A Review on In-situ Gel

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***Abstract*-The present review on in situ gelling systems has emerged as a significant and widely recognized topic within the field. These systems offer substantial advantages for drug delivery, characterized by their ease of use and straightforward manufacturing processes. They enhance patient adherence and comfort by reducing the frequency of drug administration, attributed to their distinctive sol-to-gel transition properties. The formation of gels is influenced by various factors, including temperature variations, pH alterations, ionic presence, and exposure to UV light. The gels formed in situ facilitate the sustained and controlled release of drugs. Both natural and synthetic biodegradable polymers, such as pectin, alginic acid, gellan gum, and xyloglucan, are utilized in the formulation of these gels. This review focused definitions, classifications, benefits, drawbacks, and the types of polymers employed, along with their desirable characteristics and preparation methods for in situ gels. Additionally, it addresses the approaches, applications, and evaluation methods pertinent to in situ gels.**

Index Term: **In situ gel, Mechanism, Novel drug delivery system, Polymers.**

I. INTRODUCTION

The "In-Situ Gel " system has become one of the best new drug administration systems. The sitting gelling system helps to improve sustainable and controlled drug release, patient compliance and comfort due to the special characteristics of the transition "gel ". An in-situ gelling system is a formulation that is in the form of a solution before it enters the body, but it transforms into a gel under one or combinations of a variety of physiological conditions. The sol-to-gel transition depends on a variety of factors, including temperature, pH changes, solvent exchange, UV radiation, and the presence of specific molecules or ions. Drug delivery systems with the above sol-gel properties are useful for the preparation of vehicles for the long-term administration of bioactive molecules. The "in situ gelling" systems have several advantages, such as ease of application of the dosage, reducing the frequency of administration and protecting the drug from changes in environmental conditions. A variety of natural and synthetic polymers undergo in situ gelation and can be used orally, ocularly, transdermally, buccally, intraperitoneally, parenterally, injectably, rectally, and vaginally routes . Recent advances in in situ gels have made it possible to exploit changes in the physiological uniqueness and different areas of the gastrointestinal tract to enhance drug absorption and improve patient convenience and compliance . Pectin, gellan gum, chitosan, alginic acid, guar gum, carbopol, xyloglucan, xanthan gum, HPMC, poloxamer, etc. are some of the natural polymers used in the in-situ gelling systems . This review focuses mainly on the introduction of in situ gels, the different approaches, the evaluation of the different polymers used and their applications [1]-[2]-[3].

II. ADVANTAGES

- To reduce drug loss.
- To facilitate insertion.
- To be administered to unconscious or elderly patients.
- To help prolong the sustained release of drugs.
- To provide improved patient comfort and compliance.
- To minimize drug toxicity due to low doses without drug accumulation.
- To provide higher bioavailability.
- The use of natural polymers ensures biocompatibility and biodegradation.
- The use of synthetic polymers allows for a range of applications, usually well-defined and modified to achieve acceptable degradability and functionality.
- Controlled release drug
- Easy drug Administration

- In situ gels provide an important "stealth" features of vivo due to which Hyprophilicity that increases
- vivo rotational delivery device rotation time immune response and capture phagocytic activities.

III. DISADVANTAGES

- Large volumes of liquid are required.
- Agents in ash form are more susceptible to deterioration.
- Stability issues may arise due to chemical breakdown.
- Eating and drinking may be restricted for several hours after administration of the medication.
- The amount of drug load and uniformity In particular, it may be limited to hydro gel Hydrophobic drug.
- Only small amounts can be administered.
- The form of the drug solution is more sensitive to deterioration.
- Chemical decomposition is the possibility of instability.

IV. IMPORTANCE

- The In-situ gel facilitates the controlled and sustained release of the drug through the sol-gel transition[4].
- It helps in reducing the frequency of drug administration in the body[4].
- Less amount of drug is required, no drug accumulation or side effects[5].
- Increases the bioavailability of the drug[5].
- Gel formation increases drug residence time[6].
- In situ gel drug delivery systems reduce drug wastage[6].
- A liquid dosage form would be ideal as it would sustain drug release and maintain contact with the target site for an extended period of time[6].

V. IN SITU GEL MECHANISM

A. In situ gel formation due to physical mechanism

1.Swelling: In this strategy, gelation occurs when the material absorbs water from the external environment and then expands to occupy the required space. An example of such a substance is mineral 18-99 (glycerol monooleate)[7].

Swelling-controlled mechanism

a.Solvent-activated systems: Occur when the distribution of the drug is faster than the inflammation of the hydrogel. When the hydrogel is placed in an aqueous solution, the water molecules penetrate into the polymer network and occupy some space, so other metals in the lattice start to grow and other water molecules can enter the lattice. However, inflammation is not a continuous process; the strength of the linked network or physically linked will balance the constant advice of the network to prevent its destruction. For example, drug extraction from hydrogel (HPMC) is commonly performed using this method[8].

b. Osmotic swelling: In hydrogels, the total inflammatory pressure of the gel is related to the volume fraction, free network volume, and crosslink density, but is independent of the gel pH and inflammation time[8].

2.Diffusion: In this method, the solvent diffuses out of the polymer structure into the tissue, resulting in deposition of a polymer network. N-methylpyrrolidone (NMP) is one of the useful solvents for such systems[9].

Diffusion- controlled mechanism

a.Matrix system: Strong specialists spread as easily as the force of an inert hydrogel grid broken.

- Drug release depends on:
  - Separation of water in the matrix followed by dissolution of wood and finally dispersion of the tree dissolved from the matrix.
  - The polymer interacts with the drug resulting in moderate drug release.
  - The size of the hydrated matrix is considered as the tree path length. If the polymer matrix is considered inert and the drug release is controlled by the distribution, the drug release rate can be defined by the Higuchi equation[10].

b.Reservoir system: The drug is contained in a substance (often called a reservoir) surrounded by a regulating hydrogel membrane that allows drug diffusion. As the system interacts with water, water evaporates from the system and dissolves the drug, and drug transport (from the cavity through the outer polymer membrane) occurs with the removal of another membrane interface and gradient-driven distribution in thermodynamic activity. Drug trafficking can be defined by Fick\'s first law, if the activity of the drug in the pool remains constant and unlimited immersion conditions are maintained, then the rate of drug release may continue unchanged because it depends on fluid availability and will be

independent of time, so zero-order kinetics can be achieved. Once the drug wears off, the amount released gradually increases with concentration according to first-order kinetics. These types of drug delivery systems are used to administer active ingredients orally[10].

B. In situ gel formation due to chemical reaction

1. Enzymatic crosslinking: In situ development catalyzed by conventional catalysts has not been studied in general, however, it presents several favorable circumstances compared to chemical and photochemical approaches. For example, in Under physiological conditions, the enzymatic cycle operates productively without the use of potentially hazardous chemicals such as monomers and initiators. Varying the amount of enzymes provides an advantageous system for controlling the gelation rate, allowing the combination to be introduced before gel formation[11].

2.Photopolymerization: Photopolymerization is commonly used to transform biomaterials in situ. A mixture of reactive monomer or macromer and initiator is infused into a tissue site and electromagnetic radiation is applied to produce a gel. Acrylate and related polymerizable groups are regularly used as polymerizable groups on individual monomers and macromers because they rapidly undergo photopolymerization in the presence of a suitable photoinitiator. In particular, ultraviolet and visible wavelengths are used. Short-wave ultraviolet light is less commonly used because it has limited tissue penetration and is harmful. In the case of photopolymerizable frames, they are introduced into the ideal site by perfusion, photocured in situ using a fiber optic connection, and then release the drug over a period of time. At physiological temperatures, the photoreaction results in a rapid polymerization rate[11].

3. Ionic crosslinking: There are some ion-sensitive polysaccharides, such as gellan gum, gelatin, sodium alginate, which undergo phase transition in the presence of various ions. The anionic polysaccharide, gellan gum, undergoes in situ gelation in the case of mono- and divalent cations, such as Ca2+, Mg2+, K+ and Na+[11].

VI. POLYMERS

A.Pectin

The polymer backbone of pectins, a family of polysaccharides, is primarily composed of residues of α-(1-4)-D galacturonic acid[12]. According to the egg-box model, low methoxy pectin (esterification <50%) readily gels in an aqueous solution when free calcium ions are present and crosslinks the galacturonic acid chain. H+ ions, the source of divalent ions, are necessary for pectin gelation to occur. Calcium ions are typically needed to create a gel that can be used as a drug delivery vehicle [13]. Pectin's primary benefit when used in these formulations is its water solubility, which eliminates the need for an organic solvent. When taken orally, the divalent cations in the stomach cause a pectin-to-gel transition. It is possible to incorporate complex forms of calcium ions into formulations to induce pectin gelation [14].The majority of the calcium ions added to the formulation can form a complex with sodium citrate when added to the pectin solution. This enables the formulation to stay in a fluid state (sol) until the complex breaks down in the stomach's acidic environment, where gelation is brought on by the release of calcium ions. When the formulation is given to the stomach, the amount of calcium and citrate ions can be adjusted to preserve its fluidity and cause gelation prior to administration[15].

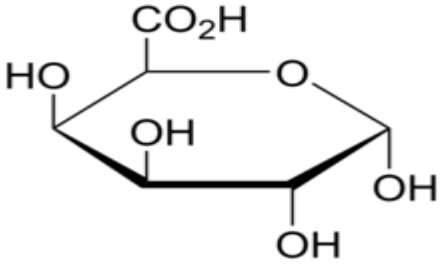

Fig 1: Structure of Pectin

B.Chitosan

Shrimp and crab shells naturally contain chitosan, which is made up of heat-sensitive, biodegradable, and polycationic polymers that are produced by alkaline deacetylation of chitin[16].It is a polymer made up of glucosamine and N-acetylglucosamine copolymers. A pH-dependent cationic polymer that is biocompatible, chitosan can dissolve in aqueous solutions up to 6.2. A hydrated gel is created when an aqueous solution of chitosan is neutralized to a pH higher than 6.2 [17]. By adding a polyol salt with a single anionic head, such as glycerin, sorbitol, fructose, or glucose phosphate salt, to the chitosan aqueous solution, the pH gelling cationic polysaccharides solution is converted into thermally sensitive pH-dependent gel forming aqueous solutions without undergoing chemical modification or cross-linking[18].

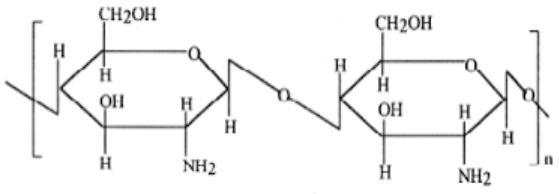

Fig 2: Structure of Chitoson

C. Xanthan gum

The gram-negative bacterium Xanthomonas campestris ferments to produce xanthan gum, a high molecular weight extracellular polysaccharide[19].This naturally occurring cellulose derivative's primary structure consists of a cellulosic backbone (βD-glucose residues) and a trisaccharide side chain made up of β-D-mannose, β-D-glucuronic acid, and α-D-mannose that is joined to the main chain's alternating glucose residues. Both pyruvate and glucuronic acid groups are present in the side chains of this polymer, which gives it its anionic characteristic. Both hot and cold water, as well as alkaline and acidic environments, can dissolve xanthan gum. exhibits strong stability in alkaline environments[20].

D. Carbopol

Carbopol is identified as a high molecular weight, cross-linked derivative of polyacrylic acid, functioning as a water-soluble vinyl polymer. It undergoes a sol-to-gel transition when the pH level surpasses a pKa of around 5.5 in aqueous solutions[21]. In acidic environments, Carbopol remains in solution, whereas it converts to a low-viscosity gel in alkaline conditions. The combination of hydroxypropyl methylcellulose (HPMC) with Carbopol serves to increase the viscosity of the solution while simultaneously lowering its acidity. Various water-soluble polymers, such as the Carbopol-hydroxypropyl methylcellulose system, polymethacrylic acid, and polyethylene glycol, are categorized as pH-induced in-situ precipitation polymer systems[22].

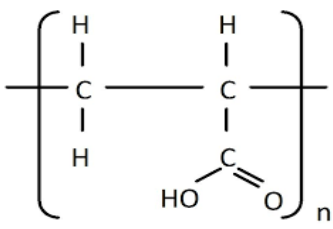

Fig 3:Structure of carbopol

E. HPMC

Hydroxypropyl methylcellulose (HPMC) is made up of glucan chains featuring repeating β-(1,4)-D-glucopyranose units. Methylcellulose, a natural polymer, is derived from native cellulose and includes alternating methyl groups along its structure[23].While cellulose materials typically show a viscosity that decreases with rising temperature, HPMC and methylcellulose present an exception to this behavior. As a water-soluble cellulosic ether, HPMC is extensively utilized due to its solubility in both organic and aqueous solvents. Its desirable characteristics, including flexibility, lack of taste and odor, and stability in the presence of heat, light, air, and moderate moisture, position it as a favorable option for drug delivery systems[24].

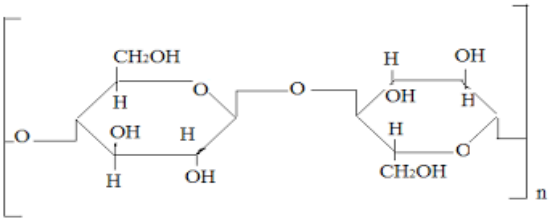

Fig 4:Structure of HPMC

F. Xyloglucan

Xyloglucan, commonly referred to as tamarind gum, is a polysaccharide extracted from the endosperm of tamarind seeds. This polysaccharide features a backbone chain of (1-4)-β-D-glucan, which is adorned with (1-6)-α-D-xylose branches that are partially substituted by (1-2)-β-D-galactoxylose[25].Xyloglucan consists of three distinct oligomers: heptasaccharide, octasaccharide, and non-saccharide, each characterized by varying quantities of galactose side chains. Upon partial degradation by β-galactosidase, xyloglucan produces a product that demonstrates thermally reversible gelation, attributed to the lateral stacking of rod-like chains. The temperature at which the sol-gel transition occurs is influenced by the extent of galactose removal. When heated to body temperature, it transitions into a thermoreversible gel[26]. Its potential application in oral drug delivery is based on the anticipated slow gelation time, which allows for in-situ gelation within the stomach following the oral intake of a chilled xyloglucan solution. Given its non-toxic, biodegradable, and biocompatible nature, xyloglucan gels are promising candidates for various drug delivery routes, including oral, intraperitoneal, ocular, and rectal administration[27].

G.Alginic acid

Alginic acid is a polysaccharide gum derived from brown algae. It is characterized as a linear block copolymer composed of β-D-mannuronic acid and α-L-glucuronic acid residues, which are interconnected through 1,4-glycosidic bonds[28]. The specific ratio of these blocks and their arrangement along the polymer chain is influenced by the algae's source. When a dilute aqueous solution of alginate is treated with divalent and trivalent metal ions, it undergoes a coordinated process that results in the formation of a robust gel, particularly involving consecutive glucuronic acid residues within the α-L-glucuronic acid segment. The α-L-glucuronic acid (G) is arranged in an alternating sequence (MG) with either the MM or GG blocks, and the interaction between the G block and the calcium ions leads to the development of a uniform gel[29]. The mechanical properties and porosity of the resulting hydrogel are contingent upon the G:M ratio, the type of crosslinking agent employed, and the concentration of the alginate solution. Alginic acid is noted for its advantageous characteristics, including biodegradability and non-toxicity, rendering it an ideal candidate for ophthalmic formulations. The prolonged retention of alginic acid-based formulations on the precorneal surface is attributed not only to their gelling capability within the eye but also to their excellent mucosal adhesion, which is facilitated by the presence of carboxylic acid groups[30].

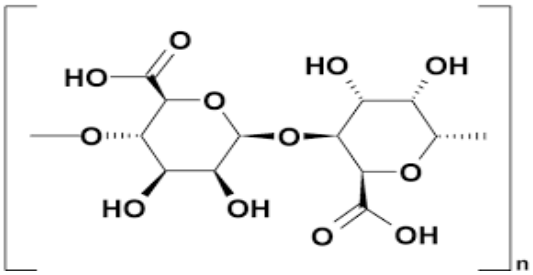

Fig 5: Structure of Aliginic acid

VII. APPROCHES

A.physiological triggered approaches –

1. Temperature triggered in situ gel technique:-

Temperature is the most widely used stimulant for environmentally friendly polymer systems in the form of in-situ gelling. Temperature changes that are easily used to control, and are easily applicable both in vitro and in vivo. In this process, gelation is caused by body temperature and there is no need for external heat. These hydrogels are not liquid at room temperature (20-25 ° C) and go into gelation on contact with body fluids (35-37 ° C), due to the increase in temperature. There are three types of temperature-sensitive systems. They are a sensitive form of thermo Esb. In this system, the thermo-reacting polymers or temperatures used show significant and permanent changes in their body properties and temperature. These polymers show a constant gap in the high or low temperature of the critical high or low temperature present[31].

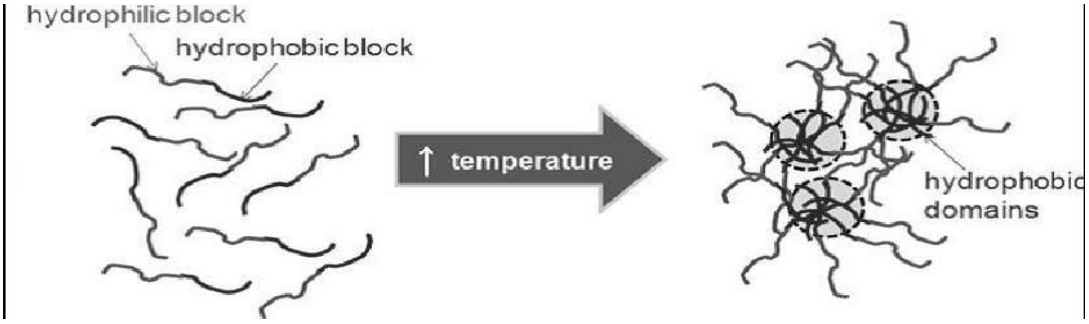

Fig 6:Mechanism of Temperature sensitive system

2.PH triggered in in situ gelation:-

The formation of the gel in this process is attributed to variations in pH levels. This technique employs polymers that are sensitive to pH changes. These pH-sensitive polymers contain acidic or basic groups that can either accept or release protons in response to fluctuations in pH. A significant number of polymers with ionizable groups are classified as polyelectrolytes. The presence of these polyelectrolytes within the structure results in an increase in external pH, which subsequently leads to the swelling of the hydrogel, functioning as an in situ gel. Certain polymers, particularly those with anionic groups, are well-suited for this method. Examples include cellulose acetate phthalate (CAP), carbomer and its derivatives, polyethylene glycol (PEG), pseudo latexes, and polymethacrylic acid (PMC)[31].

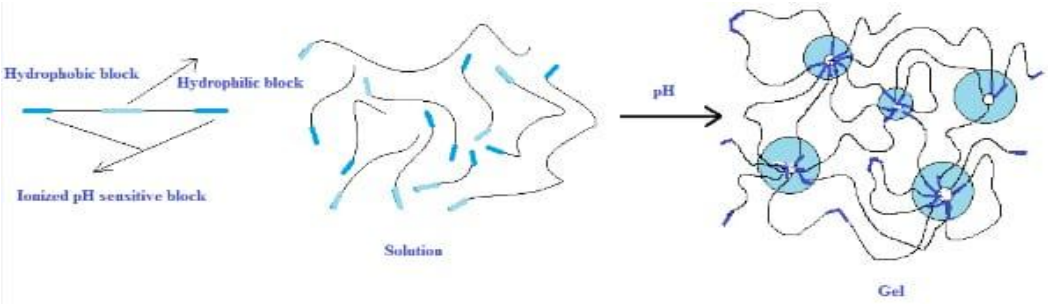

Fig 6:Mechanism of PH triggered insitu gel system

3. Ion Activated in situ gelation:-

In this approach, the gelling of the solution applied is induced by the transformation of ionic energy. It is believed that the extent of gelation is influenced by the osmotic gradient present at the surface of the gel. Examples of osmotically responsive gelation polymers include Gelrite or Gellan gum, Hyaluronic acid, and Alginates[31].

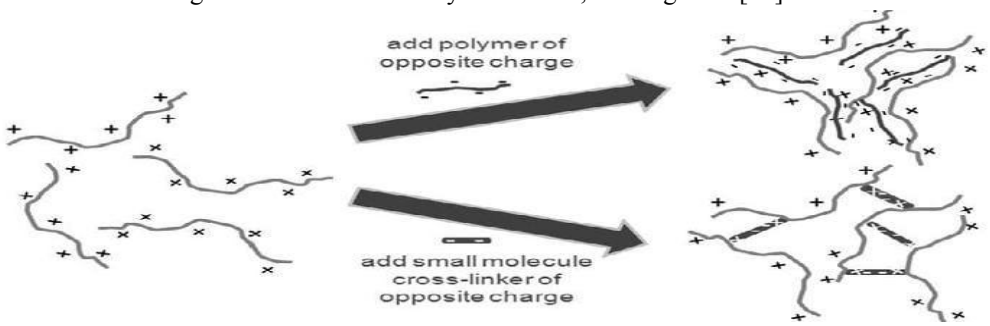

Fig 7:Mechanism of ion Activated insitu gelation

B. Chemical Triggered Approaches.

1.Enzyme-Triggered Gelation –

a. Protein-based systems -The creation of enzyme-sensitive gels can be achieved through the use of proteins, including gelatin and collagen[32].

b. Peptide-based systems -Peptides, specifically elastin-like polypeptides, serve as a basis for the formulation of enzyme-sensitive gels [33].

2. Photopolymerization –

a. Acrylate-based systems: Acrylates can be photopolymerized to create gels [34].

b. Methacrylate-based systems: Methacrylates can be photopolymerized to create gels [34].

C. External Triggered Approaches –

1. Ultrasound-Triggered Gelation

Systems that utilize ultrasound-triggered gelation agents are capable of producing gels that respond to ultrasound activation[35].

2. Magnetic Field-Triggered Gelation

The incorporation of magnetic field-sensitive lipids into liposomes allows for the production of gels that exhibit sensitivity to magnetic fields[36].

VIII. EVALUATION AND CHARACTERIZATION OF IN-SITU GELLING SYSTEM

A.Clarity

The clarity of the formulations before and after gelling is often determined by visual examination of the formulations under light alternatively against white and black backgrounds . Additionally, the contents are often set in motion with a swirling action. Also, it is observed for the formation of turbidity or any unwanted particles dispersed within the solution [37].

B.pH

pH affects both the solubility and stability of the drug in the formulation. The formulation should remain stable at its pH and at the same time be non-irritating to the patient at the time of administration. The pH is measured by a digital pH meter . It should be pre-calibrated using standard buffers of pH 4 and pH 7 according to established procedures . Texture analysis: Formulation hardness, consistency, and cohesion are assessed primarily using a texture analyzer that demonstrates the injectability of the sol, making the formulation easy to administer in vivo. To maintain close contact with surfaces such as tissue, the gel's adhesiveness value should be high. Texture analysis provides information about the mechanical properties of a sample: hardness, compressibility, and adhesion. These properties can directly correlate with

sensory parameters in vivo, helping to develop products with desirable attributes that contribute to patient acceptability and compliance [38].

C.Gelling capacity

Gelling capacity is determined for in-situ gels for ophthalmic formulations. The in-situ gel is mixed with simulated tear fluid to examine the gelling ability of ophthalmic products. This is determined by visual observation of a drop of formulation during a vial containing 2.0 ml of freshly prepared simulated tear fluid. Gelation was visually assessed by recording the time and time it took for the formed gel to dissolve [39].

D.Gel-Strength

This parameter can be evaluated using a rheometer. Depending on the gelation mechanism of the gelling agent used, a specific amount of gel is prepared from the form of the sol in the beaker. This gel, in the beaker, rises at a constant rate, so slowly push the probe into the gel. Changes in the load on the probe can be measured as a function of the probe immersion depth below the gel surface [40].

E.Rheological studies

Rheology studies should be performed on in-situ gels, as we know from our previous knowledge that gels exhibit thixotropic behaviour . Viscosity and rheological properties of polymer formulations in solution or gel can be measured with Brookfield rheometers or other types of viscometers such as research rotators and Oscillatory rheometers. The viscosity of these formulations should be such that no problems are expected during administration by the patient, especially during parenteral and intraocular administration [41].

F.Gelation pH

Gelation pH is determined by an in-situ gel formation system incorporating a pH-sensitive polymer. The formulation is then placed in a beaker and 1M NaOH was added dropwise with continuous stirring. Use a pH meter (Equiptronics digital pH meter) to check the pH and while the viscosity is also measured. Changes in viscosity at each pH are recorded. The pH at which a rapid change in viscosity is observed is referred to as gelation pH [42].

G.Gelation temperature

The gelation temperature or sol-gel transition temperature is the temperature at which the liquid-to-gel phase transition occurs. Gelation temperature is determined for an in-situ gel formation system incorporating a thermoreversible polymer and was described by Miller & Donovan technology . In this 2 ml in-situ gel is transferred to a test tube and placed into a water bath then the temperature of the water bath is increased slowly and constantly. After equilibrating the gel for 5 minutes at each setting, the gelation of the formulation is examined. The formation of the gel is indicated by the lack of movement of the meniscus when the tube is tilted. This is known as the gelation temperature when the meniscus would no longer move upon tilting to 90° [43].

H.Drug-polymer interaction study and thermal analysis

Interaction studies should be performed with Fourier Transform Infrared (FTIR) spectroscopy. During the gelation process, the nature of the interacting forces can be evaluated using techniques that employ the KBr pellet method. Thermogravimetric analysis (TGA) can be performed on in-situ polymer systems to quantify the proportion of water in hydrogels. Differential scanning calorimetry (DSC) was performed to observe if there was a change in the thermogram compared to the pure active ingredient used for gelation [44].

I.In vitro drug release studies

For in-situ gel formulations intended to be administered by the oral, ocular, or rectal route, evaluation studies must be performed to determine drug release from the formulation in vitro. The study is performed using a plastic dialysis cell or Franz diffusion cell . The cell consists of two half-cells, a donor compartment, and a receptor compartment. Both half-cells are separated with the help of semipermeable cellophane/dialysis membrane /cellulose membranes. The formulation is placed in the donor compartment and a newly prepared simulated buffer is placed in the receptor compartment. The entire assembly is placed on a thermostat-controlled magnetic stirrer. The temperature of the medium is maintained at 37ºC ± 0.5ºC. The total amount of receptor solution can be

removed at intervals and replaced with a new medium. This receptor solution can be diluted with the respective solvent as needed and the drug release can be analyzed at each nm using analytical techniques such as UV spectrophotometer using reagent blanks. For injectable in-situ gels, the formulation is placed in a vial containing the receptor medium and placed on a shaker water bath at the required temperature and vibration rate. Samples are taken and analyzed regularly . The drug content is then calculated using the formula generated from the standard calibration curve. Calculate the percentage of cumulative drug release (% CDR). The data obtained is further subjected to curve fitting of drug release data [45].

J.Accelerated stability studies

The sterile formulations are subjected to stability testing to assess shelf life. The sterile formulation is replaced in amber-coloured glass vials, closed with grey butyl rubber closures, and sealed with aluminum foils. The vials containing formulation are kept in a stability chamber, maintained at 40 ± 2°C, and 75 ± 5 % RH for one month as per the International Conference of Harmonization (ICH) State Guidelines. Samples could be withdrawn weekly and analyzed for drug content, pH, visual appearance, gelling capacity, and in vitro drug release [46].

IX. APPLICATION

A.Oral drug delivery system

The application of pH-sensitive hydrogels holds promise for the targeted delivery of pharmaceuticals to designated areas within the gastrointestinal tract. Hydrogels composed of different ratios of cross-linked polyethylene glycol (PEG) and polyacrylic acid (PAA) derivatives have enabled the development of silicone microspheres capable of releasing prednisolone in the gastric medium or exhibiting gastroprotective effects. Cross-linked dextran hydrogels demonstrate rapid swelling in alkaline conditions, while other polysaccharides, such as amidated pectins, inulin, and guar gum, have been investigated to enhance the colon-specific properties of sodium alginate. This alginate formulation incorporates complexed calcium ions that facilitate gelation through ion release in the stomach's acidic environment[47].

B.Ocular drug delivery system

Natural polymers, including alginic acid, inulin, and xyloglucan, are predominantly utilized in ocular delivery systems. In the context of local ophthalmic delivery, various agents such as autonomic drugs, anti-inflammatory medications, and antimicrobial compounds are employed to alleviate intraocular pressure associated with glaucoma. Conventional delivery systems often exhibit suboptimal bioavailability and therapeutic outcomes due to the rapid turnover of tear fluid, which results in the quick removal of drugs from the eye. To mitigate these bioavailability issues, ophthalmic in-situ gels are formulated with viscosity enhancers like Carboxy Methyl Cellulose, Hydroxy Propyl Methyl Cellulose, Carbomers, and Poly Vinyl Alcohol, which serve to prolong the precorneal residence time and improve bioavailability while being easy to produce. Furthermore, penetration enhancers, including preservatives, chelating agents, and surfactants, are utilized to enhance the penetration of drugs through the cornea[47].

C.Nasal drug delivery system

The nasal in-situ gel system incorporates xanthan gum and gellan gum as polymers that facilitate gel formation. Momethasone furoate is employed to determine its therapeutic efficacy in allergic rhinitis treatment. An animal model of allergic rhinitis was developed for this purpose, allowing for the observation of the in-situ gel's effects on nasal symptoms induced by antigens in sensitized rats. Findings revealed that the in-situ gel effectively mitigated the worsening of nasal symptoms in comparison to the commercially available product, Nasonex (Momethasone furoate suspension 0.05%)[47].

D.Rectal and vaginal drug delivery system

The rectal route serves as a viable option for the administration of diverse drug formulations, encompassing liquid, semisolid (ointments, creams, and foams), and solid dosage forms, including suppositories. Acetaminophen, known for its anti-inflammatory properties, can be developed into a rectal in situ gel using polycarbophil along with poloxamer F188 and poloxamer 407 as synthetic polymers. This innovative approach to formulating an in situ gelling liquid suppository is acknowledged

for its efficacy and ability to improve bioavailability[48].

E.Injectable drug delivery system

This drug delivery system features the formulation of in situ gels, which have become increasingly popular over the past decade due to their non-invasive nature and the resulting patient compliance. The injectable in situ gels are mainly composed of synthetic polymers and block copolymers. Bupivacaine exemplifies an anti-inflammatory drug that is formulated as an injectable in situ gel, utilizing poly(D,L-lactide), poly(D,L-lactide-co-glycolide), and PLGA as the polymer, which facilitates extended drug action in gel form[48].

F.Dermal and transedermal drug delivery

An evaluation was conducted on the use of Pluronic F127 in a thermally reversible gel as a vehicle for the percutaneous administration of Indomethacin. Results from in vivo studies suggest that a 20% w/w aqueous gel may function as a viable base for the topical delivery of the drug. Additionally, the combination of iontophoresis and chemical enhancers demonstrated a synergistic effect, leading to enhanced insulin permeation[48].

X. CONCLUSION

This review highlights that the 'in situ gel' system has emerged as a prominent novel drug delivery mechanism. This system facilitates sustained and controlled drug release, thereby enhancing patient compliance and comfort. A variety of natural and synthetic polymers are capable of forming in situ gels, making them suitable for multiple administration routes, including oral, ocular, transdermal, buccal, intraperitoneal, parenteral, injectable, rectal, and vaginal applications. There exists significant potential for further research into in situ gel systems to develop advanced drug delivery techniques.

XI. REFERENCES

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