HYDROGEL: SYMMETRIC DESCRIPTION OF DRUG DELIVERY SYSTEM**Nipuna Kumar Bhoi^{1*}, A.K Singhai¹, Gaurav Jain¹, Subhendu S. Mishra²****¹ Lakshmi Narain College of Pharmacy, Bhopal, M.P, India****² Kalinga Biomedical Research Institute & Training Establishment, Sambalpur, Odisha*****Corresponding Author's E mail: nipunabhoi68@gmail.com****Article Info :** Received 21 Feb. 2020; Revised 7 Mar. 2020; Accepted 17 Mar. 2020, Available online 15 April.2020 **Cite this article as:** Nipuna Kumar Bhoi, A.K Singhai, Gaurav Jain, Subhendu Sekhar Mishra. Hydrogel: Symmetric Description Of Drug Delivery System 2020; 9(2): 27-36.<https://dx.doi.org/10.38164/AJPER/9.2.2020.27-36>**Copyright: This is an open-access article distributed under the terms of the Creative Commons Attribution license which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use (Non Commercial, or CC-BY-NC) provided the original author and source are credited.****ABSTRACT**

Hydrogels are extensively exhausted materials that have a lot of medical presentations. These are convincing 3-D, hydrophilic, polymeric networks accomplished of absorbing huge extents of water or biological fluids. Because of their high-water subject, porosity and soft consistency, they carefully pretend natural living tissue more so than other types of mock biomaterials. The present review works deals with the formulation and evaluation of mucoadhesive hydrogel of an antiviral agent, to oppressed the poor retaining of drug (tear out from ocular cavity) and poor ocular bioavailability of drugs. Hydrogels are of great importance in providing sustained ocular drug delivery.

Keywords: Hydrogel, Polymeric network, Mucoadhesive, Bioavailability, Sustained drug delivery.**INTRODUCTION**

Hydrogels are targeted drug delivery systems that have deliberated, the early 1960s. First of all, Wichterle and Lim make notorious to a class of hydrophobic gel, cross-linked hydroxyethyl methacrylate hydrogels, developed for biological intents ^{1,2}. A hydrogel is an innovative class of functional polymer materials with a promising budding in the bio-medical field.

These are cross-linked polymers with hydrophilic sets that aid them to captivate the bulk of water. While hydrogels have abundant compensations in drug distribution as well as biocompatibility, low toxicity and good swelling behavior but reliant on chemical moieties of the gel establishing

polymers and route of administration some limitations would appear in the delivery of active pharmaceutical using hydrogel as dispensing vehicle.

In the biomedical field, the hydrogels network is sheathed in H_2O , the material fascinates the H_2O and accepts fluidic properties, that is similar to tissues in the human body^{3,4}. In the occurrence of H_2O , the surfaces of the hydrogels become watery and acquiescent. These properties duo with the steady group of the material suggestively lessens inflammation to the surrounding tissues and progresses biocompatibility⁵. Moreover, hydrogels will not mark the metabolic processes of existing organisms and metabolites can permit spontaneously over the hydrogels. These are also subtle to minor deviations in outer stimuli, such as temperature,

pH, ionic strength, electric fields, and magnetic fields, and can respond to these stimuli over volume swelling or shrinking⁶⁻¹⁰.

Fig – 1 The sketch map of the hydrogel network

Hydrogels Classification:

Classification may be established on their bases (natural or synthetic), their polymeric arrangements (homopolymer, co-polymer and multi-polymer), physical development (amorphous, semi-crystalline and crystalline hydrogels), cross-linkers (physical and chemical cross-linked), electrical charge (non-ionic, cationic, anionic, amphoteric and zwitterionic) and release mechanism (time-controlled and stimuli-induced).

Double Network Hydrogels:

Double network hydrogels contain two inter probing polymeric systems; which is an abundantly cross-linked firm polymeric network, despite the other is a frivolously cross-linked supple polymer network ¹¹. However, this edifice is linked through physical predicament, not a chemical cross-linking arises between these two jointly impartial cross-linked systems ¹². Hydrogels parade a positive viscous flow paid to the weak cross-linking of the second network, which can successfully captivate the fracture energy over the network distortion and/or the slippage of physical involvements along the polymer chain. Account to better mechanical strength, Double Network hydrogels have several pros over hydrogels with a single network edifice, such as the degree of cross-linking is relaxed to switch and amplified drug inserting bulk ¹³.

Fig – 2 Schematic descriptions of Double Network Hydrogel

Double Network hydrogels were principally collected of covalent bonds, but when covalent networks are diminished by stress, hydrogels become progressively elastic and will enduringly lose their energy ¹⁴. In recent years, a series of Double Network hydrogels have been industrialized that acquaint with noncovalent (e.g., ions or hydrogen bonds) which parade high strength and durability^{15,16}.

Nanocomposite Hydrogels

Hydrogels simulate innate tissue microenvironment owing to their leaky and hydrated molecular structure. An evolving attempt to strengthen polymeric hydrogels and to take in many functionalities efforts on integrating nanoparticles within the hydrogel web. An extensive assortment of nanoparticles, such as carbon-based, polymeric, ceramic, and metallic nanomaterials can be cohesive within the hydrogel systems to acquire nanocomposites with superior properties and

personalized functionality. Nanocomposite hydrogels can be caused to own superior physiochemical, biological and electrical properties.

This identical diffusion of inorganic elements can significantly rally the asset of hydrogels ¹⁷. Nanocomposite hydrogels are correspondingly identified as crossbreed hydrogels, that are designed by physical or chemical covalent cross-linking of the polymer network with raw material particles, together with carbon-based nanoparticles, polymeric nanoparticles, inorganic/ceramic nanoparticles, or metal/metal oxides ^{18–20}.

Fig – 3: Schematic descriptions of Nanocomposite hydrogels

An innovative biodegradable nanoscopic hydrogel was produced by photo cross-linking salt-induced polymer musters ²¹. This process was based on the incorporation of block copolymers comprising polyphosphoester (poly (ethyl ethylene phosphate) (PEEP)), which could endure a salt-induced hydrophobic-to-hydrophilic transition.

A triblock copolymer of poly (ethylene glycol) (PEG) combined with PEEP was produced, and its end groups were then functionalized with acryloyl chloride to produce an acrylate block copolymer (Acr-PEEP-PEG-PEEP-Acr). Successively, a diblock copolymer of PEG and PEEP (Acr-PEEP-PEG-Lac) containing heteroacrylate and lactosyl end functional groups was also produced to have as a feature for pointing moieties into the nanogel ²¹.

Bioadhesive and Mucoadhesive Hydrogel

The principal goal of bioadhesive targeted drug delivery is to focus on a delivery device inside the body to boost the drug fascination process in a site-specific method. Bio adhesion is affected by the

synergistic action of the biological environment, the properties of the polymeric controlled release device, and the presence of the drug itself. The delivery site and the device strategy are stated by the drug's molecular structure and its pharmacological behavior.

Mixtures of hydrogels encompassing hydroxyethyl cellulose, sodium carboxymethyl cellulose, xanthan gum, hyaluronic acid sodium salt, sodium alginate, Carbopol as well as polycarbophil and porcine mucus were analyzed for relative rheological synergism. Hydrogels were considered for their texture and mechanical possessions.

Fig – 4: Schematic descriptions of Nanocomposite hydrogels

Advantages:

- 1) Possess an excessive degree of elasticity similar to ordinary tissues due to its biocompatible, biodegradable and injectable property
- 2) Locally applied & prevent passing first-pass metabolism
- 3) Sustained and prolonged action in comparison to standard drug delivery systems
- 4) A decreased dose of administration.
- 5) Improved drug utilization and patient compliance.
- 6) Drug targeting to a specific site like the colon.
- 7) Protection of mucosa from irritating drugs.
- 8) Drug loss is blocked by broad first-pass metabolism.
- 9) Lowering of daily cost to a patient due to fewer dosage units are mandatory by the patient in therapy.

Disadvantages:

- 1) Hydrogels are high-priced
- 2) The surgical risk allied with the device imbedding and retrieval
- 3) Hydrogels are non-adherent; they may prerequisite to be protected by a secondary dressing
- 4) It used as contact lenses causes lens deposition, hypoxia, dehydration, and red-eye reactions.
- 5) It has low mechanical strength.

Hydrogel Drug Delivery:

Hydrogel drug delivery systems can influence therapeutically beneficial upshots of drug delivery and have come across clinical use. It can offer three-dimensional and sequential switch over the free of therapeutic agents, together with small-molecule drugs, macromolecular drugs, and cells. Owing to their physical properties, convenient degradability and competence to guard labile drugs from degradation, hydrogels assist as a platform in which various physiochemical interactions with the encapsulated drugs control their release. Hydrogels now a day are more attracted because of their controlled as well as the sustained release of drugs. They can release the drugs at suitable and targeted sites.

(a) Wound Healing:

Hydrogels are cross-linked materials and the ability to hold water and drug in them. Due to their water-holding ability, they can hold and retain wound exudates. Gelatine and sodium alginate-based hydrogels when applied can cover and protect the wound from bacterial infection.

(b) Oral route:

Oral route delivery of therapeutics, specifically protein-based pharmaceuticals, is of kin attention for safe and controlled drug delivery for patients. Hydrogels approach first-rate possible as oral therapeutic systems due to integral biocompatibility, diversity of both natural and synthetic material options and tuneable properties. In precise, stimuli-responsive hydrogels make use of physiological changes along the intestinal tract to achieve site-specific, controlled release of protein, peptide and chemotherapeutic molecules for both local and systemic treatment applications.

(c) Gene Delivery

Modification of hydrogel composition leads to effective targeting and delivery of nucleic acids to specific cells for gene therapy.

(d) Ocular Delivery

Conventional dosage forms like eye drops presented a poor therapeutic response and also demand frequent dosing. Hence, Hydrogel dosage deliver the drug to the target site without far loss of drug or without causing any systemic side effects.

(e) Cosmetology

Hydrogels, when instilled into the breast, emphasise them for aesthetic reasons. These implants have silicone elastomer shell and are filled with hydroxyl propyl cellulose polysaccharide gel.

Release mechanisms

- **Diffusion-controlled**

Fick's diffusion theory is used in this type of drug release, for kinetic modeling. The diffusion of a drug from hydrogels could be associated with the porosity and also the tortuosity of hydrogels. It

might be acting as a reservoir or matrix. In reservoir systems, drug molecules are captured and enclosed by polymeric hydrogels and so the release of drug primarily obeys the first law of Fick's diffusion. In matrix systems, drug molecules are equally dispersed in polymeric hydrogels and drug release generally follows the second law of Fick's diffusion.

- **Swelling-controlled**

A swelling-controlled drug release is a zero-order kinetic model. When the rate of diffusion of the drug is faster than the rate of hydrogel swelling, Swelling-controlled drug release could occur. It may have a swelling-induced transition phase from glassy to rubbery state which reasons faster drug diffusion and release from polymeric chains.

- **Chemically-controlled**

In the hydrogel matrix, enzymatic or hydrolytic cleavage of the polymeric network is accountable for drug release. Drug release could be happened by cleavage of polymeric chains through bulk or surface erosion. The polymer chain cleavage is the rate-limiting step of chemically-controlled release systems and drug molecular diffusion has no substantial effect on drug release.

Application of hydrogel

1. Superior biocompatibility
2. Good oxygen permeability
3. Low protein adsorption and cell adhesion
4. Aqueous surface environment to protect cells and therapeutic drugs (peptides, proteins, oligonucleotides, DNA)
5. Negligible frictional irritation within the surrounding tissues upon implantation
6. Soft and tissue-like physical properties
7. Micro-porous structure for additional transport channels
8. Ease of surface modification with specific biomolecules
9. It can be injected in vivo as a solution that gels at body temperature.
10. Soft Contact Lenses
11. Industrial Applicability
12. Tissue Engineering

Table – 1 Hydrogel-based Marketed Products

Brand name	Drug	Dosage form	Use
Dichol	Carbachol	Sterile solution and prefilled syringes	In ophthalmic surgery
Refresh tears	Hydroxypropyl methylcellulose	Eye drops	In dryness of eye and as eye lubricant
Restasis	Cyclosporine	Emulsion	In dry eye
Refresh Classic	Artificial tear fluid	Single use vials	Relieves dry and irritated eyes
Ciplox	Ciprofloxacin	Eye drops	In eye infection and conjunctivitis
Geltear	Carbomer	Bioadhesive gel	As a lubricant, in burning, irritated and dried eye
Timolol xe	Timolol maleate	<i>In-situ</i> gel	For dried eye and Keratoconjunctivitis
Acivir eye	Acyclovir	Ointment	For eye infection
Ocupol	Polymixin-B	Eye drops and ointment	In bacterial infection, corneal ulcer,
Pred Forte	Prednisolone acetate	Suspension	As anti allergic and anti-inflammatory
Chloromycetin	Chloramphenicol palmitate	Ointment	In conjunctivitis and eye inflammation
Betnisol N	Betamethasone	Eye drop	In eye infection
Dexcin	Dexamethasone	Eye drop	In eye infection

The Future Challenges for Hydrogel

Hydrogels are new useful polymer materials suffering rapid development. They have been practical to demonstrate improved degradation and mechanical properties.

- 1) Synthetic methods of preparation of hydrophilic polymers with required functional groups.
- 2) Multifunctional or multi-arm structures including branched or grafted copolymers.
- 3) Accepting of the criticality and the swelling/syneresis behavior of novel anionic or cationic polymers.
- 4) The advance of ultrapure polymers, such as cross-linked free PVA gels produced by freezing-thawing of aqueous solutions.
- 5) Synthesis and characterization of biomimetic hydrogels.

Conclusion:

Hydrogels suggest a flexible stand for the rehabilitation of many diseases counting cancer and diabetes. The water-loving personality of hydrogels and the capacity to shrink and swell reliant on numerous environmental indicators or the mere occurrence of water is smart for drug delivery applications. They have a high degree of permeability and the polymers structure them could be cross-linked to changing degrees by regulating their densities. With a physical structure highly co-operative to amendment in several ways, the hydrogel applications are not just restricted to targeted drug delivery. They also find requests in hygiene products, wound dressings, contact lenses and tissue engineering.

Ethical approval

This review article does not include any animal or human studies done by any of the authors.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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