IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

In Situ Gel Technique- A Modern Era Of Medicine

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ABSTRACT

The ‘in situ gel’ system has emerged as one of the best drug delivery systems; facilitates continuous and controlled release of drugs with its special feature of 'Sol to Gel' transformation.

An in situ gelling system is a solvent in solution before entering the body, but will change into a gel under various body conditions. There are varieties polymers form an in-situ gel and may be used for various drug control lines. There are several applications and benefits of the in situ gelling system in modern life. This review focuses on the introduction of in situ gel, its machine, various polymers used and their applications.[1]

Keywords: situ gel, new drug delivery system, polymers

1) Introduction:-

the 'in situ gel' system has emerged as one of The best drug delivery systems, in situ gelling the system assists in continuous and controlled drug release, improved patient compliance as well comfort1 with its special feature 'Sol to Gel' change. There are several advantages in ‘in situ gelling system’ which includes ease of application of dosage, reduced frequency of administration and even protection of drug from change in environmental conditions.[1]

Various natural and synthetic polymers go into situ gel constructive and potentially non-verbal orally, ocular, transdermal, buccal, intraperitonial, parenteral, injections, rectal veins and vagina[2)]. Recent developments in in situ gels have made it possible to apply changes to physical differences[3, 4] in different regions Stomach tract of enhanced drug absorption as and patient comfort and compliance. Pectin, gellan gum, chitosan, alginic acid, guar gum, carbopal , Xyloglucan, HPMC, poloxamer etc. some natural polymers are used in the in situ gelling system. There are a several applications [5] and in-situ benefits a gelling system in modern life. This review is very much focused introduction to situ gel, its method, various polymers used and their use.

3) Ideal characteristics of in situ gel technique:-

1. It should be biocompatible.

2. It should be capable of Stick to mucus.

3. It should have pseudo plastic behavior.

4. It should influence the tear behavior.

5. The polymer should be capable of decrease the viscosity with increasing shear rate offering lowered viscosity during blinking and stability of tear film during fixation

2) Advantages:-

- Controlled and sustained release drug
- Easy drug Administration
- Can be administered to unconscious patients
- More patient compliance and comfort
- Drug toxicity and frequency is minimized
- Bioavailability is increased
- Biocompatibility and biodegradation can be done easily by the use of natural polymers
- 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.[6]

3) Mechanisms in In situ Gel Technique

4.1) Physical mechanism:

- Diffusion: - Diffusion is physical approach involves diffusion of solvent from polymer into tissue of surrounding to form precipitation. N-methyl pyrrolidone is commonly used polymer in in-situ gelling technique.
- Swelling: - In Diffusion polymer is used around the polymer embankment and the liquid present present in the outer area and swollen from the outside to inside and the drugs come out slowly. myverol a substance used as a polar lipid flooded water into the liquid crystalline phase properties. This item contains some bio adhesive properties and can degrade in vivo by enzymatic action.[7]

4.2) Chemical Mechanisms:-

In situ gel formation based on different chemical reactions or mechanisms such as Precipitation of inorganic solids from supersaturated ionic solutions, Enzymatic processes, and photo initiated processes.

- Ionic cross linking:-

In this method, the ion sensitive polymer is used. Ion sensitive polymers may undergo phase transition in presence of various ions like Na+, K+, Ca+, and Mg+. Some polysaccharides are also in the class of ion-sensitive like. While k-carrageenan forms rigid, small amount of K+ are reply in brittle gels, elastic gels are forms in icarrageenam mainly in the presence of Ca2+. Gellan gum mainly available as Gelrite. It is an anionic polysaccharide, in the presence of mono and divalent cations that undergoes in situ gelling system [8, 9.]

- Enzymatic cross linking:-

The in-structure formation of natural enzymes has not been extensively investigated but appears to have some advantages over chemical and photochemical methods. For example, the enzymatic process works well under physiologic conditions without the need for potentially harmful chemicals such as monomers and initiators.
Intelligent stimulus delivery systems investigated using hydrogels to release insulin have been investigated. PH-sensitive polymers that contain stable insulin and glucose oxidase can be elevated due to the level of blood glucose releasing insulin-bound insulin in a way that affects the heart.
Adjusting the amount of the enzyme also provides an easy way to control the level of gel formation, allowing the compounds to be injected prior to gel formation.[10]

- Photo polymerization:-

The photo-polymerization method is electromagnetic radiation used during the formation of in situ gelation system. Active macromere solution or monomers and the invader can be injected into the tissue area as well as the use of electromagnetic radiation used to make the gel.
The most suitable polymers for image polymerization are polymers are separated a functional polymerisable group in front of the image launcher such as acrylate or similar monomers and macromers usually long ultraviolet waves are also visible using wavelengths.
Short haircuts of ultraviolet light are present they are not always used because they have limited access tissue and biologically harmful. In this way, the ketone, such as 2,2 dimethoxy-2-phenyl acetophenone, used as initiator of ultraviolet photo- polymerization. Camphorquinone and ethyl eosin initiators are used in visible light systems.[11]

4) Various approaches in in situ gel technique:-

There are various approaches are made to enter into in situ gelation method.

5.1)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.

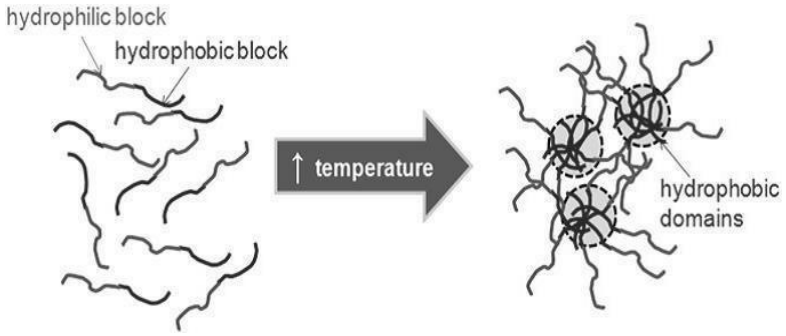

Figure 1: Mechanism of temperature sensitive system

5.2) PH triggered in in situ gelation:-

In this process the gel is formed due to changes in pH. This method uses pH-sensitive or pH-sensitive polymers. At pH sensitive polymers consist of hanging acidic or basic groups may receive or release protons against 22 pH variables. A large number of polymers of ionizable groups are known as poly electrolytes. The poly electrolytes present in the structure cause an increase in the external pH leading to the swelling of the hydrogel acting in situ gel. Some polymers are suitable for this method of those polymers with anionic groups. Other cellulose acetate phthalate (CAP), carbomer and its extracts, polyethylene glycol (PEG), pseudo latexes and poly methacrilic acid (PMC) etc.

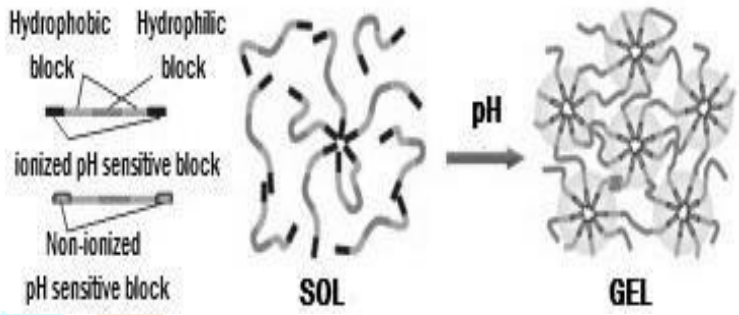

Figure 2: Mechanism of pH triggered in situ gelation

5.3)Ion Activated in situ gelation:-

In this method, the gelling of the applied solution is caused by the conversion of ionic23,24 energy. It is thought that the level of gelation depends on the osmotic inclination of the gel surface. An osmotically reflective gelation polymer is Gelrite or Gellan gum, Hyaluronic acid and Alginates etc.

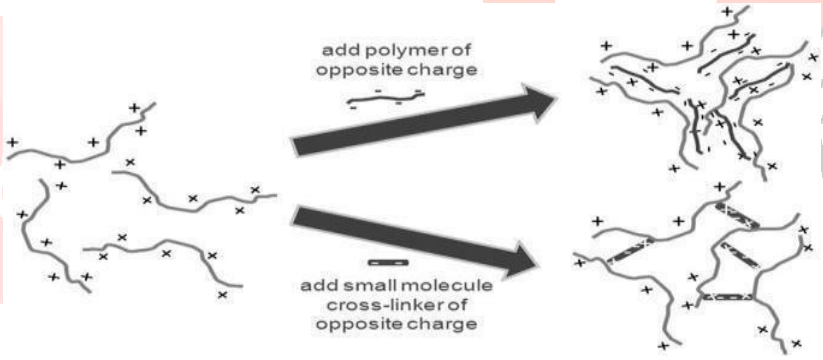

Figure 3: Mechanism of Ion activated in situ gelation.

6.0) Polymers used in in situ gelation:-

- Gellan gum:

Anionic deacetylated exocellular a polysaccharide produced by Pseudomonas elodea. temperature-dependent gelation or cation made. The construction is made of gellan solution with calcium chloride and sodium citrate complex.

When used orally, calcium ions are used extracted from the area with stomach acid leading to the flow of gellan thus creates a gel in place. In the area gelling gellan formulation as an oral delivery vehicle reported theophylline.[12]

- Xyloglucan:

Xyloglucan is a polysaccharide found from tamarind seeds and composed of (1-4) -β-Dglucan backbonechain, containing (1-6) -α-D xylose branches partially replaced by
(1-2) -βDgalactoxylose. Xyloglucan is slightly degraded by βgalactosidase, a by-product of which is expressed by heat. reverse gelation by lateral packing of the same rod chains.
The temperature change of sol-gel varies by galactose degradation rate. Build with heat gels that convert to warmth to body temperature. Yours potential use in oral delivery is advantageous the recommended slow gelation time (a few minutes) may allow in-situ gelation in the abdomen following orally cold xyloglucan solution management20.Xyloglucan gels may be used orally intramuscular delivery of intraperitoneal, ocular and rectal.[13]

- Alginic acid:

Alginic acid is a linear block copolymerpolysaccharide hlanganisa-D mannuronic acid and αL-glucuronic acid residues composed of 1, 4-glycosidiccommunication. Part of each block and the arrangement of blocks near a molecule varies depending on the source of the algal. Reduce aqueous solutions alginates form strong gels by combining di and trivalent iron ions by a cohesive process involving consecutive glucuronic residues in α-Lglucuronic acid blocks of alginate chain.
Alginic acid can be designated as an ophthalmic construction vehicle, from which it shows positive organisms such as biodegradability and nontoxicity. A long time precorneal settlement of alginic-containing structures the acid was considered, not only based on its ability to apply the gel eye, but also because of its mucoadhesive adhesive properties.[14]

- Chitosan:

Chitosan is perishable ,a thermosensitive, polycationic polymer obtained byalkaline deacetylation of chitin, a natural component of shrimp and crab shell. Chitosan is a pH of biocompatible a cationic-based polymer, which always melts internally aqueous solutions up to a pH of 6.226. The neutrality of aqueous solution of chitosan at a pH above 6.2 leadsthe formation of a liquid gel like rain.
PH The solution of cationic polysaccharides is modified in the formation of a pH sensitive temperature-sensitive gel aqueous solutions, without chemical modification or connecting by adding polyol salt containing one anionic head such as glycerol, sorbitol, fructose or glucose and phosphate salts to chitosan aqueous solution.[15]

- Carbopol :-

Carbopol is highly dependent on pH polymer, which remains in solution form at acidic pH however forms a gel of low viscosity at alkaline pH. HPMC is used in combination with carbopol to give viscosity carbopol solution, while reducing acid acid solution. These fall under the pH-induced category in-situ precipitating polymeric systems.
Based on this concept, composition and ophthalmic examination indomethacin treatment delivery system uveitis is performed. Localized pH polymeric system (aqueous solution for carbopol-HPMC system) was designed and developed by Ismail et al. plasmid DNA delivery.[16]

- Pectin:

Pectin is a family of polysaccharides, in where the polymer core primarily comprises
α- (1-4) D remnants of galacturonic acid. Low methoxy pectin (degree for esterification <50%) forms gels easily in water solution in the presence of free calcium ions, which connect galacturonic acid chains in a way described in the egg box model. Although the gelation of pectin will occur in the presence of H + ions, the source of Divalent ions, usually calcium ions, are needed to produce gels that are suitable as drug vehicles delivery. Great benefit of using pectin in these a composition that is soluble in water, organic solvents are

not required in construction. Divalent cations present in the stomach, carry out a change pectin in gel state when administered orally.[17]

- Pleuronics:

Poloxamers or pluronic (marketed by BASF Corporation) is a commercial available difunctional triblock copolymers non-ionicnature. They include the middle block of comparison hydrophobic polypropylene oxide surrounded by both on the sides with hydrophilic poly blocks ethylene oxide. Due to the PEO / PPO ratio of 2: 1, when these molecules are immersed in liquid solvents, they form micellar structures in addition to essential micellar to concentrate. .

- HPMC:-

Cellulose contains a glucan chain with a repeating unit of β- (1, 4) -D-glucopyranose. Other natural polymers such as HPMC, MC and EC are those that show the transformation of the sol-gel phase sensitive to temperature. Cellulose material will increase its viscosity when the temperature drops while output such as HPMC, MC, will increase its viscosity as the temperature rises. MC is a natural polymer composed of native cellulose with a flexible methyl group in its series. At low temperatures (300C) the solution is liquid and when the temperature rises (40-500C) and gelation[18].

7.0) Application of In situ drug delivery system:-

- Oral drug delivery system

PH-sensitive hydro gels can be used in the delivery of certain drugs to specific areas of the GI tract. Hydro gels composed of different concentrations of PAA-released PEG emissions are allowed in the preparation of silicone microspheres, which produce prednisolone in the abdominal area or exhibit gastro protective properties. Contraindicated dextran hydro gases have rapid inflammation under high pH conditions, while other polysaccharides such as amidaded pectin's, inulin and guar gum are investigated to improve the colon-specific drug delivery system. The formation of gellan and sodium alginate both contain a complex calcium ion that transcends the gelation process by releasing these ions into the acidic environment of the stomach.

- Eye drug delivery system

In the ocular delivery system natural polymers such as alginic acid, inulin, and xyloglucan, inulin are widely used. In the local system of ophthalmic delivery various compounds such as independent drugs, an anti-inflammatory agent and an anti-bacterial agent, are used to relieve intra ocular incompatibility in glaucoma. The standard delivery system often leads to poor recovery and treatment response due to high fluid retention and flexibility leads to rapid removal of the drug from the eyes and therefore, victory the bioavailability problem of the in-situ ophthalmic gel was improved. Improving viscosity bioavailability enhancements such as Carboxy Methyl Cellulose, Hydroxy Propyl Methyl Cellulose, Carbomers, Poly Vinyl alcohol used to improve the viscosity of the structure to increase the duration of pre-corneal stay and increase the availability of bioavailability, simplification. Entry enhancements such as preservatives, chelating agents, surfactants used to improve the penetration of cornea drugs.

- Nose drug delivery system

In the nasal gel system in situ xanthan gum and gallan gum are used as in-situ polymers forming the gel Momethasone furoate which is used to test its effectiveness in treating infectious rhinitis. Animal studies have been used to model rhinitis allergies and the effect of in-situ gel on antigen-treated nose signals in sensitive mice was observed. An in-situ gel was found to prevent an increase in nasal symptoms compared to nosonex for marketing preparation (suspension of Momethasone furoate 0.05%).

- Rectal and vaginal drug delivery system

The rectal route may be used to deliver many types of drugs that are formulated as liquid, semisolid (ointments, creams and foams) and solid dosage forms (suppositories). Acetaminophen an anti inflammatory drug formulated as rectal in situ gel by using polycarbophil and poloxamer F188 and poloxamer 407 as synthetic polymer forming in situ gelling liquid suppository which is considered as an synthetic polymers forming in situ gelling liquid suppository which is considered as an effective method shows enhance bioavailability.

- Skin and transdermal drug delivery system

Pluronic F127 gel that is able to reverse heat has been tested as a percutaneous handling vehicle Indomethacin. An in-vivo study suggests that 20% w / w liquid gel may be used in a practical way as a topical foundation drug administration. Poloxamer 407 gel found ready for the delivery of flexible insulin in the body73. I a combination of chemical enhancements and iontophoresis led to the synergistic development of insulin to enter.[19]

8.0) CONCLUSION

The present review concludes that 'in situ gel' system has emerged as one of the best novel drug delivery systems, the in situ gelling system helps for the sustained and controlled release of the drugs, improved patient compliance and comfort, Various natural and synthetic polymers undergo in situ gel forming and potentially can be used for oral, ocular, transdermal, buccal, intra-perotonial, parenteral, injectable, rectal and vaginal routes. There is high scope for research work on in situ gel system in order to provide advanced techniques in drug delivery systems.

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