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HYDROGELS: Classification, Preparation and Biomedical Applications

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Abstract : *Hydrophilic polymeric networks that are able of imbibing hug e volumes of water and witnessing lump and loss suitably to grease controlled medicine- release are called hydrogels. Their porosity and comity with waterless surroundings make them largely seductive biocompatible medicine delivery vehicles. Their operations are multifarious and for several biomedi cal requirements as they're malleable into varied physical fo rms similar as nanoparticles, microparticles, crossbeams, fli cks and coatings Hydrogel products constitute a group of polymeric materials, the hydrophilic structure of which renders them capable of holding large amounts of water in their three-dimensional networks. Extensive employment of these products in a number of industrial and environmental areas of application is considered to be of prime importance. This review summarizes the classification, and preparation methods, technical features ,basic benefit ,limitations and Biomedical Applications of hydrogels.*

Keywords: *hydrogels: classification, preparation. and biomedical applications*

I. INTRODUCTION

Hydrogels are formed by cross-linking polymer chains dispersed in an aqueous medium through a myriad of mechanisms, including physical entanglement, ionic interactions, and chemical cross-linking (1). Hydrogels are network polymeric materials in which the polymer chains are very hydrophilic, such that they can associate with large quantities of water without dissolving. The water can be tightly bound to the polymer network or free to move within the polymer network(2). Hydrogels are three-dimensional hydrophilic polymer networks made up of water-soluble polymers, crosslinked to form a water-insoluble hydrogel. They are able to swell and retain a significant portion of water when placed in an aqueous solution(3.) Hydrogels are waterswollen polymeric materials that maintain a distinct threedimensional structure. They were the first biomaterials designed for use in the human body(4). molt Ydtogel Water Loving 3D Network Polymer) | What is Hydrogel? (Hydrogel Structure | Hydrogel is a cross-linked L0: Polymer polymer network that can sn VA Nan i bed absorb and retain a large se oes ened) amount of water. Y ees , ©) ae 2H \, AS molecules we ON Cs; Ware, VP Key Features ‘ \ id se \ Types © High water absorption Pamir s , 7 a). | | (swelling capacity) << at i YS © Natural a © 3D crosslinked network | > * Ea ml Vie lei be © Biocompatible ‘23 Ee Fo ‘ i bose © Soft and jelly-ike , Le Matbtlies ____ Applications =| Advantages Examples => y © Excellent water absorption | | : © Controlled drug release : Agriculture : : ae ey ee sai || @ sot fl gnc goed eras Fig.1 Hydrogels

Hydrophilic gels that are usually referred to as hydrogels are networks of polymer chains that are sometimes found as colloidal gels in which water is the dispersion medium (5). hydrogels can be divided into two major categories: synthetic hydrogels and supramolecular hydrogels. synthetic hydrogels are formed by permanent chemical cross-links between the polymer chains via nonreversible covalent bonds. and Supramolecular hydrogels, which perfectly combine the advantages of synthetic hydrogels with those of supramolecular polymers(6). Then, the use of hydrogels has extended to various biomedical and pharmaceutical

applications. In comparison to other synthetic biomaterials, hydrogels resemble living tissues closely in their Physical properties because of their relatively high water content and soft and rubbery Consistency(7). Hydrogels play a pivotal role in preserving the rounded morphology and phenotype of chondrocytes or stromal cells while also establishing an

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optimal 3D local microenvironment that fosters interactions among cells and networks(8). Not only water, hydrogels may also absorb a variety of other solvents. This characteristic of hydrogels is because of the existence of hydrophilic groups for instance, -SO3H, -COOH, -OH, -NH2, -CONH2, -CONH, and so on(9). The unique properties of hydrogels have boosted them to the forefront of scientific exploration and industrial application over the past several decades. This interest can also be attributed to the remarkable versatility and adaptability of hydrogels, as well as the relatively straightforward methods available for their preparation(10).

II. STRUCTURE AND CLASSIFICATION OF HYDROGELS

2.1 Based on Origin

Natural hydrogel: Alginate: Derived from brown seaweed, commonly used _ in wound dressings and drug delivery systems(11). Gelatin: Obtained from collagen, used in food, pharmaceutic als, and tissue engineering(12) Synthetic hydrogels: Poly(ethylene glycol) (PEG): Biocompatible and widely used i n drug delivery, tissue engineering, and hydrophilic coatings(13). properties with temperature, useful drug delivery biosensor s(14).

2.2 Based on Crosslinking

Physical hydrogels: Physical crosslinking is a reversible reaction that occurs due to intermolecular interactions such as hydrogen boinding ionic/electrostatic interaction, polymeric chain entanglement, hydrophobic interactions, mTt stacking, self-assembly, crystallization/stereo-complex formation, and metal coordination(15). Chemical hydrogels: Chemical crosslinking is an irreversible process. The reaction between the crosslinker and polymer solution leads to the covalent bonds, resulting in 3D network formation, which is called chemically or permanently crosslinked hydrogels(16). 2.3SmartHydrogel pHResponsive Hydrogels: Such as poly(acrylic acid), which swell or shrink based on pH changes, useful in controlled dr ug release(17). Electroactive Hydrogels: These hydrogels can change shape in response to electrical stimuli, used in actuators and soft r obotics(18).

III. METHODS OF HYDROGEL PREPARATION

In general, hydrogels can be prepared from either synthetic polymers or natural polymers. The synthetic polymers are hydrophobic in nature and chemically stronger compared to natural polymers. Their mechanical strength results in slow degradation rate, but on the other hand, mechanical strength provides the durability as well. These two opposite properties should be balanced through optimal design(19).Also, it can be applied to preparation of hydrogels based on natural polymers provided that these polymers have suitable functional groups or have been functionalized with radically polymerizable groups(20). 4.Hydrogel technical features The functional features of an ideal hydrogel material can be listed as follows (21):

e The highest absorption capacity (maximum equilibrium swelling) in saline.
e Desired rate of absorption (preferred particle size and porosity) depending on the application requirement
e . The highest absorbency under load (AUL).
e The lowest soluble content and residual monomer.
e The lowest price.
e The highest durability and stability in the swelling environment and during the storage.
¢ The highest biodegradability without formation of toxic species following the degradation.
e pH-neutrality after swelling in water.
e Colorlessness, odorlessness, and absolute non-toxic.
e Photo stability.

ees Hydrogel reais —(Systematic Diagram) 1, Selection of Materials 2 Preparainn of Pome Sotuon Polymer Solution 3. Addition of Crosslinker —s (or Other Components)

@ Pe | * Dissolve polymer & f a eS 4 _insvitable solvent + Add croslnker — ’ ih contin (Dae es Cart n | « Heat gently if aneene) f) auc + Adjust

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+ Crossinker (eg. Glutaraldehyde, 2 - necessary. CaCl) —= + Sohent (Nts) ter aes 4, Gelation / Crosslinking | 7. Final Hydrogel ~ — = | «Allow the minture to undergo Eine lines | + Drythe hyo by + Obtain the prepared | gelation (room temperature + Ueda varersiate| | freeze-drying, oven drying hydrogel for further ‘or mild heating). heal (orair drying). use and evaluation. Fig no 2. Hydrogel Preparation

V. GENERAL BENEFITS OF HYDROGELS

The general benefits of an ideal hydrogel material can be listed as follows (22):
e Biocompatible
e Can be injected in vivo (in a whole, living organism) as a liquid
e that then gels at body temperature
e Protect cells
e Good transport properties (such as nutrients to cells or cell
e products from cells)
e Timed release of medicines or nutrients
e Easy to modify
e Can be biodegradable or bioabsorbable.
6.General limitations of hydrogels The general limitation of an ideal hydrogel material can be listed as follows (23):
e High cost
e Low mechanical strength
¢ Can be hard to handle
¢ Difficult to load with drugs/nutrients
e May be difficult to sterilize
e Non-adherent.
e Hydrogel technical feat

VI. BIOMEDICAL APPLICATIONS

Drug Delivery

Drug delivery is a prominent application of pH responsive polymers, leveraging their ability to react to environmental pH changes to control the release of therapeutic agents. This strategy takes advantage of the polymers’ reversible structural transitions under different pH conditions, enabling precise modulation of drug release profiles(24).

Wound Healing

These stages involve the commerce of colorful cell types an d matrix factors, including hemostasis, inflammation, prolife ration, and redoing, as illustrated In the hemostasis stage, pl atelets aggregate around damaged blood vessel walls to pro duce a platelet draw, while fibrin forms a blood clot at the cr ack point(25).

Hydrogel sensors and Actuators

Hydrogel sensors can be classified into two types according to hydrogels’ functions in the sensors: (a) stimuli-responsive hydrogels as sensors that can exhibit volume and/or phase changes according to environmental inputs(26). and (b) passive hydrogels as matrices to host responsive substances (e.g., free ions, nanoparticles, biomolecules, and living cells) that respond to environmental inputs(27).

Other Applications

This part describes hydrogels’ applications from various research groups and discusses their practical issues. Hydrogels that can sense various external stimuli have been presented Sensing, Array networks, fluid control and drug delivery , Artificial muscles and nerve regeneration.(28)

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VII. CHALLENGES AND FUTURE PERSPECTIVES, RESEARCH

Many techniques have been used to design porous scaffold architecture. All porosity mentioned fabrication techniques are used to prepare scaffolds of hydrogels, ceramics, and polymers for biomaterials applications. These created porous scaffolds show more suitable mechanical properties than scaffolds processed using other methods(29).Designers of these scaffolds have achieved better bone regeneration compared with other scaffolds, because of their excellent interconnected porosity(30).

MECHANICAL CONSIDERATION FOR DESIGNING INJECTABLE HYDROGELS

Appearance of Term Relating to Injectable Hydrogels in Scientific Literature K <225=) Injectable Hydrogel (Ge forms tie stent) ed rat (Gelation by temperature) A ma Injectable 1 Injectable Biomaterial pH-Responsive

2 fae) laa f (Gelaton by pH change)

<7 Sok-Gel Transition y 4 2 Shear-Thinning Sef (Soltion to gel | wy LF Injectable Hydroget ‘pon stil) F “NF Flow under shear, CES Applications H = o Sato coe H K : & fay, : & 1 Se 7 ' ey : .

‘Tissue Engineering | ing ' ControlledDrg ' {Neural Ti aa | sell ee sigalg,

Hydrogels are a broad class of materials that exhibit mechanical and chemical properties that are especially useful for a variety of medical Appearance of term relating to injectable hydrogels in scientific literature in a given diagram. interventions. (23) Noninjectable hydrogels represent the bulk of the literature as they were the first to be discovered and developed, and their usefulness for both drug and cell delivery led to broad enthusiasm for developing hydrogels for biomedical applications(24). Hydrogel design parameters Designing hydrogels with specific characteristics and functions is a complex task that requires meticulous manipulation of various factors. For cartilage regeneration (CR), the primary focus should be on selecting the appropriate hydrogel components, as the material composition directly influences the hydrogel’s properties and performance. The mechanical properties of the hydrogel scaffold must align with the target tissue to ensure proper support and functionality.(25) Hydrogels as Cancer Vaccines Delivery of more ambitious combination therapy using injectable hydrogels has led to increasingly sophisticated and complex treatment regimens. Among the more comprehensive strategies has been to use hydrogels to deliver cancer vaccines, generally multicomponent therapies designed to kick-start de novo and durable immune responses by providing the key elements of antigen (sometimes preloaded into adoptive APCs) and one or more adjuvants.(26) In this context, adjuvants are drugs that provide essential danger signals to the innate cells of the immune system (we have already discussed several adjuvants,including CpG and STING agonists). Cancer vaccines generally fall into two categories, those that mount a response to exogenous antigen and those that mount responses toendogenous antigen.(27

6. Challenges and Future Perspectives

Challenges in hydrogel development include designing scaffolds with suitable mechanical properties, and balancing mechanical strength with a slow degradation rate. Future research is focused on:

* Development of multifunctional injectable hydrogels combining cell delivery, on-demand drug release, and in situ sensing.
* Utilizing Bio-orthogonal click chemistries for safer in vivo crosslinking.
* Implementing Machine-learning-driven design to predict network properties.
* Developing Sustainable hydrogels from renewable monomers and Green synthesis techniques.
* Advancements in Personalized medicine applications.

Hydrogels are a versatile platform with a promising future in regenerative medicine and broad industrial application.

VIII. LITERATURE SURVEY

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e Desired rate of absorption (preferred particle size and porosity) depending on the application requirement
e . The highest absorbency under load (AUL).
¢ The lowest soluble content and residual monomer.
e The lowest price.

IX. CONCLUSION

Novel hydrogel systems have been devised in current years. In terms of application, hydrogels are under research as matrices for the living cells encapsulation and for the pharmaceutically active proteins controlled release. Hydrogels are an essential tool for regenerative drug and biomedical engineering; their operations have been and are still being tested in utmost org an systems due to the promising results formerly attained. T hese biomaterials are so extensively studied that their parcels include water immersion, biocompatibility, and the capabil ity to mimic native towel for cell proliferation and isolation.

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