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HYDROGEL – A COMPHREHENSIVE REVIEW

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ABSTRACT

A hydrogel is a water-insoluble three- dimensional polymers network that has the ability to absorb body fluids in a biological environment. Hydrogels are soft cross-linked polymeric materials that can store drug, and biomolecules for hydration and therapeutic applications. Hydrogels have been settled in pharmaceutical applications and become very popular due to their high-water content, soft consistency, flexibility and bioavailability. Hydrogel formulation were white, viscous creamy preparation with glossy texture. Natural and synthetic hydrophilic polymers can be cross-linked and modified in physical or chemical manner to obtain hydrogel. A properly cross-linked hydrogel can be converted by body to less toxic or non-toxic intermediate. The well -shaped hydrogels exhibited remarkable wet-tissue adhesion, suitable swelling and mechanical properties, sustained probiotic release and excellent storage durability.[1]

KEYWORDS: Hydrogel, Micro emulsion, Polymers, Tropical application.

INTRODUCTION

Many scientific research has been done in the field of biomaterials that play a vital role in human health. Hydrogels are polymeric network that holds water in their three -dimensional structure. They are not soluble in water and show flexibility similar to natural tissues. They are stable in sharp and strong fluctuation in temperature. Hydrophilic gels that are usually referred to as network of polymer chains that are sometime found as colloidal gels in which water is the dispersion medium. Natural hydrogels were gradually replaced by synthetic types due to their higher water absorption capacity, long service life and wide variety of raw chemical resources. They are providing better benefits in drug therapies and thus involved in various applications. This review article deals with classification, general methods and a view with their applications.[1,15]

Classification[15,16]

According to polymeric composition

- Homo polymeric hydrogels - have cross-linked skeletal structure according to nature of monomer and polymerization technique.
- Copolymeric hydrogels- comprised of two or more different monomeric species
- Multipolymer Interpenetrating polymeric hydrogel (IPN)- It is made up of two independent cross- linked synthetic / natural polymer compound.

Based on configuration

- Amorphous (Non-crystalline)
- Semi crystalline: a complex mixture of amorphous and crystalline phases.
- Crystalline

Based on type of cross- linking

- Chemically cross- linked network: Have permanent junctions
- Physically cross-linked network: Have transient junctions

Based on physical appearance

- Matrix
- Film
- Microsphere

Based on network electric charge

- Non-ionic (Neutral)
- Ionic (Cation/anion)
- Amphoteric electrolyte (Ampholytic)-contains both acidic and basic group
- Zwitterionic (Polybetaines)-contains both anionic and cationic groups in each structure

Methods or technologies adopted in hydrogel preparation[9,16,17,1]

Bulk polymerization

Many vinyl monomers are used in this method. Bulk hydrogels are formed with one or more monomers. Small amount of cross-linking agent is added. The polymerization is normally initiated with radiation, ultraviolet or chemical catalyst. It is notable that it is a simplest technique which involves only monomer or monomer soluble initiators. As the concentration of monomer increases, the degree of polymerization also increases. This method usually

produces a transparent, glassy polymer matrix which is very hard. But when it is immersed in water, it swells to become soft and flexible.

Solution polymerization/ cross linking

In this method, the ionic or neutral monomers are mixed with the multi- functional cross-linking agent. The method is initiated by redox initiator or UV-irradiation. The prepared hydrogel is washed with distilled water to remove monomer, cross-linking agent, the initiator or other impurities. Advantage: The presence of solvent serving as a heat sink Disadvantage: If the water amount exceeds the actual limit to get equilibrium swelling then phase separation occurs. Water, ethanol, benzyl alcohol, water-ethanol mix can be used as a solvent. These solvents can be removed after formation of gel by swelling hydrogel in water.

Suspension polymerization

Since water-in-oil (w/o) process is chosen instead of oil-in-water (o/w) the polymerization is referred to as inverse suspension. The monomers and initiator are dispersed in hydrocarbon phase. This dispersion results in homogenous mixture. Dispersion polymerization often results in product as powder or microsphere (beads) so no grinding is required.

Grafting to a support

This technique involves generation of free radicals onto a stronger support surface. Here the monomers are directly added onto the supporting material surface. This occurs due to result of covalent bond between chain of monomers and the support. This method improves the mechanical properties of hydrogel since it can be grafted on surface coated on to a stronger support.

Polymerization by irradiation

Ionizing high energy radiation like gamma rays and electron beams are used as initiators to prepare hydrogels. The irradiation taking place on polymeric solution results in the formation of radicals on the polymeric chains first and usually the radiolysis of water molecules results in the formation of hydroxyl radicals. These hydroxyl radicals also attack the polymeric chains which further results in the formation of macro-radicals. The recombination of macro-radicals on different chains helps in the formation of covalent bonds directly. Due to this phenomenon the cross-linked structure is formed. By this method we can obtain relatively pure and initiator-free hydrogels. The examples of polymers cross-linked by this method are polyvinyl alcohol, poly ethylene glycol and polyacrylic acid.

Microemulsion- based hydrogel

Drug was added to the mixture of oil, surfactant and cosurfactant with varying component ratio. Then appropriate amount of water was added drop by drop with stirring at ambient temperature. Xanthium gum was selected as the gel matrix which is slowly mixed with micro emulsion.

Sprayable hydrogel

Placebo hydrogels were prepared by addition of CMC to dispersant (high purified water or phosphate buffered saline PBS pH 7.4) under stirring. The mixture was heated and got steam sterilized.

Hydrogel formation by enzymatic route

Gel, PVA, and mTGase solutions were prepared individually, the solution of mTGase was prepared by dissolving the enzyme in distilled water and the polymer blend (gel and PVA) solutions were prepared in a weight-polymer ratio of 1:1 under mechanical stirring until homogeneous suspensions were obtained. Hydrogels were formed by adding amounts of mTGase solution into the gel-PVA blend. This mixture was then poured into molds of a cylinder like shape. The molds were incubated subsequently the enzyme was inactivated. Then the polymer samples were cooled down, kept overnight, frozen before lyophilization.

Technical feature of hydrogel

- Highest absorption capacity in saline.
- Preferred rate of absorption and highest bio degradability.
- The top most absorbency under load (AUL).
- The lowest price.
- The utmost robustness and steadiness in the swelling environment as well as during storage.
- pH- neutrality after swelling in water
- Colourless, odourless and non-toxic.
- Photostability

Advantages

- Methotrexate a most frequently used DMARD due to its high functionality on joints in RA patients. But it is highly toxic to normal body cells orally/parenterally. It slows down RA auto immune damage meanwhile it weakens body immune system. Targeted local

delivery of hydrogels can overcome these problems and even improve its low bio-compatibility after oral administration.[21]

- Studies have shown that injectable hydrogels and transdermal hydrogels are the two major types suitable for RA treatment.[18]
- Hydrogels offer many advantages which included providing a moist environment to the wound area and it also acts as an excellent carrier for the topical application.[19]
- Tacrolimus composite hydrogel was designed to have superior pharmaceutical formulation properties delivery efficiency and local bio-availability compared to currently available paraffin-based TAC ointments.[11]
- Water-based hydrogel have in addition the advantage of rapid evaporation with minimal formulation residue at application site.[12]
- More over chemically modified hydrogel formulation provides elastic nature of swollen and after being applied they show non-irritation to the surrounding tissue.[15]
- Chitosan is a suitable polymer for the intelligent delivery of macromolecular compounds. By modification of chitosan with thiol groups, muco- adhesion and controlled drug delivery release is achieved.[3]
- The proteinaceous cowpea mosaic virus (CPMV) nanoparticles are rapidly degraded in-vivo. For this, CPMV nanoparticle in injectable hydrogel formulation was prepared to achieve slow particle release and prolonged immune stimulation.[5]
- The studies also shown that the formulation containing high molecular weight chitosan and 0-4.5 mg CPMV gelled rapidly and slowly released for several months with conserved immunotherapeutic efficiency.[5]
- Bio active hydrogels show superior therapeutic capability for promoting ulcer healing in vivo by enhancing cell migration, inducing epithelial formation and orderly collagen fibre deposition as well as facilitating neovascularization.[12]
- Hydrogel sunscreen show high SPF value and UV protection both in-vivo and in-vitro.[17]
- Hydrogels can influence cell behaviour by mimicking the extravascular matrix and they can influence the cell behaviour and its biochemical and biophysical processes.[7]
- Hydrogels are biocompatible, can be injected, easy to modify, have good transport properties.[7]
- Timed release of growth factors and other nutrients to ensure proper tissue growth.[5]
- Hydrogels possess a degree of flexibility very similar to natural tissue, due to their significant water content.[4]

- Environmentally sensitive hydrogels have the ability to sense changes in Ph, temperature, or the concentration of metabolite and release their load as result of such a change.[7]
- Entrapment of microbial cells within hydrogel beads has the advantage of low toxicity.[16]
- A sprayable hydrogel allows a cutaneous application with minimal risk of contamination.[18]
- A properly cross-linked hydrogel can be converted by body to less toxic or non-toxic intermediate.[14]
- Recently different hydrogel matrices such as carbomer 940, xanthium gum and carrageenan have been used to increase the viscosity of microemulsion.[7]

Applications

Osteoporosis: The aceclofenac hydrogel for topical preparation was prepared by using guar gum and Carbopol 940. The formulated gels showed good homogeneity, good stability and better drug release rate. It was concluded that developed formulations deliver the drug for the treatment of osteoporosis.[9]

Rheumatoid arthritis: Hydrogel lubricate the articulating joint surfaces to prevent degradation of synovial surfaces of bones and cartilage. The BPN/chitosan/PRP thermos-responsive hydrogel has shown significant potential for RA treatment through anti-inflammatory and osteogenesis mechanisms. Due to softness and elasticity, hydrogel act as an excellent mechanical cushion for the mechanical support of joints and bone. They reduce the friction between the internal lining of joints and protect the joints comprehensively.[21]

Wound healing: Anti-oxidant activity of n-hexane hydrogel of Moringa oleifera seeds showed the highest scavenging at the concentration of 160 microgram /ml. It possesses both gram positive and gram-negative bactericidal potential thus can be used as therapy to treat wound infections.[17,18,19]

Psoriasis: Nano carriers contain a high payload for hydrophobic tacrolimus (TAC), a potent immunosuppressive drug and currently approved for atopic dermatitis. Water based hydrogel have in addition the advantage of rapid evaporation with minimal formulation residue at application site. TAC hydrogel composite formulation delivers higher drug doses into the skin, compared to a conventional ointment formulation.[3]

Dental application: Fibroblast growth factor-2 (FGF-2) which is normally stored in the extra cellular matrix, plays a role in physiologic conditions such as enamel and dentin formation of the tooth gum as well as pathologic condition.[19]

Hydrogels as soft contact lenses: The most used polymer exploited to produce soft-lenses is silicone, which is five times safer and more over it possess good permeability to oxygen. The silicone hydrogel lenses can be designed to release ophthalmic drugs for an extended period of time varying from 10 days to a few months**.**[8,10,16]

Drug delivery application: Hydrogels and smart hydrogels can be a very interesting solution in reaching a sustained and targeted release of pharmaceuticals, both increasing the effect of drug itself and lowering side effects at the same time.[7]

Cardiac applications: Hydrogels have also been shown to improve cell retention when co-injected for cellular cardio myoblasts and to prolong release of therapeutics when used as a delivery vehicle. Thereby hydrogels alone or in conjunction with cells or therapeutics can be insist for cardiac repair.[11]

Bone regeneration: Alginate hydrogel has been used as a tool for producing bone and cartilage tissues. It is a naturally occurring polymer found in kelp sea weed that is commonly used in gel formation.[19,18]

Tissue engineering: Hydrogel acts as a natural extra-cellular matrix that subsequently promotes cell proliferation and tissue re-growth. The pseudo-extra-cellular matrix, comprised of growth factors, metabolites and other materials, brings cell together and controls tissue structure with the ultimate goals of the natural tissue that was lost or damaged.[15,12]

Electrophoresis: Gel electrophoresis currently represents one of the most standard techniques for protein separation. Polyacrylamide cross-linked hydrogels, acrylamide agarose copolymers have been proposed as promising system for separation matrices in 2D electrophoresis.[5]

Bacterial culture: Hydrogels can hold inside the matrix a significant number of micro-organisms for purification of water, for production of biomolecules or for simple culture of bacteria. Agar is famous as the golden standard substrate for bacterial culture in biotechnology application.[14]

Immunotherapy and Vaccine: A nano-vector composed of peptide-based nanofibrous hydrogel can condense DNA to result in strong immune responses against HIV. Supra molecular hydrogel is composed of nanofibers formed by self-assembly of small molecules. They can rapidly respond to pH, temperature, ionic concentration or addition of enzymes. They show a good biosafety and dramatically improve the immune responses due to their high efficacy to condense DNA, promote DNA efficiency transfection and enhance gene expression in-vitro.[5]

Plastic surgery: Promising use of hydrogels is bulking agents for treatment of urinary incontinence. Smart injectable gels can be involved in clinical procedures where these materials can be used to tighten the urethral channel and reduce patient`s incontinence.[19,11]

Cosmetics: Pecogel by phoenics chemical in.is a wide selection of hydrogel and are suitable for cosmetic purposes such as sunscreen cream or mascara.[6]

Perfume delivery: Used to develop devices capable of slowly dispense fragrances to the surrounding.[6]

Domestic use: The production of super-adsorbent diapers with the property of being dry even after a considerable adsorption of fluids.[11,19]

Dressings for burn wounds: Hydrogel dressings can absorb wound exudate, the amount of water absorbed by a hydrogel is 100 times its dry weight. Maintain the moist environment. Hydrogel dressing can be customized into any shape hydrophilicity, good compatibility and suitable pore structure can meet the demand in burn wound healing process. They can improve the healing rate of burn wounds, accelerate fibroblast proliferation wound Epithelization.[11,12,18,19]

Agriculture: Hydrogels increase the water holding capacity of soil and increases permeability and enhance infiltration rates. They decrease the irrigation frequency and the fertilizer leaching. They reduce the compaction tendency of soil and soil erosion, water run-off and thus they reduce the water stress of plants. Most of the hydrogels marketed for agriculture come from cross-linked acrylamides and acrylamide-acrylate copolymers, as they remain active for much time. Rough powders of polyacrylamide used as long- term reservoir of water for plant growth in gardening.[7]

Sunscreen: The development of novel hydrogel sunscreen based on the yeast and gelatin demonstrated the excellent uv- protection property, biocompatibility, high fluidity and ROS scavenging capacity.[2]

CONCLUSION

Hydrogels are a family of bio-inspired, bio-mimetic and bio-functional materials with crosslinked hydrophilic networks and high-water contents. In the present review article, the classification, methods, advantages and application of hydrogels were discussed. Hydrogels are considered to be an attractive biomaterial for various medical applications due to their special technical features and their structural similarity to ECM.

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