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GENERAL REVIEW ON *IN-SITU* GELLING DRUG DELIVERY SYSTEM FOR TREATMENT OF VARIOUS DISEASES

Pawan P. Jadhav[1], S.N.Nagoba[1]*

Department of Pharmaceutics, Channabasweshwar Pharmacy College(Degree)Latur-413512 Maharashtra, India.

Abstract:

The current review on in situ gelling systems becomes one of the most popular and prominent. It had a tremendous potential advantage of delivery systems due to many benefits like easy to use, simple manufacturing, improve both adherence and patient comfort by minimizing the frequency of drug administration by its unique characteristics feature of sol to gel transition. The drawbacks associated with conventional systems of both solutions and gels, such as accurate dosing, ease of administration overcome by using in situ gelling systems. This review covers introduction, polymers used in in situ gel, *in-situ* gel for different diseases, Advantages and Disadvantages, preparation and evaluation, Recent Advancement.

Keywords: *in-situ* gel, natural and synthetic polymers, drug delivery systems, sol to gel form, onychomycosis.

Introduction:

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, presence of ions, etc.[12]. *In situ* gel produces a constant plasma drug profile in the body by extending the release of a drug. Sol to gel transition can be widely used for sustained delivery vehicle preparation of bioactive molecules [14]. *In situ* gels, potentially used for oral, buccal, subcutaneous, transdermal, intraperitoneal, ocular, nasal, rectal, vaginal, and parenteral routes [15].

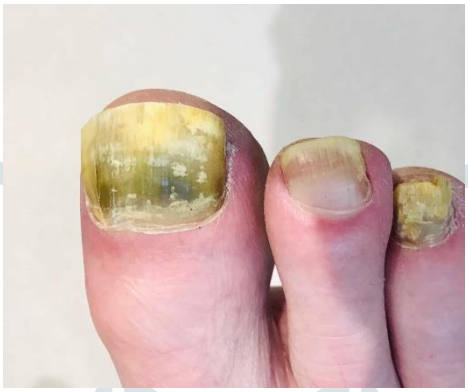
In-Situ Gel Delivery Systems:

In-situ gelation is a process of gel formation at the site of application after the composition or formulation has been applied to the site. As a drug delivery agent, the in-situ gel has an advantage related to the gel or polymer network being formed *in-situ* providing sustained release of the drug. At the same time, it permits the drug to be delivered in a liquid form. A film forming polymer and a gel forming ionic polysaccharide. These compositions employed two separately applied components, one being a solution of cross-linking cations, which is applied to the site, and a second

liquid component comprising the drug, film forming polymer and an ionic polysaccharide, which is then applied to react with the cross-linking ions and form a gel.

1. *In-situ* gels for treatment of onychomycosis:(14).

"Onychomycosis" traditionally referred to a non-dermatophytic infection of the nail but is now used as a general term to denote any fungal nail infection (tinea unguium specifically describes a dermatophytic invasion of the nail plate). Onychomycosis is all too often regarded as merely a cosmetic problem of relatively minor importance that is hardly worth the effort to resolve. Onychomycosis in immunocompromised patients, such as those infected with HIV, can pose a more serious health problem.

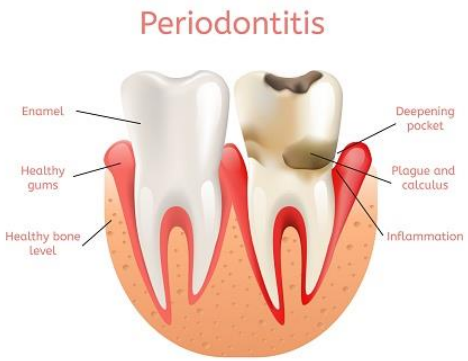


2. *In-situ* gel for ophthalmic preparation: (15)

One of the major limitations faced in ophthalmic delivery is the attainment and retention of optimum drug concentration at the site of action within the eye. Various ophthalmic dosage forms, like solutions, ointments, gels and polymeric inserts have been investigated in an attempt to extend the ocular residence time of medications for topical application to the eye. The corneal contact time has been increased to varying degrees by these dosage forms. But, they have not been unanimously accepted, because of blurred vision (e.g., ointments) or lack of patient compliance (e.g., inserts).Ease of administration in case of highly viscous solution and gel forms retard its use and patient compliance.

3. *in situ* gel for periodontal:

Periodontal disease is term used to ascribe to some pathological conditions characterized by degeneration and inflammation of gums, periodontal ligaments, alveolar bone, and dental cementum. *In situ* gel forming formulations current a novel idea of deliver drugs to patients as a liquid dosage form, yet achieve sustained release of drug for the desired period.[4]



4. Floating oral in-situ gel:

Floating Drug Delivery System is one of the novel systems of drug delivery. *In-situ* gelling system is a new trend in floating DDS. The formulation of floating *in situ* gelling solution may sustain and prolong drug action, improve patient compliance and reduce frequency of administration of the drug in comparison to conventional drug delivery system. FDDS is an effective technology to prolong the gastric residence time in order to improve the bioavailability of the drug. Floating drug delivery systems meant for gastric retention, float on the surface of the gastric fluids, due to their low density and produce prolonged effect by showing the controlled release.

Advantages

- To decrease the wastage of drug.
- To ease of administration.
- It helps to extended or prolonged release of drugs.
- It allows more patient comfort and compliance.
- Due to the low dose, there will be no drug accumulation and minimize the drug toxicity.
- It offers more bio-availability.
- By using synthetic polymers usually well defined that can be modified to yield tolerable degradability and functionality.
- It exhibits bio-adhesiveness to facilitate drug targeting, primarily through mucus membranes, for non-invasive drug administration.

Disadvantages :

- Requires a high level of fluids.
- The solution form of the drug is more susceptible to degradation.
- Due to chemical degradation, there is a chance of stability problems.
- Eating and drinking restricted for a few hours after placing the drug.
- Due to low mechanical strength, it may result in premature dissolution.

Classification Of *In-Situ* Gelling Polymers

i. Natural polymers (e. g., Alginic acid, carrageenan, chitosan, guar gum, gellan gum, pectin, xanthan gum, xyloglucan, etc.)

ii. Synthetic or semi-synthetic polymers (e. g., CAP, HPMC, MC, PAA, PLGA, poloxamers)

Preparation of in situ gel :

The polymer may differ based on the development of in situ gelling systems. The polymeric solution was prepared by dispersing required quantities of polymers and copolymers in distilled water using a magnetic stirrer until the polymers completely dissolve. After the preparation of an aqueous drug solution, transferred to a primarily prepared polymeric solution with continuous stirring until to get a homogeneous solution, and then add excipients based on the delivery system. Finally, make up the volume with distilled water.

Evaluation Of *In-Situ* Gels :

Physical evaluation

1. Compatibility studies:

for a physical mixture of interaction between drug and excipients by FTIR or DSC.

2. Appearance :

Preferably, the gels should be transparent. The formulations were observed for a general appearance by the naked eye, such as color, odor.

3. Clarity test :

Checked by using a black and white background.

4. pH:

By using a calibrated digital pH meter immediately after preparation.

5. Homogeneity:

By placing the preparation between two glasses, then observe particle roughness under the light

6. Isotonicity :

The formulation is mixed with few drops of blood, observe under a microscope, and compare with standard preparations.

7. Sol-gel transition temperature:

The temperature of the phase transition of 'sol' meniscus was noted first and then heated at a specified rate. 'Gel' formation is indicated by a lack of movement of the meniscus on tilting the tube and note down the temperature.

8. Gelling time:

Gelling time is the time required for the first detection of gelation..

9. Texture analysis :

The cohesiveness, consistency, firmness of in situ gels assessed using a texture profile analyzer, which mainly indicates the syringe ability of 'sol' so the formulation can be quickly administration via in vivo.

10. Spreading coefficient :

To check the spread ability of *in situ* gel.

11. Gelling strength :

It can be determined with the help of Brookfield viscometer.

Recent Advances:

One of the challenges facing today's pharmaceutical industry centers on coming up with efficient treatment options that are readily acceptable to physicians and patients. In situ gel formulations are one of the challenging drug delivery systems. Various biodegradable polymers are used for formulation of in situ gels, but there are fabrication problems, difficult in processing, use of organic solvents for their preparation, burst effect and irreproducible drug release kinetics. Natural polymers satisfy the characteristics of an ideal polymer but batch to batch reproducibility is difficult therefore synthetic polymers are used. Hydrogels showing improved biocompatibility, biodegradability, reduced

burst effect, better mechanical strength and processability. The recent advancement of biotechnologies has led to the development of labile macromolecular therapeutic agents that require complex formulations for their efficient administration.

Conclusion:

The utilization of *in situ* gels providing various advantages over conventional dosage forms. The use of biocompatible, biodegradable, and water-soluble polymers for the *in situ* gel formulation can make excellent and excellent drug delivery systems. A novel carrier can incorporate in these systems to obtain sustained drug delivery in a much improved and extreme manner. These systems, as they can administer in solution form, undergo gelation at the site of action. Finally, *in situ* gels are easy to apply and offer patient comfort and compliance.

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