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Review Article

IN-SITU DRUG DELIVERY SYSTEM: A REVIEW

Hapse Sandip A.[1*], Gunjal Mrunal M.[2], Jadhav Ajinkya B.[3], Gunjal Sahil A.[4]

1. Dr.V.V.P.F's College of Pharmacy, Vilad Ghat, Ahilyanagar.

Address for correspondence:

Hapse Sandip A., Dr.V.V.P.F's College of Pharmacy, Vilad Ghat, Ahilyanagar.

Email Id: - sandiphapse@gmail.com

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ABSTRACT

Controlled and sustained drug delivery has become standard in modern drug design. The in situ gel system is one of the best novel drug delivery system. In situ gelling formulations are drug delivery system which exist in a liquid form at room temperature and change into gel state after application to the body. In situ gelling system explain about gels which are defined as intermediate state of matter consist of liquid and solid components. In - situ gels are type of hydrogel, which are in solution form and undergoes gelation under various physiological conditions. The formation of gel depends on temperature, PH changes, viscosity, ion exposure, radiation, enzyme, molecular weight, polymers, UV light. Both natural and synthetic biodegradable polymers are used for formulation of in situ gels such as Poloxamer, Pectin, HPMC (Hydroxypropyl methyl cellulose), Xyloglucon, Carbopol, Guar gum, Gellan gum, Xanthan gum, Alginic acid. Method includes in In situ gel formulation are solvent evaporation method, phase transition method, eletrospinning process, self emulsifying drug delivery system, iontophoresis process, hydrogels systems process. In situ gel to be used in different drug delivery systems like Oral, Ocular, Nasal, Buccal, Vaginal, Rectal, Dermal, Intravesical. This review mainly focuses on introduction to in situ gel, various applications of in situ gel, methods for preparation, drug criteria for selection, various polymers used in In situ gel formulation.

KEY WORDS: Polymers, In situ gel, application, gels, controlled and sustained release.

INTRODUCTION

In situ gelling system is liquid formulation which forms a solid-like depot after injection in to body or applied to topical site. The development of in situ gel system has received attention over the past few years. In situ forming polymeric delivery system ease the administration, reduce frequency of administration and improve patient comfort. They are injectable depot systems such as wafers or implants because they can easily prepared with lower costs. They are injectable using smaller gauge needles; could be self administered using autoregulators. In situ gel deliver accurate dose to prolong residence time of drug. In situ gel formulation occurs due to combination of one or more stimuli like temperature, PH changes, solvent exchange and ulta violet irradiation. Topical administration using this system is also attractive and allows processes like spraying. From the 1970's natural and synthetic polymers began to be investigated for controlled release formulations.

Hydrogels are three dimensional structures that have polymeric networks. They have capacity to absorb and retain large amount of water and biological fluid to swell. There are two types of hydrogels 1.preformed hydrogels 2.in situ gels. In this In situ solution undergo gelation after reaching particular site. In situ is a Latin word which means 'in position'. In situ gelling system is lighter than gastric fluid. It float over stomach contents. In in situ drug delivery system various routes of administration are involved such as oral, ocular, topical, rectal, vaginal, nasal, intravenous, intraperitoneal.

Gelation is achieved with polymer solutions, through some inorganic. Sometimes gelation achieved with small organic. The primary aim of this drug delivery system is to modified the pharmacokinetics parameters at the tissue distribution of the drug. In situ drug delivery system low doses of drug are required and there will be no drug accumulation and side effects, it increases bioavailability of drug and resistance time of drug will be increase, it decreases wastage of drug.

Ideal Characteristics of Polymers for Preparation of In Situ Gel[14,15,16,17,18]

- Biocompatible and non-irritating
- Pseudo-plastic behaviour, with decrease in viscosity and increased shear rate 3] Non- toxic and free of adverse effects
- Well tolerated and gentle on tissues
- Muco-adhesion: Capable of adhering to mucous membranes 6] Tear dynamics: Influences tear behaviour positively
- Clarity: Optically clear and transparent.

Importance of In Situ Gelling System[19,20,21]

- Controlled and sustained drug release via sol gel transition, enabling gradual and consistent therapeutic effect.
- Reduce frequency of drug administration, as the gel formation allows for prolonged release of the drug.
- Lower doses of drugs are required, minimising risk of accumulation and associated side effects.
- Enhanced bioavailability of drugs, ensuring more effective absorption and utilisation.
- Increased residence time of drug in the body, allowing for more sustained therapeutic effect.
- Accurate and reproducible doses delivery, unlike conventional gel formulation, which can be inconsistent.
- Improved patient compliance and comfort due to ease of administration, from the physical form of in situ gels.

Advantages of In-Situ Drug Delivery System[22,23,24]

- Controlled and sustained release of drug, providing a consistent and gradual therapeutic effect.
- Ease of administration, facilitating hassle-free drug delivery.
- Ability to administer to unconscious patients, ensuring continuous therapy.
- Enhanced patient compliance and comfort, reducing the burden of frequent dosing. 5] Decreased dose frequency and drug toxicity.
- Minimize side effects and improve safety.
- Increased bioavailability, ensuring more effective drug absorption and utilization.
- Utilization of natural polymers, providing biocompatibility and biodegradation, reducing the risk of adverse reactions.

Disadvantages of In-Situ Drug Delivery System[25,26]

- High fluid requirement: in situ gel formation necessitates a significant amount of fluids, which may be challenging in certain clinical settings.
- Instability of sol form: the sol form of the drug is more prone to degradation, potentially compromising its efficacy.
- Stability concerns: chemical degradation may occur, leading to stability problems and impacting drug effectiveness.
- After administration patients may need to restrict eating and drinking for several hours, potentially impacting their quality of life.
- Limited drug loading: the quantity of homogeneity of drug loading into hydrogels may be limited, particularly for hydrophobic drugs.

- Dose limitations: only drugs with small dose requirements are suitable for delivery via in situ gel formation.
- Lower mechanical strength may result in premature dissolution or flow away of the hydrogel from the targeted local site, reducing its effectiveness.

In Situ Gel Forming Polymers[27,28]

1. Pectin
2. Xyloglucan
3. Gellan gum
4. Alginic acid
5. Xanthum gum
6. Chitosen
7. Carbopol
8. Poly(DL-lactic acid)
9. Poly(DL-lactide co glycolide) 10] Poly caprolactone
10. Guar gum
11. HPMC (hydroxypropyl methyl cellulose)

1. **PECTIN**[29,30,31]

Pectin are family of polysaccharides characterized by polymer backbone primarily composed of alpha – (1-4)-D-galacturonic acid residue. Low methoxy pectin (esterification<50%) readily forms a gel in aqueous solutions containing free calcium ions, which cross link the galacturonic acid chain via the egg-box model. Pectin gelation occurs in the presence of H+ ions and divalent ions, with calcium ions typically required to produce a gel suitable for drug delivery. The primary advantage of using pectin in this formulation is its water soluble, eliminating the need for organic solvents. In the stomach, divalent cations induce a pectin-to- gel transition upon oral administration. To induce pectin gelation, complex forms of calcium ions can be incorporated in to formulations. Additionally, sodium citrate can be added to the pectin solution to form complex with most calcium ions, maintaining the formulation in fluid state (sol) until degraded in the acidic stomach environment, where calcium ion release induces gelation. Optimisation of calcium and citrate ion concentration enables the formulation to remain fluid until administration, followed by gelation in stomach. This PH- dependant gelation mechanism allows for targeted drug delivery application.

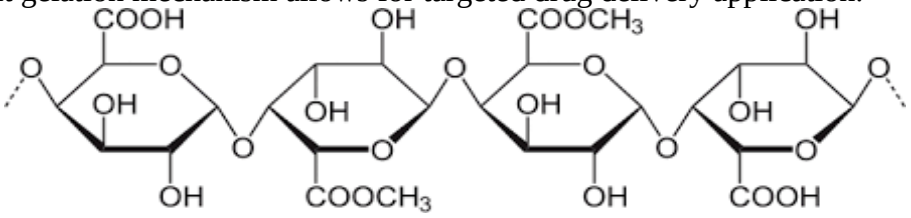

Fig.1.1. Structure of Pectin

2. **Xyloglucan**[32,33,34]

It also known as tamarind gum, is polysaccharide derived from tamarind seeds. It is made up of long chain of glucose molecules with side branches of xylose and galactose. When this polysaccharide is broken down slightly, it forms a gel that can change shape in response to temperature changes. Xyloglucan composed of three different oligomers: 1] Heptasaccharide 2] Octasaccharide 3] Non-saccharide. The gelation temperature varies based on the amount of galactose removed. When heated to body temperature, the substance forms a reversible gel. This property makes it suitable for oral drug delivery, as it can slowly gel in the stomach over minutes after swallowing a chilled xyloglucan solution, allowing for targeted drug release. This gel can be used to deliver drugs to the body through various routes, including orally, injectable, eye drop and rectal suppositories. The gel forms slowly over minutes, allowing it to gel in the stomach after swallowing a cold solution. Xyloglucan is non toxic, biodegradable and biocompatible making it promising material for drug delivery.

3. **GELLAN GUM**[35,36]

Gellan gum is an anionic polysaccharide secreted by pseudomonas elodea, comprising tetra saccharide repeat unit of alpha-L-rhamnosa, beta-D-glucuronic acid and two beta-D- glucuronic acid

residue. Commercially available as GelriteTM and kelcogel TM, it undergoes temperature-dependent or cation-indused gelation. This process involves double helix junction zone formation, followed by agglomeration and complexation with cations (Ca2+, Mg2+) and hydrogen bonding with water, resulting in a three dimentional network. Gellan gum exibits cation-induced in-situ gelation, with divalent ions (Ca2+, Mg2+) more effective than monovalent cations (Na+,K+) in promoting gelation this properties prolongs drug residence time at the absorption site, enhancing bioavailability.

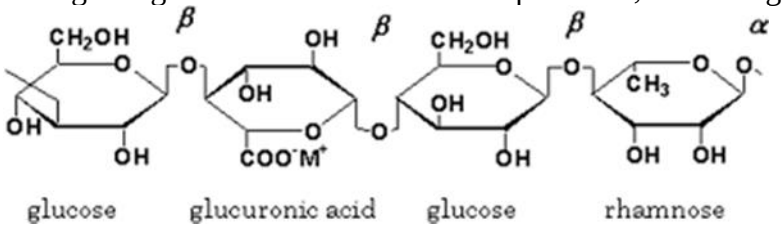

Fig.1.2. Structure of Gellan gum

4. **ALGINIC** ACID[37,38,39]

Alginic acid, a polysaccharide extracted from brown algae, is a linear block copolymer consisting of beta-D-mannuronic acid and alpha-L-glucuronic acid residue linked by 1,4- glycosidic bonds. The block composition and arrangement vary depending on the algal source. In aqueous solution, alginate forms a hard gel upon addition of divalent and trivalent metal ions, coordinated by consecutive glucuronic acid residues within the alpha-L- glucuronic acid block. The G block, placed in a alternative sequence (MG) with MM or GG blocks, interacts with calcium ions to form a homogeneous gel. Hydrogel mechanical strength and porosity depends on the G:M ratio, crosslinker type and alginate solution concentration. Alginic acid's biodegradability and non-toxicity make it an ideal vehicle for ophthalmic formulation offering long term precorneal retention due its gelation and adhesion properties, attributed to carboxylic acid groups.

5. **XANTHAM GUM**[40,41]

Xantham gum is high-molecular-weight extra cellular polysaccharide derived from fermentation of Xanthomonas campestris, a gram-negative bacterium. Its primary structure comprises cellulosic backbone of beta-D-glucose recidues, with a trisacchride side chain(beta-D-mannose-beta-D-glucuronic acid-alpha-D-mannose) attached to every other glucose residue. The presence of glucuronic acid and pyruvate groups in the side chains imparts anionic properties to the polymer.

This polysaccharide exhibits excellent solubility in:

1. Cold and hot water
2. Alkaline conditions
3. Acidic conditions

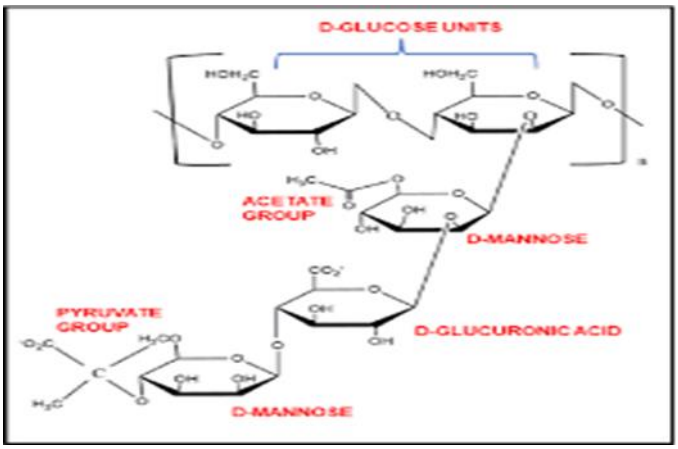

Fig.1.3 Structure of Xantham gum

6. **Chitosan**[42,43,44]

Chitosan is a biodegradable, heat-sensitive and poly-cationic polymer derived from shrimp and crab shells through alkaline de-acetylation of chitin. It is copolymer of glucosamine and N-acetylglucosamine. Chitosan is biocompatible, PH-dependent cationic polymer that remains dissolve in aqueous solutions upto PH 6.2. Above this PH, it forms a hydrated gel the addition of polyol salts with single anionic head,

such as glycerine, sorbitol, fructose or glucose phosphate salt, transforms the PH-gelling polysaccharide solution into a thermally sensitive, PH-dependent gel-forming aqueous solutions without chemical modification or crosslinking.

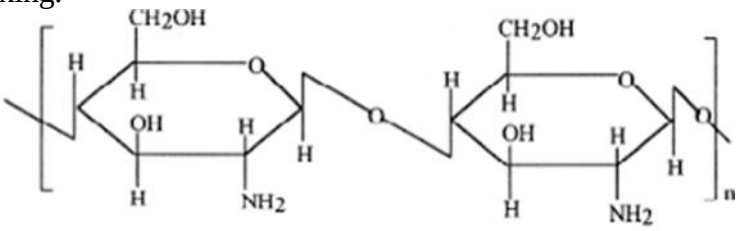

Fig.1.4. Structure of Chitosan

7. **CARBOPOL**[45,46]

Carbopol is high molecular weight crosslinked polyacrylic acid derivative and water soluble vinyl polymer. It undergoes a sol-to-gel transition at PH >5.5, remaining in solution at acidic PH but forming a low viscosity gel at alkaline PH. Combining carbopol with HPMC increases the viscosity and reduces the acidity of solution. Carbopol molecule are tightly coiled and partially dissociate in water, forming a flexible coil. As PH rises, the polymer
swells due to electrostatics repulsion between anionic groups. The gelling effects occurs in two stages: dispersion and hydration of carbopol, followed by neutralization with sodium hydroxide, triethanolamine, or potassium hydroxide. Poloxamer is water-soluble triblock copolymer consisting of two polyethylene oxide (PEO) blocks and one polypropylene oxide (PPO) block. It exhibits thermoreversible gelation and forms hydrogel at concentrations
>20%. Poloxamer's gelation temperature rheological properties can be tailored by adjusting its molecular weight and PEO/PPO ratio.

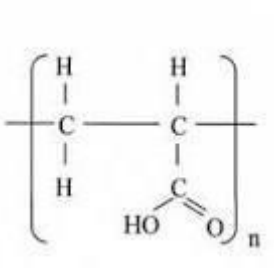

Fig.1.5. Carbopol

8. **POLOXAMER**[47]

Poloxamer: A Thermoresponsive triblock copolymer
Poloxamer, commercially known as pluronic, is water soluble triblock copolymer consisting of two hydrophilic polyethylene oxide (PEO) blocks surrounding hydrophobic polypropylene oxide(PPO) core (ABA configuration).

The hydrophobic PPO core is flanked by hydrophilic PEO blocks, enabling poloxamers unique properties:

1. Excellent thermosetting properties.
2. Enhanced drug resistance time.
3. Clear, colourless and transparent gel formation.

Poloxamers are available in various molecular weights, influencing their gelling properties. The proportion and distribution of hydrophilic and hydrophobic chains determine their behaviour.

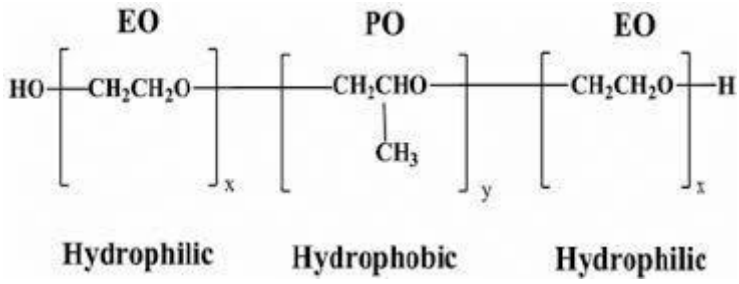

Fig.1.6 Structure of Poloxamer

9. **HPMC**[49,50]

Hydroxypropyl methylcellulose (HPMC) is a water soluble cellulosic ether composed of glucan chain with repeating beta-(1,4)-D-glucopyranose units it is versatile polymers with unic properties, including viscosity inversely proportional to temperature, solubility in organic and aqueous solvents and stability against heat, light, air and moisture. HPMC solutions exhibits a sol-gel transition at temperatures between 30 degree to 50 degree, primarily due to hydrophobic intereaction between methoxy-substituted molecule. At low temperature, the polymer hydrates and exhibits minimal polymer-polymer intereaction. As temperature increases, the polymer gradually loses hydration water, leading to decrease relative viscosity. upon sufficient dehydration polymer-polymer association occurs, resulting in an infinite network structure and a sharp rise in relative viscosity. This sol-gel conversion is exploited in the design of in-situ gelation system for drug delivery application.

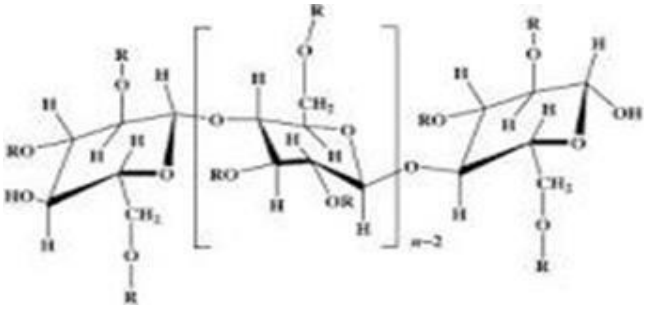

Fig.1.7. Structure of Hydroxypropyl Methylcellulose(HPMC)

9. **GUAR GUM**[51]

A versatile natural polymer, guar gum also known as guaran, is a naturally occurring gum extracted from the endosperm of seeds.

Properties:

1. Insoluble in hydrocarbons, fats, esters, alcohols and ketones
2. Soluble in water, dispersible in both cold and hot water
3. Forms colloidal solutions in small amounts

Derivatives and applications:

Guar gum derivatives are used in:

1. Coating matrix systems
2. Nano particles
3. Hydrogels for targeted delivery system
4. Graft polymers (e.g. Polyacrylamide-grafted guar gum) for colon targeting
5. Sustained-release matrix tablets as a polymer

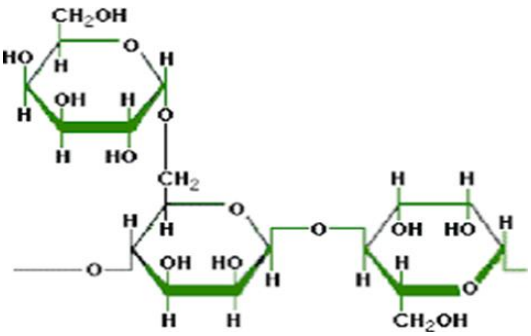

Fig.1.8. Structure of guar gum

Selecting A Drug for In Situ Drug Delivery System Involves Several Criteria[52,53,54]

Physiochemical properties:

- **Solubility:** The drug should be soluble in the formulation medium to insure adequate release.
- **Stability:** The drug must remain stable under condition of the delivery system (e.g. PH, Temperature)
- **Molecular weight:** Idealy, drug should have a molecular weight conducive to diffusion and permission.
- **Release mechanism:** The should be ameneble to the desired release mechanism, such as diffusion, swelling or degradation.
- **Biocompatibility:** The drug should exhibit low toxicity and high compatibility with the surrounding tissues to avoid adverse reaction.
- **Therapeutic window**: A suitable therapeutic window is crucial to insure efficacy without toxicity.
- **Targeted delivery:** If the goal is to target specific tissues or cells, the drugs properties should allow for this targeted action.
- **Regulatory status:** The drug should have an established safety profile and be compliant with regulatory requirement.
- **Efficacy and pharmacokinetics:** understanding the drugs pharmacokinetics helps predicts its behaviour in the body and its effectiveness in the delivery system.

Method of Preparation Involves In In Situ Drug Delivery System[55,56,57,58,59,60]

1. SOLVENT EVAPORATION METHOD PROCESS:

- Preparation: The drug is dissolve in suitable organic solvents. A polymer such PLGA, is added and the mixture is homogenised.
- Casting: The solution is cast into molds or onto a substrate.
- Evaporation: the solvent is evaporated, leaving behind a solid drug polymer matrix.
- Mechanism: The polymer chains come together as a solvent evaporates, encapsulating the drug within the solid structure allowing for controlled release.
- Applications: Used for encapsulating drugs like paclitaxel for cancer treatment .

2. PHASE TRANSITION METHOD PROCESS:

- Preparation: A solution of temperature-sensitive or PH-sensitive polymer is prepared.
- Administration: The solution is injected in the body; it undergoes a phase change in response to physiological conditions (e.g. temperature increase or PH change).
- Mechanism: The liquid polymer solution transitions to a gel state upon exposure to body temperature or PH, forming a depot for drug release.
- Applications: used for local anaesthesia delivery, such as poloxamer-based systems.

3. ELETRO-SPINNING PROCESS:

- Preparation: A polymer solution (e.g. PCL) is prepared and loaded with the drug.
- Electro-spinning: The solution is eletrospun to form nanofibers, which can be controlled on a substrate.
- Mechanism: The eletrospinning processes produces fibers with high surface area, allowing for controlled drug release as the fibers degrade.
- Applications: Used for wound healing applications, with fibers containing antibiotics like

ciprofloxacin.

4. SELF-EMULSIFYING DRUG DELIVERY SYSTEM (SEDDS) PROCESS:

- Preparation: The drug is mixed with lipids (oils), surfactants and co-surfactant to form homogeneous mixture.
- Emulsification: Upon ingestion, the mixture emulsifies in gastrointestinal fluids, forming fine droplets.
- Mechanism: The emulsification enhances drug solubility and bioavailability due to increased surface area.
- Applications: Effective for poorly soluble drugs, such as Fenofybrate, leading to improved oral absorption.

5. IONTOPHORESIS PROCESS:

- Preparation: A drug solution is prepared, usually containing charged molecules.
- Administration: An electric current is applied to drive the charged drug ions through the skin.
- Mechanism: The electric field enhances drug permeability through the stratum corneum' promoting transdermal delivery.
- Application: Used for delivering drugs like Lidocaine and Insulin transdermal.

6. HYDROGEL SYSTEMS PROCESS:

- Preparation: Hydrophilic polymers are mixed with the drug' and crosslinking agent is added to form a gel.
- Administration: The gel can be injected or apply directly to the site of action.
- Mechanism: The gel swells in response to environmental changes, allowing for sustained and controlled drug release.
- Applications: Injectable alginate hydrogels are used for localised delivery of anti- inflammatory drugs.

Applications of In Situ Drug Delivery System[61,62,63,64,65,66,67,68,69,70,71,72,73]

Oral drug delivery system: Natural polymers for insitu oral drug delivery systems- pectin, xyloglucan, gellan gum. Researchers have explored pectin's potential for sustained paracetamol delivery via orally administrated in situ gelling formulations. Pectin's water solubility eliminates the need for organic solvents making it an attractive option. Gellan- based in-situ gelling formulations have been developed for oral theophylline delivery these formulations comprise gellan solution, calcium chloride and sodium citrate complex. Upon oral administration.

I. Calcium ions are released in the stomach's acidic environment.
II. Gellan gum gelates, forming a gel in-situ.
III. Sustained drug release and increased bioavailability of theophylline were observed in rats and rabbits.
IV. Gellan formulations out performed commercial sustained released liquid dosage form.

Nasal drug delivery system: A nasal drug delivery system using an in-situ gel was developed an evaluated for treating allergic rhinitis. Gallan gum and xanthan gum were used as polymers to create gel. Animal studies showed that the in-situ gel reduced nasal symptoms in sensitized rats, outperforming the marketed formulation nasonex. Histopathology results confirmed the safety of formulations for nasal administration. Additionally a thermo-sensitive hydrogels was designed for nasal insulin delivery.

Rectal and vaginal delivery: In-situ gel also show promise for drug delivery via rectal and vaginal routes. For instance, xyloglucan based thermo-reversible gels have been explored for rectal drug delivery of indomethacin. In rabbits studies, these gels demonstrated broader drug absorption peaks and longer drug residence times compared to commercial suppositories. This formulations aimed to improved therapeutic efficacy and patient compliance. notably the in-situ polymeric system reduced the maximum drug concentration, potentially minimizing indomethacin's adverse effects on the nervous system.

Occular drug delivery system: In situ gels can be used to enhance drug retention in the eye. For example, formulations that transition from a liquid to a gel upon contact with tear fluid can provide sustained release of anti-glaucoma medications.

Injectable hydrogels: These can be injected into tissues and solidify upon injection. They are used in cancer therapy to deliver chemotherapeutic agents directly to tumor sites, minimizing systemic toxicity.

Local anesthesia: In-situ drug delivery system for local anaesthesia can provide prolonged analgesia by forming gels at the injection site, allowing for sustained drug release.

Orthopedic applications: Injectable systems can deliver growth factors or antibiotics directly to bone defects or surgical sites, enhancing healing and preventing infections.

Wound healing: Hydrogel-based dressing can release anti-inflammatory or anti-microbial agents in-situ, promoting healing and reducing infection risks.

Buccal drug delivery system: Over the past decade, intra-oral in-situ gelation systems have revolutionized the treatment of oral mucositis a common and debilitating site effect of chemotherapy and radiation in head and neck cancer patients. Oral mucositis causes severe pain, bleeding and ulceration, significantly impacting patient's quality of life and nutritional status. Current treatments, such as oral rinses with local anaesthetics, have limited efficacy and duration. Traditional formulations like mouthwashes and polymer gels also fall short due to their short residence time in oral cavity. Protective layer on ulcerative lesions ensure extended residence time and sustained drug release, improving patient compliance and reducing treatment failure.

This system have shown promise in:

1. Controlling pain
2. Regulating inflammation
3. Enhancing wound healing
4. Treating bacterial and fungal infections.

Advances In In-Situ Drug Delivery System[74,75,76,77]

Advances in In-situ drug delivery system have a significantly improved the efficacy and safety of therapeutic agents. These systems allow for localised and controlled release of drugs, enhancing patients compliance and minimizing side effects.

Polymeric system hydrogels: Smart hydrogels responds to physiolocal conditions (e.g.PH, temperature) to release drug. Recent developments include stimuli-responsive hydrogels that can deliver drug at specific sites based on environmental triggers.

Nanoparticles: biodegradable nanoparticles can encapsulate drugs and release them in controlled manner. Recent innovation focus on targeting specific cells or tissues, such as using surface modification for enhance targeting.

Micro-needle arrays: Micro-needle technologies allow for minimally invasive drug delivery. Recent studies shown improvements in the design and materials used, such as dissolving micro-needles that dissolve into the skin, releasing the drug directly into the blood stream.

Implantable systems: Biodegradable implants provide long term drug release without the need for repeated administrations. Recent advancement focus on enhancing the release profile and biocompatibility of these systems.

Smart drug delivery system bio-responsive system: Systems that responds to specific biological signals (e.g. enzymes, antibodies) for localized drug release are gaining traction. These allows for precision therapy and reduced systemic side effects.

Self-regulated systems: recent research has led to the development of systems that can adjust the drug release rate based on feedback from the body, offering the more personalised treatment approach.

Targeted delivery mechanism: Techniques such as ligand-mediated targeting have been developed to enhance the delivery of drugs to specific cells such as cancer cells. This approach minimizes side effects and enhances therapeutic index of drug.

3D bio-printing: Advances in 3D printing technologies allow for the fabrication of complex drug dekivery system that can be tailored to individual patients needs. This approach facilities the design of structures that can release drug in controlled manner.

Microspheres and nano-fibers: these systems provide sustained release of drugs and can be engineered for specific release profiles. Recent innovations include electro-spinning techniques to create nanofibers that can deliver drug over extended periods.

Combination therapies: Systems that can deliver multiple drugs simultaneously are being explored to enhanced therapeutic outcomes, especially in chronic diseases and cancer treatment. This allows for synergistic effects while reducing drug resistance.

Challenges In In-Situ Drug Delivery System[78,79]

In situ drug delivery system (IDDS) are innovative approaches that allow for localized and controlled drug release at the site of action, often enhancing therapeutic efficacy while minimizing systemic side effect. However, there are several challenges associated with their development and implementation:

1. Biocompatibility and safety: Ensuring that the materials used in IDDs are biocompatible and do not elicit adverse immune responses is crucial. Materials must be safe for long term implantation if needed.
2. Drug stability: Maintaining stability of drug within the delivery system is essential. Factors such as temperature, PH and enzymatic degradation can affect drug potency.
3. Controlled release mechanism: Designing systems that provide predictable and sustained drug release profiles can be challenging. Achieving the desired release kinetics often requires sophisticated engineering.
4. Targeting accuracy: Ensuring that the drug is deliver precisely to the entended site of action can be difficult, particularly in complex anatomical regions or when treating conditions like cancer.
5. Manufacturing consistency: Scalability and reproducibility of IDD systems must be established to ensure that each batch meets the necessary quality standards.
6. Patient compliance: Some IDDs may requires specific patient compliance, such as adhering to a schedule for administration or managing device maintenance, which can affect treatment outcomes.
7. Regulatory challenges: Navigating regulatory landscape for novel drug delivery system can be complex. Approval processes can be lengthy and require extensive testing.
8. Cost and accessibility: The development and production cost of IDDs may be high, impacting their accessibility and widespread using in clinical settings.

CONCLUSION

In-situ gel drug delivery systems are promising approach to control and sustained drug release these systems offer several advantages, including ease of administration, enhanced patient compliance and increased bioavailability. However, there are also challenges and limitation to consider, such as high fluid requirements, instability and limited drug loading capacity. The choice of polymer and preparation method in crucial to the success of these systems. By understanding the properties and behaviors of various polymers and methods, researches and developers can design and optimize in-situ drug delivery systems for specific applications. Further research and development are needed to fully realize the potential of these systems and to overcome the existing challenges. Ultimately, in-situ gel drug delivery systems have the potential to improve patient outcomes and quality of life and there continued development and optimization are warranted.

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