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Review Article

In Situ Gelling Systems: A Smart Approach to Controlled Drug Release

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ABSTRACT

Over the past decades, gel-based system has been gained greater attention as an innovative approach in drug delivery, particularly for developing regulated and sustained drug delivery system can improving therapeutic outcomes. Among these, in-situ gel systems have gained prominence as one of the most promising innovative drug delivery systems, primarily due to their unique ability to transform 'liquid into gel' transition is broadly accepted. In-situ gels are hydrogels that exist in solution before administration. They undergo gelation when physiological conditions change such as temperature fluctuation, pH changes, presence of ions and UV radiation, solvent exchange and others. This transformation increases how long the drug stays at the targeted site, improves bioavailability, and enhances the patient compliance and comfort. These systems are designed to reduce the dose frequency and enhance the drug effectiveness by ensuring localised drug delivery, minimizing dosage requirements and providing consistent drug release. Various polymers such as natural and synthetic ones, forms in-situ gels at the targeted site, and are used across various ways of delivering the drug to the body, including oral, ocular, rectal, nasal, vaginal and transdermal routes.in situ gelling system offers several advantages and have a wide range of applications in today's advanced methods of delivering the medicine. The review provides an overview of in-situ gels, covering their mechanism of action, method of preparation, types of polymers used, evaluation parameters and their roles in various drug delivery system.

INTRODUCTION

'In situ gel' technology has become one of the most promising and effective drug delivery systems because of its unique ability to transform from a liquid(sol) to Gel at the site of action. "In-situ" is a Latin term that means 'in position' [1]. The in-situ gelling systems helps to deliver the drug slowly and exactly where it's needed. They improve patient compliance and comfort due to their unique

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characteristic feature of 'liquid to Gel transition 'at the site of action. This has led to widespread acceptance in the medical field .The liquid to gel transition i.e., the solution or suspension (before administration in the body),which after reaching to specific site, undergoes gelation to form gel upon contact with fluids in the body .The gel formation occurs i.e., transition from a liquid to gel can occur under different physiological condition such as changes in temperature, pH ,solvent exchange ,external triggers ,concentration of ions, uv radiation and presence of certain biomolecules or ions , among others .Various polymers ,both naturally derived and synthetic such as guar gum ,pectin ,Carbopol, poloxamer etc are incorporated into this system for their properties .This system is designed to deliver the medications through various routes, including oral ,ocular ,transdermal ,buccal ,intraperitoneal ,parenteral ,injectable, as well as vaginal and rectal .[2,3] Increased bioavailability, reduced dosing frequency and less dose required for the treatment, and better ability to stay at the site of drug absorption are the key characteristics of the system.[2] The in-situ gel-forming polymer-based formulation offer several significant benefits which includes easy administration and better stability of the drug against environmental factors. It also improves patient compliance, enhance drug absorption and reduce the local and systemic side effects.[1] Moreover, system shows better patient compliance among patients. Stability issues, homogeneity in drug loading, mechanical strength are the key factors that can influence the performance of the system .[2] Recent research has been exploring the use of in situ gelling system and nanoparticulate gel formulations for delivering the drug through buccal, ocular, nasal, and vaginal routes. Advances in in situ gels have made it possible to use the physiological changes that occur in different regions of the gastrointestinal tract to optimize drug absorption, while also increasing patient comfort and acceptance.[4]

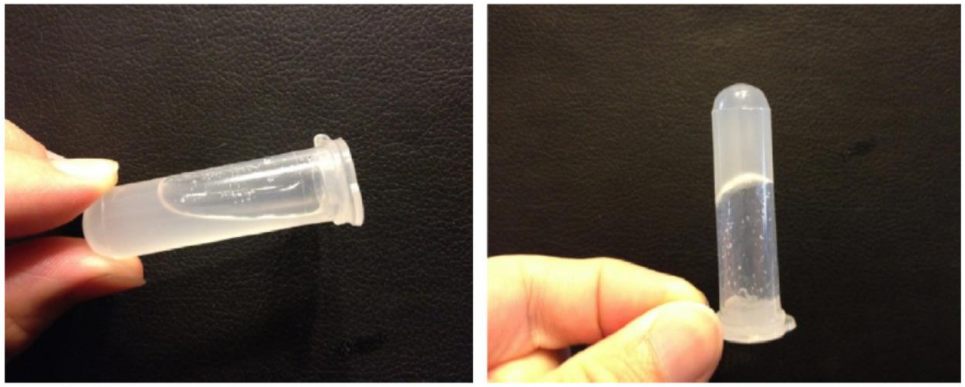

Fig :1. In-situ gel at room temperature and body temperature

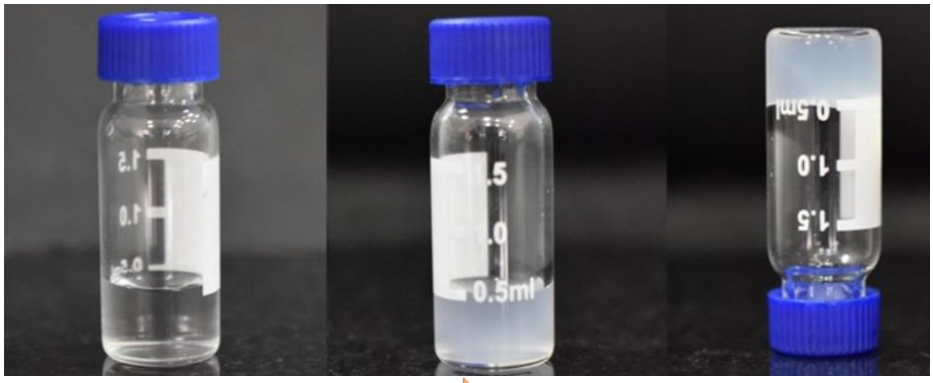

Fig: 2. Sol State@<20°C → Gel State@≤33±1°C,In ≤45 Sec

Importance Of In-Situ Gelling System

1. In-situ gel enables slow and steady release of the drug by transforming from a liquid into a gel at the site of administration.[1,5]
2. It helps to reduce how often the medicine need to be taken.
3. Low doses of drugs are required. [3]
4. ease of application .[6]
5. The gel formation increases drug's residence time, allowing for prolonged therapeutic action and better contact with target tissue.[1,7,8]
6. The in-situ gel system reduces the drug wastage .[1,5]
7. For effective treatment, a liquid formulation should remain at the site of actions and release the drug gradually over an extended period .[1]
8. Because of their physical structure, in- situ gel systems are easy to administer, which improves patient comfort and compliance. [1,5]

Suitable Drug Candidate for In-Situ Gel

1. Narrow absorption window in GI tract, e.g., riboflavin and levodopa, cyclosporine.[9]
2. Primarily absorbed from stomach and upper part of GI tract, e.g., calcium supplements, chlordiazepoxide and cinnarizine .[10]
3. Drugs that act locally in stomach, e.g., antacids and misoprostol. [9]
4. Ideally, drug should have a molecular weight conductive to diffusion and permeation.
5. The drug should exhibit low toxicity and high compatibility with the surrounding tissues to avoid adverse reaction. [10]

ADVANTAGES

1. Provide controlled and sustained release of drug, providing consistent and gradual drug release.[1,8]
2. Easy of the drug administration, facilitating Hassel -free drug delivery. [3,8]
3. Improved patient compliance and comfort. [5,11]
4. It decreases the wastage of drug. [12]
5. It works directly at the targeted site, providing localized action and reducing effects on non-targeted areas.[9,10]
6. It tends to produce less unwanted effects compared to conventional dosage forms.26
7. Reduction in plasma level fluctuation. [13]
8. It helps to reduce how often the drug needs to be taken and lowers the risk of side effects.[1,5]
9. Its simple production process reduces both setup and operational costs. [14]
10. Increased local bioavailability. [5,14]
11. 11.To enable drug targeting mainly via the mucus membrane especially in cases where invasive drug administration is required.[12,15]
12. Formulations made with naturally occurring polymers are less likely to produce unwanted reactions, as they are easily tolerated and safely eliminated by the body. [8,15]

DISADVANTAGES

1. High fluid intake is necessary.[1,16]
2. The sol formulation is more prone to deterioration, potentially compromising the efficacy .[8,17]
3. Stability problems may arise as a result of chemical degradation (oxidation, hydrolysis etc.,) or microbial degradation.[1,3,13]
4. The patient may be advised not to eat or drink for a few hours after taking the medication.[3,5]
5. Drug must have a low dose requirement to be suitable for this route .[1,3]

6. Due to lower mechanical stability, the hydrogel may dissolve prematurely or move away from the targeted area .[1,3]

7. For hydrophobic drugs, achieving both the quantity and even distribution of the drug loading in hydrogels may be limited. [1,3,16]

8. Toxicity because of organic solvents used.[19]

9. High viscosity of polymeric solution sometimes which may lead to problems during administration.[19]

Criteria For Selecting Polymers In In-Situ Gel Formulation

1. polymers need to stick effectively to the mucus membrane to ensure proper retention.[1,12]

2. It must be well-tolerated and non-irritant. [1,8,15]

3. It should be non-toxic .[1,3]

4. It should exhibit pseudoplastic flow properties.

5. The polymer should be capable of decreasing the viscosity with increase in shear rate.[3,15]

6. It should help to maintain or improve tear film behavior.[10,12,20]

7. It should be optically clear and transparent. [8,15]

Polymers Employed In In-Situ Gelling System

Polymers	Properties
1.Pectin	❖ Pectin's are complex carbohydrates that mainly consist of α-(1-4)-D-galacturonic acid residues. ❖ One of its biggest benefits is that it dissolves easily in water, which eliminate the requirement for organic solvents in formulation. ❖ When pectin is taken orally, divalent cations in the stomach help convert it into a gel form .[1,5,15,20.]
2.Guar gum	❖ Guar gum is also known as guaran, is a natural gum that comes from the endosperm of guar plant seed. ❖ It does not dissolve in hydrocarbons, esters, fats, ketones and alcohols. However, these substances dissolve in water (both cold and hot). ❖ Derivatives of guar gum are used in targeted delivery systems, including coating matrices, nanoparticles, and hydrogels. ❖ They can be added to matrix tablets to allow the drug to releasee in a slow and controlled manner.[1,20]
3.Carbapol	❖ This polymer, derived from polyacrylic acid and known for its high molecular weight, is commonly recognised for its pH sensitivity. Carbopol transforms from a liquid to a gel as the pH increases from 4.0 to 7.4. ❖ Carbopol remains in liquid form under acidic conditions but turns into low - viscosity gel when the pH becomes alkaline. It is primarily used in liquid or semisolid pharmaceutical formulation such as gels, suspensions and emulsions. ❖ HPMC is often combined with Carbopol to enhance the thickness of the solution and help lower its acidity.[1,2,13-16,20,21]
4.Xyloglucan	❖ It is also known as tamarind gum, as it is a natural polysaccharide extracted from endosperm of tamarind seed. ❖ It is mainly used in drug delivery systems targeting the peritoneal cavity, mouth, eyes and rectum because it is safe for the body, ecofriendly and well tolerated nature. The sol-to gel transition temperature differs based on amount of galactose eliminated. ❖ It forms gel either when heated from refrigerated temperature to body temperature or when cooled down from higher temperature.[13-16,20,21]

5.Gellan gum	❖ Gellan gum is a negatively charged, naturally derived from polysaccharide made by the microorganism Pseudomonas elodea (sphingomonas elodea) through fermentation. It consists of a repeating tetra saccharide unit composed of α-L-rhamnose, one β-D-glucuronic acid residues. Commercially called as Gelrite or Phytagel. ❖ Gellan gum forms gel in response to temperature changes or due to presence of cations (e.g., Na+, K+, Ca2+ and Mg2+). ❖ Gellan gum in widely employed in food business as a stabilizing and suspending agent. Gellan gum is recognised as a suitable polymer for developing nasal formulation and a water-soluble polymer for developing oral floating sustained-release dosage form.[1,3,5,13,14]
6.Alginic acid	❖ It is a type of copolymer composed of β-D-mannuronic acid and α-L-glucuronic acid units, which are linked together through 1,4-glycosidic bonds. ❖ A dilute solution of alginate turns into a firm gel when exposed to divalent or trivalent metal ions, as these ions binds with continuous α-L-glucuronic acid segment in the alginate chain. ❖ It is commonly applied in formulation of gel-forming solutions for the delivery of drugs, peptides, proteins. It functions as a carrier in ophthalmic gel systems due to its bio adhesive, non-toxic nature and biodegradable properties.[1,11,13,21]
7.Xanthum gum	❖ Xanthum gum is an extracellular polysaccharide known for its large molecular size, produced by fermenting the gram-negative bacterium Xanthomonas campestris.[1,16,20] ❖ It shows good stability in alkaline environment. It is employed in pharmaceutical formulation to stabilize the emulsion and suspension.[2,22] ❖ It dissolves easily in both hot and cold water, and maintains its stability across a wide pH range .[1] ❖ This natural cellulose derivative has a backbone of β-D-glucose with a side chain of three sugars of β-D-mannose-α-D-mannose linked to alternating glucose units in the main chain.[21] ❖ This natural cellulose derivative has a backbone of β-D-glucose with a side chain of three sugars of β-D-mannose-α-D-mannose linked to alternating glucose units in the main chain.[21]
8.Chitosan	❖ Chitosan is an eco-friendly, temperature-responsive polymer with a natural positive charge. It is an amino -based polysaccharide derived by chemically modifying chitin, a substance commonly found in the shells of crabs and shrimp, through an alkaline deacetylation process.[12,14] ❖ Chitosan undergoes gel formation in response to changes in pH and thermal conditions. It is a non-toxic, pH -sensitive polymer with a positive charge that stays dissolved in water up to approximately pH 6.2.[4] ❖ When the pH of a chitosan solution rises above 6.2, it loses its solubility and forms a hydrated, gel-like precipitate .[1,20] ❖ The pH responsive, positively charged polysaccharide solution is transformed into potent gel-based pH solutions by adding polyol salt, without involving any chemical modification or bonding.[14,20]
9.HPMC	❖ Cellulose is made up of glucan chain that contains repeating β-(1,4)-D-glucopyranose units. ❖ As the temperature drops (30^0**C**), the cellulose material becomes thickens, but it undergoes gelation as the temperature rises to 40-50^0**C** ❖ MC is a cellulose -based polymer derived from native cellulose, in which a flexible methyl groups are alternately substituted along the polymer chain.[1,11,23]

10.Poloxamer	❖ Poloxamers are water- soluble triblock copolymers composed of two polyethylene oxide (PEO) segments flanking a central block of polypropylene oxide (PPO), forming an ABA-type structure.[2] ❖ commonly sold under the brand name Pluronic. It shows excellent thermosetting property and extends the drug residence time at site of application, thereby increasing the bioavailability and effectiveness. It forms a clear, colourless and translucent gel.[6,8] ❖ It undergoes gelation in response to temperature changes.[6] ❖ Widely used in formulations, it helps stabilize mixtures, improves solubility, and create gel-like textures.[2] It contains more than 30 different non-ionic surfactants.[10] ❖ Its ability to form gel is influenced by how the water- attracting and water-repelling chains are arranged and balanced. Different molecular weights provide various gelling performances .[1,6]

Mechanism Of In-Situ Gel

The in-situ gel formulation is mainly occurred in 2 different mechanism they are

1)Physical mechanism

2)Chemical mechanism

Physical Mechanism

a) Diffusion:

Diffusion acts as a physical mechanism in the development of in situ gels, where the solvent within the polymer mixture slowly disperses into surrounding tissue environment [2]. During the process, the polymer gradually becomes less soluble as the liquid components migrate into the surrounding tissue, which results in the solidification of the polymer matrix at the application site. N- methyl pyrrolidone (NMP) is a commonly used in the development of in-situ gel systems.[1]

b) Swelling:

Swelling is another important physical mechanism applied in the design of in-situ gel systems. In this method, the polymer takes up fluids from the surrounding environment, swells from outside inward, and enables steady drug release. Myverol, a polar lipid, is known for forming lyotropic liquid crystalline phase structures upon hydration. It can degrade enzymatically within the body and also exhibits bio adhesive properties.[2]

c) Bio-erosion:

In this mechanism, the drug is dispersed through an inserted body structure made of a matrix of bio erodible materials. The bio-erosion matrix allows the tear drops to interact with the insert, which can lead to the sustained release of medications as the bioerosion matrix gradually breaks down this results in even drug distribution and controlled release. A basic viscosity -based gel remains unchanged after administration. However, at the site of application, the solution transforms into a gel due to its chemical properties.[24]

Chemical Mechanism:

a) Enzymatic cross-linking:

Enzymatic cross-linking is considered one of the most effective and suitable methods for developing in-situ gelling systems. In this approach, the in-situ gel forms as a result of the polymer cross-linking with enzymes that are naturally present in the body's fluids**.** Although enzyme-catalysed in-situ gel formation using natural enzymes has not been widely explored, it offers certain advantages compared to chemically and light-induced methods.[20] For example, it functions effectively under the physiological condition and removes the need for potentially hazardous substances like initiators and monomers. Changing the enzyme's concentration

while maintaining a suitable established mechanism that regulate the rate at which gel forms, ensuring that the mixtures is administered before gelation begins.[2]

b) Photo polymerization:

Photo polymerization is a widely used technique in the development of biomaterials. In this method, a gel forms directly at the site of application through exposure to light or other forms of electromagnetic radiation, allowing the material to set in place and form an in-situ gel. Electromagnetic radiation which is used to create a gel after invader and reactive macromer and monomer solution of injected within a tissue location. The good polymers for photo polymerisation which are exposed to a photo initiator like acrylate or a comparable monomer will breakdown by a polymerizable functional group. This technique typically uses long-wavelength UV and visible light, as shorter wavelengths are avoided due to their harmful effects on biological tissues and their limited ability to penetrate the skin. This method makes use of ketones like 2,2-dimethoxy-2-phenylacetophenone as ultraviolet photopolymerization initiators. The formulation is injected directly at the targeted site, where it undergoes photo-curing in situ with the help of Fiber optic cables. This allows the drug to be released over an extended period. This system also enables fast polymerization at body temperature, making it suitable for biomedical applications.[21]

c) Ionic cross linking:

This method utilizes ion-sensitive polymers that undergo phase transitions when exposed to ions such as Na^+, K^+, Ca^{2+}, and Mg^{2+}. Certain polysaccharides belong to this category of ion-sensitive materials. For example, κ-carrageenan forms a firm gel structure in the presence of small amounts of potassium ions. Depending on the type and concentration of mono- or divalent cations, κ-carrageenan can produce either brittle or elastic gels, making it suitable for in situ gel-forming systems.[1]

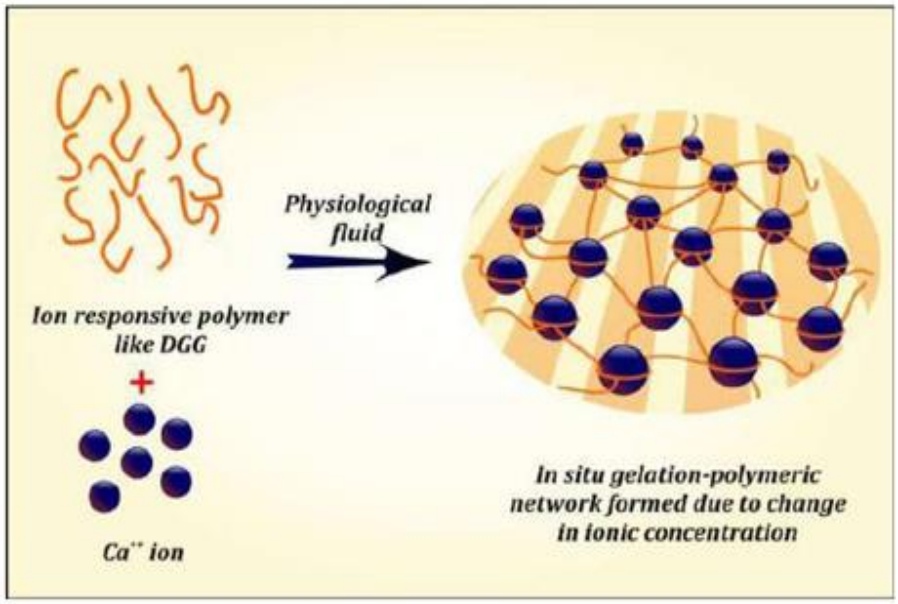

Fig 3: Mechanism involved in ionic cross-linking system

d) Temperature triggered gelation:

In this type of formulation, temperature is one of the most commonly employed triggers in polymer systems that respond to environmental changes. The use of temperature-sensitive methods is convenient and adaptable for applications in both laboratory (in vitro) and living systems (in vivo) conditions, body temperature triggers gelation: external heat is not required. When the liquid form (in room temperature) changes to a gel state (35-

37^0C), this happens when the hydrogels come into contact with the body fluid and as a result of rise in the temperature.[2]

Type	Example
Negative thermos sensitive	Poly (N-isopropyl acrylamide)
Positive thermos sensitive	Polyacrylic acid
Thermally reversible	Poloxamer, tetronics

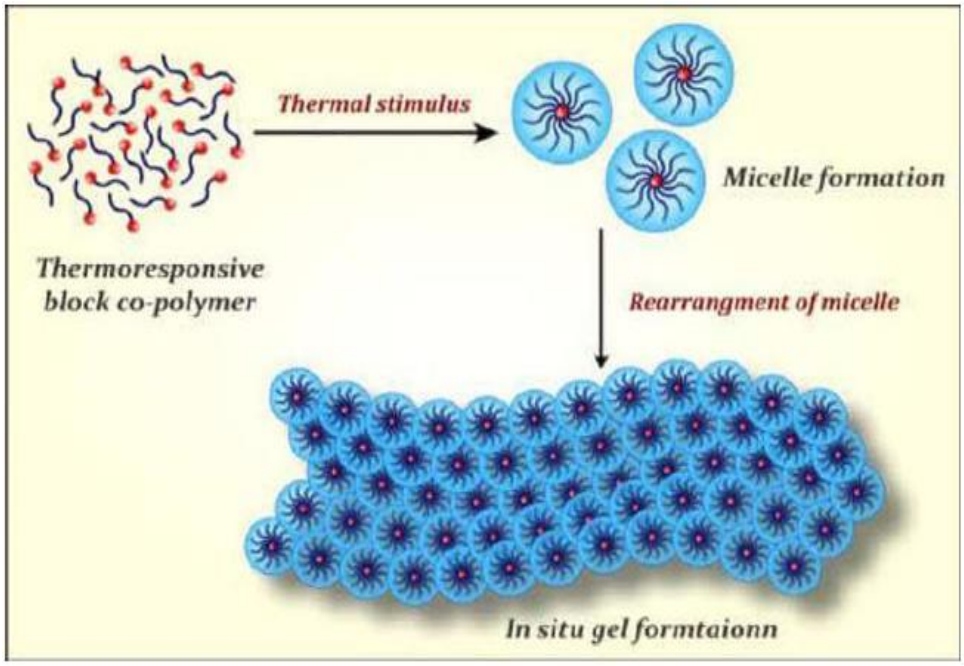

Fig 4: Mechanism involved in temperature triggered system

e) pH Triggered in-situ gelation

Gel formation in this method is triggered change in the pH. This method makes use of pH-sensitive or pH-responsive polymers. Pendant basic or acidic groups found in pH-sensitive polymers can either accept or donate protons in response to changes in the surrounding pH**.** Large-scale ionizable group polymers are often referred as ionic or ion-sensitive polymers. Because the formulation contains polyelectrolytes, the hydrogel swells and forms an in-situ gel when the external pH rises. Several anionic polymers are considered suitable for this method, such as polyethylene glycol (PEG), cellulose acetate phthalate (CAP), carbomer and its various forms, pseudo-latexes, and polymethacrylic acid (PMC), and similar compounds used in this context. Polyacrylic acid, commonly known as Carbopol is a well-known pH sensitive polymer. It stays in solution at lower pH values but forms gels with less dense gel at higher pH values.[2]

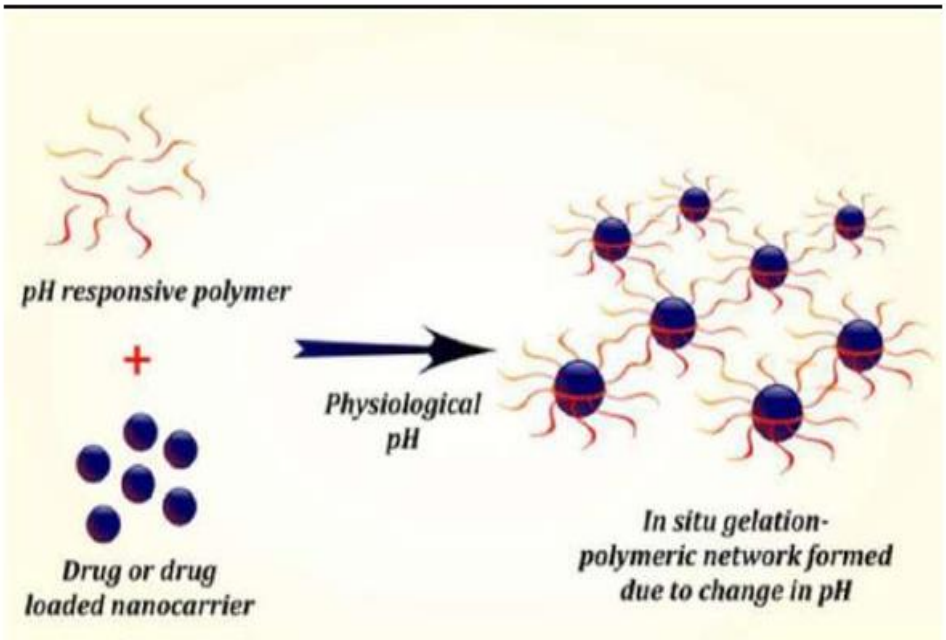

Fig 5: Mechanism involved in pH sensitive system

General Method of In-Situ Gel Preparation

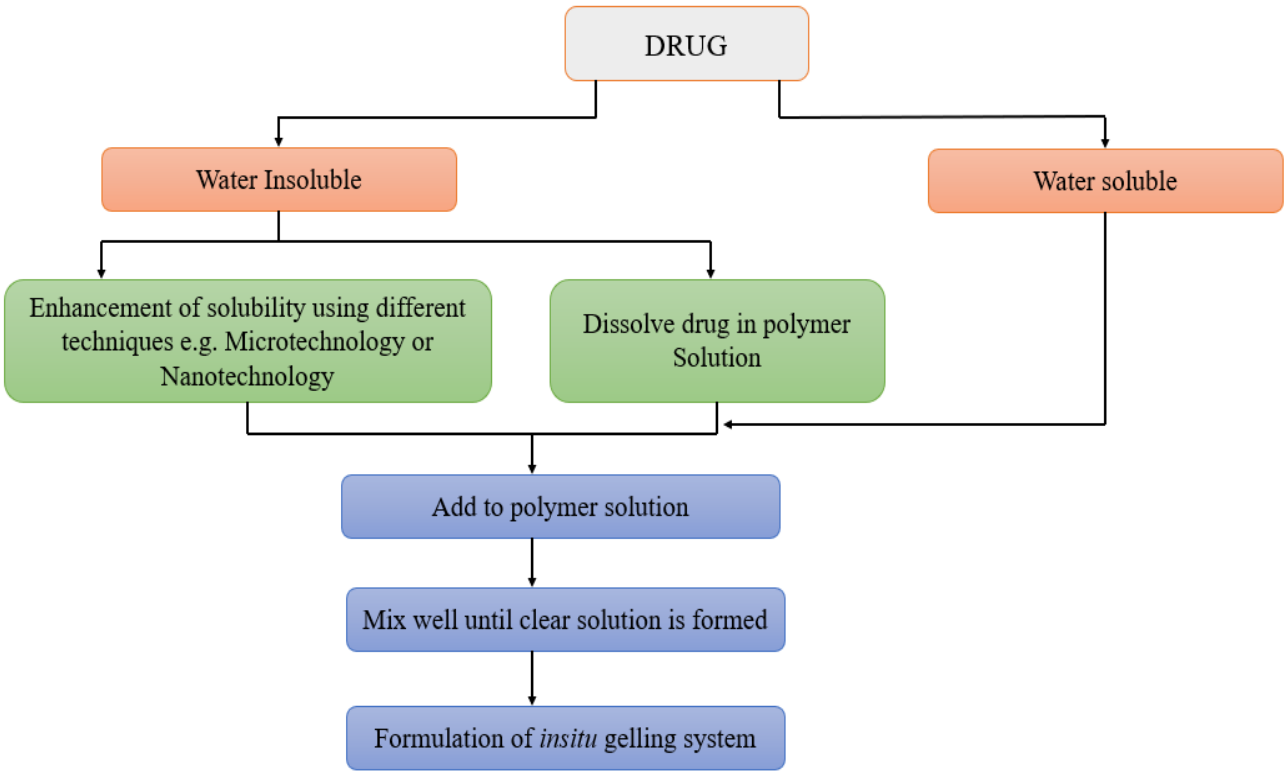

Fig 6: General method of preparation of in-situ gel

Application Of In-Situ Gel[1-9,11,17,18,22]

1.Oral drug delivery system

pH- sensitive hydrogels are particularly useful for delivering drugs to targeted areas within the gastrointestinal (GI) tract. Hydrogels made from

varying combinations of cross-linked polyethylene glycol (PEG) and polyacrylic acid (PAA)derivatives have been used in the formulation of silicone microspheres, which help release prednisolone specifically in the abdominal region, offering gastroprotective effects. Cross-linked dextran-based hydrogels quickly swell in response to change in pH, making them suitable for such applications. Additionally, other natural polysaccharides like amidated pectin, insulin, and guar gum have been explored to enhance colon-targeted drug delivery. Gellan gum and sodium alginate, both of which can form gels in the presence of calcium ions, also show promise; in acidic stomach conditions, theses ions are released, triggering the gelation process.

2.Ocular drug delivery system

In ocular drug delivery, natural polymers such as alginic acid, inulin, and xyloglucan are commonly used, with inulin being the most common. For local eye treatments, drugs such as autonomic agents, anti-inflammatory medicines and antimicrobials help relieve discomfort in conditions like glaucoma. To enhance drug bioavailability, viscosity enhancers like carboxymethyl cellulose, hydroxypropyl methyl cellulose, carbomers, and polyvinyl alcohol are added to formulations. These substances help increase the formulations thickness, thereby prolonging its retention on the eye's surface and improving drug availability, while also offering manufacturing ease. Additionally, penetration enhancers often the same classes of drugs used therapeutically, such as anti-inflammatory drugs, autonomic agents, and antimicrobials aid in reducing ocular discomfort and improving drug absorption. Traditional eye drops systems frequently suffer from poor drug retention and reduced therapeutic effects due to rapid tear turnover and drainage. To address these limitations and improve bioavailability, in-situ gelling systems were developed, which transform into gels upon contact with the eye, allowing the drug to stay longer at the site of the action.

3.Nasal drug delivery system

In nasal in-situ gel systems, polymers like xanthan gum and gellan gum are utilized for their ability to form gel upon administration. Mometasone furoate was evaluated for its effectiveness in treating infectious rhinitis. To assess its therapeutic potential, an animal model of allergic rhinitis was developed, and the impact of the in-situ gel on antigen-induced nasal symptoms was studied in sensitized rats. The results showed that the in-situ gel formulation significantly reduced nasal symptoms compared to the commercially available Nasonex (Mometasone furoate suspension 0.05%).

4.Rectal and Vaginal drug delivery system

The rectal route allows for the administration of a wide variety of drugs in multiple dosage form, including liquids, semisolids such as creams, foams, and ointments, as well as solid forms like suppositories. Similarly, the vaginal route, apart from its role in the reproductive system, is recognised as an effective pathway for drug delivery. Acetaminophen, known for its anti-inflammatory effects, has been formulated as a rectal in situ gel using synthetic polymers like Polycarbophil, Poloxamer F188, and Poloxamer 407. These polymers contribute to the formation of a thermosensitive liquid suppository that gels upon administration. This approach not only simplifies delivery but also enhances the drug's bioavailability.

5.Injectable drug delivery system

In situ gels have emerged as a preferred drug delivery option in recent years because they don't require surgery and are easier for patients to use. Sustained drug release can effectively be achieved by incorporating the therapeutic agent into a delivery matrix that is administered through injection or implantation. Thermoresponsive gels, especially those based on poloxamers, are frequently utilized due to their reversible phase transition capabilities. Many synthetic polymers and block copolymers are commonly incorporated in the formulation of injectable in situ gel injection. One example of anti -inflammatory drug is Bupivacaine which is formulated as an

injectable in situ gel using poly (D, L-lactide), poly (D, L-lactide coglycolide) and PLGA as the polymer that exhibits a prolonged duration of action in gel state.[5]

6.Dermal and Transdermal drug delivery system

Due to the skin's unique structure and composition, the pharmaceutical research has found it extremely difficult to deliver the medication molecules across the skin barrier. The Pluronic F127 has been evaluated for its effectiveness as a thermoresponsive gel base for delivering Indomethacin through the skin. In vivo studies indicated that a 20% w/w aqueous gel formulation could be practically used for topical drug applications. Poloxamer 407 gel also demonstrated potential as a suitable medium for transdermal insulin delivery 73. Additionally, combining iontophoresis with chemical penetration enhancers resulted in a synergistic enhancement in insulin absorption through the skin.[9]

General Evaluation Parameters of In-Situ Gelling System

1.Clarity

The prepared solution is visually inspected under the light against both black and white backgrounds to assess its clarity. download file.[5,6]

2.Appearance

Ideally, the gels should be transparent. The formulations underwent visual inspection to observe general characteristics such as colour, Odor, and any suspended particulate matter.[15]

3.pH

pH can be determined by taking the formulation in a beaker and gradually introducing 1 ml of NaOH while stirring the solution continuously. The pH is then measured using a pH meter.[5,6]

4.Texture analysis

Texture analysis is commonly used to evaluate the firmness, uniformity, and cohesiveness of hydrogels by using texture analyser. This helps determine how easily the sol can be injected, ensuring that the formulation can be comfortably and effectively delivered in the body.[20]

5.Sol-gel transition temperature and gelling time

In in situ gelling systems containing temperature - sensitive polymers, the phase transition temperature refers to the point at which a visible change in the sol's meniscus is first noticed, indicating the onset of gel formation. To evaluate this, the sample is kept in a test tube and gradually heated to a set temperature and gel formation is confirmed by the lack of meniscus movement when the tube is tilted.[3,20]

6.Gelling capacity

The gelling capacity of the in- situ gel is evaluated for ophthalmic formulation.[7]To mimic real eye conditions, the formulation is combined with artificial tear solution in a 25:7 ratio (i.e.,25μl of the gel to 7μl of typical tear fluid). The gel's ability to form and maintain its structure was observed. the gel formation process was observed visually, recording how long it took for the gel to form, and the duration taken for complete dissolution.[7,9,15,20,25]

7.Gel strength

A rheometer was used to evaluate this property, which depends on the gelation behaviour of the specific gelling agent used in the formulation. A specific quantity of gel was prepared from the sol form in a beaker. During the measurement, the beaker containing gel was steadily moved upward, allowing the probe to gradually penetrate through the gel. The variation in the load applied to the probe was measured in relation to how deep it reached beneath the surface of the gel.[7,15,25]

8.Drug content

Approximately 1 ml of prepared formulation is accurately measured and transferred into a 10 ml volumetric flask, then diluted to the mark with distilled water. From this,1ml is withdrawn and further diluted to 10ml using distilled water. The resulting solution is then analysed using UV-visible spectrophotometry by measuring the absorbance at specific wavelength.[25]

9.Viscosity and rheological studies

Evaluating the viscosity is essential in the development of in situ gel formulation, as it significantly influence both their performance and ease of application.[7]The flow behaviour and consistency of the gel system are typically examined using instruments like Brookfield viscometer or traditional ones such as the Ostwald viscometer. In situ gels should have a viscosity that allows easy and trouble-free application, especially when delivered through the eye or via injection, ensuring patient comfort during administration. The formulation should have the viscosity between 5 and 100 mPas.[3]

10.Spreading coefficient

The apparatus is composed of a ground glass slide fixed on to the wooden block. Each sample, weighing approximately 2 grams, was positioned and examined on this group slide. Subsequently, gel preparation was sandwiched between this slide and second slide having some dimension to the fixed glass slide. The second slide was equipped with a hook. Approximately1 gram of weight is placed on the top of the two slides for 5min to eliminate the air bubbles and ensure the uniform gel film between them. A calibrated weight was positioned on a pan linked with pulley system through a hook. The duration it took for the upper slide to detach from the ground slide was recorded. Short duration indicates a great the spreading coefficient (S).[15]

$$s = \frac{M \times L}{T}$$

Where,

M=Weight tied to upper slide

L=Lenth of glass slides

T=time taken to separate the slides

11.Sterility testing

Sterility testing is performed in accordance with IP 1996. The sample is incubated for a minimum period of 14 days. To check the bacterial contamination, the sample is placed in fluid thioglycolate medium at 30-35℃ and for fungal contamination, it is incubated in Soya casein digest medium at 20-25℃.[20,25]

CONCLUSION AND FUTURE REMARKS

The present review concludes that the in-situ gel technology stands out as a highly innovative and effective method for drug delivery. The main aim is to enhance patient adherence to therapy and comfort by offering controlled and reliable drug release, which is effectively achieved by in situ gels. The utilization of polymer -based in-situ gels enables precise and consistent release of therapeutic agents, offering significant over traditional dosage forms. These systems are capable of maintaining drug levels for extended durations, thereby ensuring sustained therapeutic action. Additionally, the exhibit excellent chemical stability and well-tolerated by biological tissues and ease of application, reduced dose frequency, making the in-situ gel dosage forms highly reliable and safe. The formulation often includes polymers that are both biodegradable and easily dissolves in water. This formulation approach improves the acceptability and overall performance of the drug delivery system. This system utilizes synthetic polymers that forms gel at the site of application, making it suitable for oral use, eye application, through the skin, inside the cheek, within the abdominal cavity, by injection, as well as through rectal and vaginal routes. There is considerable scope on in situ gel systems to develop advanced techniques in drug delivery system.

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