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COMPREHENSIVE REVIEW ON HYDROGELS FOR CONTROLLED DRUG RELEASE

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ABSTRACT

This review provides a comprehensive overview of the use of polymer gel in drug administration mechanism. In 1891, to their modern practices in reparative drug, towel design, and agriculture. It highlights the part of hydrogels in prolixity controlled, swelling-controlled, and chemically controlled medicine delivery systems. It also explores the use of hydrogels in colorful medicine delivery routes, including subcutaneous, oral, rectal, and topical transdermal administration and provides exemplifications of retailed hydrogel products for medicine delivery.

INTRODUCTION

Novel drug delivery systems (NDDS) are one type of pharmaceutical device that has been the subject of much research and development in recent years. Van n Bemmelen was the first to create the word "hydrogel" in 1884. A type of hydrophobic gel known as cross-linked hydroxyethyl methacrylate (HEMA) hydrogels was first presented by Lim in 1960 and was created for biological purposes [1].

This characteristic is pivotal in the conception of dynamic hydrogel systems that can adjust to varying physiological conditions, paving the way for advanced applications in smart drug delivery systems, adaptive tissue scaffolds, and responsive biomedical devices. The introduction of injectable hydrogels, characterized by their shear thinning and self-healing properties, represents significant progress towards the development of less invasive therapeutic modalities. Recent advancements in nanotechnology have precipitated the emergence of angels , a novel class of hydrogel-based nanomaterials with promising prospects in drug delivery and tissue engineering. In the realm of drug delivery systems, hydrogels encounter limitations pertaining to biocompatibility, safe assembly, and controlled drug release [2]. Hydrogels are the hydrophilic polyelectrolyte polymeric system of three dimensional which are physically or chemically cross-linked structures that absorb considerable quantity of water with tunable biocompatibility, acute environmental sensing, biodegradability, and mechanical properties. The hydrogels can be proposed by the incorporation of natural or synthetic polymers through physical or covalent cross linking. The swelling, softness, elasticity, flexibility, absorbent nature, and capacity to store water are among the crucial characteristics of hydrogels. The hydrophilic functional group connected to polymeric support gives hydrogels. Although the term "hydrogels" indicates that the substance has already swelled in water, another name for dried hydrogels is "Xerogels" [3]. More than other kinds of artificial biomaterials, hydrogels most closely mimic natural living tissue. Great attention in the use of hydrogels in drug delivery applications has been inspired by their distinctive physical characteristic. Because they can stay longer at the delivery site, hydrogels are also utilized as carriers that can interact with mucosa lining of the GI tract, colon, vagina, nose, and other regions of the body [4].

1.CLASSIFICATION OF HYDROGELS

1.1 Based on Source

- Natural source
- Synthetic source
- Semi synthetic source

1.2 Based on Polymeric Composition

- Homo polymeric hydrogels
- Co polymeric hydrogels
- inter penetrating polymeric hydrogel

1.3 Based on structure

- Amorphous
- Semi crystalline
- hydrogen bonded

1.4 Based on Physical Appearance

- Matrix
- Film
- Microsphere

1.5 Based on Type of Cross Linking

- Physical cross linking
- Chemical cross linking

1.6 Based on Network Electrical Charges

- Non-ionic hydrogel
- Ionic hydrogel
- Zitter ionic hydrogel

2.PROPERTIES OF HYDROGEL

2.1Swelling Properties [5].

The hydrogel polymer has chains which are crosslinked to each other either chemically or physically. The slight changes in environmental factors may response rapidly to reversible changes in hydrogel as shown by the followingequation

Percentage swelling =[(Ws-Wd)/Wd] x 100 WereWs is weight of swollen gel and

Wd is weight of dry gel [6].

2.2 mechanical properties

These properties of the hydrogels can vary relying on the purpose of use of the substance. A gel with high rigidity can be obtained by increasing the cross-linkages in it [7].

2.3. biocompatibility

A material's biocompatibility refers to its capacity to function in each application with a favorable host reaction. The hydrogels should be nontoxic and biocompatible, making them particularly useful in biomedical applications [8].

2.4. porosity and permentation

The factors the effect the hydrogel matrix include the interconnections between the pores, the average size of the pore and the distribution of pore size.

- Chemical cross-link concentrations of the polymer strands.
- Physical entanglements present in the polymer strands [9].

2.5. polymers

- Hydrogels are produced from natural and synthetic polymers.
- Natural polymers like chitosan, gelatin, alginates, fibrin [10].
- Synthetic polymers such as vinyl acetate, acrylic acid, methacrylate-vinyl-2-pyrrolidine.

3.CHARACTERIZATION OF HYDROGELS

This section delves into the crucial properties of hydrogels, such as mesh size, swelling behavior, porosity, microstructure, mechanical strength, and degradability. We start by examining why these characteristics are vital for the effectiveness of hydrogel-based drug delivery systems [11].

3.1 Morphological characterization

The morphology of hydrogels includes its shape, form, and structure and it is determined through a stereomicroscope. The texture of the polymers such as starch, can be assessed by the SEM technique [12].

3.2 X-ray diffraction [12].

Xray diff reaction is employed to evaluate the molecular organization and nanoscale structure of an organic hydrogel in its hydrated form. It may also be used to the transition of polymers from their crystalline form to another during the processing.

3.3 Mesh Size and Swelling Behavior [13-14].

The swelling behavior of hydrogels in drug delivery significantly impacts drug re lease and diffusion, making it a crucial factor in their applicationand immerse it in a substantial volume of water or specific buffer solutions for predetermined durations such as 16, 24, or 48 followed by filtration and measurement of the swollen hydrogel's weight (Ws) to determine the degree of swelling using the formula.Q= Ws−Wd Wd The immersion time is critical and varies based on the time to reach swelling equilibrium which presents a limitation due to the difficulty in precisely determining this point. This method directly correlates isotropic swelling behavior with volumetric changes, emphasizing the importance of precise measurement techniques for thickness determination [14].

3.4 FTIR

The IR absorption spectra of the hydrogels changes if there is any alteration in their morphology. These changes in the spectra can be determined by using FTIR. The appearance of bands shows the cross-linking of the polymers.

3.5 Rheology

The viscosity of the hydrogels can be evaluated by the Cone plate viscometer at a constant temperature, i.e., 4°c.

3.6 Measurement of gel content

The gel content can be determined by putting the sample in 200 mesh and washing it three times with distilled water following extraction at 80°C in distilled water for 24 h. The remaining gel was dried [15].

4. MACROSCOPIC DESIGN

Almost any size and shape can be achieved by casting or shaping hydrogels to fit the specifications of the delivery pathway into the human body. Based on their size, hydrogel delivery systems fall into three primary categories: macro-gels, microgels, and nanogels

4.1 Macroscopic hydrogels

Macroscopic hydrogel is often surgically inserted into the body. Clinical application has proven successful, as demonstrated by Infuse, a type I collagen gel that secretes recombinant human bone morphogenetic protein and is surgically inserted into the body to treat long bone fractures and spinal fusions. There are some

categories of delivery routes: (1) Macro-porous gels (2) shear-thinning gels (3) In situ-gelling gels.

4.2 Macro-porous gels

Manufacturing sizable hydrogels with interconnected holes that have the ability to physically collapse and recover reversibly is another method for making injectable hydrogels. Here, hydrogel is injected using a syringe and needle.

4.3Shear thinning Hydrogels

It is possible to pre-gel some hydrogels outside of the body and then inject them by applying shear force. Under shear tension during injection, these hydrogels behave like low-viscosity fluids, but as soon as the shear stress in the body is removed, they rapidly return to their original stiffness [16].

4.4 In Situ-Gelling Hydrogels

These systems can be injected into the body in liquid form, where they go through a Sol-gel transition the in situ antitumor effects of peptide hydrogels loaded with emo din (EM) Before drug administration, these systems are injectable solutions, and at the site of drug administration, in situ hydrogels that are either solid or semi-solid are created. Conditions from the outside, such as light, temperature, or pH, induce this phase shift [17].

5. RELEASE MECHANISM

5.1 Diffusion-controlled drug delivery system

Calculations for controlled-release drug diffusivity are based on ideas related to volume, hydrodynamics, or blockage. Diffusion types are separated into two categories: polymer hydrogel membrane and reservoir system.

5.2 Swelling Controlled delivery system.

The rate of swelling in the swelling-controlled hydrogel is substantially slower than that of drug diffusion.

5.3 Chemically Controlled delivery system.

The release of molecules that is controlled by reactions that take place inside a delivery matrix is referred to as chemically-controlled release. This system is either an erodible system or a suspended chain system, depending on the drug release mechanism [18].

6. HYDROGEL FOR THERAPEUTIC DRUG DELIVERY CURRENT

6.1 Biorthogonal cross-linking methods

for biomedical applications, the use of in situ forming hydrogels is preferred over preformed hydrogels since there is no need for surgical interventions as gelation can take place under physiological conditions upon injection.

6.2 Multicomponent hydrogels.

Early hydrogels were mostly based on a single (co)polymer and often designed to perform only one task. In the past few decades, research shifted increasingly to multicomponent hydrogels that better capture the multifunctional nature of native biological environments, including living tissues [19].

6.3 Stimulus-Responsive Hydrogels

They can swell, shrink, degrade, or exhibit a soul−gel phase transition upon changes in pH, temperature, solvent, pressure, ionic strength, light, and concentration of specific biomolecules such as enzymes [20-23].

7. APPLICATION

Hydrogel applications are widespread in various fi elds, due to their compatibility with different usage conditions and their specific structures.

7.1 Drug delivery in oral cavity

Drug administration to the oral cavity can be very beneficial for the local treatment of oral problems like periodontal disease, stomatitis, fungal and viral infections, and oral cavity cancers.

7.3 Rectal drug Delivery

Rectal administration has several benefits, including regulated release of the substance, minimal adverse responses, quick absorption of the compound, and avoidance of the gastrointestinal tract.

7.4 Ocular drug delivery

Additionally, hydrogels were being injected into the vitreous humor or implanted in the subconjunctival area before being delivered to the back of the eye [24].

7.8 Tissue engineering

In regenerative medicine, tissue engineering (TE) is important. It is divided into three categories: implantation and/or grafting, scaffold and cell/tissue, and. Scaffolds have >80um-sized pores are coupled with ceramics or polymers.

7.9 Biosensing

A biosensor is created by combining chemical and physical sensors. A biosensor is regarded of as a tool that can detect and report biophysical characteristic of system being studied or as a tool that can offer relevant analytical information by changing biochemical dates [25].

7.11 Miscellaneous

Various other applications of hydrogel are Gene delivery, Watering beads for plants, Diapers preparation, Perfume delivery, Plastic surgery, Sealant and adhesive, Water purification, Regenerative medicine, Dyes and heavy metal ion removal, Colon specific hydrogels, etc [26-28].

8. LIMITATIONS OF HYDROGELS

- High cost
- Little mechanical strength
- Challenging to sterilize
- Difficult to load
- In contact lens less deposition hypoxia, dehydration, and red eye reactions.

9. CHALLENGES AND PERSPECTIVES

In the domain of drug delivery, the evolution of hydrogels from traditional chemical-based compositions to advanced supramolecular structures represents a paradigm shift. This transition has been facilitated by significant advancements in material

chemistry and polymer science and complemented by cutting-edge fabrication techniques such as three dimensional (3D) printing and micro fluid The capacity to engineer complex microscale and nanoscale architectures not only augments the versatility of hydrogels but also substantially amplifies their applicability in surmounting intricate delivery challenges [29].

10. FUTURE PERSPECTIVES

This Perspective reflects the tremendous progress that has been achieved in the field of hydrogels for therapeutic delivery in the past 50 years. With improvements in bioinks and additive manufacturing techniques, 3D printed hydrogels increasingly mimic the complex biological and functional organization n of native tissues. Future perspectives focus on stimuli-responsive "smart" hydrogels for targeted, on-demand drug release (pH, temperature, light), personalized therapies, and enhanced biocompatibility for chronic disease management, including cancer and regenerative medicine.

11. CONCLUSION

Hydrogels have emerged as versatile materials with a wide range of applications in drug delivery systems. Their ability to absorb water and transition from a liquid to a gel state makes them ideal for the controlled release of drugs. Additionally, the development of microgels and nanogels for least invasive drug administration further expands the scope of hydrogel applications in drug delivery.

12. AUTHOR CONTRIBUTIONS

All authors are contributed equally.

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The authors have no conflicts of interest to declare.

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16. REFERENCE

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