — requirements that are met when drug loading is moderate and the physical properties of the polymer and drug particles are compatible [2]. Where powder properties are cooperative, direct compression is the method of choice — fewest steps, lowest cost, easiest to validate. But cohesive blends, high drug loads, and low-density materials frequently produce tablets that either lack mechanical integrity or fail content uniformity testing, sometimes both. A binder solution is used to granulate the drug and polymer together; the granules are dried, milled to size, and compressed. Content uniformity and compressibility both typically improve substantially [8]. Roller compaction offers a dry alternative: ribbons are formed under mechanical pressure, milled to granule size, and compressed without any water contact at any stage.

5.2. Factors That Determine Drug Release

The release profile from a swellable matrix emerges from the interaction of a relatively small number of formulation and environmental variables. Polymer concentration is the primary control lever. As the proportion of matrix polymer in the tablet increases, the gel that forms during dissolution becomes thicker and more cohesive, slowing both diffusion and surface erosion. For many HPMC systems, a concentration window of roughly 20 to 40% w/w is needed to maintain adequate gel integrity for sustained release over 8 to 12 hours, though this range shifts depending on polymer viscosity grade and drug load [3].

Drug solubility has a strong influence on which release mechanism predominates. For poorly soluble drugs, dissolution within the gel is the rate-limiting step, and release is inherently slow even at moderate polymer concentrations. Freely soluble drugs represent the more demanding formulation challenge: they dissolve quickly within the gel and depend almost entirely on gel layer thickness to retard outward movement, which places heavy demands on polymer performance. Tablet geometry is a non-trivial variable as well — flat-faced tablets expose more surface area per unit mass than biconvex designs, and the initial release rate is consequently faster. For biconvex tablets, the curved surfaces reduce effective release area, and the ratio of surface area to tablet volume changes as the tablet erodes, producing a more complex release-time pattern [4, 5].

The effect of pH on polymer swelling deserves more attention than it routinely receives. Ionizable polymers such as Carbopol change their hydration state substantially as pH shifts from gastric to intestinal values. Even nominally pH-independent cellulosic polymers may be indirectly affected through pH-driven changes in drug solubility. Evaluating dissolution behaviour across the full physiological pH range — not only at a single buffer pH — is therefore standard practice for matrix systems intended for oral administration [6].

6. Evaluation of swellable matrix tablets

Table 3 Mathematical Models Applied to Drug Release Data from Swellable Matrix Systems

Model	Equation	Parameters	Release Pattern	Application to Swellable Systems
Zero-Order	$Q = Q_0 + K_0t$	K_0 = release rate constant	Constant rate; independent of amount released	Ideal for narrow therapeutic index drugs; few purely zero-order systems in practice
First-Order	$\ln Q = \ln Q_0 - K_1t$	K_1 = first-order rate constant	Rate proportional to remaining drug; declines over time	Common for water-soluble drugs; simpler pharmacokinetic modelling
Higuchi	$Q = KH\sqrt{t}$	KH = Higuchi diffusion constant	Diffusion from planar matrix; Q vs $\sqrt{t}$ is linear	Applies to insoluble matrices with drug dispersed in the solid phase
Korsmeyer–Peppas	$Mt/M\infty = ktn$	k = kinetic constant; n = diffusion exponent	$n \leq 0.45$: Fickian; 0.45–0.89: anomalous; n = 0.89: Case II	Most diagnostic for swellable systems; n value identifies dominant mechanism
Hixson–Crowell	$Q_0{}^1/^3 - Qt^1/^3 = KHCt$	KHC = cube root dissolution constant	Accounts for changing surface area as tablet erodes	Useful for eroding hydrophilic matrices where geometry changes over time

The evaluation framework for swellable matrix tablets includes standard compressed tablet quality tests plus additional tests specific to controlled release behaviour. Table 3 presents the mathematical models used to characterize drug release kinetics, and Table 4 summarizes the full evaluation parameter set with acceptance criteria and formulation significance.

6.1. Physical and Mechanical Tests

Weight variation, hardness, and friability are measured routinely for all compressed tablets and are no less important in swellable systems. Hardness deserves particular attention here because the compression force used during manufacture directly affects matrix porosity — the network of spaces between particles through which water enters and drug exits. Tablets compressed at too high a force exhibit reduced porosity, impede initial water entry, and may produce release profiles that differ substantially from pilot batches prepared at lower forces. Tablets compressed at too low a force may be mechanically fragile and show poor dissolution reproducibility because of premature surface disintegration [2].

6.2. Swelling Index Determination

The swelling index is specific to swellable systems and is not part of the standard evaluation set for conventional tablets. It is determined by placing a weighed tablet in dissolution medium and recording the wet weight at timed intervals over several hours. The percentage increase relative to the original dry weight gives the swelling index at each time point. The result is a profile — not a single endpoint — that shows how quickly and to what extent the polymer absorbs water under the test conditions. Formulations with higher polymer concentrations or higher viscosity grades generally develop larger and more sustained swelling indices, and this tends to correlate inversely with drug release rate. The swelling index can therefore serve as a rapid, inexpensive screening parameter during early formulation work, used alongside full dissolution testing [3].

6.3. *In Vitro* Drug Release and Kinetic Analysis

Dissolution testing provides more useful information about a controlled release tablet than any other single evaluation. For swellable matrix systems, the USP Type II paddle apparatus is used most commonly, operated at 50 to 100 rpm in 900 mL of buffer — usually phosphate buffer at pH 6.8 or 7.4, or USP simulated intestinal fluid — maintained at 37°C. Samples are withdrawn at timed intervals over 8, 12, or 24 hours depending on the intended release period, and drug concentrations are quantified by UV spectrophotometry or HPLC. Cumulative percentage released is plotted against time, and the resulting profile is compared to target specifications and, where applicable, to a reference product using the similarity factor f_2 [12].

To extract mechanistic information from the data, the release profile is fitted to the models listed in Table 3. The Korsmeyer–Peppas model is most diagnostic for swellable systems. The diffusional exponent n separates Fickian diffusion ($n \leq 0.45$ for a cylinder), anomalous transport ($0.45 < n < 0.89$), and Case II transport ($n \approx 0.89$) where release is governed primarily by polymer relaxation and swelling. An n value approaching or exceeding 1.0 indicates Super Case II transport, where chain relaxation outpaces diffusion and the release pattern approximates zero-order behaviour [6].

Table 4 Evaluation Parameters for Swellable Matrix Tablets: Methods, Acceptance Criteria, and Formulation Significance

Parameter	Method / Instrument	Acceptance Criteria	Key Variables	Formulation Significance
Weight Variation	Analytical balance; individual tablet weights	±5% for tablets >80 mg; ±7.5% for <80 mg (USP)	Blend uniformity, feeder performance	Critical for dose accuracy; directly impacts bioavailability
Hardness	Monsanto / Erweka tester	6–12 kP (typical for CR tablets)	Compression force, binder level	Over-compression suppresses swelling and distorts dissolution profile
Friability	Roche friabilator; 100 rpm, 4 min	NMT 1.0% weight loss (USP)	Granule strength, lubricant level	Ensures physical integrity during coating, packaging, and transit

Swelling Index	Gravimetric method; timed intervals	Formulation-specific; higher polymer → higher SI	Polymer concentration, viscosity grade	Directly reflects gel-forming capacity; correlates inversely with release rate
In Vitro Dissolution	USP Type II paddle; 50–100 rpm, 900 mL buffer	NLT 80% release at Q-hour (product-specific)	pH, ionic strength, agitation, tablet geometry	Most informative test; mandatory for controlled release characterisation
Drug Content Uniformity	UV spectrophotometry / HPLC on extracted tablets	90–110% of labelled content (USP/ICH)	Blend homogeneity, sampling strategy	Ensures dose consistency; critical for narrow therapeutic index drugs
Accelerated Stability	40°C ± 2°C / 75% RH ± 5% for 6 months (ICH Q1A)	No significant change in assay, dissolution, or appearance	Moisture, oxidation, polymer hydration	Moisture uptake by HPMC can alter gel formation; necessitates barrier packaging

6.4. Stability Testing

Stability testing follows the ICH Q1A(R2) guidance framework. Accelerated conditions of 40°C ± 2°C and 75% relative humidity ± 5% are maintained for six months, with parallel long-term studies at 25°C ± 2°C and 60% RH for up to 24 months or the full intended shelf life. Tablets are evaluated at intervals for assay, dissolution profile, physical appearance, and hardness. The susceptibility of hydrophilic polymers — HPMC in particular — to moisture absorption from the surrounding environment makes packaging selection a critical formulation decision rather than an afterthought. Moisture uptake alters the degree of polymer chain mobility even in the solid tablet, and prolonged storage under humid conditions has been shown to shift drug release profiles in ways that resemble formulation changes rather than ordinary analytical variability [7].

7. Recent research on Swellable matrix formulations

Table 5 presents findings from selected published studies across several therapeutic drug classes, illustrating the versatility of the swellable matrix platform and the continued importance of HPMC and natural gum polymers in current research. The studies also show how transport mechanism — identified through the Korsmeyer–Peppas exponent — varies in a predictable way with drug solubility and polymer selection.

Table 5 Summary of Selected Swellable Matrix Formulation Studies Across Drug Classes

Drug	**Polymer(s)**	**Release Type**	**Key Observation**	**Transport Mechanism**	**Reference**
Metformin HCl	HPMC K4M, K100M, PVP K30	Sustained (8–12 h)	K100M + PVP K30 combination gave optimal controlled release; dosing reduced from three times to once daily	Anomalous (n = 0.67–0.78)	Patil et al., 2023
Diclofenac Sodium	HPMC K15M, Carbopol 934	Extended (12 h)	20–30% polymer blend substantially slowed release; dissolution medium pH noticeably shifted the release pattern	Erosion + diffusion	Caraballo et al., 2004
Carbamazepine	HPMC K15M, Compritol 888 ATO	Non-Fickian / Case II	HPMC concentration inversely related to release rate; higher drug load shifted n toward Case II transport	Case II (n ≥ 0.89)	Barakat et al., 2009

Tramadol HCl	Xanthan gum, HPMC K4M	Sustained (10 h)	Xanthan gum maintained consistent swelling regardless of pH; binary blend produced near zero-order release	Near zero-order	Talukdar & Kinget, 1995
Ketoprofen	HPMC K4M, HPMC E15, Ethylcellulose	Anomalous diffusion	HPMC viscosity grade was the main determinant of gel integrity and drug permeation through the swollen matrix	Anomalous (n ≈ 0.5–0.75)	Vueba et al., 2004
Clarithromycin	HPMC K15M, Carbopol 934, HPMC K4M	Gastroretentive floating (8 h)	Floating lag time under 3 min; buoyancy maintained ≥8 h; adequate release and stability at 40°C/75% RH	First-order / anomalous	Rao et al., 2009

Across a broad reading of the published literature on swellable matrices, two variables appear more consistently than any others as determinants of release rate: polymer concentration and viscosity grade. This is not surprising — it confirms what experienced formulators have known empirically for a long time — but the consistency across compounds, research groups, and experimental conditions gives it weight beyond received wisdom. Binary and ternary polymer combinations tend to produce release profiles closer to zero-order than single-polymer systems do. This has been observed with Carbopol, with xanthan gum, and with waxy materials as the second component, suggesting it reflects something general about polymer interaction rather than a property of any specific combination. Poorly soluble compounds fairly reliably show anomalous or Case II transport, indicating that polymer relaxation and erosion contribute meaningfully alongside diffusion. For soluble drugs, the exponent values point toward Fickian diffusion as the governing process.

8. Advantage, limitations, and future perspectives

8.1. Summary Comparison

Table 6 The principal advantages and limitations of swellable hydrophilic matrix systems side by side.

Table 6 Advantages and Limitations of Swellable Hydrophilic Matrix Drug Delivery Systems

Advantages	**Limitations and Challenges**
Manufactured on standard tablet presses without coating infrastructure	*In vivo–in vitro* correlation is often imprecise; GI motility and fed/fasted state alter polymer swelling behaviour
Once or twice daily dosing supports adherence in chronic disease management	High-dose, highly soluble drugs need impractically large polymer proportions to retard release adequately
Flattened plasma concentration curve limits peak-related toxicity and trough-related therapeutic failure	Resulting tablet dimensions may exceed patient-acceptable limits, particularly in elderly populations
Gel layer provides mucosal protection for irritant drugs delivered at controlled concentrations	Dose dumping — though uncommon in well-designed systems — is a concern if matrix integrity is compromised
Raw materials, especially HPMC, are pharmacopoeially recognised with broad regulatory acceptance	Hydrophilic polymers absorb moisture; inadequate barrier packaging leads to drug release drift on storage
Scalable from laboratory to commercial production with minimal process changes	pH variation along the GI tract influences ionizable polymer swelling in ways that are difficult to predict
Release profile adjustable by varying polymer type, grade, concentration, and tablet geometry	Less suitable for drugs with significant presystemic metabolism or narrow absorption windows

8.2. Advantages

The sustained commercial use of swellable matrix tablets rests on practical strengths that competing oral controlled release platforms — membrane-coated multiparticulates, osmotic pumps, ion-exchange resins — do not all share at once. Manufacture requires no coating infrastructure, no complex multi-layer assembly, and no specialized facilities beyond those needed for conventional tablet compression. Development timelines are comparatively short, in part because HPMC behaviour is thoroughly characterized and the formulation design space is well mapped from many decades of published work. Clinically, extending dosing to once or twice daily carries genuine benefits for medication adherence in chronic conditions, and a smoother concentration-time profile reduces both the pharmacodynamic and toxicological problems associated with the high peaks seen with immediate-release formulations [1, 2].

8.3. Limitations and Outstanding Challenges

The limitations of swellable matrix systems deserve direct acknowledgment rather than minimization. The most clinically significant is the persistent difficulty of establishing reliable in vitro–in vivo correlations. Dissolution testing, conducted under standardized but highly artificial laboratory conditions, frequently fails to predict in vivo performance with the precision needed for confident biowaiver applications or product bridging studies. Gastrointestinal motility, fluid volume in the lumen, the fed versus fasted state, and gut transit time all vary within and between individuals, and each can meaningfully alter how the polymer swells and how fast drug is released [4].

The clearest limitation of swellable matrices involves high-dose, freely water-soluble drugs. Metformin is the case that comes up most often, and for good reason. Achieving adequate retardation at the doses required means incorporating enough polymer that the resulting tablet may be too large for routine patient use. There is no clean formulation solution to this — it is a genuine constraint of the platform. Physical damage to the tablet, extreme pH excursions, or storage at inappropriate humidity can all compromise matrix integrity, and when that happens, the controlled-release mechanism no longer functions as intended. These are not hypothetical failure modes. Stress testing during development needs to systematically probe them. [5].

8.4. Future Directions

Gastroretentive swellable matrix systems are among the technically most interesting developments currently being pursued. The strategy involves engineering the tablet to expand rapidly upon contact with gastric fluid under fed conditions — reaching dimensions that prevent transit through the pylorus. By extending gastric residence from the typical one to three hours to five to eight hours or more, such systems can meaningfully improve bioavailability for drugs whose absorption is confined to the upper small intestine. Current research focuses on the mechanical design of the swollen tablet — it must resist pyloric passage yet eventually collapse for safe downstream transit — and on developing predictive models of behaviour within the gastric environment [3, 20].

Hybrid systems that combine synthetic polymers with natural gums are attracting real formulation interest, not just academic curiosity. The synthetic component typically contributes processing reliability; the natural gum brings biocompatibility and, in some cases, properties — prebiotic activity, for instance — that may carry independent value. Ternary blends of HPMC, xanthan gum, and sodium alginate have produced release profiles that single-polymer systems could not replicate, and the ability to use each component at a lower individual level has practical implications for both tablet size and cost. Stimulus-responsive matrices — designed to react to the pH gradient at the ileocolonic junction or to the reductive environment of the colon — are being studied with increasing seriousness. The motivation is site-specific delivery for colorectal cancer and inflammatory bowel disease, conditions where getting the drug to the right location is not just convenient but therapeutically necessary [9]. Computational modelling is improving steadily, and dissolution apparatus is getting meaningfully closer to replicating actual gastrointestinal conditions — mechanical forces, pH transitions, fluid volume and composition. The goal of designing a formulation backward from a specified in vivo performance target is not yet routine, but it is becoming less distant.

9. Conclusion

Swellable hydrophilic matrix tablets have held their position in the oral drug delivery landscape not through inertia but because they genuinely work, and their mechanism is scientifically well understood. The gel barrier that forms when the tablet contacts fluid simultaneously controls drug diffusion and polymer dissolution — its properties can be adjusted within a clearly defined formulation design space. HPMC is available in multiple viscosity grades that provide continuous and predictable control over release rate.Natural gums bring additional properties that HPMC alone does not provide, widening what the formulation can accomplish. Standard compression equipment handles these blends

without modification. Development and production costs stay lower than they would for more sophisticated controlled-release architectures.

Challenges remain.The gap between dissolution testing and clinical performance remains stubborn. Meanwhile, squeezing enough polymer into a high-dose soluble formulation without producing an oversized tablet is still a puzzle that formulators are actively trying to solve. These are not unaddressed problems — they are the focus of ongoing research.Gastroretentive swellable systems, hybrid blends, and stimuli-responsive designs have already shown that this platform can do more than originally thought. Innovation is clearly still possible. Among the options for oral sustained release, the swellable matrix stands out. It is thoroughly validated, practically straightforward, and still scientifically rewarding for formulators seeking prolonged drug exposure.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Author Contribution

First author: Conceptualization, Literature Search, Data Curation, Writing – Original Draft. Second author: Data accumulation. Third author: Design and drafting. Fourth author: Data validation. Corresponding author: Overall validation.

Data Availability

Data is available from the corresponding author on request.

Statement of Usage of Artificial Intelligence

Open AI platforms were used for grammatical corrections only.

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