INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Article

A Review On Ocular Drug Delivery System

Gaurav Haware[1]*

[1]-*Karmayogi Tatyasaheb Bondre Institute of Pharmacy, Chikhli*

ARTICLE INFO

Published: 30 July. 2026

Keywords:
Opthalmic Formulation; In Situ Gels; Stimuli-responsive polymers

DOI:
10.5281/zenodo.21701863

ABSTRACT

The ocular drug delivery system is crucial due to the isolation of the human eye and its challenges in administering drugs. Traditional opthalmic formulations have a short pre-corneal residence time and poor bioavailability, as medications are eliminated from the pre-corneal lachrymal fluid quickly and extensive. Newer research aims to develop stable sustained release in-situ gels to overcome these limitations. In situ gel systems are formulated as liquid preparations suitable for instillation into the eyes, which transform into gels when exposed to the physiologic environment. This increases the pre-corneal residence time of the delivery system, increasing the ocular bioavailability of the drug. The production of gels depends on changes in physicochemical parameters such as pH, temperature, or ion-sensitivity, allowing for controlled and sustained delivery of medication. Evaluations of these systems include drug content, clarity, pH, gelling capacity, viscosity, in vitro drug release tests, texture analysis, sterility testing, isotonicity assessment, accelerated studies, and irritancy tests. FT-IR spectroscopy was used to determine incompatibilities between drugs and polymers. Various innovative dosage forms are available, such as insitu gel, collagen shield, minidisc, ocular film, ocusert, nanosuspension, nanoparticulate system, liposomes, niosomes, dendrimers, ocular iontophoresis, and more. However, the development of ophthalmic drug delivery systems has been challenging due to difficulties associated with the ocular route, such as non-productive absorption, drainage, induced lacrimation, tear turn over, and impermeability of medications to the cornea. In situ gel formation can be triggered by various physical and chemical stimuli, including temperature, pH, electric field, magnetic field, and light. Stimuli-responsive polymers, both naturally occurring and manufactured, are viable options for developing in situ gels. Oral, ophthalmic, rectal, vaginal, injectable, and intra-peritoneal administration methods can be used to give in situ gels. In situ gel systems address limitations related to conventional methods of both solutions and gels.

***Corresponding Author:** Gaurav Haware
Address: *Karmayogi Tatyasaheb Bondre Institute of Pharmacy, Chikhli*
Email ✉: gauravhaware2002@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

In situ gel systems address limitations related to conventional methods of both solutions and gels, such as the inability to accurately dose and the difficulty of administration. This review discusses the introduction, advantages, disadvantages, suitable polymer characteristics, approaches, applications, evaluation, and marketing products of in situ gels, as well as reported studies and recent advancements.

1. INTRODUCTION

The ocular drug delivery system (Figure 1) is regarded to be both essential and problematic due to the fact that the human eye is an isolated organ that presents a number of challenges when it comes to the administration of drugs. Furthermore, the typical opthalmic formulations have a short precorneal residence time and poor bioavailability. This is because the medications are eliminated from the pre-corneal lachrymal fluid in a quick and extensive manner through the processes of solution drainage, lachrymation, and non-productive absorption by the conjunctiva. It is (1).

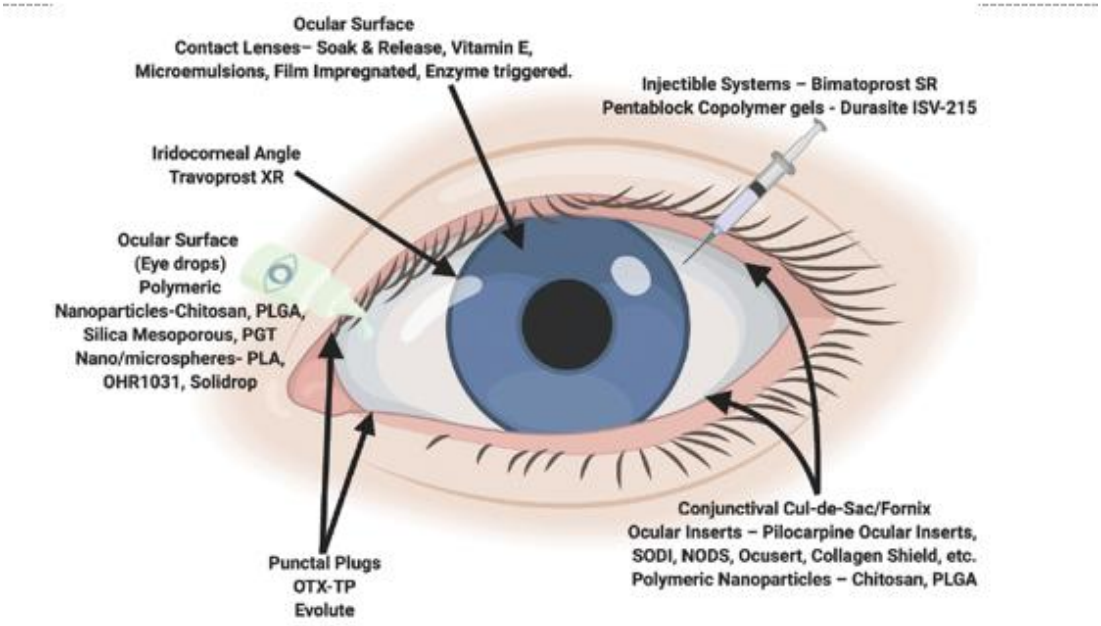

Figure 1: Ocular Drug Delivery System

There have been a number of different attempts made towards the creation of stable sustained release in-situ gels in order to overcome the limitations that are connected with the current formulations of ophthalmic medications. Newer research in ophthalmic drug delivery systems is aimed at incorporating multiple drug delivery technologies. This includes the development of systems that not only extend the contact time of the vehicle at the ocular surface, but also slow down the removal of the drug. This is an important factor in the development of these systems. Specifically, the in situ gel system is formulated as a liquid preparation that is suitable for instillation into the eyes. When the liquid is exposed to the physiologic environment, it transforms into gel, which results in the formation of in-situ gel. This results in an increase in the precorneal residence time of the delivery system, which in turn increases the ocular bioavailability of the drug (2). The production of gels is dependent on elements such as changes in a particular physicochemical parameter (such as pH, temperature, or ion-sensitivity), which allows for the medication to be delivered in a controlled and sustained way. The following characteristics of these systems were

evaluated: drug content, clarity, pH, gelling capacity, viscosity, in vitro drug release tests, texture analysis, sterility testing, isotonicity assessment, accelerated studies, and irritancy test. In order to determine the incompatibilities between drugs and polymers, FT-IR spectroscopy was utilised (3). There are many different innovative dosage forms available, such as insitu gel, collagen shield, minidisc, ocular film, ocusert, nanosuspension, nanoparticulate system, liposomes, niosomes, dendrimers, ocular iontophoresis, and so on. Because of the difficulties associated with the ocular route, such as non-productive absorption, drainage, induced lacrimation, tear turn over, and impermeability of medications to the cornea, the development of ophthalmic drug delivery systems has always been a hard endeavour. When it comes to the treatment of a variety of eye disorders, such as dryness, conjunctivitis, keratitis, eye flu, and others, the highly established method of administration for administering pharmaceuticals to the eye is the topical application of the drug. The use of polymers, which play a significant role in the transport of medications to the pre and intra ocular tissues, has been the subject of research for the purpose of developing new methods for the delivery of pharmaceuticals to the eye (4). These consistent efforts have resulted in the achievement of the goal of increasing the bioavailability of the ocular medicine and extending the duration of its therapeutic activity. The use of intelligent polymeric systems has been demonstrated to be a potential method of administering the medications. Immediately upon administration, these polymers go through a sol-gel transition. Before they are administered, they are in the solution phase, but when they are under physiological conditions, they are gels. By raising the corneal permeability of the medications and extending the amount of time they spend in the cul-de-sac, it is possible to increase the ocular bioavailability of the pharmaceuticals (5). In situ gel formation can be triggered by a number of different physical and chemical stimuli, including temperature, pH, electric field, magnetic field, and light, among others. A stimuliresponsive polymer is a type of polymer that resembles biological systems in a primitive manner (6). This type of polymer is characterised by the fact that an external stimulus, such as temperature and pH, alters the characteristics of the formulation. Naturally occurring polymers as well as manufactured polymers are both viable options for the development of in situ gels. Oral, ophthalmic, rectal, vaginal, injectable, and intra-peritoneal administration are the many methods that may be utilised to give in situ gels (7). In situ gels and the numerous methods for in situ gelling systems are discussed in this review, which provides a concise synopsis of the subject matter. The evaluation of polymeric in situ gel, as well as the many types of smart polymers, their methods of gel production from sol forms, and the evaluation of the gels themselves. It is well acknowledged that the ocular medication delivery system is both essential and difficult to implement since the distribution of drugs is highly hard. Moreover, the traditional opthalmic formulations demonstrate a short pre-corneal residence period and limited absorption. The creation of stable sustained release in-situ gels has been the subject of a number of different attempts on several occasions (8). Newer research in ophthalmic drug delivery systems is aimed at incorporating multiple drug delivery technologies. This includes the development of systems that not only extend the contact time of the vehicle at the ocular surface, but also slow down the removal of the drug. This is an example of how the research is being directed. The evaluation that is now being conducted on in situ gelling systems develops become one of the most well- known and famous (9). It was a delivery method that had a significant potential advantage due to various benefits, such

as being easy to use and simple to manufacture; improving both adherence and patient comfort by minimising the frequency of drug administration through its distinctive features feature of transitioning from sol to gel. In addition to that, it offers nanoemulsions that gel in situ, nanospheres, microspheres, and liposome technologies. The in situ gelling systems are able to address the limitations that are connected with conventional methods of both solutions and gels (10). These problems include the inability to accurately dose and the difficulty of administration. Within the scope of this review, the definitions, kinds, benefits, drawbacks, polymers employed, and appropriate features of polymers were the primary topics of discussion. In this review, they mainly focussed on introduction, advantages, disadvantages, suitable polymer characteristics, approaches, applications, evaluation, and marketing products of in situ gels. It also focused on some reported studies as well as recent advancements of in situ gels. The intention of writing this review article to describes every aspect of in situ gels, which near the readers a specific feature and might contribute to research and development.

2. In Situ Gels

A gel (Figure 2) is a substance that is soft, stable, or solid-like in nature, and it is composed of at least two components, one of which is a liquid, that are present in a significant number (11). Gels, which are a transitory state of matter, are composed of liquid as well as dependable components, which may be classified as semi-liquids or semi-liquids. Gels combine the cohesive qualities of solids with the diffusive transport characteristics of fluids (12). Gels are a special type of material. In addition to being stable and secure, it is composed of a component network that is threedimensional (13). Gels are characterised by the production of a polymer network by the process of cross-linking polymer chains. This can be accomplished through the formation of covalent bonds (chemical cross-linking) or non-covalent links (physical cross-linking). Gels may be divided into two categories, namely physical and chemical, according to their natural characteristics. Physical gels are characterised by the presence of weak links such as electrostatic, hydrogen, and Vander Waal linkages (14). There is a growing interest in physically crosslinked gels, which are chemical gels that arise when strong covalent connections are formed (15). This is because of the worry of toxicity. The chains of polymeric molecules that make up three-dimensional (3-D) formations are known as hydrogels. Therefore, they are straightforward to produce in a wide range of sizes and shapes (16). These hydrogels are a sort of hydrophilic preparations, and they have a high absorption capacity that allows them to shift between being liquid-gel and becoming themselves (17).

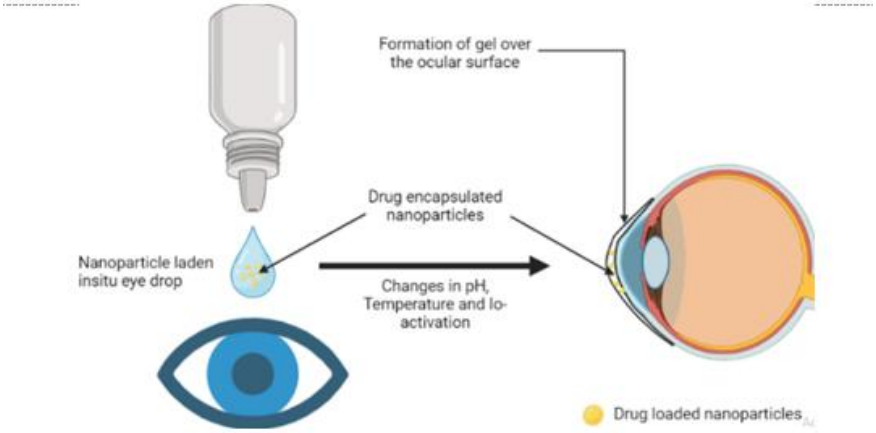

Figure 2: In situ gel for Ocular Drug Delivery System

For the purpose of accommodating a significant quantity of air, hydro-gels are made up of cross-links. Additionally, it is able to hold a substantial amount of water and biological fluids, which allows it to expand. There are also two forms of hydrogels, which are referred to as preformed hydrogels and in situ gels (18). In situ gels are the solutions or suspensions that undergo gelation after reaching the particular site due to contact with body fluids or physicochemical changes such as pH, temperature, ionic concentration, UV radiation, presence of specific molecules, or ions, external triggers, etc. (19). In situ gel produces a constant plasma drug profile in the body by extending the release of a drug, so it is attached and absorbed in gel form and is known to prolong the life of the drug in the mucosa (20). The drug delivery systems having the properties, as mentioned earlier, of sol to gel transition can be widely used for sustained delivery vehicle preparation of bioactive molecules (21). In situ gels, potentially used for oral, buccal, subcutaneous, transdermal, intraperitoneal, ocular, nasal, rectal, vaginal, and parenteral routes (22). From a manufacturing point of view, less complicated and thus lowers the investment and manufacturing cost (23). In the discovery phase, the gel formulations are used to enhance the local and systemic exposure of potential lead compounds, which is ideal for establishing animal models for various conditions quickly and cost-effective (24). Despite the massive diversity of gels, a particular class of gels, namely smart polymer gels, are in the focus of pharmaceutical research during the last decades (25). These intelligent polymers change their physicochemical properties in response to an altered environment. In recent advances, in situ gels have made it possible to exploit the changes in physiological uniqueness (26). Comprehensive research has been carried in designing of in situ gels, emerged as one of the best novel drug delivery systems (NDDS) (27).

3. Mechanism of Sol-Gel Formulation

In situ forming hydrogels are liquid preparations that, following instillation, undergo phase transition in the ocular cul-de-sac leading to the formation of viscoelastic hydrogels, gel, and with this, a reaction to changes in the surrounding environment is provided (28). In situ gel- forming ocular drug delivery systems are made from polymers that exhibit reversible phase transitions (sol–gel–sol) and pseudoplastic behavior (29). These methods are designed to minimise interference with blinking. The formulation of such a system can be in the form of a liquid dosage

form that is suited for instillation into the eye (30). This liquid dosage form, when subjected to physiological circumstances, transforms into a gel phase, which results in an increase in the pre-corneal residence period of the delivery system (31). Polymeric polymers, which, when administered, create gel matrices, are the foundation of the vast majority of the in situ forming drug delivery systems that have been documented. Polysaccharides such as alginate, gellan, and xyloglucan; (32) polyesters such as PLA and PLGA; (33) polyethers such as PEGPPG-PEG (Poloxamers); and (34) mixed polyesters and polyethers such as PEG-PLGAPEG are examples of polymers that have been explored before (Figure 3).

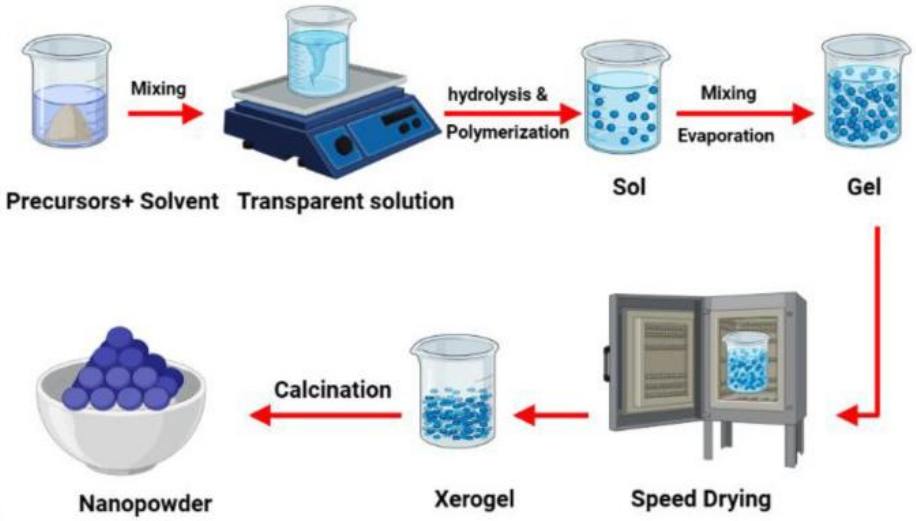

Figure 3: Mechanism of Sol-Gel Formulation

4. Advantages over Conventional Eye Preparations

Because of the quick turnover of tear fluid and the dynamics that induce rapid precorneal removal of the medication, eye drops that are known as traditional ophthalmic administration methods frequently result in low bioavailability and therapeutic response (35). There is a correlation between the patient's non-compliance and the high frequency of eye drop instillation performed (36). If the medication solution that is drained from the eye is systemically absorbed from the naso lacrimal duct, then the inclusion of extra drug in the formulation is an attempt to solve the bioavailability problem (37). This might possibly be harmful. There are many different types of ophthalmic vehicles that have been created in order to increase the ocular bioavailability and extend the residence duration of the dosage that has been injected (38). These vehicles include inserts, ointments, suspensions, and aqueous gels (39). Like ointments, gels are also difficult to administer for some patients. In this respect In situ gels are interesting since these are conveniently dropped as a solution into the conjunctival sac, where they undergo a transition into a gel with its favourable residence. The sol-gel-sol transition occurs as a result of chemical and physical change induced by the physiological environment. Liquid-gel phase transition dependent delivery system vary according to the particular polymer employed and their mechanism for triggering the transition to gel phase in the eye take advantage of change in temperature, pH, ion sensitivity or lysozymes upon contact with tear fluid. However, due to a number

of limitations, such as hazy vision caused by ointments or limited patient compliance with inserts, these ocular drug delivery methods have not been utilised to a significant extent (40).

5. Classification of In Situ Gel forming Hydrogels

5.1 Temperature triggered:

As a result of an increase in temperature, formulations become gelled when they come into contact with the application site, which is between 35 and 37 degrees Celsius. Formulations are liquid at room temperature (20-25 degrees Celsius). Temperature-sensitive hydrogels go through a volume phase transition or a sol–gel phase transition when they reach a critical temperature, often known as the lower critical solution temperature (LCST) or the upper critical solution temperature (UCST). After an increase in temperature, there is a progressive desolvation of the polymer and an increase in micellar aggregation, which is entanglement of the polymeric network. This is the process that is involved in the solto-gel transition. Micelles are formed as a result of the dehydration of the polyoxy propylene block; at a certain point, micelles come into contact with one another and cease to move (41). Examples: Pluronic (Poloxamer), Cellulose derivatives, Polymethacrylates.

5.2 PH triggered:

After application at the target location, formulations are polymeric dispersions in an aqueous solution that spontaneously gelate in response to changes in pH. This occurs after the formulation has been applied. At a particular pH, electrostatic and hydrophobic interactions, as well as hydrogen bonding, take place, which ultimately results in interdiffusion. The ionisation of carbopol polymer is responsible for the phase transition that was seen for carbopol solution. This phase transition was mediated by the change in pH from 4.0 to 7.4 and may be attributed to the change (42). Example: Cellulose acetate phthalate, Polyacrylic acid (Carbopol), Polycarbophils

5.3 Ion activated:

In this particular category of in situ hydrogels, the sol-to-gel transition is brought about by the presence of monovalent or divalent cations, such as sodium ions, potassium ions, calcium ions, and magnesium ions. After being injected into the cul-de-sac in the form of a liquid solution, the electrolytes that are present in the tear fluid, and in particular the cations of sodium, calcium, and magnesium, are particularly well-suited to commence the gelation of the polymer. The negatively charged polysaccharide and the cations are linked together in a cross-linking process (43). Examples: Gellan gum (Gelrite R), Sodium Alginate.

6. Evaluations

If Insitu Gel System Clearness, pH measurement, gelling capability, drug content, rheological research, in vitro diffusion study, isotonicity, antibacterial activity, in vivo visual testing in rabbits, and accelerated stability tests are some of the evaluation factors that are utilised for insitu gel formulations (44, 45). It is essential that the formulation possess an optimal viscosity that would facilitate the instillation of the liquid into the eye in the form of drops (46). This liquid would then undergo a quick transition from a sol-to-gel state, which might be triggered by pH, temperature, or ion exchange (47-53).

6.1 Physical parameters

Physical parameters to be tested for insitu gel solution are clarity, pH, gelling capacity, and drug content estimation.

6.2 Gelling capacity

The gelling capacity of the prepared formulation is determined by placing a drop of the formulation in a vial containing 2.0 ml of freshly prepared simulated tear fluid and visually observe.

6.3 Rheological studies

The viscosity measurements can be calculated using Brookfield viscometer, Cone and Plate viscometer. In-situ gel formulation is placed in sample tube. Formulation should have viscosity of 5-1000 m Pas, before gelling & after formation of gel should have viscosity from about 50- 50,000 m Pas.

6.4 In vitro drug release studies

In vitro release study of insitu gel solution is carried out by using Franz diffusion cell. The best fit model is check for Krosmeyers Peppas and Fickinian diffusion mechanism for their kinetics.

6.5 Texture analysis

The consistency, firmness and cohesiveness of insitu gel are assessed by using texture profile analyzer which mainly indicated gel strength and easiness in administration in vivo. Higher values of adhesiveness of gels are needed to maintain an intimate contact with mucus surface.

6.6 Isotonicity evaluation

Isotonicity is important characteristic of the ophthalmic preparations. Isotonicity has to be maintained to prevent tissue damage or irritation of eye. All ophthalmic preparations are subjected to isotonicity testing, since they exhibited good release characteristics and gelling capacity and the requisite viscosity.

6.7 Drug-polymer interaction study and thermal analysis

Interaction study should be performed with Fourier Transform Infra Red (FTIR). 6.8 Antibacterial activity The microbiological growth of bacteria is measured by concentration of antibiotics and this has to be compared with that produced by known concentration of standard preparation of antibiotic (56).

6.9 Ocular irritancy test

The Draize irritancy test should designed for the ocular irritation potential of the ophthalmic product prior to marketing. According to the Draize test, the amount of substance applied to the eye is normally 100µl placed into the lower culdesac with observation of the various criteria made at a designed required time interval of 1hr, 24hrs, 48 hrs, 72hrs, and 1week after administration. Three rabbits (male) weighing 1.5 to 2kg are used for the study (57). The sterile formulation is instilled twice a day for a period of 7 days, and a cross-over study is carried out (a 3 day washing period with saline was carried out before the cross-over study). Rabbits are observed periodically for redness, swelling, watering of the eye (58).

7. Applications

7.1 Oral drug delivery systems

Gellan gum, pectin, xyloglucan, etc., are used for oral in situ gels. The pH-sensitive gels have potential use in site-specific delivery of drugs to specific regions of the gastrointestinal tract (GIT), and some of the reported polymers and drugs, including the route of administration of in situ gelling systems (59). Gellan gum has the tendency

of gelation, which is temperaturedependent or cations induced. The in situ gelling systems consisted of a gellan solution with calcium chloride and sodium citrate complexes. When it's administered orally, the calcium ions were released in the acidic environment of the stomach leading to the gelation of gellan, thus form an in situ gel (60). Gelation of pectin will occur in the presence of H+ions, a source of divalent cations; generally, calcium ions are required to produce the gels that are suitable as vehicles for drug delivery (61). The main advantage is that it is water-soluble, so there is no need for organic solvents in the formulation. Divalent cations present in the stomach carry us the transition of pectin to gel state when it is administered orally (62). Xyloglucan is partially degraded by β-galactosidase, resultant product exhibits thermally reversible gelation by the lateral stacking of the rod-like chains or on warming to body temperature (63). Depends on the degree of galactose elimination, sol-gel transition temperature also varies. Its potential application in oral drug delivery exploits the proposed slow gelation time that would allow in situ gelations in the stomach following the oral administration of chilled xyloglucan solution (64). The gelation behavior of xyloglucan is similar to Pluronic F127, but it forms a 'gel' at a much lower concentration (65).

7.2 Ocular Drug Delivery Systems

Because of the high tear fluids that are produced by conventional administration methods, the bioavailability and therapeutic impact of the medication are frequently diminished. On the other hand, dynamics lead to the quick drug removal (66). When it comes to ocular medication administration, the most frequent ingredients employed are alginic acid, gellan gum, and xyloglucan. There are medications that have a local effect, including as antibacterial, anti-inflammatory, and autonomic medicines, that are used to alleviate intraocular tension in patients with glaucoma (67). There are several other water-soluble polymers and pH-induced in situ precipitating polymeric systems, such as carbopol, HPMC, and PMA-PEG (68).

7.3 Nasal drug delivery systems

Nasal drug administration has been considered as an alternative route for systems use of drugs restricted to intravenous administration. Nasal drug delivery can also provide a way of entry to the brain that circumvents the blood-brain barrier (BBB) because the olfactory receptor cells are in direct contact with the central nervous system (69). Because of the large absorptive surface and low proteolytic activity, the nasal mucosa is considered an attractive site for the delivery of vaccines. Nasal vaccines will improve patient compliance and reduce production costs compared with parental products. Mostly protein and peptides can deliver by this route (70).

7.4 Parenteral drug delivery systems

Chitosan is a pH-dependent cationic polymer that remains dissolved in an aqueous solution under conditions exceeding 6.2, resulting in a hydrated gel-like precipitate. However, its nonbiodegradability is a major issue. To address this, polyol salts with a single anionic head, such as glycerol, sorbitol, fructose, and glucose phosphate salts, are added to the chitosan solution to transform it into a thermally sensitive solution without chemical modification or cross-linking. This resolves the problem of chitosan's inability to biodegrade (71). Synthetic polymers, such as aliphatic polyesters like PLA, PGA, PLCG, PDL, and PCL, have been the focus of extensive research (72). Lactide or glycolide polymers have been shown to be viable options for controlled release of bioactive substances. Despite thorough

testing on both animals and humans, these materials have no adverse consequences. Upon implantation, the polymers do not show any signs of inflammatory response or other detrimental consequences when produced under GMP conditions from purified monomers (73). The systems are positioned in complex-shaped volumes, leading to the development of implants. Photoreactions enable fast polymerization rates at physiological temperatures (74). When heated, thermosetting systems transform into their final form, a "gel." The curing process involves the development of covalent cross-links between polymer chains, producing a macromolecular network. However, further heating may result in degeneration (75). In situ precipitating polymeric systems can result in the formation of a gel due to temperature changes, solvent removal, or pH changes (76). NIPAAm is an example of a thermosensitive polymer with a phase separation at a lower critical solution temperature of 32 degrees Celsius (77). Poloxamers and pluronic are examples of triblock copolymers with POE and POP units, which are subject to variations in solubility due to temperature (78).

7.5 Dermal And Transdermal Drug Delivery Systems

Skin is considered an essential route of administration of drugs for both local and systemic effects. Common preparations for topical and dermatological administration of drugs have certain limitations like poor adherence, reduced permeability, and compromised patient compliance (79). In vivo studies suggest that 20 % w/w aqueous gel maybe it is used as a base for topical administration of the drug. The combination of iontophoresis and chemical enhancers results in a synergistic enhancement of insulin permeation (80).

7.6 Rectal Drug Delivery Systems

Although the oral route is the most convenient route for drug administration, this is not possible from either a clinical or pharmaceutical perspective. In these cases, the rectal way may represent a practical alternative and can be used to administer drugs for both local and systemic effects. The environment in the rectum is considered relatively constant and stable and has low enzyme activity in comparison to other sections of the GIT. However, the rectal cavity can be challenged by erratic drug absorption due to the low adhesion to the rectal membrane and the potential expulsion of the dosage form. These can prevent dosage form leakage, which is familiar with rectal suspensions and enemas (81-84).

8. CONCLUSIONS

The ocular drug delivery system is crucial due to the isolation of the human eye and its challenges in administering drugs. Traditional opthalmic formulations have a short pre-corneal residence time and poor bioavailability, as medications are eliminated from the pre-corneal lachrymal fluid quickly and extensive. Newer research aims to develop stable sustained release in-situ gels to overcome these limitations. In situ gel systems are liquid preparations suitable for instillation into the eyes, which transform into gels when exposed to the physiologic environment, increasing the pre-corneal residence time and ocular bioavailability of the drug. The production of gels depends on changes in physicochemical parameters such as pH, temperature, or ion-sensitivity, allowing for controlled and sustained delivery of medication. Evaluations of these systems include drug content, clarity, pH, gelling capacity, viscosity, in vitro drug release tests, texture analysis, sterility testing, isotonicity assessment, accelerated studies, and irritancy tests. FT-IR spectroscopy was used to determine incompatibilities between drugs and polymers. Various innovative dosage forms are

available, such as insitu gel, collagen shield, minidisc, ocular film, ocusert, nanosuspension, nanoparticulate system, liposomes, niosomes, dendrimers, and ocular iontophoresis.

9. Conflict of Interest

None

REFERENCES

1. Rogovina LZ, Vasilev VG, Braudo EE. Definition of the concept of the polymer gel. Polym Sci Series C 2008;50:85-92.
2. Whitlock DR, Weiss L, Ambrogio LN, Inventors, AOBIOME LLC, Assignee. Ammonia oxidizing microorganisms for use and delivery to the gastrointestinal system. United States patent application US 16/318,583; 2019.
3. Carlfors J, Edsman K, Petersson R, Jornving K. Rheological evaluation of gelrite in situ gels for ophthalmic use. Eur J Pharm Sci 1998;6:113-9.
4. Ullah F, Othman MB, Javed F, Ahmad Z, Akil HM. Classification, processing and application of hydrogels: a review. Mater Sci Eng C 2015;57:414-33.
5. Crini G. Recent developments in polysaccharide-based materials used as adsorbents in wastewater treatment. Prog Polym Sci 2005;30:38-70.
6. Kuo CK, Ma PX. Ionically cross-linked alginate hydrogels as scaffolds for tissue engineering: part 1. Structure, gelation rate and mechanical properties. Biomaterials 2001;22:511-21.
7. Peak CW,WilkerJJ,Schmidt G. A review on tough and stickyhydrogels. ColloidPolym Sci 2013;291:2031-47.
8. Fuchs S, Shariati K, Ma M. Specialty tough hydrogels and their biomedical applications. Adv Healthcare Mater 2020;9:1901-396.
9. Zhao X, Sun X, Zhang J, Bai B. Gel composition and brine concentration effect on hydrogel dehydration subjected to uniaxial compression. J Petrol Sci Eng 2019;182:106358.
10. Bai B, Zhou J, Yin M. A comprehensive review of polyacrylamide polymer gels for conformance control. Petrol Explor Dev 2015;42:525-32.
11. Sarada K, Firoz S, Padmini K. In-situ gelling system: a review. Int J Curr Pharma Rev Res 2014;15:76-90.
12. Bhardwaj L, Sharma PK, Malviya R. A short review on gastroretentive formulations for stomach specific drug delivery: special emphasis on floating in situ gel systems. Afr J Basic Appl Sci 2011;3:300-12.
13. Prabaharan M, Mano JF. Chitosan-based particles as controlled drug delivery systems. Drug Delivery 2004;12:41-57.
14. Kaur P, Garg T, Rath G, Goyal AK. In situ nasal gel drug delivery: A novel approach for brain targeting through the mucosal membrane. Artificial Cells Nanomed Biotech 2016;44:1167-76.
15. Browning TR, Heath RD. Reconceptualizing the effects of lean on production costs with evidence from the F-22 program. J Operations Management 2009;27:23-44.
16. Dai T, Huang YY, K Sharma S, T Hashmi J, B Kurup D, R Hamblin M. Topical antimicrobials for burn wound infections. Recent Pat Anti-infect Drug Discovery 2010;5:124-51.
17. Figueira RB, Silva CJ, Pereira EV. Organic–inorganic hybrid sol– gel coatings for metal corrosion protection: a review of recent progress. J Coat Technol Res 2015;12:1-35.
18. Kumar A, Srivastava A, Galaev IY, Mattiasson B. Smart polymers: physical forms and bioengineering applications. Prog Polym Sci 2007;32:1205-37.

19. Mishra M, Kumar P, Rajawat JS, Malik R, Sharma G, Modgil A. Nanotechnology: revolutionizing the science of drug delivery. Curr Pharm Des 2018;24:5086-107.
20. Langmaier F, Mokrejs P, Kolomaznik K, Mladek M. Biodegradable packing materials from hydrolysates of collagen waste proteins. Waste Management 2008;28:549-56.
21. HB N, Bakliwal SR, Pawar SP. In-situ gel: new trends in controlled and sustained drug delivery system. Inter J Pharm Tech Res 2010;2:1398-408.
22. Jadhav UG, Dias RJ, Mali KK, Havaldar VD, Additional MI. Development of in situ- gelling and mucoadhesive liquid suppository of ondansetron. Int J Chem Tech Res 2009;1:953-61.
23. Packhaeuser CB, Schnieders J, Oster CG, Kissel T. In situ forming parenteral drug delivery systems: an overview. Eur J Pharm Biopharm 2004;58:445-55.
24. Hatefi A, Amsden B. Biodegradable injectable in situ forming drug delivery systems. J Controlled Release 2002;80:9-28.
25. Lin Z, Gao W, Hu H, Ma K, He B, Dai W, et al. Novel thermosensitive hydrogel system withpaclitaxelnanocrystals:highdrug-loading,sustaineddrugreleaseandextendedloca l retention guaranteeing better efficacy and lower toxicity. J Controlled Release 2014;174:161-70.
26. Malik K, Singh I, Nagpal M, Arora S. Atrigel: a potential parenteral controlled drug delivery system. Pharm Sin 2010;1:74-81.
27. Jeong B, Kim SW, Bae YH. Thermosensitive sol–gel reversible hydrogels. Adv Drug Delivery Rev 2012;64:154-62.
28. Baldwin AD, Kiick KL. Polysaccharide-modified synthetic polymeric biomaterials. Pept Sci: Original Res Biomolecules 2010;94:128-40.
29. Grassin Delyle S, Buenestado A, Naline E, Faisy C, Blouquit Laye S, Couderc LJ, et al. Intranasal drug delivery: an efficient and non-invasive route for systemic administration: focus on opioids. Pharmacol Ther 2012;134:366-79.
30. Soppimath KS, Aminabhavi TM, Kulkarni AR, Rudzinski WE. Biodegradable polymeric nanoparticles as drug delivery devices. J Controlled Release 2001;70:1-20.
31. Jothi M, Harikumar SL, Aggarwal G. In-situ ophthalmic gels for the treatment of eye diseases. Inter J Pharm Sci Res 2012;3:1891.
32. Almeida H, Amaral MH, Lobao P, Lobo JM. In situ gelling systems: a strategy to improve the bioavailability of ophthalmic pharmaceutical formulations. Drug Discover Today 2014;19:400-12.
33. Ruel Gariepy E, Leroux JC. In situ-forming hydrogels-review of temperature-sensitive systems. Euro J Pharm Bio-Pharm 2004;58:409-26.
34. Singh NK, Lee DS. In situ gelling pH-and temperature-sensitive biodegradable block copolymer hydrogels for drug delivery. J Controlled Release 2014;193:214-27.
35. Kempe S, Mader K. In situ forming implants-an attractive formulation principle for parenteral depot formulations. J Controlled Release 2012;161:668-79.
36. Sudhakar Y, Kuotsu K, Bandyopadhyay AK. Buccal bio-adhesive drug delivery-a promising option for orally less efficient drugs. J Controlled Release 2006;114:15-40.
37. NagarwalRC,KantS,SinghPN,MaitiP,PanditJ K.Polymericnanoparticulatesystem:a potential approach for ocular drug delivery. J Controlled Release 2009;136:2-13.
38. Hoare TR, Kohane DS. Hydrogels in drug delivery: progress and challenges. Polym 2008;49:1993-2007.

39. Gu D, O'Connor AJ, GH Qiao G, LadewigK. Hydrogels with smart systems for delivery of hydrophobic drugs. Expert Opin Drug Delivery 2017;14:879-95.
40. Abdelkader H, Mansour HF. Comparative studies for ciprofloxacin hydrochloride preformed gels and thermally triggered (in situ) gels: in vitro and in vivo appraisal usinga bacterial keratitis model in rabbits. Pharm Dev Technol 2015;20:410-6.
41. Kumbhar AB, Rakde AK, Chaudhari PD. In situ gel forming injectable drug delivery system. Int J Pharm Sci Res 2013;4:597-609.
42. Mundada AS, Avari JG. In situ gelling polymers in ocular drug delivery systems: a review. Crit Rev Ther Drug Carrier Syst 2009;26:85-118.
43. Mahajan HS, Shah SK, Surana SJ. Nasal in situ gel containing hydroxy propyl β-cyclodextrininclusioncomplex ofartemether:developmentandinvitroevaluation.J Incl Phenom Macrocycl Chem 2011;70:49-58.
44. SinghRM,KumarA,PathakK.Mucoadhesivein situnasalgellingdrugdeliverysystems for modulated drug delivery. Expert Opin Drug Delivery 2013;10:115-30.
45. Matanovic MR, Kristl J, Grabnar PA. Thermoresponsive polymers: insights into decisive hydrogel characteristics, mechanisms of gelation, and promisingbiomedical applications. Inter J Pharm 2014;472:262-75.
46. Coviello T, Matricardi P, Marianecci C, Alhaique F. Polysaccharide hydrogels for modified release formulations. J Controlled Release 2007;119:5-24.
47. Malafaya PB, Silva GA, Reis RL. Natural–origin polymers as carriers and scaffolds for biomoleculesandcelldeliveryintissueengineering applications.AdvDrugDeliveryRev 2007;59:207-33.
48. Gil ES, Hudson SM. Stimuli-responsive polymers and their bioconjugates. Prog Polym Sci 2004;29:1173-222.
49. Gulrez SK, Al-Assaf S, Phillips GO. Hydrogels: methods of preparation, characterisation and applications. Progress in molecular and environmental bioengineering from analysis and modelling to technology applications; 2011. p. 117-50.
50. Brinker CJ, Scherer GW. Sol-gel science: the physics and chemistry of sol-gelprocessing. Academic Press; 2013.
51. Radivojsa M, Grabnar I, Grabnar PA. Thermo-reversible in situ gelling poloxamer-based systems with chitosan nanocomplexes for prolonged subcutaneous delivery of heparin: design and in vitro evaluation. Eur J Pharm Sci 2013;50:93-101.
52. Devasani SR, Dev A, Rathod S, Deshmukh G. An overview of in situ gelling systems. Pharm Biological Eva 2016;3:60-9.
53. Parekh HB, Jivani R, Jivani NP, Patel LD, Makwana A, Sameja K. Novel in situ polymeric drug delivery system: a review. J Drug Delivery Ther 2012;2:136-45.
54. Liu L, Gao Q, Lu X, Zhou H. In situ forming hydrogels based on chitosan for drug delivery and tissue regeneration. Asian J Pharm Sci 2016;11:673-83.
55. Saini R, Saini S, Singh G, Banerjee A, Railmajra DS. In situ gels-a new trends in ophthalmic drug delivery systems. Int J Pharm Sci Res 2015;6:386-90.
56. Brun Graeppi AK, Richard C, Bessodes M, Scherman D, Merten OW. Thermoresponsive surfaces for cell culture and enzymefree cell detachment. Prog Polym Sci 2010;35:1311-24.
57. Darge HF, Andrgie AT, Tsai HC, Lai JY. Polysaccharide and polypeptide based injectable thermo-sensitive hydrogels for local

biomedical applications. Inter J Biol Macromol 2019;133:545-63.
58. TaylorMJ,TomlinsP,SahotaTS.Thermo-responsivegels.Gels2017;3:4.
59. Jagur Grodzinski J. Polymeric gels and hydrogels for biomedical and pharmaceutical applications. Polym Adv Technol 2010;21:27-47.
60. Cole MA, Voelcker NH, Thissen H, Griesser HJ. Stimuliresponsive interfaces and systems for the control of protein– surface and cell-surface interactions. Biomaterials 2009;30:1827-50.
61. He C, Kim SW, Lee DS. In situ gelling stimuli-sensitive block copolymer hydrogels for drug delivery. J Controlled Release 2008;127:189-207.
62. Masteikova R, Chalupova Z, Sklubalova Z. Stimuli-sensitive hydrogels in controlled and sustained drug delivery. Medicina 2003;39:19-24.
63. Ju XJ, Xie R, Yang L, Chu LY. Biodegradable 'intelligent' materials in response to physical stimuli for biomedical applications. Expert Opin Ther Pat 2009;19:493-507.
64. Agarwal P, Rupenthal ID. Injectable implants for the sustained release of protein and peptide drugs. Drug Discover Today 2013;18:337-49.
65. Rajak P, Nath LK, Bhuyan B. Liquid crystals: an approach in drug delivery. Indian J Pharma Sci 2019;81:11-21.
66. Hassan RM, Khairou KS, Awad AM. New aspects to physicochemical properties of polymer gels in particularly the coordination biopolymeric metal–alginate ionotropic hydrogels. In: Polymer Gels, Springer, Singapore; 2018. p. 275-354.
67. Qazvini NT, Bolisetty S, Adamcik J, Mezzenga R. Self-healing fish gelatin/sodium montmorillonite biohybrid coacervates: structural and rheological characterization. Biol Macromol 2012;13:2136-47.
68. Migneault I, Dartiguenave C, Bertrand MJ, Waldron KC. Glutaraldehyde: Behaviour in aqueous solution, reaction with proteins, and application to enzyme cross-linking.Biotech 2004;37:790-802.
69. Oryan A, Kamali A, Moshiri A, Baharvand H, Daemi H. Chemical cross-linking of biopolymeric scaffolds: current knowledge and future directions of cross-linked engineered bone scaffolds. Int J Biol Macromol 2018;107:678-88.
70. Vibha B. In-situ gel nasal drug deliverysystem-a review. Inter J Pharma Sci 2014;4:577- 80.
71. Wu Y, Liu Y, Li X, KebebeD, Zhang B, Ren J, et al.Research progress of in-situ gelling ophthalmic drug delivery system. Asian J Pharm Sci 2019;14:1-5.
72. Kumar L, Verma R. Chemical stability studies of bioadhesive topical gel. Int J Pharm Pharm Sci 2011;3:101-4.
73. YadavKS,RajpurohitR,SharmaS.Glaucoma: currenttreatmentandimpactofadvanced drug delivery systems. Life Sci 2019;221:362-76.
74. Karthikeyan D, Bhowmick M, PandeyVP, Nandhakumar J, Sengottuvelu S, Sonkar S, et al. The concept of ocular inserts as drug delivery systems: an overview. Asian J Pharm 2014;2:192- 200.
75. Morsi N, Ibrahim M, Refai H, El Sorogy H. Nanoemulsion-based electrolyte triggered in situ gel for ocular delivery of acetazolamide. Eur J Pharm Sci 2017;104:302-14.
76. Jones DS, Yu T, Andrews GP. A statistical determination of the contribution of viscoelasticity of aqueous carbohydrate polymer networks to drug release. Carbohydr Polym 2019;206:511-9.
77. Jain D, Kumar V, Singh S, Mullertz A, Bar-Shalom D. Newer trends in in situ gelling systems for controlled ocular drug delivery. J Anal Pharm Res 2016;2:00022.

78. BashirR,MajeedA, Ali T,FarooqS,KhanNA. Floatingoral insitugel: areview.J Drug Delivery Ther 2019;9:442-8.
79. Majeed A, Khan NA. Ocular in situ gel: an overview. J Drug Delivery Ther 2019;9:337-47.
80. Soliman KA, Ullah K, Shah A, Jones DS, Singh TR. Poloxamerbased in situ gelling thermoresponsive systems for ocular drug delivery applications. Drug Discovery Today 2019;24:1575-86.
81. Pandya Y, Sisodiya D, Dashora K. Atrigel, implants and controlled released drugdelivery system. Int J Biopharm 2014;5:208-13.
82. Radivojsa M, Grabnar I, Grabnar PA. Thermo-reversible in situ gelling poloxamer-based systems with chitosan nanocomplexes for prolonged subcutaneous delivery of heparin: design and in vitro evaluation. Eur J Pharm Sci 2013;50:93-101.
83. Devasani SR, Dev A, Rathod S, Deshmukh G. An overview of in situ gelling systems. Pharm Biological Eva 2016;3:60-9.
84. Parekh HB, Jivani R, Jivani NP, Patel LD, Makwana A, Sameja K. Novel in situ polymeric drug delivery system: a review. J Drug Delivery Ther 2012;2:136-45.

HOW TO CITE: Gaurav Haware1*, A Review On Ocular Drug Delivery System, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 7, 5803-5817. https://doi.org/10.5281/zenodo.21701863