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Hydrogels: Classification, Preparation Methods, Characterization, and Biomedical Applications - A Comprehensive Review

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Abstract - This review highlights the fundamental aspects of hydrogels, including their classification, materials used in preparation, crosslinking mechanisms, and various fabrication techniques such as solvent casting, freeze-thaw, chemical crosslinking, and radiation-induced methods. The article also discusses important evaluation parameters including pH, viscosity, spreadability, tensile strength, rheological behavior, drug content, in vitro drug release, stability studies, and cytotoxicity assessment. Furthermore, the growing applications of hydrogels in drug delivery systems, wound healing, tissue engineering, and controlled therapeutic release are summarized. Owing to their versatility and ability to mimic biological tissues, hydrogels continue to emerge as promising biomaterials for advanced healthcare applications. Future developments in polymer design and crosslinking strategies are expected to further enhance their clinical and pharmaceutical potential.

Keywords : Hydrogel, Crosslinking, Drug Delivery System, Tissue Engineering, Wound Healing, Biomedical Applications, Polymer Networks.

INTRODUCTION:

Extensive scientific investigation has been conducted in the area of biomaterials that contribute to human health. This article focuses on hydrogels, a significant subject within biomaterials research. Hydrogels consist of three-dimensional polymer networks that are not soluble in water and can retain substantial quantities of water or biological fluids due to hydrophilic groups found within their structure. The main polymer chains of hydrogels contain various hydrophilic functional groups such as hydroxyl (OH-), carboxyl (COOH-), amine (NH2), and sulfate (SO3H). Polymeric hydrogels can be produced through either physical crosslinking, chemical crosslinking, or a combination of both methods.(1) The rheological approach can also be used to investigate hydrogels. "Newtonian" behavior is typically seen in solutions of water-soluble polymers at low or intermediate concentrations where there is little to no chain tangling. Additionally, networks formed by adding cross-links between polymeric chains exhibit viscoelastic and occasionally completely elastic behavior. Because of their capacity to absorb water, hydrogels are being studied to investigate the principles of swollen polymer networks. They are also widely used in a variety of technical fields, including contact lens and protein separation materials, cell encapsulation dies, and devices for the controlled release of medications and proteins.(2)

HYDROGELS:

Cross-linked polymeric polymers known as "hydrogels" have proved important in a number of disciplines. When Wichterle and Lim created the first synthetic hydrogels in 1954, hydrogel gained notoriety. A significant amount of water and biological fluids can be retained in the swelled condition by hydrogels, which are three-dimensional (3D), insoluble, crosslinked, and tissue-like networks of polymers. The expansion of polymeric chain networks is caused by the counterbalanced capillary,

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osmotic, and hydration forces that interact with water or biological fluids. The degree of these opposing effects defines the hydrogel's equilibrium state and some of its intrinsic qualities, such as internal transport, diffusion properties, and mechanical strength.[3]

TYPES OF HYDROGEL:

Hydrogels can be classified as natural or synthetic based on the type of polymer they include. Natural or synthetic polymers that have been hydrogenated are regarded as raw materials for use in medicine. Hydrogels must be made of both natural and synthetic polymers that are biocompatible, biodegradable, and blood compatible in some situations where the hydrogel comes into contact with blood. [4] Hydrogels fall into a variety of categories. Nonetheless, because the hydrogels are essentially made of networks of cross-linking, they are divided into two groups according to cross-linking: (a) chemically cross-linked hydrogel and
(b) physically cross-linked or self-assembled hydrogel. Different kinds of physical and chemical hydrogels are made.[5]

NATURAL HYDROGELS:

Gels using polymers derived from natural sources are known as natural hydrogels. Benefits of using natural polymers to create hydrogels include non-toxicity, biocompatibility, and biodegradability. The goal of using biomaterials determines whether natural polymers are used to make hydrogels. For instance, hydrogels utilized for products with controlled release need to be informal, biocompatible, and biodegradable . Polysaccharides and associated proteins, which are frequently employed as transporters for the release of chemicals, are examples of natural polymers. These polymers' biocompatibility was demonstrated by in-body testing; of these, polysaccharides are more appropriate because of their biocompatibility, enzymatic breakdown, high durability, and non-toxicity.[4]

SYNTHETIC HYDROGELS:

Synthetic polymers like polyamides and polyethylene glycol (PEG) are used to create synthetic hydrogels. In hydrogel manufacturing, synthetic polymers have recently replaced natural polymers because of their longer lifespan, higher water absorption capacity, and gel strength. Hydrogels are made from synthetic polymers and have a number of medical uses. The mechanical structure and chemical composition of synthetic polymers are superior to those of natural polymers, and they are hydrophobic. These polymers include PEG, polyvinyl alcohol, and polyacrylamide and its derivatives. One of the most widely utilized polymers for synthetic hydrogenation in a variety of medical applications, including tissue engineering, medication release, bone prostheses, and wound dressings, is PEG.[4]

PHYSICAL CROSSLINKING:

Physically crosslinked hydrogels are often made from multiblock or graft copolymers. The latter can consist of a water-soluble polymer backbone, such as a polysaccharide, to which hydrophobic units are connected, or hydrophobic chains with water-soluble grafts. Other documented methods for crosslinking include hydrogen bonding, suspension polymerization, irradiation chemical reaction of similar groups, and protein crosslinking, but all need the application of a crosslinking agent, which is frequently toxic and raises questions about gel durability. For these reasons, physically crosslinked hydrogels, which can be generated using numerous crosslinking processes such as ionic interaction crystallization, hydrogen bonding, protein contact, and hydrophobic interaction.[6]

CHEMICAL CROSSLINKING:

Chemically cross-linked hydrogels have gained popularity in recent years due of their high mechanical strength.[7] Chemical crosslinking of hydrogels involves the formation of covalent bonds between polymer chains, creating a stable three-dimensional network capable of retaining large amounts of water. This process typically occurs through reactions such as free-radical polymerization, click chemistry, condensation reactions, or the use of multifunctional crosslinking agents (e.g., glutaraldehyde, genipin, or diacrylates). Chemical crosslinking provides hydrogels with enhanced mechanical strength, structural stability, and resistance to dissolution compared with physically crosslinked systems. The crosslink density can be precisely controlled to tune key properties including swelling behavior, porosity, degradation rate, and mechanical stiffness. As a result, chemically crosslinked hydrogels are widely employed in applications such as drug delivery systems, tissue engineering scaffolds, wound dressings, and biosensors, where long-term stability and predictable performance are required.

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MATERIALS :

Hydrogel are prepared from natural and synthetic polymers. Common natural polymers include chitosan, gelatin, alginate, hyaluronic acid, and fibrin. These materials are often combined with synthetic monomers or polymers to enhance mechanical strength, stability, and functional properties. Some commonly used synthetic monomers include hydroxyethyl methacrylate (HEMA), vinyl acetate (VAc), acrylic acid (AA), N-(2-hydroxypropyl) methacrylate (HPMA), N-vinyl-2-pyrrolidone (NVP), and N-isopropylacrylamide (NIPAM). For example, chitosan can be combined with HEMA or NIPAM, gelatin can be used with vinyl acetate, alginate with acrylic acid, and hyaluronic acid with HPMA to form composite polymer systems with improved performance for applications such as drug delivery, tissue engineering, and hydrogel formation.[8]

METHODS OF PREPARATION:

1. SOLVENT CASTING METHOD:

The solvent casting method is one of the most widely used techniques for preparing hydrogel films and membranes. In this method, polymers are dissolved in a suitable solvent to form a homogeneous solution, followed by casting and solvent evaporation to obtain a hydrogel matrix.The solvent casting technique is based on the dissolution of hydrophilic polymers in a solvent, followed by crosslinking and controlled solvent evaporation. As the solvent evaporates, the polymer chains interact and form a three-dimensional network structure, resulting in hydrogel formation.

2. FREEZE-THAW METHOD:

Polymers are dissolved in distilled water to create a homogenous solution using the freeze-thaw process. After being put into molds, the solution is repeatedly frozen and thawed. While thawing stabilizes the hydrogel network, freezing causes ice crystals to form and encourage physical crosslinking between polymer strands. A stable hydrogel with good elasticity and water absorption capacity is produced after a number of cycles.

3. CHEMICAL CROSSLINKING METHOD:

The chemical crosslinking method involves dissolving polymers in a suitable solvent and then adding a chemical crosslinking agent, like genipin or glutaraldehyde. The slurry is placed into molds for gel formation after being constantly agitated to guarantee even crosslinking. After a thorough washing to get rid of any unreacted chemicals, the hydrogel is either dried or kept in an appropriate environment for later usage.

4. RADIATION INDUCED METHOD:

To create a homogenous solution for radiation-induced hydrogel synthesis, a polymer such PVA, chitosan, or gelatin is first dissolved in distilled water. After that, the mixture is transferred onto a mold or petri dish, and nitrogen purging can be used to eliminate oxygen. The polymer solution is then subjected to UV, gamma, or electron beam radiation, which produces free radicals that cause polymer chains to crosslink and create a three-dimensional hydrogel network. The resulting hydrogel is then dried for additional analysis and use after being cleaned with distilled water to get rid of any unreacted components.

EVALUATION OF HYDROGEL:

1. Appearance, feel, color, and smell:

Organoleptic qualities are often evaluated subjectively. While variations in appearance can provide important details about a product during its shelf life, changes in color and odor can be signs of oxidation in gels. The prepared gel was put to cellophane, and its color, clog presence, and feel were all visually examined.[9]

2. pH determination:

A digital pH meter was used to measure the hydrogel compositions' pH. After dissolving one gram of gel in twenty-five milliliters of distilled water, the electrode was submerged in the gel formulation for thirty minutes until a consistent reading was achieved. After that, continuous reading was observed. Each formulation's pH was measured three times, and average values were determined.[10]

3. Viscosity

The Brookfield digital viscometer was used to measure the produced hydrogel's viscosity. Spindle number six was used

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to measure the viscosity at 250C and 10 rpm. A suitable wide-mouth container was filled with an adequate amount of gel. The wide-mouth container was filled with hydrogel so that the viscometer's spindle could be suitably dipped. Before the measurements, hydrogel samples were let to settle for 30 minutes at a constant temperature of 25 ±/10C.[11]

4. Coefficient of Spreading:

Spreadability research was conducted using a laboratory setup that had been appropriately adapted. The device consisted of a glass slide with a pan fixed to a pulley and a wooden block with scale. The excess formulation was sandwiched between the smooth polish board and the glass slide. To compress the mixture to a consistent thickness, a 100g weight was applied on the upper glass slide for five minutes. The pan was filled with weight (100 g). Spreadability was measured by the number of seconds needed to separate the slides. The following formula was used to determine the spreadability: S is equal to (m × l)/t where l is the length of the glass slide, t is time, m is weight attached to the top slides, and S is spreadability.[12]

5. Tensile strength:

Properties of tensile strength Sufficient mechanical strength to replicate the mechanical properties of skin tissue is one of the most important aspects of skin structure in tissue engineering.[13] hydrogels were evaluated for tensile strength in order to ascertain their mechanical stability and elasticity under applied stress. Using a universal testing equipment, hydrogel samples were put through tensile testing at a steady stretching rate until they broke. The stress-strain curve was used to record parameters like Young's modulus, elongation at break, and tensile strength. The findings shed light on the hydrogel's adaptability, robustness, and appropriateness for pharmaceutical and biological uses.

6. Invitro drug release test:

Using USP apparatus I (AT8XTEND, rotating basket, Sotax, Switzerland), the drug release test was carried out at a temperature of 37.0 ± 0.5 ◦C and a rotation rate of 100 rpm. Phosphate buffer (pH 7.4, 900 ml) that had been filtered and degassed was utilized as a dissolving media. Samples were gathered, passed through a 0.45 µm filter, and then replaced with new dissolving medium. The obtained samples were examined for 5-FU content at 266 nm using UV/spectrophotometry (LKB, USA).[14]

7. Determination of Drug Content:

One gram of hydrogel was precisely weighed and dissolved in one hundred milliliters of phosphate buffer (pH 7.4). To ensure appropriate mixing, the volumetric flask was shaken vigorously in a shaker for four hours. The solution was filtered by passing it through the filter paper. A 10 ml volumetric flask was filled with 1 ml of the solution, and 7.4 phosphate buffer was used to create the final volume (Khullar et al., 2011). Following the proper dilution against the corresponding phosphate buffer pH 7.4 as a blank, the absorbance was measured spectrophotometrically at 378 nm.[12]

8. Rheological studies:

Carbopol hydrogels were rheologically examined using a Dynamic-Hybrid Rheometer (TA Instruments, New Castle, DE) with a cone plate fixture (40 mm cone diameter and 1.99° cone angle). The Peltier heating system regulated the temperature. Data analysis was done using the Dynamic-Hybrid Rheometer's TRIOS software (version 2.6.1, TA Instruments, New Castle, DE). The Carbopol hydrogel formulation was applied to the Peltier plate just enough to cover the cone at the top of the plate before the rheological experiment. Before and after lowering the cone over the peltier plate, the Carbopol hydrogel on the plate was allowed to equilibrate for three minutes at a regulated temperature, contingent on the experimental conditions. After lowering the cone, the rheometer's "trim gap" option was used to close the gap between the cone and plate, creating a thin, even layer of Carbopol hydrogel beneath the cone. The excess Carbopol hydrogel on the sides of the cone was removed carefully without disturbing the film between plate and cone.[15]

9. Stability studies:

The goal of stability testing is to demonstrate how a drug's or its product's quality changes over time due to environmental factors including temperature, humidity, and light. It is necessary to determine shelf life, retest time, and recommended storage conditions. The stability test required for drug registration applications in the United States, Japan, and the European Union is outlined in the International Conference on Harmonization (ICH) Guidelines titled "Stability testing of New Drug substance and product" (QIA). The duration of the investigation and storage conditions are specified by ICH.

Long-Term Testing: 60% at 25°C ± 2°C RH ± 5% for a full year.

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Accelerated Testing: 40oC ± 2oC / 75% RH ± 5% for 6 months Stability studies were carried out at 25oC/60% RH, 30oC/65% RH and 40oC/75% RH for the selected formulation for 3 months.[10]

10. Cytotoxicity Testing by MTT and Neutral Red (NR) Assay:

sterile hydrogel pieces weighing fifty milligrams each were cultured in ten milliliters of DMEM at 37 degrees Celsius. This extract, which contained the membrane leach-out products, was filtered through a 0.22 l filter in order to assess how the leachout products affected the viability of the cells. HeLa (CCL-2, human epitheloid cervical cancer) and NIH3T3 (CRL-1658 embryo, NIH Swiss mouse) cells were procured from ATCC (USA), seeded on 96-well plates, and cultured at 37±C in 5% CO2 and 95% air. After that, these cells were exposed to hydrogel extracts at different concentrations (5–40%) for a full day. To evaluate cell viability, MTT and NR tests were carried out in accordance with conventional procedures (Doyle, Grifths, and Newell 1995).[16]

CONCLUSION:

Overall, hydrogels continue to gain attention in modern biomedical research due to their versatility and ability to mimic biological tissues. Their applications in drug delivery systems, wound healing, tissue engineering, and controlled therapeutic release highlight their growing significance in healthcare. Future research focusing on advanced polymer combinations, improved crosslinking strategies, and enhanced biological compatibility will further expand the potential of hydrogels in pharmaceutical and biomedical fields.

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REFERENCES:

1. Chamkouri H. A Review of Hydrogels, Their Properties and Applications in Medicine. Am J Biomed Sci Res. 2021 Feb 3;11(6):485–93. doi:10.34297/AJBSR.2021.11.001682
2. Akhtar MF, Hanif M, Ranjha NM. Methods of synthesis of hydrogels … A review. Saudi Pharm J. 2016 Sep;24(5):554–9. doi:10.1016/j.jsps.2015.03.022
3. Varaprasad K, Raghavendra GM, Jayaramudu T, Yallapu MM, Sadiku R. A mini review on hydrogels classification and recent developments in miscellaneous applications. Mater Sci Eng C. 2017 Oct;79:958–71. doi:10.1016/j.msec.2017.05.096
4. Chamkouri H. A Review of Hydrogels, Their Properties and Applications in Medicine. Am J Biomed Sci Res. 2021 Feb 3;11(6):485–93. doi:10.34297/AJBSR.2021.11.001682
5. Varaprasad K, Raghavendra GM, Jayaramudu T, Yallapu MM, Sadiku R. A mini review on hydrogels classification and recent developments in miscellaneous applications. Mater Sci Eng C. 2017 Oct;79:958–71. doi:10.1016/j.msec.2017.05.096
6. Ullah F, Othman MBH, Javed F, Ahmad Z, Akil HMd. Classification, processing and application of hydrogels: A review. Mater Sci Eng C. 2015 Dec;57:414–33. doi:10.1016/j.msec.2015.07.053
7. Akhtar MF, Hanif M, Ranjha NM. Methods of synthesis of hydrogels … A review. Saudi Pharm J. 2016 Sep;24(5):554–9. doi:10.1016/j.jsps.2015.03.022
8. Nandini Sahu, Diksha Gupta, Ujjwal Nautiyal. Hydrogel: Preparation, and Applications. Asian Pac J Nurs Health Sci. 2020 Jun 30;3(1):1–11. doi:10.46811/apjnh/3.1.2
9. Tyagi S, Panda A, Khan S. FORMULATION AND EVALUATION OF DICLOFENAC DIETHYL AMINE MICEROEMULSION INCORPORATED IN HYDROGEL.
10. Gehalot N, Chourasiya A, Kushwaah P, Aole S, Jain V. Formulation and evaluation of Hydrogel for wound healing. Vol. 8. 2023;8(1).
11. Singh V, Chaubey N. Design and Evaluation of Topical Hydrogel Formulation of Aceclofenac for Improved Therapy. J Drug Deliv Ther. 2019 Sep 15;9(5):118–22. doi:10.22270/jddt.v9i5.3605
12. Formulation and Evaluation of Microemulsion Based Topical Hydrogel Containing Lornoxicam. J Appl Pharm Sci. 2014 Dec 30. doi:10.7324/JAPS.2014.41214
13. Shamloo A, Aghababaie Z, Afjoul H, Jami M, Bidgoli MR, Vossoughi M, et al. Fabrication and evaluation of chitosan/gelatin/PVA hydrogel incorporating honey for wound healing applications: An in vitro, in vivo study. Int J Pharm. 2021 Jan;592:120068. doi:10.1016/j.ijpharm.2020.120068
14. Elsayed EW, El-Ashmawy AA, El-Bassyouni GT, Mousa SM, El-Manawaty M, Emara LH. Formulation and evaluation of alginate-gelatin hydrogel scaffolds loaded with zinc-doped hydroxyapatite and 5-fluorouracil. Int J Biol Macromol. 2023 May;237:124147. doi:10.1016/j.ijbiomac.2023.124147
15. Jain S, Patel N, Madan P, Lin S. Formulation and rheological evaluation of ethosome-loaded carbopol hydrogel for transdermal application. Drug Dev Ind Pharm. 2016 Aug 2;42(8):1315–24. doi:10.3109/03639045.2015.1132227
16. Makarand V. Risbud, Ramesh R. Bhond. Polyacrylamide-Chitosan Hydrogels: In Vitro Biocompatibility and Sustained Antibiotic Release Studies. Drug Deliv. 2000 Jan;7(2):69–75. doi:10.1080/107175400266623