

Review on injectable hydrogel

Sakshi Vijay Phalke, Jagruti Gawali

Delonix Society, Baramati College of Pharmacy, Maharashtra, India

Abstract

Hydrogel have three-dimensional structure which is hydrogel is simply a hydrophilic polymeric network cross-linked in some fashion to form generate an elastic structure. Injectable hydrogel is technique in which active substance and biomaterials is injected into body fluid formation of situ solid hydrogel. Active substance such as drugs, Protein, genes, virus Injectable hydrogel are developed by photo cross linking polymerization by two types chemical and physical cross linking. Injectable hydrogel improve some properties such as good biocompatible, good biodegradable, controlled drugs release ability. Injectable hydrogel is injected into body fluid and formation of situ solid hydrogel.

Injectable hydrogel delivery variety of bimolecule to site of action. When hydrogel injected into the body fluid their will be contionus exchange of body fluid and hydrogel. Injectable hydrogel are used for tissue engineering, tissue regeneration and madical device.

Keywords: injectable hydrogel, chemical cross linking, physical cross linking, biocompatibility

Introduction

Hydrogel are three-dimensional network structure which drink large amount of water. Hydrogel are involved sample reaction between monomers and associated bond such as hydrogen bond, Vander walls bond. Hydrogel are a hydrophilic in nature which absorb water when it contact with body fluid and then it will be swell

Hydrogel can be used for delivery bioactive molecules which help for tissue regeneration. Injectable hydrogel is technique in which biomaterials is injected into body tissue and formation of situ solid hydrogel. Situ solid hydrogel means healthy cells are mixed with polymer and solutions and other bioactive materials and then injected into body body fluid. Injectable hydrogel are prepared by using hydrophilic monomer polymerization with existing ploy functional cross linking agent. Cross linking agent include

glutaraldehyde (GTA) or genipin and enzymes. Injectable hydrogel are developed by chemical and physical cross linking. Injectable hydrogel are three-dimensional structure of which absorb water in biological fluid Natural polymer used in injectable hydrogel is collage and gelatin and polysaccharides such as alginate and agrose. Synthetic polymers are used in injectable hydrogel are vinyl alcohol polyethylene oxide and polyethylene glycol

Injectable hydrogel are based on situ formation. Injectable hydrogel is fill active substance in body fluid and then formation of situ solid hydrogel. Active substance include protein drug genes and virus. Injectable hydrogel can be used for good biocompatible, good biodegradable, minimal invasion, versatility, High drug release ability. It also used for control released and tissue engineering.

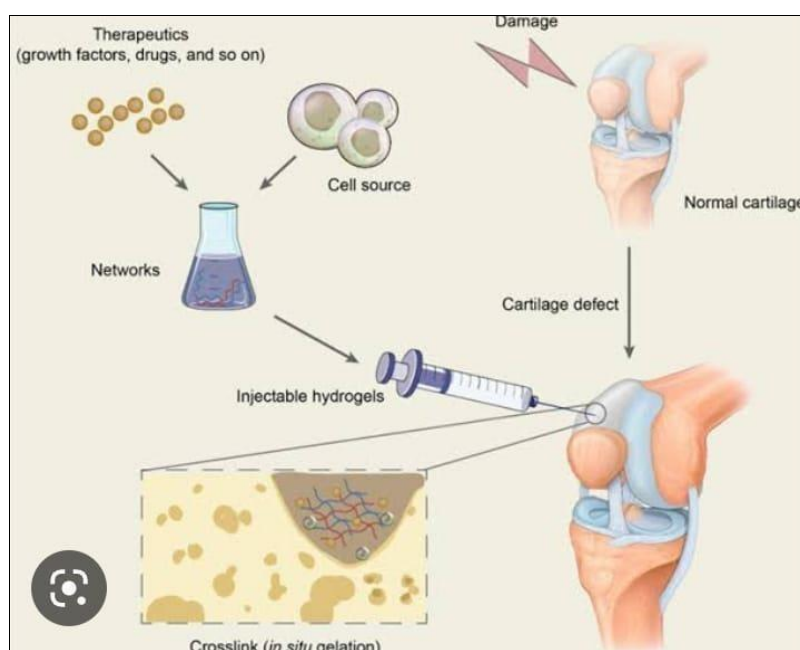


Fig 1

Mechanism of action

Injectable hydrogel when mixed with polymer and solutions and then injected into body fluid it will be swell and then continues exchange occurs between polymer and body fluid. Bio materials are release by ensured entrapped practical carried out by diffusion. When biomaterials is injected into body fluid formation situ solid hydrogel it absorb the water form the body fluid

Polymer used in preparation of injectable hydrogel is collage, gelatin, vinyl alcohol, polyethylene oxide and polyethylene glycol. Injectable hydrogel are developed by hydrophilic monomer with ployfunctional cross linking agent

Advantages of injectable hydrogel

Injectable hydrogel is improved some properties include good biocompatible and biodegradability

It have High drugs laoding capacity

It also controlled drug release ability

It also contains excellent cytocompatibility

It required minimal invasion surgery

It is suitable for thermolabile drugs

It easily control stimulus and trigger mechanism

Disadvantage of injectable hydrogel

Production cost of injectable hydrogel are high

It have poor mechanical strength

It as low reproducibility

It as lack of biocompatibility with some polymer

It required specialised service for non biodegradable device

Development of injectable hydrogel

Injectable hydrogel developed by two methods

Injectable hydrogel developed by physical cross linking

Injectable hydrogel developed by physical cross linking - it is crosslinking reaction which is used for fabrication of hydrogel. It involves some interaction such as non covalent interaction, hydrophobic interaction, van der wals forced including dipole dipole interaction and Landon dispersion force. Injectable hydrogel developed by physical cross linking reaction

Physical cross linking reaction is occur between between a structural unit of polymer chain and structural unit of another chain. Physical cross-linking is the development of a bond between polymer chains through weak physical interactions. Physical hydrogel are reversible

For example

sodium aliginated gel are formed by when it contact with calcium ion and formation of ionic bond that are bond between alignate chain. Redox active injectable gel are developpe for controlled local delivery of protein by the formation of ionic bond.

Physical injectable hydrogel are used for delivery of therapeutic agent and tissue engineering

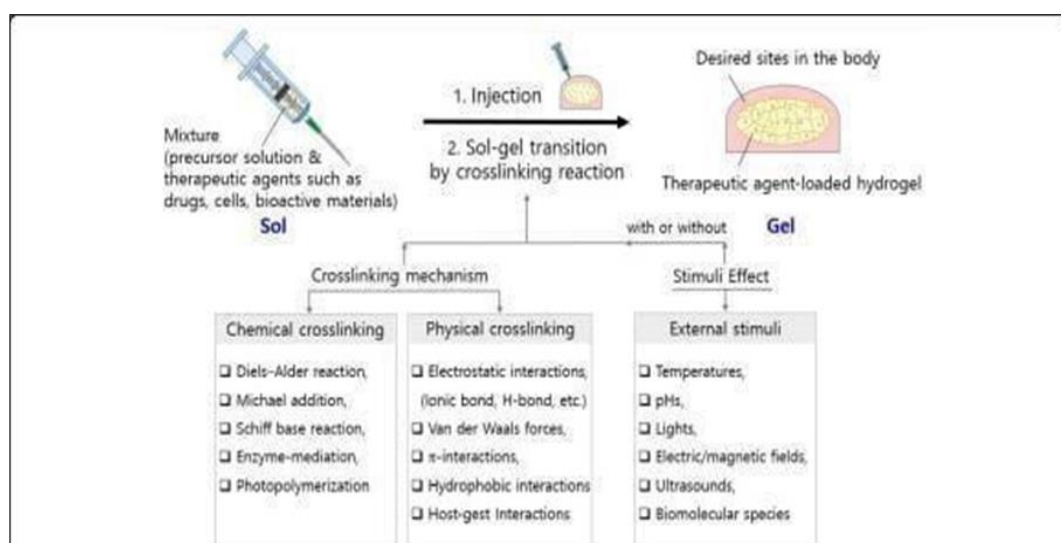


Fig 2

Injectable hydrogel are developed by chemical cross linking

Chemical cross linking are developed by chain growth polymerization, condensation polymerization and electronic beam polymerization. Chemical cross linking reaction involved covalent bond formation. Covalent bond are formed by mutul sharing of one and more pair of electrons between two atom crosslinked polymer are formed by adding of small cross linking molecule, polymer - polymer conjugated photosensitive agent or by enzyme catalysed reaction. Chemical cross linking agent are used for chemical crossing linking reaction Agents are glutaraldehyde or genipin and enzyme. Chemical cross linking consist some chemical reactions such as diels alder

reaction, Michael reaction, schiffs base reaction or enzyme or photo mediated reaction. Diels alder reaction are reaction occurs between conjugated diene to an alkene or alkyne it formed cyclic rings structure. Michael addition reaction are the addition of conjugated nucleophile with electrons poor olefin to formed unsaturated carbonyl compound it required base catalysed and nucleophile catalysed. Schiff base addition reaction is involved addition of nucleophile and formation of imine bond from an amine and a carbonyl compound

Application of injectable hydrogel

Injectable hydrogel have many used for biomedical applications such as tissue engineering and tissue regeneration medicine drug and other therapeutic agent delivery and medical devices and etc

Tissue engineering

tissue engineering is technology in which damage tissue and damage organ can transplant with health tissue and organ. Injectable hydrogel are used for regeneration of tissue include bone, cartilage, alginate, fibre elastin, heparin and hyaluronic acid. Tissue engineering required some biomaterials which provides injectable hydrogel Hydrogel are fill vacant Space by bioactive substance or device which is regeneration of tissue

Medical device

Injectable hydrogel are also used as medical device Injectable bone filler categories into medical devices.

Injectable hydrogel used to deliver therapeutic agent

injectable hydrogel are also carriers the Protein, drug, gens and other biomolecules. It is help to deliver the drug at specific site and also help to regeneration of tissue. It also deliver the bioactive to specific site. Injectable hydrogel are also design for Target drugs delivery of therapeutic agent.

Wound healing

Hydrogel dressing have excellent antibacterial properties, bioadhesiveness, good compatibility and biodegradability are used for wound healing it used to to control infection and improve angiogenesis Hydrogel have ability to convert NIR radiation, intensity time, cycling time. It increases temperature and inhibit bacteria growth effectively. Non particle of Cooper have good photothermal capability under NIR radiation. It's play important role in accelerating angiogenesis and propagation of for fibroblast

Drug therapy

Conventional drug delivery are associated with some undesirable effect such as drug absorption, rapid metabolism repeated dosing systemic toxicities and degradation. Injectable hydrogel improve some properties such as degradability and physical properties which overcome the disadvantage. It improves biocompatibility, good syringe ability and stimuli to the enzyme which improves drug delivery System. Active substance such as genes peptides protein or even living cells and organ encapsulated in hydrogel.

Cancer therapy

Systemic cytotoxicity is connected with the conventional chemotherapy of cancer injectable hydrogel control toxicity and ensure drug sustain release. injectable hydrogel are response to some stimuli include ph, temperature and immuno sensitivity which is used for cancer chemotherapy and gene therapy.

Some examples of of injectable Hydrogels TraceIT® and Space OAR®, are therapeutically used for cancerous cell it is protect the natural cell from damage by radiotherapy injectable hydrogel are used for the treatment of carcinomas and tumor

Conclusion

Review has focused on the different mechanisms of injectable hydrogel. This review article it covered injectable hydrogel developed by chemical and physical cross-linking system. It has covered variety of injectable hydrogel studies for drugs delivery system. It has also covered mechanism action of the Injectable hydrogel The major application of the Injectable hydrogel were covered This field required of novel hydrogel design with melodious properties.

Acknowledgment

With lots of respect to my family and my colleague, I would like to grateful thanks to my college B.C.O.P college of pharmacy for permitting me to do this review article. Special thank to my Friends, respected Teacher's and Co-authors give us lots of information and valuable time, thank for support. I also thankful of, who gives me this opportunity to publish our review article.

Reference

- Hoffman as. Hydrogels for biomedical applications. *Adv drug deliv rev*,2012:64:18-23.
- Caló e, khutoryanskiy vv. Biomedical applications of hydrogels: a review of patents and commercial products. *Euro polym j*,2015:65:252-67.
- Dimatteo r, Darling nj, Segura t. in situ forming injectable hydrogels for drug Delivery and wound repair. *Adv drug deliv rev*,2018:127:167-84.
- Yang ja, Yeom j, Hwang bw, Hoffman as, Hahn sk. In situ-forming injectable Hydrogels for regenerative medicine. *Prog polym sci*,2014:39(12):1973-86.
- Van tomme sr, Storm g, Hennink we. In situ gelling hydrogels for pharmaceutical and biomedical applications. *Int j pharm*,2008:355(1-2):1-18.
- Klouda l, Mikos ag. The rmoresponsive hydrogels in biomedical applications. *Euro j Pharm bio pharm*,2008:68(1):34-45.
- Klouda l. The rmoresponsive hydrogels in biomedical applications: a seven-year Update. *Eur j pharm bio phar*,2015:97:338-49. [4/28, 10:53 am]: jeong b, kim sw, bae yh. Thermosensitive sol– gel reversible hydrogels. *Adv drug Deliv rev*,2012:64:154-62.
- Csóka g, Gelencsér a, Makó a, Marton s, Zelkó r, Klebovich I, *et al.* potential Application of metolose® in a the rmoresponsive transdermal therapeutic system. *Int J pharm*,2007:338(12):1520.
- Chenite a, Chaput c, Wang d, Combes c, Buschmann m, Hoemann c, *et al.* novel Injectable neutral solutions of chitosan form biodegradable gels in situ. *Biomaterials*,2000:21(21):2155-61.
- E duhamel c, Hellio d, Djabourov m. All gelatin networks: 1. Biodiversity and Physical chemistry. *Langmuir*,2002:18(19):7208-17.
- Lanzalaco s, Armelin e. Poly (n-isopropylacrylamide) and copolymers: a review on Recent progresses in biomedical applications. *Gels*,2017:3(4):36.
- Mellati a, Kiamahalleh mv, Dai s, Bi j, Jin b, Zhang h. influence of polymer molecular weight on the *in vitro* cytotoxicity of poly (n-isopropylacrylamide). *Mater sci eng c*,2016:59:509-13.
- Alexandridis p, Hatton ta. Poly (ethylene oxide)-poly (propylene oxide)-poly (ethylene Oxide) block copolymer surfactants in aqueous solutions and at interfaces: thermo dynamics, structure, dynamics, and modeling. *Colloids surf a*,1995:96(1-2):1-46.
- Jung ys, Park w, Park h, Lee dk, na k. Thermo-sensitive injectable hydrogel based on the physical mixing of hyaluronic acid and pluronic f-127 for sustained n said Delivery. *Carbohydr polym*,2017:156:403-8.
- Oh sh, kang jg, Lee Jh. Co-micellized pluronic mixture with thermo-sensitivity and Residence stability as an injectable tissue adhesion barrier hydrogel. *J biomed mater Res b*,2018:106(1):17282.
- Choi wi, Hwang y, Sahu a, Min k, Sung d, Tae g, *et al.* an injectable and physical Levan-based hydrogel as a

- dermal filler for soft tissue augmentation. *Bio mater sci*,2018;6(10):2627-38.
17. Alexander a, Khan j, Saraf s, Saraf s. poly (ethylene glycol)–poly (lactic-co-glycolic acid) based thermosensitive injectable hydrogels for biomedical applications. *J Control release*,2013;172(3):715-29.
 18. Gong c, Shi s, Wu l, Gou m, Yin q, Guo q, *et al.* biodegradable in situ gel forming controlled drug delivery system based on thermosensitive pcl–peg–pcl Hydrogel. Part 2: sol–gel–sol transition and drug delivery behavior. *Acta bio mater*,2009;5(9):3358-70.
 19. Ren Y, Zhao X, Liang X, Ma PX, Guo B. Injectable hydrogel based on Quaternized chitosan, gelatin and dopamine as localized drug delivery System to treat Parkinson’s disease. *Int J Biol Macromol*,2017;105:1079–87.
 20. Ruirui X, Kai L, Tifeng J, Ning Z, Kai M, Ruiyun Z, *et al.* An injectable self assembling collagen–gold hybrid hydrogel for Combinatorial antitumor Photothermal/photodynamic therapy. *Adv Mater*,2016;28(19):3669–76.
 21. Zubik K, Singhsa P, Wang Y, Manuspiya H, Narain R. Thermo-responsive poly (Nisopropylacrylamide)-cellulose nanocrystals hybrid hydrogels for wound Dressing. *Polymers*,2017;9(4):119.
 22. Baral A, Roy S, Dehsorkhi A, Hamley IW, Mohapatra S, Ghosh S, *et al.* Assembly of an injectable noncytotoxic peptide-based Hydrogelator for Sustained release of drugs. *Langmuir*,2014;30(3):929–36.
 23. Feng H, Du Y, Tang F, Ji N, Zhao X, Zhao H, *et al.* Silver ions blocking Crystallization of guanosine-based hydrogel for potential antimicrobial Applications. *RSC Adv*,2018;8(28):15842–52.
 24. Cinar G, Ozdemir A, Hamsici S, Gunay G, Dana A, Tekinay AB, *et al.* Local delivery of doxorubicin through supramolecular peptide amphiphile Nanofiber gels. *Biomater Sci*,2017;5(1):67–76.
 25. Payyappilly S, Dhara S, Chattopadhyay S. The rmoresponsive biodegradable PEG-PCL-PEG based injectable hydrogel for pulsatile insulin delivery. *J Biomed Mater Res A*,2014;102(5):1500–9.
 26. Li G, Wu J, Wang B, Yan S, Zhang K, Ding J, *et al.* Self-healing Supramolecular self-assembled hydrogels based on poly (l-glutamic acid *Biomacromolecules*,2015;16(11):3508–18.
 27. Loebel C, Rodell CB, Chen MH, Burdick JA. Shear-thinning and self-healing Hydrogels as injectable therapeutics and for 3D-printing. *Nat Protoc*,2017;12:1521.
 28. Sim HJ, Thambi T, Lee DS. Heparin-based temperature-sensitive injectable Hydrogels for protein delivery. *J Mater Chem B*,2015;3(45):8892–901.
 29. Pacelli S, Acosta F, Chakravarti AR, Samanta SG, Whitlow J, Modaresi S, *et al.* Nanodiamond-based injectable hydrogel for sustained growth factor release: preparation, characterization and *in Vitro* analysis. *Acta Biomater*,2017;58:479–91.
 30. Li X, Fu M, Wu J, Zhang C, Deng X, Dhinakar A, *et al.* pH sensitive peptide hydrogel for glucose-responsive insulin delivery. *Acta Biomater*,2017;51:294–303.
 31. Ye X, Li X, Shen Y, Chang G, Yang J, Gu Z. Self-healing pH-sensitive Cytosine- and guanosine modified hyaluronic acid hydrogels via hydrogen Bonding. *Polymer*,2017;108:348–60.
 32. Qu J, Zhao X, Ma PX, Guo B. Injectable antibacterial conductive hydrogels with dual response to an electric field and pH for localized “smart” drug Release. *Acta Biomater*,2018;72:55–69.
 33. Wu H, Song L, Chen L, Zhang W, Chen Y, Zang F, *et al.* Injectable magnetic supramolecular hydrogel with magnetocaloric Liquid-conformal property prevents the postoperative recurrence in a Breast cancer model. *Acta Biomater*,2018;74:302–11.
 34. Ballios Brian G, Cooke Michael J, Donaldson L, Coles Brenda LK, Morshead Cindi M, van der Kooy D, *et al.* A Hyaluronan-based injectable Hydrogel improves the survival and integration of stem cell progeny Following transplantation. *Stem Cell Reports*,2015;4(6):1031–45.
 35. KP M, SR A, OL P, LP J, Emanuel M, KK L, *et al.* Controlling the Release of Small, Bioactive Proteins via Dual Mechanisms with Therapeutic Potential. *Adv Healthc Mater*,2017;6(24):1700713.
 36. Wu C, Zhao J, Hu F, Zheng Y, Yang H, Pan S, *et al.* Design Of injectable agar-based composite hydrogel for multi-mode tumor therapy. *Carbohydr Polym*,2018;180:112–21.
 37. Huebsch N, Kearney CJ, Zhao X, Kim J, Cezar CA, Suo Z, *et al.* Ultrasound-triggered disruption and self-healing of reversibly cross-linked Hydrogels for drug delivery and enhanced chemotherapy. *Proc Natl Acad Sci*,2014;111(27):9762–7.
 38. VJ A, Fayekah A, Nicole P, Yasemin K, Varun V, NL S, *et al.* Mechanically loading cell/hydrogel constructs with low-intensity
 39. Mironi Harpaz I, Wang DY, Venkatraman S, Seliktar D. Photopolymerization of cell- Encapsulating hydrogels: Crosslinking efficiency versus cytotoxicity. *Acta Biomater*,2012;8(5):1838-48.
 40. Yue K, Trujillo de Santiago G, Alvarez MM, Tamayol A, Annabi N, Khademhosseini A. Synthesis, properties, and biomedical applications of gelatin methacryloyl (GelMA) Hydrogels. *Biomaterials*,2015;73:254-71.
 41. Lin H, Cheng AWM, Alexander PG, Beck AM, Tuan RS. Cartilage tissue engineering Application of injectable gelatin hydrogel with in situ visible-light-activated gelation Capability in both air and aqueous solution. *Tissue Eng A*,2014;20(17-18):2402-11.
 42. Park H, Choi B, Hu J, Lee M. Injectable chitosan hyaluronic acid hydrogels for Cartilage tissue engineering. *Acta Biomater*,2013;9(1):4779-86.
 43. Cai S, Liu Y, Shu XZ, Prestwich GD. Injectable glycosaminoglycan hydrogels for controlled release of human basic fibroblast growth factor. *Biomaterials*,2005;26(30):6054-67.
 44. Steinwachs M, Cavalcanti N, Mauuva Venkatesh Reddy S, Werner C, Tschopp D, Choudur HN. Arthroscopic and open treatment of cartilage lesions with BST- CARGEL scaffold and microfracture: A cohort study of consecutive patients. *The Knee*,2019;26(1):17484.
 45. Rhee C, Amar E, Glazebrook M, Coday C, Wong IH. Safety profile and short-term Outcomes of BST Car Gel as an adjunct to microfracture for the treatment of chondral Lesions of the hip. *Orthop J Sports Med*,2018;6(8):2325967118789871.
 46. Guvendiren M, Lu HD, Burdick JA. Shear-thinning hydrogels for biomedical applica- Tions. *Soft Matter*,2012;8(2):260-72.

47. Gupta D, Tator CH, Shoichet MS. Fast-gelling injectable blend of hyaluronan and methylcellulose for intrathecal, localized delivery to the injured spinal cord. *Biomaterials*,2006;27(11):2370-9.
48. Gaharwar AK, Schexnailder PJ, Jin Q, Wu CJ, Schmidt G. Addition of chitosan to Silicate crosslinked PEO for tuning osteoblast cell adhesion and mineralization. *ACS App Mater Interfaces*,2010;2(11):3119-27.
49. Jin Q, Schexnailder P, Gaharwar AK, Schmidt G. Silicate cross-linked Bio-nanocomposite hydrogels from PEO and chitosan. *Macro mol Bio sci*,2009;9(10):1028-35.
50. Yalanis GC, Reddy S, Martin R, Choi J, Brandacher G, Mao H-Q, *et al.* An injectable Nanofiber hydrogel composite with interfacial bonding for soft tissue filling and Regeneration. *Plast ReconstrSurg*,2015;136(4S-1 (Supplement)):153-4.