WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.63
Volume 15, Issue 5, 1151-1176. Review Article ISSN 2277–7105

IN SITU FLOATING GEL SYSTEMS: SOPHISTICATED APPROACHES FOR GASTRO-RETENTIVE AND CONTROLLED DRUG ADMINISTRATION

Aynul Haniya M.[1], Pravin Babu J.[1], Sarjin Sam S.[1], Mr. Jayachandran D. L.[1*], Dr. Helen Sonia A.[1], Dr. Venkateshwaran K.[1]

Department of Pharmaceutics, S. A. Raja Pharmacy College, Raja Nagar, Vadakkangulam-627116, Tirunelveli, Tamilnadu, India.

Article Received on 04 Feb. 2026,
Article Revised on 24 Feb. 2026,
Article Published on 01 March 2026,

https://doi.org/10.5281/zenodo.18813675

***Corresponding Author**

Mr. Jayachandran D. L.

Department of Pharmaceutics, S. A. Raja Pharmacy College, Raja Nagar, Vadakkangulam-627116, Tirunelveli, Tamilnadu, India.

How to cite this Article: Aynul Haniya M.[1], Pravin Babu J.[1], Sarjin Sam S.[1], Mr. Jayachandran D. L.*[1], Dr. Helen Sonia A.[1], Dr. Venkateshwaran K.[1] (2026). In Situ Floating Gel Systems: Sophisticated Approaches For Gastro-Retentive And Controlled Drug Administration. World Journal of Pharmaceutical Research, 15(5), 1151–1176.

ABSTRACT

This article provides an in-depth overview of in situ floating gel systems designed for advanced gastro-retentive drug delivery. These systems begin as liquids that transform into gels upon contact with physiological triggers such as changes in stomach pH, temperature, or ionic strength, leading to sustained, site-specific drug release. Their buoyancy in gastric fluids allows for prolonged stomach retention, making them especially valuable for drugs with absorption limitations or instability in the intestines. The review covers the use of various biopolymers such as gellan gum, sodium alginate, and pectin, as well as synthetic polymers like Carbopol and hydroxypropyl methylcellulose (HPMC), examining their roles in gelation, mechanical strength, and the regulation of both buoyancy and drug release. Key gelation mechanisms, including pH sensitivity, temperature responsiveness, and ion activation, are discussed along with vital formulation techniques and process variables for ensuring optimal performance. The document addresses practices for incorporating drugs and excipients and outlines methods for evaluating physicochemical properties, muco-adhesion, gastric retention, and drug release profiles in vitro. A range of clinical applications is highlighted, such as the gastric delivery of anti-ulcer, antihypertensive, and antibiotic medications, supported by practical case studies. Additionally, the review discusses challenges like formulation stability, reproducibility,

industrial scaling, and regulatory matters. It also examines recent progress in stimulus-responsive smart gels and combinatorial delivery approaches. In summary, in situ floating gel systems are presented as innovative solutions for achieving extended, controlled drug release with improved patient adherence, and the text outlines both current approaches and emerging directions for research and therapeutic application in this dynamic field.

KEYWORDS: Additionally, the review discusses challenges like formulation stability, reproducibility, industrial scaling, and regulatory matters.

Overview of In Situ Floating Gels

The notion of in situ floating gels as sophisticated drug delivery systems is substantiated by recent scientific literature. These gels are often liquid formulations that convert into gels upon exposure to physiological stimuli in the stomach, such as alterations in pH, temperature, or ionic strength. This gelation facilitates buoyancy in stomach fluids, so extending gastric residence duration and permitting regulated, sustained medication release.[1]

Definition and significance of in situ gels

In situ gels are sophisticated drug delivery systems that are initially in a liquid (sol) state before administration and undergo a transformation to a gel state upon exposure to specific physiological stimuli such as changes in temperature, pH, or ionic strength within the body. This sol-to-gel transition enables the formulation to remain localized at the site of administration, allowing for controlled and sustained release of the drug over an extended period. As a result, this leads to enhanced drug bioavailability, reduced dosing frequency, improved patient compliance, and the possibility of targeted therapy. The gel acts as a reservoir, gradually releasing the drug in a controlled manner and protecting it from environmental degradation. These advantages make in situ gels particularly useful for various administration routes, including oral, ocular, nasal, buccal, and others. Natural and synthetic polymers that exhibit stimuli-responsive gelation are employed to achieve this effect, facilitating both localized and systemic drug delivery efficiently.[2]

Significance of floating medication delivery devices in gastric retention

Floating drug delivery systems (FDDS) improve gastric retention by remaining buoyant on stomach contents for extended durations, hence inhibiting premature gastric emptying. The prolonged stomach retention facilitates continuous drug release, enhancing absorption and bioavailability, particularly for medications with a limited absorption window in the upper

gastrointestinal tract or those that are unstable or poorly soluble in intestinal fluids. FDDS decreases dosing frequency, minimizes fluctuations in plasma drug concentrations, and consequently improves therapeutic efficacy and patient adherence. These systems are especially beneficial for medications necessitating localized gastric action, such as antacids, by minimizing systemic side effects through targeted administration. Effective buoyancy, however, relies on adequate stomach fluid and a minimal floating force, rendering FDDS inappropriate for some medications or situations characterized by low gastric content.[1]

Mechanisms of Buoyancy and Gelation in In Situ Floating Gels

pH-Responsive Gelation

Polymers employed in pH-sensitive in situ gels possess acidic or basic functional groups that either take or release protons in response to the ambient pH. This proton exchange induces conformational alterations and crosslinking, culminating in gel formation. For instance, Carbopol (a derivative of polyacrylic acid), sodium alginate, and chitosan demonstrate gelation induced by alterations in physiological pH. In ophthalmic applications, the shift from acidic to neutral pH triggers gelation, thereby stabilizing the drug formulation and enhancing ocular residence time through the formation of hydrogen bonds with mucin on the ocular surface.[3]

Thermally Induced Gelation

Specific polymers, such as poly(N-isopropyl acrylamide) (PNIPAM), experience a sol-gel transition at a defined temperature known as the Lower Critical Solution Temperature (LCST), around 32 °C. At temperatures beneath the Lower Critical Solution Temperature (LCST), PNIPAM polymers exhibit hydrophilicity and manifest as soluble coils in aqueous solutions. Upon heating beyond the Lower Critical Solution Temperature (LCST), they exhibit hydrophobic properties and aggregate into a gel network as a result of hydrophobic interactions and intrachain bonding. The gelation process is reversible, facilitating simple administration in liquid form and subsequent gel formation at body temperature, which renders PNIPAM extensively utilized in thermo-responsive drug delivery systems.[4]

Ion-Induced Gelation

Ionic gelation transpires when polymers, such Gellan gum, pectin, or alginate, engage with divalent cations such as Ca^{2+} or Mg^{2+} found in physiological fluids. The cations interlink the negatively charged polymer chains via electrostatic interactions, resulting in gel formation. This method is extensively employed in gastrointestinal and ocular drug delivery, wherein

variations in ionic strength induce gelation that prolongs drug release. The crosslinking strength and gel characteristics are influenced by the kind and concentration of cations, in addition to the polymer structure.[5]

Principles of buoyant behavior

Low Density: The principle states that floating dosage forms possess a bulk density inferior to that of gastric fluids (approximately 1 g/cm³), enabling them to remain buoyant on stomach contents without interfering with gastric emptying. Upon interaction with gastric fluids, the polymers and gel-forming agents in the formulation expand and encapsulate air within the matrix, preserving a density inferior to that of the gastric fluid. This buoyancy extends gastrointestinal residence time, facilitating continuous drug release while ensuring the dose form stays buoyant during its activity.[5]

Gas Formation: The principle of gas formation involves the incorporation of gas-generating chemicals, such as sodium bicarbonate or calcium carbonate, in floating medication delivery systems to generate carbon dioxide upon reaction with gastric acid. The produced gas becomes confined within the gel or polymer matrix, decreasing the system's density and allowing it to buoy on gastrointestinal juices. This buoyancy extends stomach residence time, facilitating extended medication release without influencing gastric emptying.[6]

Swelling and Expansion: Specific floating drug delivery systems expand upon interaction with stomach fluids, resulting in an increase in size that reduces their density and inhibits rapid transit through the pyloric sphincter. The swelling is mainly attributed to hydrophilic polymers such as hydroxypropyl methylcellulose (HPMC) and sodium alginate, which absorb water and create a gel matrix that encapsulates air. The augmented size and buoyancy extend stomach retention, hence improving sustained medication release and absorption.[7]

Maintenance of buoyancy: A minimal buoyant force is crucial for sustaining the dosage form's flotation on gastric contents, necessitating sufficient gastric fluid volume and an optimal formulation. The floating force is the disparity between the buoyant force and the weight of the dose form, ensuring it remains suspended for the intended stomach residence duration. The appropriate density, dimensions, and morphology of the dose form, together with adequate gastric fluid, facilitate the preservation of buoyancy during the drug release interval.[8]

Hydrophobic interaction: Nonpolar polymer segments combine to reduce their exposure to water, creating hydrophobic domains that reinforce the gel network. Block copolymers, such as poloxamers, undergo self-assembly via hydrophobic contacts, resulting in a gel matrix that underpins the structure and function of the formulation.[9]

Ionic/Charge Interaction: Polymers possessing charged groups (e.g., carboxylates, amines) can establish ionic crosslinks via electrostatic attraction, exemplified by alginate crosslinking with calcium ions or chitosan interacting with negatively charged entities. pH variations can influence charge interactions, hence impacting gelation and drug release.[9]

Hydrogen Bonding: Polymers establish hydrogen bonds between functional groups (e.g., hydroxyl/carboxyl), facilitating the creation of gel networks. Combinations of natural polymers (e.g., gelatin with agar or starch with carboxymethyl cellulose) utilize hydrogen bonding to enhance gel strength and injectability.[10]

Covalent cross-linking: Refers to the formation of chemical connections between polymer chains by covalent links, which augment the mechanical strength and stability of gels. This is typically accomplished using crosslinking chemicals or click chemistry, such as Michael addition reactions.[11]

Gel Matrix Formation: Gelation transpires by the formation of a three-dimensional polymer network that encapsulates water and medicament molecules. This network is established through physical connections (hydrophobic, ionic, hydrogen bonding) or chemical interactions (covalent crosslinking), contingent upon the polymer system. The gel matrix regulates drug diffusion rate, swelling behaviour, mechanical properties, and biodegradation profile, all of which are essential for targeted and sustained drug release.[12]

Polymers Utilized in In Situ Floating Gel Formulations

Biopolymers

Gellan gum is a bacterial exopolysaccharide known for its excellent gelling, stabilizing, and bioadhesive properties. It forms gels in the presence of cations and is biocompatible, biodegradable, and extensively used for controlled drug delivery and tissue engineering applications.[13]**,** alginate is a naturally occurring anionic polysaccharide extracted from brown seaweed. It gels through ionic crosslinking with divalent cations like calcium, making it suitable for encapsulation and sustained drug release in oral and topical formulations.[14]

Pectin is a plant-derived polysaccharide rich in galacturonic acid residues. It forms gels primarily via calcium-mediated ionic interactions and pH-dependent gelation, widely applied in drug delivery systems for colon targeting and controlled release.[14,15]

Synthetic polymers: Carbopol is a synthetic high molecular weight polymer of acrylic acid known for its excellent swelling capacity and bio-adhesive properties. It gels rapidly upon neutralization with body fluids, making it ideal for controlled and sustained drug release formulations, especially in topical and oral systems.[16] Methyl cellulose is a semisynthetic, inert, and viscoelastic polymer widely used as a controlled-release matrix former. It hydrates and swells in aqueous media, forming a gel barrier that modulates drug diffusion and release rates, and is commonly utilized in oral tablets, capsules, and gel formulations.[17]

The significance of polymer blends in gel strength and buoyancy

The role of blending polymers in gel strength involves enhancing the mechanical and rheological properties of gels through increased cross-link density and the optimization of polymer interactions, including hydrogen bonding, ionic interactions, and entanglements. Hybrid hydrogels that integrate natural and synthetic polymers have higher mechanical stability and elasticity owing to the synergistic properties of polymer chains and greater network interconnectivity. This produces gels capable of enduring physiological stressors while preserving structural integrity.[18] In floating medication delivery systems, polymer blends can regulate swelling behaviour and density. The swelling ability of hydrophilic polymers enhances gel volume, decreases overall density, and fosters buoyancy. Moreover, polymer blends can promote gas entrapment inside the gel matrix, hence improving flotation. The equilibrium between polymer hydrophilicity and hydrophobicity, in conjunction with the degree of crosslinking, determines the gel's capacity to remain buoyant for extended durations.[19]

Methods for the Preparation of In Situ Floating Gels

Essential formulation strategies for in situ floating gels employ certain stimuli that convert the formulation from a liquid to a gel post-administration, facilitating buoyancy and prolonged drug release can be achieved by Employing alterations in temperature, pH, or solvent composition to initiate gelation. Certain polymers, for instance, undergo gelation in reaction to gastric pH or body temperature, facilitating the creation of a buoyant gel within the stomach.[20] The application of cross-linking chemicals, such as calcium ions in conjunction with sodium alginate, induces gelation upon interaction with gastric juices.

Alternative approaches depend on chemical interactions between polymers and excipients that promote in situ gel formation.[20] The ambient physiological conditions, such as ionic composition or pH levels, induce gelling of the formulation upon administration, facilitating buoyancy and regulated drug release.[20]

Methods of preparation and process parameters

The formulation of in situ floating gels generally entails dissolving polymers such as sodium alginate and HPMC in distilled water through mild heating and continual agitation to obtain a uniform solution. Upon cooling below 40°C, the medication and cross-linking agents, including calcium carbonate, are integrated while stirring continuously to prevent drug degradation and achieve homogeneous dispersion. The concentrations of polymers and cross-linkers are refined to attain the intended gelation characteristics and prolonged drug release profile. The resulting gel solution is stored correctly until needed.[21]

Critical process parameters for the formulation encompass

pH kept between neutral and slightly acidic (6.7–7.2) to guarantee stability and good gelation. Viscosity is affected by the concentrations of polymers and cross-linkers, which in turn determine gel strength, drug release, and buoyancy. Heating to a temperature of 60°C is required for polymer dissolution, followed by cooling prior to drug incorporation to avert deterioration. Buoyancy lag time and length assessed to guarantee rapid gelation and extended flotation (often exceeding 12 hours). The in vitro gelling capacity was evaluated in simulated stomach fluid to verify quick gel formation and the stability of the gel over time.[21]

Integration of pharmaceuticals and excipients

Drugs and excipients are integrated into in situ floating gels by dispersing or dissolving them in a pre-prepared polymer solution, commonly composed of polymers such as sodium alginate or HPMC. Subsequent to the preparation of the polymer solution, the medicine is uniformly integrated or dissolved inside it, guaranteeing homogeneous distribution. Cross-linking compounds, including calcium carbonate or calcium chloride, are then included to facilitate gelation upon interaction with gastrointestinal juices. Furthermore, buoyancy agents such as sodium bicarbonate are integrated to enhance flotation. This procedure yields a gel in the stomach, facilitating sustained medication release, enhanced bioavailability, and extended gastric retention.[22]

Strategies for optimizing stability and gelation duration: Optimization solutions for in situ floating gels entail refining formulation and process parameters to improve stability and regulate gelation duration. Essential tactics encompass.

Modifying Polymer Concentration: Polymers such as Poloxamer 407 and Carbopol 934P are adjusted to regulate viscosity and gelation temperature; elevated concentrations enhance viscosity and lower gelation temperature, hence expediting gel formation. Enhancing Cross-linking Agents: Calcium carbonate and additional cross-linkers are modified to augment gel strength, buoyancy, and floating lag time by creating a more compact gel network that efficiently entraps gas. pH Regulation: Sustaining the formulation's pH within an appropriate range (~6.9–7.4) is essential for preserving drug stability and ensuring uniform gelation. Temperature management: Precise heating during polymer breakdown and regulated cooling prior to drug integration avert deterioration and facilitate consistent gelation. Viscosity Monitoring Consistent monitoring informs modifications to achieve an equilibrium between ease of administration and optimal gel strength for gastric retention. In Vitro Gelation Testing: Visual and instrumental evaluations validate the prompt and enduring gel formation together with appropriate buoyancy behaviour. The application of statistical designs, such as factorial design and response surface methods, facilitates the simultaneous optimization of numerous parameters, hence ensuring the optimal gelation duration, stability, and drug release profiles.[23]

Assessment Techniques for In Situ Floating Gels

Common evaluation methods are, Visual inspection for colour, odour, and clarity; pH measurement to ensure compatibility and stability, typically maintaining pH between 6.9 and 7.4.[24] Measurement of solution viscosity using instruments like Brookfield viscometers; gelation time is assessed by adding the formulation to simulated gastric fluid (0.1N HCl) and recording the time for gel formation.[25] Determine floating lag time (time taken to float) and floating duration (how long it remains buoyant) in simulated gastric fluids to evaluate gastric retention, Quantitative analysis often by UV spectrophotometry, to confirm uniform drug distribution and content within the gel.[25] Dissolution studies measure the rate and pattern of drug release from the gel, often fitted to kinetic models like zero-order or Higuchi.[26] Evaluation under different storage conditions to monitor changes in pH, viscosity, drug content, and buoyancy over time to check the stability.[27]

Physicochemical characterisation (viscosity, gel strength, pH)

Viscosity is Measured using instruments like the Brookfield viscometer to assess flow properties of the gel before and after gelation. Viscosity increases with higher polymer and cross-linker concentrations, impacting gel strength and drug release.[28] Gel strength, indicating firmness, is evaluated visually or via texture analysers. Gelation time is determined by introducing the formulation to simulated gastric fluid (0.1N HCl, pH 1.2) at 37°C and recording the time for gel formation.[29] The gel solution pH is recorded with a calibrated pH meter, typically ranging from 6.9 to 7.6 for optimal drug stability and patient comfort.[30] Physical Appearance such as observations of colour, clarity, and homogeneity to ensure formulation consistency and acceptability.[31]

Tests for floating lag time and duration

Floating lag time and duration tests for in situ floating gels are essential for assessing the formulation's stomach retention capability.

Floating Lag Time refers to the duration required for the gel to ascend and remain buoyant on the surface of the simulated stomach fluid (typically 0.1N HCl, pH 1.2) at 37°C. The formulation is gradually put into the medium, and the duration of flotation is visibly documented. Brief lag durations (ranging from seconds to a few minutes) are advantageous for immediate stomach retention.[32] Floating Duration period during which the gel maintains buoyancy on the surface of the medium without submerging is observed post-floating. Effective formulations frequently exhibit buoyancy for extended durations (e.g., >12 hours), guaranteeing prolonged stomach retention for regulated drug release.[33] Testing Procedure is generally performed in vitro utilizing beakers or USP dissolving device containing simulated stomach fluid, maintained at a controlled temperature of 37°C. Minimal disruption during introduction mitigates turbulence that could influence floating behaviour. Observations are conducted visually or through image-analysis techniques.[34]

In vitro pharmacological release and absorption assessments

In vitro drug release investigations for in situ floating gels are often conducted utilizing USP dissolution apparatus (Type II, paddle method) at 37°C with 0.1N HCl as the dissolution media. Samples are extracted at specified intervals, filtered, and analysed spectrophotometrically (often using UV-visible methods) to quantify the drug release over time. This facilitates the depiction of cumulative drug release profiles, typically exhibiting an initial burst release succeeded by persistent release attributable to gel swelling and diffusion

mechanisms. Swelling experiments entail submerging the gel in simulated stomach fluid and occasionally assessing weight increase to determine the degree of swelling. The swelling behaviour correlates with drug release kinetics, demonstrating the polymer matrix's capacity to absorb fluid and regulate drug diffusion.[35]

Assessment of muco-adhesion and gastric retention

The assessment of muco-adhesion and stomach retention of in situ floating gels encompasses several essential methodologies. Employing a texture analyser or a modified bio-adhesion apparatus, the gel is interposed between mucosal tissues or model membranes. The force necessary to separate the gel from the tissue surface is quantified to assess adhesive strength. The contact duration is optimized, generally around 10 minutes, to enhance muco-adhesion. Animal investigations, frequently utilizing imaging or pharmacokinetic monitoring, ascertain the duration of gel occupancy in the stomach, confirming improved gastric retention and extended drug release.[36]

Utilization of In Situ Floating Gels in Pharmacological Delivery

These systems extend gastric residence time by floating and forming gels within the stomach, thereby enhancing the bioavailability of drugs characterized by narrow absorption windows or instability in intestinal pH. This results in sustained drug release, decreased dosing frequency, and improved patient adherence.[38]

These gels effectively regulate drug release in the gastrointestinal tract, mitigating rapid stomach emptying by creating low-density floating gel barriers. This facilitates the sustained maintenance of therapeutic medication concentrations over prolonged durations.[39] In situ gels are utilized for ocular, nasal, buccal, vaginal, and rectal administration, wherein localized gel production facilitates extended drug efficacy and diminishes systemic exposure.[40] The integration of mucoadhesive polymers with in situ gelation prolongs residence time at mucosal locations, hence boosting medication retention and absorption.[41] They can act as carriers for drug-loaded nanoparticles or microparticles, enhancing controlled release and mucosal adhesion, thus improving therapeutic effects.[41]

Provision of anti-ulcer medications, antihypertensive agents, and antibiotics

Compounds such as famotidine, ranitidine, liquorice extract, and andrographolide have been effectively developed into floating in situ gels. These gels prolong gastric residency length, facilitate sustained release, diminish ulcer index, and safeguard the gastric mucosa to enhance

therapy efficacy.[42] Formulations utilizing antihypertensives such as losartan potassium employ floating gels to facilitate regulated drug release and enhance bioavailability by improving retention and absorption in the upper gastrointestinal tract.[43] In situ gels that float have been formulated for antibiotics like ciprofloxacin and amoxicillin, providing focused local distribution in the stomach, which is advantageous for situations such as Helicobacter pylori infection. These systems enhance drug stability, extend stomach retention, and maintain drug release, resulting in improved eradication rates.[44]

Advantages of pharmaceuticals with limited absorption windows

In situ floating gels function by converting from a liquid to a gel state when subjected to gastrointestinal conditions, influenced by factors such as temperature, pH, or ions. Upon oral administration, the solution transforms into a gel that is less dense than gastric fluids, allowing it to float and maintain buoyancy on the stomach contents. The buoyancy and gelation extend gastric retention period, facilitating the regulated and sustained release of pharmaceuticals. The drug release process predominantly adheres to a diffusion-controlled paradigm (Higuchi model), wherein the drug diffuses through the hydrated gel matrix over time. The swelling of the gel matrix and the thickness of the gel network govern the diffusion path length, hence regulating the release rate. Moreover, polymer concentration and cross-linking density affect gel strength, viscosity, buoyancy, and drug release characteristics. This regulated release, along with enhanced gastric retention, enhances bioavailability and therapeutic efficacy for drugs with limited absorption windows or unstable intestinal conditions.[47]

Case studies of commercially available or clinically studied formulations

A representative case study of carbamazepine (CBZ) floating in situ gel formulation highlights its practical development and performance characteristics A example case study of the in-situ gel formulation of carbamazepine (CBZ) underscores its practical development and performance attributes: Sodium alginate and hydroxypropyl methylcellulose (HPMC) serve as the primary polymers, with calcium carbonate (CaCO3) functioning as the cross-linking agent. The drug is first dissolved in propylene glycol and subsequently integrated into the polymer solution, which experiences a sol-to-gel transition induced by the acidic gastric environment. The CaCO3 generates carbon dioxide in the stomach, forming a porous gel matrix that ensures buoyancy with a floating lag time of approximately 28 seconds and sustains buoyancy for over 20 hours. The formulation prolongs carbamazepine release for up

to 24 hours, enhancing drug bioavailability and therapeutic efficacy while minimizing dosing frequency. Evaluation encompasses the assessment of drug entrapment, viscosity alterations during gelation, pH appropriateness, and in vitro drug release kinetics. Recent advancements investigate thermo-reversible in situ gels for intranasal administration of carbamazepine, employing poloxamers and carrageenan to formulate gels that solidify at nasal temperatures. This approach enhances cerebral targeting via the nasal mucosa, exhibiting substantial mucoadhesive properties and prolonged drug release. This instance illustrates how carbamazepine floating in situ gels facilitate enhanced patient compliance and regulated drug delivery for chronic epilepsy treatment.[48]

OBSTACLES AND CONSTRAINTS

Issues of stability

In situ gels may encounter stability issues due to chemical breakdown, particularly when sensitive medicines or polymers are utilized. Temperature and storage conditions can profoundly affect the stability and viscosity of the gel. Formulations maintained at ambient temperature may undergo alterations in drug content due to dehydration, whereas those preserved at lower temperatures (approximately 4°C) generally exhibit greater stability. Chemical degradation may be expedited by inappropriate pH levels, exposure to light, or interactions with excipients, resulting in diminished efficacy. Physical stability (e.g., clarity, phase separation, gelling strength) must be provided to preserve the gel's qualities throughout time.[49]

Challenges in Reproducibility

In situ gel preparation is sensitive to the concentration and type of polymers, the presence of ions (in ion-sensitive systems), and environmental conditions like temperature or pH changes, which may result in inconsistent gelation and drug release profiles. Batch-to-batch reproducibility can be a challenge due to small variations in raw material quality, mixing procedures, and environmental control during production. The sol-gel transition temperature, gelation time, and mechanical properties may vary, impacting therapeutic outcomes and patient experience.[50]

Challenges in scaling and manufacturing

The scale-up and production of in situ gels face numerous significant hurdles due to the intricate characteristics of stimuli-responsive polymers and the exacting requirements of formulation parameters.

Batch-to-batch reproducibility Variability in polymer molecular weight, concentration, and solvent interactions leads to discrepancies in gelation duration, viscosity, and drug release characteristics between batches. Ensuring consistent polymer characteristics over extensive production is highly challenging.[51] Regulation of stimulus responsiveness in situ gels rely on physiological triggers, including pH, temperature, and ions, to facilitate the sol-to-gel transition. Minor differences in environmental or polymer properties can substantially influence gel formation and drug delivery behaviour, complicating scale-up processes.[52] The stability of the formulation during production: The sol form of the gel and the included pharmaceuticals are vulnerable to degradation from pH, temperature, and ionic strength variations during processing, necessitating strictly regulated manufacturing settings.[53]

Optimization of rheological properties achieving Optimization of rheological properties uniform mechanical strength, viscosity, and mucoadhesive characteristics on a wide scale necessitates meticulous process regulation and thorough analytical assessment to ensure the gel's efficacy and patient comfort.[54] Expanding sterile manufacturing escalates expenses and intricacy. Moreover, regulatory approval is obstructed by the absence of standardized production processes and proven reproducibility, thereby prolonging commercialization.[55] The absence of standardized synthesis methods for smart polymers, elevated manufacturing expenses, and rigorous quality control standards are significant impediments to large-scale production.[56] Patient adherence and safety are significant benefits and critical factors in the formulation of in situ gels for ocular medication administration.

Advantages over other formulations

In situ gels convert from liquid to gel upon exposure to physiological stimuli (pH, temperature, ions) in the eye, hence extending precorneal residency duration and maintaining medication release. This decreases dose frequency, hence increasing treatment convenience and improving adherence. The simplicity of administration and less discomfort enhance patient adherence.[57] Prolonged local release restricts systemic medication absorption, hence diminishing the likelihood of systemic side effects and enhancing overall safety.[58] Frequently utilized polymers (e.g., Gellan gum, Carbopol, poloxamers, chitosan) exhibit biocompatibility and non-irritating properties. Research, encompassing ocular toxicity and histology, demonstrates that these gels are typically well tolerated, exhibiting minimal discomfort or toxicity when properly prepared.[59] An appropriate balance of viscosity and gel

strength prevents discomfort, blurred vision, or reflex tearing, which may adversely affect compliance and safety.[60]

Prospective Outlooks and Advancements

Progress in polymer science has markedly improved the formulation of floating in situ gels, especially for gastro-retentive purposes. Principal innovations encompass. Optimized Alginate Systems: The adjustment of guluronic and mannuronic acid concentrations in alginates enhances calcium-mediated crosslinking, yielding stronger, more resilient gels with extended floating duration and regulated drug release under gastrointestinal circumstances.[61] Hybrid Natural-Synthetic Matrices**:** The amalgamation of sodium alginate with cellulose ethers (such as HPMC, HEC), sodium CMC, konjac glucomannan, or psyllium husk facilitates the customization of gel viscosity, strength, and drug release characteristics while stabilizing encapsulated CO2, which is crucial for buoyancy.[62] Dietary Fiber-Based Gels: The application of food-grade dietary fibres facilitates swift gelation, negligible floating lag time (<5 seconds), and prolonged buoyancy, accompanied by improved mechanical resistance to gastric motility stresses.[63] Gas Retention and Buoyancy Control: Optimization of gas formers, including sodium bicarbonate and calcium carbonate, by factorial design enhances CO2 generation, minimizes lag time, and guarantees buoyancy for over 8-12 hours. Polymer content and viscosity are essential factors influencing gel buoyancy and raft stability, effectively analysed by design-of-experiments (DoE).[64] Mechanically Resilient Networks: Enhanced Ca2+-mediated crosslinking in alginate domains increases gel strength, enabling gels to endure peristaltic stresses without failure. The co-formulation of cellulose derivatives with glucomannan improves network flexibility, diminishes erosion, and facilitates diffusion-controlled release.[65] Design-of-Experiments (DoE) Optimization: Modern formulation methodologies utilize factorial and Box-Behnken designs to co-optimize polymer ratios, gas former concentrations, and rheological properties, resulting in rapid floating onset (approximately 20–120 seconds), prolonged buoyancy (exceeding 10–12 hours), and regulated drug release over a duration of 10–16 hours. Regression-based predictive models and desirability functions facilitate reliable scale-up intervals.[66]

Possibility for combinatorial therapy and multi-drug administration

A Gellan gum/CaCO3-based clarithromycin floating in situ gel exhibited extended stomach retention, buoyancy, and sustained release; the incorporation of sucralfate inhibited clarithromycin breakdown at low pH and enhanced its efficacy. Comparison of pylori

clearance and suspension in infected gerbils, demonstrating a combinatorial method for synergistic therapy and stability preservation.[67]

Exemplars of clarithromycin floating in situ gels: Various formulations employing sodium alginate, Gellan gum, xanthan gum, and CaCO3/NaHCO3 demonstrated floating lag times of under one minute and buoyancy exceeding 12 hours, with first-order/Higuchi release kinetics, thereby endorsing combination or sequential regimens in gastroretentive therapy.[68]

Stomach-targeted dual-drug strategies: Documentation and references suggest the advancement and refinement of stomach-specific in situ gels that co-deliver clarithromycin alongside another antibiotic, such as metronidazole benzoate, with the objective of combination eradication therapies for H. pylori via a singular gastroretentive platform utilizing calibrated polymer ratios and gas formers.[69]

Amoxicillin floating in situ gels: Previous formulations of amoxicillin floating in situ gels utilizing alginate/HPMC with effervescent gas formers demonstrated rapid flotation and sustained release over 10–12 hours, establishing a foundation for triple-therapy combinations when combined with macrolides or mucosal protectants in compatible matrices.[70]

Comprehensive design insights from reviews: In situ gel reviews enumerate polymer selections (alginate, Gellan, xanthan, pectin) and co-excipient methodologies facilitating the co-loading of pharmaceuticals with varying solubilities, while buoyancy is sustained by CaCO3/NaHCO3 and release is regulated by principles of polymer concentration and crosslink density, directly relevant to multi-drug systems.[71]

Guidance for practical formulation

Utilize an alginate/Gellan matrix with a cellulose ether thickener to separate buoyancy from release; integrate CaCO3 for ion-activated gelation and as a gas producer, optionally combine with NaHCO3 to adjust floating lag and duration. For acid-sensitive compounds (e.g., clarithromycin), incorporate sucralfate to safeguard against low-pH degradation and enhance local efficacy; optimize polymer and sucralfate concentrations through Design of Experiments (DoE) to achieve an equilibrium of gel strength, buoyancy, and release. Validate the performance of the combination through in vitro assessments of buoyancy (lag time, total floating duration), rheology, and release kinetics, subsequently confirming synergy or additivity in the relevant conditions. Models of pylori when applicable.[74]

Developing trends in intelligent and stimuli-responsive in situ floating gels

Recent developments in intelligent and stimulus-responsive floating in situ gels for drug delivery highlight the utilization of sophisticated polymers that respond to physiological stimuli such as temperature, pH, ionic strength, enzyme presence, and redox conditions. These technologies improve targeted, regulated, and prolonged medication delivery in diverse medicinal applications. Thermoresponsive gels: Polymers like Pluronic F127 remain in a liquid state at ambient temperature and transition to a gel at physiological temperature (about 37°C), enabling facile administration and extended retention, commonly utilized in ocular and injectable formulations.[75] pH-sensitive gels: Polymers such as chitosan and polyacrylic acid gel in designated pH ranges, facilitating site-specific medication release in conditions like the acidic stomach or tumour microenvironments, hence enhancing targeted therapy and reducing adverse effects.[76] Ion-triggered and enzyme-responsive gels: Polysaccharides like alginate and Gellan gum Gelate through divalent cation crosslinking, especially in the stomach, whereas enzyme-responsive gels react to disease-related enzymes to facilitate targeted and regulated drug release.[77] Redox-sensitive systems: These hydrogels react to oxidative stress or reductive conditions present in malignancies or inflammatory disorders, facilitating on-demand medication release and potential applications in gene delivery.[78] Recent advancements in self-healing and injectable smart hydrogels demonstrate rapid gelation, injectability, and self-healing capabilities via nanocomposite hydrogels with dynamic covalent connections, hence improving minimally invasive delivery methods.[79] Challenges and future work: Despite their promising characteristics, these smart gel systems encounter obstacles such as biocompatibility, batch repeatability, scalability, and regulatory approval. Research is actively focused on the integration of nanotechnology, personalized medicine, and hybrid polymers to enhance therapeutic effects.[80]

CONCLUSION

In conclusion, in situ gel systems represent a significant advancement in drug delivery, facilitating the steady and controlled release of drugs while simplifying administration for patients. These formulations utilize specific polymers that transition from liquid to gel upon exposure to physiological conditions, facilitating sustained retention at the site of action and minimizing both dosage frequency and the potential for drug loss. In situ gels, owing to their versatile characteristics, can be delivered via multiple routes, including oral, ophthalmic, injectable, and rectal, thereby accommodating various medical applications. Furthermore, these technologies enhance local drug concentration, reduce systemic side effects, and

optimize the manufacturing process, potentially decreasing production costs. The primary advantage of in situ gels is their capacity to enhance therapeutic efficacy and patient convenience by extending drug availability and assuring accurate dosage at specific locations. Future research and development are anticipated to solidify these delivery platforms as essential elements of contemporary pharmacological care.

REFERENCES

1. In-situ gel formation of pectin, 2001 Feb 28.
2. Kumar SC, Sheeba FR. Stomach Specific Novel Floating In-situ Gel for Sustained Drug Delivery: Overview. Res J Pharm Technol [Internet], 2024 Jun 25 [cited 2025 Nov 1]; 17(6): 2990–6. Available from: https://rjptonline.org/AbstractView.aspx?PID=2024-17-6-86
3. Basu A, Shashidhar Masareddy R, Patil A, Bolmal U. Design and Characterization of Sustained Release in situ Gastric Floating Gel of Ropinirole Hydrochloride. Indian Journal of Pharmaceutical Education and Research | [Internet]. [cited 2025 Nov 1]; 55. Available from: www.ijper.org
4. Kurniawansyah IS, Rusdiana T, Sopyan I, Desy Arya IF, Wahab HA, Nurzanah D. Comparative Study of In Situ Gel Formulation Based on the Physico-Chemical Aspect: Systematic Review. Gels [Internet], 2023 Aug 1 [cited 2025 Nov 1]; 9(8): 645. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC10453730/
5. Kurniawansyah IS, Rusdiana T, Sopyan I, Desy Arya IF, Wahab HA, Nurzanah D. Comparative Study of In Situ Gel Formulation Based on the Physico-Chemical Aspect: Systematic Review. Gels [Internet], 2023 Aug 1 [cited 2025 Nov 1]; 9(8): 645. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC10453730/
6. Arora S, Ali J, Ahuja A, Khar RK, Baboota S. Floating drug delivery systems: A review. AAPS PharmSciTech [Internet], 2005 Oct 19 [cited 2025 Nov 1]; 6(3): E372. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC2750381/
7. Gopalakrishnan S, Chenthilnathan A. Floating Drug Delivery Systems: A Review.
8. Hoare TR, Kohane DS. Hydrogels in drug delivery: Progress and challenges. Polymer (Guildf) [Internet], 2008 Apr 15 [cited 2025 Nov 1]; 49(8): 1993–2007. Available from: https://www.sciencedirect.com/science/article/pii/S0032386108000487
9. Thang NH, Chien TB, Cuong DX. Polymer-Based Hydrogels Applied in Drug Delivery: An Overview. Gels [Internet]. 2023 Jul 1 [cited 2025 Nov 1]; 9(7): 523. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC10379988/

10. Hoare TR, Kohane DS. Hydrogels in drug delivery: Progress and challenges. Polymer (Guildf) [Internet]. 2008 Apr 15 [cited 2025 Nov 1]; 49(8): 1993–2007. Available from: https://www.sciencedirect.com/science/article/pii/S0032386108000487
11. Hoare TR, Kohane DS. Hydrogels in drug delivery: Progress and challenges. Polymer (Guildf) [Internet]. 2008 Apr 15 [cited 2025 Nov 1]; 49(8): 1993–2007. Available from: https://www.sciencedirect.com/science/article/pii/S0032386108000487
12. Liechty WB, Kryscio DR, Slaughter B V., Peppas NA. Polymers for Drug Delivery Systems. Annu Rev Chem Biomol Eng [Internet]. 2010 Jul 15 [cited 2025 Nov 1]; 1: 149. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC3438887/
13. Muthukumar T, Song JE, Khang G. Biological Role of Gellan Gum in Improving Scaffold Drug Delivery, Cell Adhesion Properties for Tissue Engineering Applications. Molecules [Internet]. 2019 Dec 10 [cited 2025 Nov 1]; 24(24): 4514. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC6943741/
14. Liechty WB, Kryscio DR, Slaughter B V., Peppas NA. Polymers for Drug Delivery Systems. Annu Rev Chem Biomol Eng [Internet]. 2010 Jul 15 [cited 2025 Nov 1]; 1: 149. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC3438887/
15. Muthukumar T, Song JE, Khang G. Biological Role of Gellan Gum in Improving Scaffold Drug Delivery, Cell Adhesion Properties for Tissue Engineering Applications. Molecules [Internet]. 2019 Dec 10 [cited 2025 Nov 1]; 24(24): 4514. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC6943741/
16. Maji K, Dasgupta S, Pramanik K, Bissoyi A. Preparation and Evaluation of Gelatin-Chitosan-Nanobioglass 3D Porous Scaffold for Bone Tissue Engineering. Int J Biomater. 2016; 2016.
17. Englert C, Brendel JC, Majdanski TC, Yildirim T, Schubert S, Gottschaldt M, et al. Pharmapolymers in the 21st century: Synthetic polymers in drug delivery applications. Prog Polym Sci [Internet]. 2018 Dec 1 [cited 2025 Nov 1]; 87: 107–64. Available from: https://www.sciencedirect.com/science/article/abs/pii/S0079670017301612
18. Chelu M, Musuc AM. Polymer Gels: Classification and Recent Developments in Biomedical Applications. Gels [Internet]. 2023 Feb 1 [cited 2025 Nov 1]; 9(2): 161. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC9956074/
19. Lafta Rashid F, Hashim A, Lafta RASHID F. Structural, Swelling and Water Absorption Properties of New Polymer Blends for Modern Applications.
20. Mahagen Y, V, Patidhar ana, Y B, P G, G S. Formulation and Evaluation of Floatable In-situ Gel for Stomach-Specific Drug Delivery of Carbamazapine. Research & Reviews:

Journal ofÂ Pharmacy and Pharmaceutical Sciences [Internet]. 1970 Jan 1 [cited 2025 Nov 4]; 3(1): 37–43. Available from: https://www.rroij.com/open-access/formulation-and-evaluation-of-floatable-insitu-gel-for-stomachspecific-drug-delivery-of-carbamazapine.php?aid=34768

21. Jivani RR, Patel CN, Patel DM, Jivani NP. Development of a Novel Floating In-situ Gelling System for Stomach Specific Drug Delivery of the Narrow Absorption Window Drug Baclofen. Iran J Pharm Res [Internet]. 2010 [cited 2025 Nov 4]; 9(4): 359. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC3870059/
22. Jivani RR, Patel CN, Patel DM, Jivani NP. Development of a Novel Floating In-situ Gelling System for Stomach Specific Drug Delivery of the Narrow Absorption Window Drug Baclofen. Iran J Pharm Res [Internet]. 2010 [cited 2025 Nov 4]; 9(4): 359. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC3870059/
23. Raghuwanshi N, Patel V. Improved Hypertensive Therapy via Gastric Retention. International Journal of Drug Delivery Technology. 2025; 15(2): 770–7.
24. Sharma A, Sharma J, Kaur R, Saini V. Development and Characterization of In Situ Oral Gel of Spiramycin. Biomed Res Int [Internet]. 2014 [cited 2025 Nov 5]; 2014: 876182. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC4094871/
25. Hasanji FM, Patel AK, Patel VM. Formulation and Evaluation of In-Situ Sustained Release Gelling System of Famotidine. International Journal of Pharmaceutical Research and Applications [Internet]. [cited 2025 Nov 5]; 7: 2456–4494. Available from: www.ijprajournal.com
26. Patel DM, Patel DK, Patel CN. Formulation and Evaluation of Floating Oral In Situ Gelling System of Amoxicillin. ISRN Pharm [Internet]. 2011 Jul 28 [cited 2025 Nov 5]; 2011: 276250. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC3263723/
27. Mahagen Y, V, Patidhar ana, Y B, P G, G S. Formulation and Evaluation of Floatable In-situ Gel for Stomach-Specific Drug Delivery of Carbamazapine. Research & Reviews: Journal of Â Pharmacy and Pharmaceutical Sciences [Internet]. 1970 Jan 1 [cited 2025 Nov 5]; 3(1): 37–43. Available from: https://www.rroij.com/open-access/formulation-and-evaluation-of-floatable-insitu-gel-for-stomachspecific-drug-delivery-of-carbamazapine.php?aid=34768
28. Patange BS, Deshmukh DVN, Scholar R. Issue 2 www.jetir.org (ISSN-2349-5162). JETIR2202254 Journal of Emerging Technologies and Innovative Research [Internet]. 2022 [cited 2025 Nov 5]; 9. Available from: www.jetir.orgc274

29. Pumjan S, Praparatana R, Issarachot O, Wiwattanapatapee R. Dietary fiber-based floating in situ gels for improved gastric delivery of roselle extract. J Appl Pharm Sci [Internet]. 2025 Mar 5 [cited 2025 Nov 5]; 15,(4): 084–94. Available from: https://japsonline.com/abstract.php?article_id=4496&sts=2
30. |Review INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES 278 | P a g e. [cited 2025 Nov 5]; Available from: https://www.ijpsjournal.com
31. Jadhav R, Jadhav P, Gondkar S, Bachhav R. A REVIEW ON STOMACH SPECIFIC FLOATING IN-SITU GEL. Certified Journal │ Jadhav et al World Journal of Pharmaceutical Research [Internet]. 2023 [cited 2025 Nov 5]; 12(11): 1235. Available from: www.wjpr.net
32. Mahagen Y, V, Patidhar ana, Y B, P G, G S. Formulation and Evaluation of Floatable In-situ Gel for Stomach-Specific Drug Delivery of Carbamazapine. Research & Reviews: Journal ofÂ Pharmacy and Pharmaceutical Sciences [Internet]. 1970 Jan 1 [cited 2025 Nov 7]; 3(1): 37–43. Available from: https://www.rroij.com/open-access/formulation-and-evaluation-of-floatable-insitu-gel-for-stomachspecific-drug-delivery-of-carbamazapine.php?aid=34768
33. Sharma A, Sharma J, Kaur R, Saini V. Development and Characterization of In Situ Oral Gel of Spiramycin. Biomed Res Int [Internet]. 2014 [cited 2025 Nov 7]; 2014: 876182. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC4094871/
34. View of FORMULATION AND EVALUATION OF FLOATING IN SITU GEL OF CIPROFLOXACIN | International Journal of Applied Pharmaceutics [Internet]. [cited 2025 Nov 7]. Available from: https://journals.innovareacademics.in/index.php/ijap/article/view/28603/16857
35. Patel DM, Patel DK, Patel CN. Formulation and Evaluation of Floating Oral In Situ Gelling System of Amoxicillin. ISRN Pharm [Internet]. 2011 Jul 28 [cited 2025 Nov 7]; 2011: 276250. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC3263723/
36. Yan J, Chen X, Yu S, Zhou H. Comparison of different in vitro mucoadhesion testing methods for hydrogels. J Drug Deliv Sci Technol [Internet]. 2017 Aug 1 [cited 2025 Nov 7]; 40: 157–63. Available from: https://www.sciencedirect.com/science/article/abs/pii/S1773224717302745
37. Sen J, Pillai S, P G, G S. Formulation and Evaluation of Muco-adhesive In-situ Gel for Site-Specific Delivery of Clotrimazole. Research & Reviews: Journal ofÂ Pharmaceutics and Nanotechnology [Internet]. [cited 2025 Nov 7]; 2(3): 1–8. Available from:

https://www.rroij.com/open-access/formulation-and-evaluation-of-mucoadhesive-insitu-gel-for-sitespecific-delivery-of-clotrimazole-.php?aid=34365

38. Patel DM, Patel DK, Patel CN. Formulation and evaluation of floating oral in situ gelling system of amoxicillin. ISRN Pharm [Internet]. 2011 Jul 28 [cited 2025 Nov 7]; 2011: 276250. Available from: http: //www.ncbi.nlm.nih.gov/pubmed/22389849
39. Vigani B, Rossi S, Sandri G, Bonferoni MC, Caramella CM, Ferrari F. Recent Advances in the Development of In Situ Gelling Drug Delivery Systems for Non-Parenteral Administration Routes. Pharmaceutics [Internet]. 2020 Sep 1 [cited 2025 Nov 7]; 12(9): 859. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC7559482/
40. Kolawole OM, Cook MT. In situ gelling drug delivery systems for topical drug delivery. European Journal of Pharmaceutics and Biopharmaceutics [Internet]. 2023 Mar 1 [cited 2025 Nov 7]; 184: 36–49. Available from: https://www.sciencedirect.com/science/article/pii/S0939641123000073
41. Sen J, Pillai S, P G, G S. Formulation and Evaluation of Muco-adhesive In-situ Gel for Site-Specific Delivery of Clotrimazole. Research & Reviews: Journal ofÂ Pharmaceutics and Nanotechnology [Internet]. [cited 2025 Nov 7]; 2(3): 1–8. Available from: https://www.rroij.com/open-access/formulation-and-evaluation-of-mucoadhesive-insitu-gel-for-sitespecific-delivery-of-clotrimazole-.php?aid=34365
42. Development of floating in-situ gelling system as an efficient anti-ulcer formulation: In-vitro and in-vivo studies.
43. FORMULATION AND EVALUATION OF FLOATING ORAL IN-SITU GELLING SYSTEM OF LOSARTAN POTASSIUM | INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH [Internet]. [cited 2025 Nov 8]. Available from: https://ijpsr.com/bft-article/formulation-and-evaluation-of-floating-oral-in-situ-gelling-system-of-losartan-potassium/
44. Patel DM, Patel DK, Patel CN. Formulation and Evaluation of Floating Oral In Situ Gelling System of Amoxicillin. ISRN Pharm [Internet]. 2011 Jul 28 [cited 2025 Nov 8]; 2011: 276250. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC3263723/
45. Development of floating in-situ gelling system as an efficient anti-ulcer formulation: In-vitro and in-vivo studies.
46. FORMULATION AND EVALUATION OF FLOATING ORAL IN-SITU GELLING SYSTEM OF LOSARTAN POTASSIUM | INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH [Internet]. [cited 2025 Nov 8].

Available from: https://ijpsr.com/bft-article/formulation-and-evaluation-of-floating-oral-in-situ-gelling-system-of-losartan-potassium/

47. Patel DM, Patel DK, Patel CN. Formulation and Evaluation of Floating Oral In Situ Gelling System of Amoxicillin. ISRN Pharm [Internet]. 2011 Jul 28 [cited 2025 Nov 8]; 2011: 276250. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC3263723/
48. Mohananaidu K, Chatterjee B, Mohamed F, Mahmood S, Hamed Almurisi S. Thermoreversible Carbamazepine In Situ Gel for Intranasal Delivery: Development and In Vitro, Ex Vivo Evaluation. AAPS PharmSciTech [Internet]. 2022 Dec 1 [cited 2025 Nov 8]; 23(8). Available from: https://pubmed.ncbi.nlm.nih.gov/36271212/
49. Verma R, Singh Rathore K, Saurabh SS. A review: In-situ gel drug delivery system. International Journal of Comprehensive and Advanced Pharmacology Journal homepage. 2024; 9(3): 177–82.
50. Garg A, Agrawal R, Singh Chauhan C, Deshmukh R. In-situ gel: A smart carrier for drug delivery. Int J Pharm [Internet]. 2024 Mar 5 [cited 2025 Nov 4]; 652: 123819. Available from: https://www.sciencedirect.com/science/article/abs/pii/S037851732400053X
51. Wagay ZA, Rongpi S. International Journal of Research Publication and Reviews Stimuli-Responsive In-Situ Gelling Systems: Smart Polymers for Enhanced Drug Delivery. International Journal of Research Publication and Reviews [Internet]. 2025 [cited 2025 Nov 8]; (6). Available from: www.ijrpr.com
52. Waghmode RR, Mali DP, Salve P, Dhadde SB. A Bird Eye View on In-situ Ophthalmic Gel: Challenges and Opportunities. International Journal of Drug Delivery Technology. 2024; 14(3): 1801–10.
53. Wagay ZA, Rongpi S. International Journal of Research Publication and Reviews Stimuli-Responsive In-Situ Gelling Systems: Smart Polymers for Enhanced Drug Delivery. International Journal of Research Publication and Reviews [Internet]. 2025 [cited 2025 Nov 8]; (6). Available from: www.ijrpr.com
54. Durgun ME, Mesut B, Hacıoğlu M, Güngör S, Özsoy Y. Optimization of the Micellar-Based In Situ Gelling Systems Posaconazole with Quality by Design (QbD) Approach and Characterization by In Vitro Studies. Pharmaceutics [Internet]. 2022 Mar 1 [cited 2025 Nov 8]; 14(3): 526. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC8954786/
55. Shreya L, Suma US, Zohmingliani R. Recent advances in oral in situ gel drug delivery system: a polymeric approach. Drug Dev Ind Pharm [Internet]. 2025 [cited 2025 Nov 8]; Available from: https://www.tandfonline.com/doi/abs/10.1080/03639045.2025.2559033

56. Jeoh T, Wong DE, Strobel SA, Hudnall K, Pereira NR, Williams KA, et al. How alginate properties influence in situ internal gelation in crosslinked alginate microcapsules (CLAMs) formed by spray drying. PLoS One [Internet]. 2021 Feb 1 [cited 2025 Nov 8]; 16(2): e0247171. Available from: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0247171
57. Verma R, Singh Rathore K, Singh Saurabh S. A review: In-situ gel drug delivery system. IP International Journal of Comprehensive and Advanced Pharmacology [Internet]. 2025 Jul 20 [cited 2025 Nov 8]; 9(3): 177–82. Available from: https://ijcap.in/archive/volume/9/issue/3/article/3421
58. Paul S, Majumdar S, Chakraborty M, Mukherjee S, Sarkar N, Prajapati B, et al. In-situ gel bases ocular delivery system of Ganciclovir, in-vivo and in-vitro investigation. BMC Pharmacol Toxicol [Internet]. 2025 Dec 1 [cited 2025 Nov 8]; 26(1): 102. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC12076903/
59. Nair AB, Shah J, Jacob S, Al-Dhubiab BE, Sreeharsha N, Morsy MA, et al. Experimental design, formulation and in vivo evaluation of a novel topical in situ gel system to treat ocular infections. PLoS One [Internet]. 2021 Mar 1 [cited 2025 Nov 8]; 16(3): e0248857. Available from: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0248857
60. Ahmed B, Jaiswal S, Naryal S, Shah RM, Alany RG, Kaur IP. In situ gelling systems for ocular drug delivery. Journal of Controlled Release [Internet]. 2024 Jul 1 [cited 2025 Nov 8]; 371: 67–84. Available from: https://www.sciencedirect.com/science/article/abs/pii/S0168365924003158
61. Pumjan S, Praparatana R, Issarachot O, Wiwattanapatapee R. Dietary fiber-based floating in situ gels for improved gastric delivery of roselle extract. J Appl Pharm Sci [Internet]. 2025 Mar 5 [cited 2025 Nov 8]; 15,(4): 084–94. Available from: https://japsonline.com/abstract.php?article_id=4496&sts=2
62. Wiwattanapatapee R, Klabklay K, Raksajit N, Siripruekpong W, Leelakanok N, Petchsomrit A. The development of an in-situ biopolymer-based floating gel for the oral delivery of metformin hydrochloride. Heliyon [Internet]. 2023 Apr 1 [cited 2025 Nov 8]; 9(4): e14796. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC10070646/
63. Pumjan S, Praparatana R, Issarachot O, Wiwattanapatapee R. Dietary fiber-based floating in situ gels for improved gastric delivery of roselle extract. J Appl Pharm Sci [Internet]. 2025 Mar 5 [cited 2025 Nov 8]; 15,(4): 084–94. Available from: https://japsonline.com/abstract.php?article_id=4496&sts=2

64. Vipul V, Basu B. Formulation and characterization of novel floating in-situ gelling system for controlled delivery of ramipril. International Journal of Drug Delivery [Internet]. 2013 [cited 2025 Nov 8]; 5: 43–55. Available from: http: //www.arjournals.org/index.php/ijdd/index
65. Vipul V, Basu B. Formulation and characterization of novel floating in-situ gelling system for controlled delivery of ramipril. International Journal of Drug Delivery [Internet]. 2013 [cited 2025 Nov 8]; 5: 43–55. Available from: http: //www.arjournals.org/index.php/ijdd/index
66. Moazen M, Shafaghi A, Ebrahimi-Najafabadi H, Ghasemi S, Ashoobi MT, Manoochehri S. Optimization of pH-sensitive ingredients and characterization of raft-forming alginate-based oral suspensions as reflux suppressant. J Drug Deliv Sci Technol [Internet]. 2022 Feb 1 [cited 2025 Nov 8]; 68: 103124. Available from: https://www.sciencedirect.com/science/article/abs/pii/S1773224722000338
67. Rajinikanth PS, Mishra B. Floating in situ gelling system for stomach site-specific delivery of clarithromycin to eradicate H. pylori. Journal of Controlled Release [Internet]. 2008 Jan 4 [cited 2025 Nov 8]; 125(1): 33–41. Available from: https://www.sciencedirect.com/science/article/abs/pii/S0168365907003872
68. Okunlola A, Durodola IA. Evaluation of Khaya gum (Khaya senegalensis) as a polymer in the formulation of floating in situ gels of metoprolol succinate. BJPharm [Internet]. 2023 [cited 2025 Nov 8]; 8(1): 1011. Available from: http: //doi.org/10.5920/bjpharm.1011
69. Sen O, Manna S, Nandi G, Jana S, Jana S. Recent advances in alginate based gastroretentive technologies for drug delivery applications. Med Nov Technol Devices [Internet]. 2023 Jun 1 [cited 2025 Nov 8]; 18: 100236. Available from: https://www.sciencedirect.com/science/article/pii/S2590093523000310
70. Patel DM, Patel DK, Patel CN. Formulation and Evaluation of Floating Oral In Situ Gelling System of Amoxicillin. ISRN Pharm [Internet]. 2011 Jul 28 [cited 2025 Nov 8]; 2011: 276250. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC3263723/
71. Research Journal of Pharmaceutical Dosage Forms and Technology [Internet]. [cited 2025 Nov 8]. Available from: https://rjpdft.com/HTMLPaper.aspx?Journal=Research+Journal+of+Pharmaceutical+Dosage+Forms+and+Technology%3BPID%3D2014-6-2-11
72. FORMULATION AND EVALUATION OF STOMACH SPECIFIC FLOATING IN-SITU GEL OF CLARITHROMYCIN | INTERNATIONAL JOURNAL OF

PHARMACEUTICAL SCIENCES AND RESEARCH [Internet]. [cited 2025 Nov 8]. Available from: https://ijpsr.com/bft-article/formulation-and-evaluation-of-stomach-specific-floating-in-situ-gel-of-clarithromycin/

73. Rajinikanth PS, Mishra B. Floating in situ gelling system for stomach site-specific delivery of clarithromycin to eradicate H. pylori. Journal of Controlled Release [Internet]. 2008 Jan 4 [cited 2025 Nov 8]; 125(1): 33–41. Available from: https://pubmed.ncbi.nlm.nih.gov/18006101/
74. Raghuwanshi N, Patel V. Improved Hypertensive Therapy via Gastric Retention. International Journal of Drug Delivery Technology. 2025; 15(2): 770–7.
75. Pandey M, Choudhury H, Aziz ABA, Bhattamisra SK, Gorain B, Su JST, et al. Potential of Stimuli-Responsive In Situ Gel System for Sustained Ocular Drug Delivery: Recent Progress and Contemporary Research. Polymers (Basel) [Internet]. 2021 Apr 2 [cited 2025 Nov 8]; 13(8): 1340. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC8074213/
76. Pandey M, Choudhury H, Aziz ABA, Bhattamisra SK, Gorain B, Su JST, et al. Potential of Stimuli-Responsive In Situ Gel System for Sustained Ocular Drug Delivery: Recent Progress and Contemporary Research. Polymers (Basel) [Internet]. 2021 Apr 2 [cited 2025 Nov 8]; 13(8): 1340. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC8074213/
77. Pandey M, Choudhury H, Aziz ABA, Bhattamisra SK, Gorain B, Su JST, et al. Potential of Stimuli-Responsive In Situ Gel System for Sustained Ocular Drug Delivery: Recent Progress and Contemporary Research. Polymers (Basel) [Internet]. 2021 Apr 2 [cited 2025 Nov 8]; 13(8): 1340. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC8074213/
78. Pandey M, Choudhury H, Aziz ABA, Bhattamisra SK, Gorain B, Su JST, et al. Potential of Stimuli-Responsive In Situ Gel System for Sustained Ocular Drug Delivery: Recent Progress and Contemporary Research. Polymers (Basel) [Internet]. 2021 Apr 2 [cited 2025 Nov 8]; 13(8): 1340. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC8074213/
79. Pandey M, Choudhury H, Aziz ABA, Bhattamisra SK, Gorain B, Su JST, et al. Potential of Stimuli-Responsive In Situ Gel System for Sustained Ocular Drug Delivery: Recent Progress and Contemporary Research. Polymers (Basel) [Internet]. 2021 Apr 2 [cited 2025 Nov 8]; 13(8): 1340. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC8074213/

80. Pandey M, Choudhury H, Aziz ABA, Bhattamisra SK, Gorain B, Su JST, et al. Potential of Stimuli-Responsive In Situ Gel System for Sustained Ocular Drug Delivery: Recent Progress and Contemporary Research. Polymers (Basel) [Internet]. 2021 Apr 2 [cited 2025 Nov 8]; 13(8): 1340. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC8074213/