Journal of Biomedical and Pharmaceutical Research
Available Online at www.jbpr.in
CODEN: - JBPRAU (Source: - American Chemical Society)
NLM (National Library of Medicine): ID: (101671502)
Index Copernicus Value 2021: 83.38
Volume 12, Issue 2, March - April: 2023, 20-33

ISSN (Online): 2279-0594
ISSN (Print): 2589-8752

Research Article

A Review of Hydrogels, with its Properties and Applications in Medicine

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Article Info: Received: 23-01-2023 / Revised: 04-02-2023 / Accepted: 22-02-2023
DOI: https://doi.org/10.32553/jbpr.v12i2.970
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Conflict of interest statement: No conflict of interest

Abstract:
A hydrogel is an insoluble in water three-dimensional polymer network that has the potential to absorb bodily fluids in a biological setting. Hydrogels may also be used in medical applications. Chemical crosslinking mechanisms such as optical polymerization, enzymatic reactions, and physical crosslinking mechanisms such as temperature- and pH-dependent processes, as well as ionic crosslinking, are all responsible for the formation of a network of polymers of this kind. Both physical and chemical hydrogels may be generated by the application of weak secondary forces, but chemical hydrogels can also be formed through the application of covalent forces. Hydrogels may be made from a wide variety of polymers derived from either natural or synthetic sources. The swelling, the mechanical characteristics, and the biological properties of hydrogels are some of the most essential aspects of hydrogels, and each of these qualities may have an effect on the structure and morphology of the hydrogel. Hydrogen is utilized in a variety of medical applications, including tissue engineering, contact lenses, wound dressings, and the release of therapeutic agents. This is possible because hydrogen has a structure that is analogous to the extracellular matrix (ECM), and it also has the ability to absorb water. There is a discussion on hydrogels, the many varieties of hydrogels, the characteristics of hydrogels, and their uses in medicine.

1. Introduction

There has been a significant amount of scientific investigation carried out in the subject of biomaterials that have an impact on human health [1]. The study of hydrogels, which is one of the primary focuses of research on biomaterials, is the subject of the present article. The presence of hydrophilic groups within the structure of hydrogels gives them the capacity to absorb significant quantities of water or biological fluid in the body [2-5]. Hydrogels are water-insoluble three-dimensional polymer networks that have the potential to absorb enormous volumes of water.

In the primary polymer chain that makes up hydrogels, hydrophilic functional groups may be found in the form of hydroxyl groups (OH-), carboxyl groups (COOH-), amine groups (NH2), and sulphate groups (SO3H-). [6] These groups can be identified by their prefixes: hydroxyl, carboxyl, amine, and sulphate. Polymeric hydrogels may be created using either chemical crosslinking, physical crosslinking, or a mixture of the two forms of crosslinking [7].

Properties like as mechanical strength and intracellular and extracellular transport are affected by the chemical structure of the hydrogel, as well as its shape and equilibrium swelling [1]. Hydrogels because of their ability to absorb water, their soft structure, their biocompatibility, their low protein adsorption due to low surface tension and their similarity to the structure of ECM, their special attraction for a variety of medical applications including tissue engineering, and their ability to release therapeutic agents (proteins, drugs, genes) The use of contact lenses and dressings for wounds [6-10]. There are a few different approaches that may be used when developing hydrogels. These approaches include the major source of the hydrogel (natural or synthetic polymer), homopolymer network, copolymer network, and permeable network. Both physical and chemical cross-links, including cationic and anionic anion loads, as well as biodegradable hydrogen gel loads (and biodegradable) Biologically degradable and biologically stable (split by [1,4]). Researchers have recently begun to focus more of their attention on hydrogels that may react to different biological circumstances [11]. When a patient gets rid of the consequences of surgery for implantation, such as discomfort and inflammation, by using this form of hydrogel, which is also called injectable hydrogen, the patient saves a lot of time and money. Hydrogels are created in the body at the site of their intended use in accordance with the local biological environment [6].

In these types of systems, the liquid solution of the polymer is injected into the body, where it is then transformed into a solid hydrogel by the use of both chemical and physical crosslinking agents [6,7]. Alterations in temperature, pH, the presence of ions, and exposure to UV light are all conditions that may stimulate the formation of hydrogels [12,13]

The process of crosslinking has an effect on characteristics such as molecular mass, mechanical strength, and resistance to heat and solvents. Both physical and chemical cross-linking contribute to the formation of the hydrogel's three-dimensional structure, which makes it possible for therapeutic agents (drugs and biomolecules) to be trapped inside the structure and then released from it [1]. For example, the characteristics of hydrogels and their applications in a wide variety of medical sectors are explored in this article. Hydrogels that range in size, function, and design have the potential to be excellent drug delivery vehicles (Figure 1).

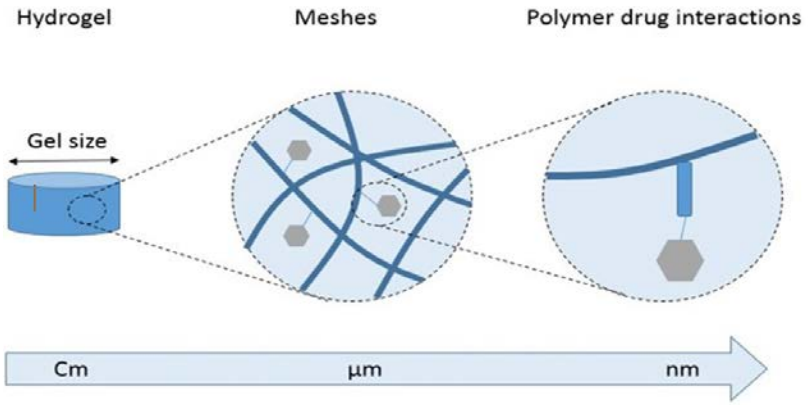

Figure 1: Multiscale properties of hydrogels

Mechanism of Hydrogel Formation

Polymers are a kind of carbohydrate material that has seen widespread use in the production of both chemical and physical hydrogels owing to their accessibility, existence of functional groups that may be modified, biocompatibility, and a variety of other qualities [6]. It is possible to tailor hydrogels to the requirements of a particular application by tailoring both the kind of monomer or polymer used and the reactions that are used to generate the hydrogel. Chemical crosslinking and physical crosslinking are the two ways that may be used in the production of hydrogels [14].

Chemical Crosslinking

Chemical cross-linkable hydrogels are a specific kind of hydrogel that, thanks to the formation of covalent bonds, can be transformed from a liquid state into a solid one. This approach is also employed in hydrogel systems that are created in situ. In this technique, hydrogels are produced by the use of a number of different processes, including enzyme reactions, click reactions, and optical polymerization. In the following paragraphs, we will go through the various techniques that were stated for producing these hydrogels [15]. Because of their high level of mechanical strength, hydrogels produced by chemical crosslinking have been given some consideration [16].

Optical Polymerization

One of the ways of chemical cross-linking in the creation of hydrogen is known as optical polymerization. This process has a number of benefits, including the need for very little energy and the absence of a solvent throughout the reaction. This technique makes use of hydrophilic polymers that contain molecules that are sensitive to light. When the polymer solution is subjected to either visible light or ultraviolet light,

The process of polymerization begins simultaneously with the formation of the optical decomposition initiator and free radicals. Polymers that cross-link in this manner often include groups of acrylates and methacrylates, both of which are polymerized when exposed to light. This approach allows for precise control over the pace of gelling, and the hydrogen produced during the process may be put to use to facilitate the release of therapeutic substances such proteins and medicines [15]. Via the use of an optical initiator, a monomer may be turned into a polymer using this approach [17], and it is one of the most efficient methods to do so. The hydrogel may be strengthened using optical polymerization, which also makes it possible for the cells to disappear during gel formation. This is useful for therapeutic applications. Moreover, a porous lattice structure is produced for the hydrogel using this approach [18]. At healthy temperatures and pH levels, optical polymerization may be accomplished with relative ease either within or outside of the body. It is recommended that a non-toxic optical primer with the appropriate light wavelength radiation from a light source be used for hydrogels used in the medical field. For instance, a mechanism of gelling by optical crosslinking through the failure of vinyl groups in contact with UV radiation [19] should be used.

Enzymatic reactions

Enzymatic reactions are only able to take place when enzymes are present in the biological milieu where they occur. Because of this, a lot of interest has been shown in using this approach for cellular applications. In order to crosslink via enzymatic processes, optimal conditions for crosslinking must be present. These conditions include natural pH, a biological habitat, and the optimal temperature. The use of a unique enzyme substrate that has the capacity to inhibit the creation of hydrogels is a significant benefit of this technology for the production of hydrogels.

The introduction of poisonous compounds as a result of unintended reactions. In the process of preparing hydrogel systems for use in tissue engineering, one of the chemicals employed as an enzymatic catalyst is horseradish peroxidase (HPR). Other compounds used include

modified glutamines and tyrosinases. Because of its great mechanical stability and simplicity of purification, HPR is one of the enzymes that is employed to make hydrogels in this manner. As a result, HPR is used in a wide variety of medical applications, including drug release, tissue engineering, and reconstruction and repair. The HPR-H2O2 enzyme water system is extensively employed in the development of natural hydrogels such as chitosan, hyaluronic acid, dextran, and gelatin to generate hydrogels. This system is also used in the production of artificial hydrogels. It was generated by enzymatic processes in the study that Kurosawa et al. conducted, and it was used to facilitate the release of therapeutic proteins. Throughout the course of this research project, hyaluronic acid was functionalized with the help of tyramine and then tagged with the fluorescent marker amino fluorescein. Because of its selectivity and its compatibility with cells, the employment of enzymatic processes to generate cross-linking is an appropriate strategy for the development of hydrogels since the time required for subcutaneous gelling was significantly decreased.

Click reaction

According to Sharples et aldefinition, .'s click chemistry is defined as certain types of reactions that take place in the presence of a catalyst and have a high speed and efficiency, excellent biological properties, and favourable reaction conditions [1,20]. [Click chemistry] is a term that was coined by Sharples et al. The synthesis and activation of polymers both make extensive use of click chemistry, which also serves as an efficient and versatile approach for the functionalization of molecules. Click chemistry plays a crucial part in both of these processes. This technique is used for the production of hydrogels, nanogels, and microgels because of the many advantages offered by click chemistry.

Moreover, it has been used as a substrate in the processes of tissue engineering and medication delivery. In the field of polysaccharide-based hydraulic chemical crosslinking, click chemistry is recognized as a newly developing substrate. In general, click reactions consist of a wide variety of reactions, such as the following: cop- per (I) reactions (catalyzed by alkyne azide sequestered, catalytic reactions of free pair of alkyne azides, silicosterone reaction with disaccharide (DA), among which the intergroup reaction is included), silicosterone reaction with disaccharide (DA), catalytic reactions of free pair of alkyne azides, etc. Because of their many benefits, including great selectivity and high levels of efficiency even in the physiological settings of the body, alkynes and azides are the most visible examples of click chemistry. [1] These two types of compounds are also the most common. The reaction takes proceed even in the absence of a catalyst or primer, which preserves the biocompatibility of the material [20]. This is because the lack of side-products that are thermally reversible and enable the degree of reaction to be regulated are required for the reaction to take place. The synthesis of starch-based hydrogels for use in biomedical and tissue engineering applications was accomplished by a click reaction between the thiol and allyl groups of starch. The hydrogel that was produced as a consequence exhibited desirable swelling behaviour as well as biodegradability [21].

Physical Crosslinking

It is possible to generate hydrogels formed by physical bonding by modifying intramolecular forces such as hydrogen bonding, hydrophobic interaction, and electrostatic ionic force. Hydrogels may then be formed by physical bonding. while the chemical technique has the possibility of an increase in the toxicity of the crosslinker, this method makes it feasible to create hydrogel using methods that are both easy and risk-free. Ionic methods, temperature-dependent methods, and pH-dependent cross-linking methods are examples of physical cross-linking techniques [20].

Ionic crosslinking: The ion crosslinking reaction is one of the physical methods of crosslinking, and it is distinguished from other physical methods by the fact that it does not involve the formation of a covalent bond

between the polymer chains. Instead, the ion crosslinking agent is used to form the gel in this method [6,13]. This approach is used in order to provide hydrogels with a high degree of tenacity [22]. Natural alginate is a polysaccharide, and its polymer solution has the capacity to form gels when exposed to divalent cations like Ca2+. Alginate is a naturally occurring carbohydrate. The presence of these ions is responsible for the formation of ionic bonds within the polymer chain as well as the bonding of gluronic acid groups in the alginate chain. As an example of an ECM, hydrogen alginate is often employed. Current research efforts have concentrated on minimizing the amount of time required for gelation, enhancing their mechanical characteristics, and developing more effective biological interactions. They may be manufactured for use in injectable biomaterials and cultivated in vitro if certain parameters, such molecular weight, concentration of alginate and calcium, and the composition of alginate in the made hydrogel are controlled [13,14]. Chitosan is one example of an application that makes use of another natural polymer called chitosan, which has the capacity to crosslink ionically and is one of the natural polymers listed in [7].

Temperature dependent methods: In the process of forming hydrogen by the use of physical cross-linking, temperature plays an important role as a parameter. Hydrogels that are sensitive to temperature turn into liquids at low temperatures and solids when they reach body temperature [23]. Applications of hydrogels, which are formed when water-soluble polymers are subjected to temperature changes and cause them to assume a gel-like state, have been found useful in the field of tissue engineering. In order to crystallize, these hydrogels do not need the addition of any chemical stimulants. They can have their gel point changed to a temperature that is somewhat similar to that of the human body, which enables them to be injected into a liquid and then solidified within the body. This technique makes use of both natural and man-made polymers in its construction. The derivatives of cellulose, chitosan, and gelatin are examples of natural polymers. Examples of synthetic polymers include poly-isopropyl acrylamide (PNIPAAM) and its copolymers, as well as plux- amer. Current studies on the usage of PNIPAAM copolymers in tissue engineering applications have focused on the release of chondrocytes and growth factors. Moreover, ploxamers have been examined for their potential use in lung tissue engineering. In order to increase the mechanical qualities necessary to trap cells, a physical gelling of ploxamer combined with a chemical crosslinking agent has been applied. Researchers have also taken into consideration a temperature-sensitive hydrogel of hyaluronic acid that can be injected owing to the fact that it has a high level of biocompatibility and a high level of sensitivity to body temperature [24].

pH-dependent methods: Since each place in the human body is associated with a different pH [15], it should be used as a stimulant in hydrogels. Among stimulus-responsive hydrogels, pH-sensivity etc. Many studies and research projects have made extensive use of sitive hydrogels. Hydrogels that are pH-sensitive have the capacity to expand and contract dynamically as a function of the pH of their surrounding environment on average. The presence of side acidic groups that are capable of being ionized at a certain pH is a characteristic that is shared by many pH-sensitive hydrogels. Because of their capacity to stimulate and react to changes in their surrounding environment, pH-sensitive hydrogels have found widespread usage in a variety of medical applications, including controlled drug delivery systems and heart valves. In certain applications, particularly those involving the release of drugs, hydrogels are subjected to a range of temperatures inside the body. Alterations in temperature are required in order to comprehend the process of the development of pH-sensitive hydrogels [15]. Carboxymethyl chitosan was combined with an unstable acid crosslinking agent and ideal circumstances in a research study

conducted by Hu et al. to create pH-sensitive hydrogels. The work was published in the journal Polymer. The material known as carboxymethyl chitosan is non-toxic, as well as bio-degradable and biodegradable. It is compatible and has been exploited to a large extent in the medical and medical fields [25].

Types of Hydrogels

Natural hydrogels and synthetic hydrogels are the two kinds of hydrogels that may be differentiated based on the type of polymer used. Materials for medical purposes that have been hydrogenated by natural or synthetic polymers are regarded to be raw materials. In order to be employed in the production of hydrogels, natural and synthetic polymers must first be biocompatible, then biodegradable, and in certain applications, the hydrogel must also be blood compatible [26].

Natural Hydrogels

Natural hydrogels are a kind of gel in which the polymers that make up the gel come from natural sources. The formation of hydrogels by the use of natural polymers offers a number of benefits, including biocompatibility, biodegradability, and non-toxicity. The function that biomaterials are intended to serve determines whether or not natural polymers can be used in the production of hydrogels. For instance, hydrogels that are employed for controlled material release need to be biocompatible, biodegradable, and informal [27]. Polysaccharides and the proteins that are derived from them are examples of natural polymers. They may both function as carriers for the release of chemicals. The findings of in-body testing of these polymers demonstrated that they are biocompatible. Among these polymers, polysaccharides are the most appropriate choice because of their biocompatibility, enzymatic breakdown, high durability, and lack of toxicity [28]. Natural hydrogels such as alginate, collagen, gelatin, and fibrin are all used in therapeutic settings. Other examples include gela- tin. For instance, alginate has been shown to successfully restore normal functioning in the left ventricle of the heart after a heart attack. Furthermore, collagen has been employed in place of vascular bundles in several applications. Gelatin may be used in the creation of artificial structures, and fibrin may be utilized in tissue engineering, in addition to serving as an adhesive and an anticoagulant during surgical procedures [29].

Synthetic Hydrogels

Hydrogels made from synthetic polymers, such as polyamides or polyethylene glycol, are the building blocks of synthetic hydrogels (PEG). Synthetic polymers have lately replaced natural polymers in the manufacture of hydrogels owing to the many benefits offered by synthetic polymers, including a longer shelf life, better gel strength, and an increased capacity to absorb water. Many medical applications make use of the synthetic polymers that are put to use in the production of hydrogels. Natural polymers tend to be hydrophilic, whereas synthetic polymers are hydrophobic, and in terms of mechanical structure and chemicals, synthetic polymers are superior to natural polymers. Polyacrylamide and its derivatives, polyvinyl alcohol, and polyethylene glycol are examples of these polymers. PEG is one of the most widely used polymers for synthetic hydrogenation, which is used in a wide variety of medical applications including drug release, tissue engineering, bone prostheses, and wound dressings. PEG is also one of the most widely used polymers. Because of its biocompatibility, non-stimulating effects on the immune system, and resistance to protein adsorption, this polymer is put to use in a wide variety of medical applications. These qualities allow it to avoid protein absorption. PEG has the capacity to build its own insoluble network structures when used alone. Nonetheless, by incorporating factor groups into it, the crosslinking in the structure of the hydrogen network may be improved. [27].

Properties of Hydrogels

Because of their capacity to take in and hold water, network polymers known as hydrogels tend to expand when exposed to water [30].

Hydrogels may be thought of as network sponges.

Swelling of hydrogel

Equilibrium swelling of hydrogels is obtained from the follow- ing formula:

swelling ratio=(w_t-w_d)/w_d

Where Wt is the weight of the swollen hydrogels and Wd is the weight of the dried hydrogels in freeze-drying.

In conventional hydrogel delivery methods, drug release takes place primarily as a result of swelling or contraction of the hydrogel, in addition to the diffusion of the drug via the polymer network. When the characteristics of a hydrogel, such as its swelling behaviour, structure, mechanical strength, or permeability, may alter in response to different stimuli, one can refer to that particular kind of hydrogel as either a stimulus-responsive hydrogel or a physiologically sensitive hydrogel. These compounds are able to efficiently be employed to change the release of drug agents from hydrogels for the purpose of controlled drug release [6]. The hydrogen swelling ratio of adipic acid dehydrated, poly- glutamic acid, and hyaluronic acid is shown in Figure 2. There is a significant inflation rate associated with hydrogen in general, with the maximum inflation rate reaching up to 70 percent. The hydrogel was able to be dissolved in the buffer phosphate salt solution, as shown in Figure 2. This occurred when the solid concentration was 1% by weight. Xiobin et al. have developed a high-swelling injectable hydrogel to regulate protein release by copolymerizing hyaluronic acid and polyglutamic acid. Their method utilizes the copolymerization process. Because of the correlation between the reduction in the percentage of swelling and the rise in the amount of crosslinking in the structure, the weight percentage of polymer components should be raised. Their investigation also revealed that the molar ratio of NH2 to CHO may have an effect on the proportion of the hydrogel that swells. As can be seen in Figure 2, when the molar ratio of NH2 to CHO reached 1: 2, the swelling rate was almost twice as fast as it was when the ratio was 2: 1 for the hydrogel, and when it was 1: 3 for NH2 to CHO, the pace was slow because of the low ratio. After the completion of the structural cross-linking, the hydrogel was dissolved in phosphate buffer solution (PBS) [24].For the purpose of the regulated release of pharmacological agents, the swelling behaviour of pH-sensitive polymers has been used. The most essential characteristics that determine the swelling behaviour and the pace of release are a polymer's molecular weight and the degree of crosslinking that exists between any two locations. Regulates the levels of medication and oxygen that may pass through [14]. Hydrogens have the ability to expand and hold significant quantities of water when placed in biological settings. The prevention of disintegration and the maintenance of the network's dimensions are both achieved by the use of cross-linking between the structural chains. The collapse or phase transition of the hydrogel may be caused by a number of external conditions, including temperature, pH, ion concentration, and others. The hydrogel is extremely dependent on these elements. Swelling of a hydrogel is the primary mechanism by which drugs are released, and the method of drug release can be controlled to be either inflation or diffusion or both by adding PEG to the PNIPAAM polymer system to improve the swelling ability of the copolymer [12]. Swelling of a hydrogel is the primary mechanism by which drugs are released.

Mechanical Properties

Injectable chemical hydrogels have better mechanical properties and longer stability than physical hydrogels. However, the use of toxic crosslinking agents in the preparation of chemical hydrogels can have a negative effect on biocompatibility. Hydrogels, on the other hand, establish physical-chemical interactions and avoid such toxic initiators [6]. When it comes to the engineering design of hydrogels for use in medical applications, one of the most essential characteristics that must be taken into consideration is the hydrogel's mechanical

qualities. The mechanical characteristics of scaffolds, both on a macroscopic and a microscopic size, play an essential role in the regulation of cell behaviour in the area of tissue engineering. This significance may be seen at both scales.

The form of cells is directly influenced by both biomechanical cues and interactions between cells and extracellular matrix. For instance, the rigidity of the extracellular matrix has an effect on the fibroblasts seen in adult human skin. Moreover, cells that are subjected to more robust substrates are able to arrange a greater elastic modulus in the plasma membrane along with an improved cytoskeleton. In addition, the rate of cell proliferation and migration is significantly increased when cells are cultivated on harder substrates as compared to softer substrates. The time-independent and time-dependent viscoelastic theories are used to examine the structure of the hydrogel and determine the effective crosslinking ratio (Figure 3) [31]. These theories are the primary means by which the mechanical characteristics of hydrogel biomaterials are described. Since the PNIPAAM hydrogel produced using the free radical polymerization approach is so fragile, conventional mechanical identification techniques are unable to be used in order to ascertain its mechanical characteristics. The initial monomer concentration, the amount of crosslinking agent, the polymerization temperature, the degree of swelling at the time of measurement, and the method of measurement are some of the parameters that can influence the mechanical properties of hydrogels. Other parameters include the temperature of polymerization. Because of this, it is very difficult to compare any mechanical characteristic in an exact manner [32]. In order to improve the mechanical characteristics of PAA that was bound with amylose, Reza Abdollahi and his colleagues utilized graphene oxide. They are of the opinion that because of its high aspect ratio and unique mechanical strength, graphene oxide provides a sufficient strengthening effect for tensile properties, making it an ideal candidate for use in this application.

Biological Properties

Injectable hydrogels must possess essential features such as biocompatibility and nontoxicity before they may be used in a variety of medical applications. These properties include adequate mechanical properties, excellent viscosity, stability, biodegradability, and others. The hydrogel must possess appropriate mechanical and biological qualities, and these properties must be comparable to those of the tissue that it is intended to replace [6]. In various research, Zhao et al. have combined cross-linking and electrospinning in an effort to attain the highest possible levels of both the mechanical and biological qualities of the material. UV light was used to create crosslinks in gelatin methacrylate fibres that were electrospun. The findings shown that the physical and biological characteristics of electro spinning hydrogel may be altered by manipulation of the exposure period [33]. It is essential to build a hydroxyapatite in order to simulate the appearance of actual bone tissue.

/ carbon nanotube / hydroxyapatite CNT composite that has superior mechanical and biological qualities for the purpose of being used as bone replacements.

The unique top of the composite not only promotes the circulation of body fluids, but it also reveals a wet and uneven surface, which is a desired property for cell adhesion, proliferation, and development. In addition, the particular top of the composite assists the circulation of bodily fluids. Consequently, the HA/CNT composite, which has superior mechanical and biological characteristics, has a significant amount of promise for usage in bone replacement applications as well as the production of highly active tissue scaffolds. Expansion of osteoblast cells in biological material is a necessary phase for the development of osteoblasts' fundamental biological features [34]. In the process of developing an injectable hydrogel, its

biocompatibility has to be investigated. This is because the hydrogel ought to encourage the expansion and differentiation of cells without causing the host to experience toxicity or immunological responses. Because the majority of the components of natural hydrogels are analogous to ECM, their biocompatibility is significantly higher than that of artificial hydrogels. The structure of the hydrogel needs to be compatible with cells, tissues, and body fluids; it also needs to be non-cancerous and non-toxic, and it can't trigger any chronic physiological or inflammatory reactions after it is destroyed [6].

Application of Hydrogels in Medicine

Tissue Engineering

Hydrogels are similar to ECMs in that they are made up of highly hydrated polymer networks. ECMs have garnered a lot of interest for their potential uses in tissue engineering and regenerative medicine. To this day, many kinds of hydrogels that are generated from natural or synthetic polymers have been used in order to successfully restore osteocortical joints or articular cartilage tissue that has been damaged. In most cases, brown seaweed and a wide variety of microorganisms are used to extract alginate, which is a kind of naturally occurring polysaccharide polymer. The ability of alginate to physically cross-link by divalent cations such as Ca2+ at ambient temperature is one of its distinguishing characteristics. Because of this ability, alginate may be used in a wide variety of biotechnological processes, including moulding, spraying, and even 3D printing.

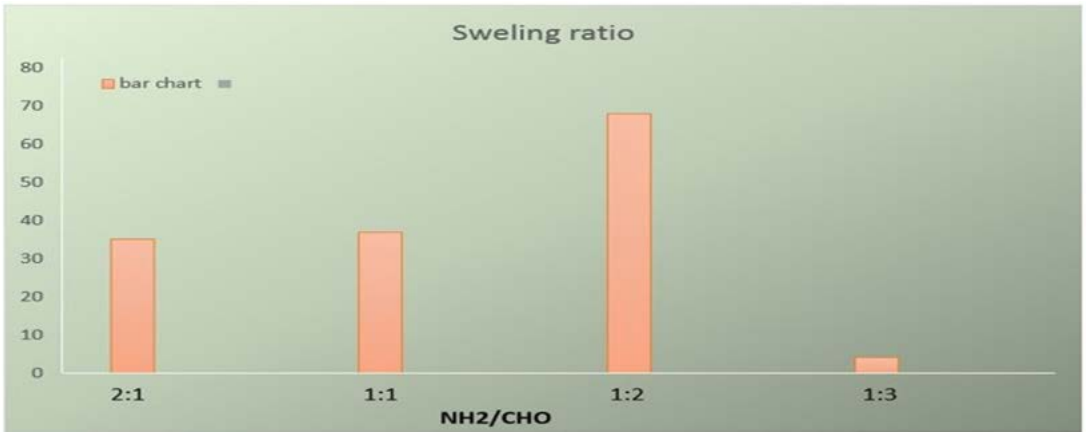

Figure 2: Swelling ratio of dehydrated adipic acid / polyglutamic acid and hyaluronic acid hydrogels [24].

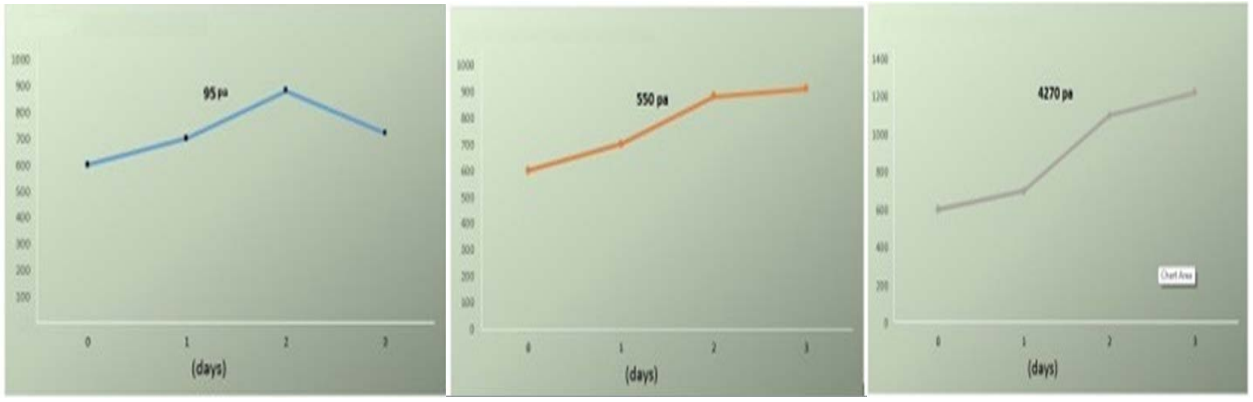

Figure 3: Comparison diagram of hydrogel stiffness with respect to cell proliferation [31].

Physical Hydrogels:

The goods offer favourable biocompatibility in addition to minimal toxicity and a relatively affordable price. It is possible for alginate hydrogel to sustain the chondrogenic phenotype while also promoting the development and proliferation of encapsulated chondrocytes, which is a desirable outcome. Inoculation of chondrocytes over a period of 21 to 28 days results in the formation of type II collagen in addition to the advanced cartilage gene. In addition, primary bone cells, including chemical stem cells (MSCS), may be produced from alginate and employed for the bone regeneration process. Encapsulated MSCS are able to generate their own own collagen extracellular matrix (ECM), which interacts with the host tissue.

It is the second most prevalent natural biopolymer and may be derived from renewable sources such as marine trash, oyster shells, insects, and fungus. Chitosan is a substance that is appropriate for applications involving tissue engineering as a result of its high biocompatibility and capacity for biodegradation. The production of chitosan by enzymatic grafting may be beneficial to the multiplication of both chondrocytes and stem cells.

Sustain chondrogenic phenotype and shape and increase extracellular matrix deposition in vitro [ECM.] 36 has been recognized for a long time as a support material that is created by cells and serves as the sole scaffold on which cells rest. Neutral materials have a higher biocompatibility compared to other materials, and because of their ineffectual qualities, they are suitable for a wide variety of applications [36]. Some of these applications include tissue engineering and the replacement of artificial hip joints. By copolymerizing PEG and PNIPAAM, Alexander et al. were able to produce temperature-sensitive injectable hydrogels that might be used in tissue engineering applications. They are of the opinion that hydrogels based on PNIPAAM have a low compressive modulus and poor mechanical characteristics. This material is a good candidate for the creation of an injectable biological material that may be used in the regeneration or replacement of soft tissue [12] because of the temperature sensitivity of the PNIPAAM polymer.

Because they are able to mimic the extracellular matrix (ECM) structure of body tissues and provide biochemical signals to support cell proliferation and differentiation, hydrogels made from natural materials are frequently used as scaffolds in tissue engineering. This is because of the combination of these two properties. For the creation of polymer scaffolds to be used in tissue engineering, optical crosslinking has received a lot of attention recently. This is because these hydrogels are able to rapidly cure under biological circumstances at physiological temperatures while also providing a particular level of control over the gel dynamics. As a result, they may be used to create scaffolds with complicated morphologies. It is essential for hydrogels that are going to be employed in biomedical and tissue engineering that their mechanical characteristics are going to be comparable to those of real tissue [37].

Wound Dressing:

As an alternative to traditional wound dressings, Min Hee Kim and his colleagues were successful in producing MC methylcellulose hydrogels that included silver oxide particles. For the purpose of this experiment, they utilized Sprague field hairs that were four weeks old. The field work was carried out in an environment where the temperature, humidity, and light levels were all under strict control [38]. According to the findings of their histological investigation, the portion of the wound that had been treated with MC hydrogel containing silver oxide nanoparticles had a higher rate of success compared to the portion that had not been treated. There have been reports that treating burn wounds with MC hydrogel greatly increases the pace at which they recover [38]. Also, the treatment pattern of burn wounds was explored in order to investigate untreated tissue. On days 1, 3, 7, 14, and 21, particles

were subjected to an analysis using biological dyes. According to the findings, MC hydrogels that did not include silver nanoparticles were responsible for tissue necrosis and inflammation, but hydrogels that did contain silver nanoparticles did not produce tissue necrosis or inflammation [38]. Dressings made of hydrogel have the ability to absorb water at a rate that is many times higher than their dry weight. These dressings are effective for absorbing wound secretions, assisting in maintaining a cooler temperature at the wound site, and producing a more humid environment. The currently available wound dressings suffer from a variety of drawbacks, including a lack of antibacterial activity, inadequate oxygen permeability and water permeability, and poor mechanical qualities [39]. Antibiotics were included into a nanocomposite hydrogel that Hassan Namazi and his colleagues utilized in order to circumvent the issues described above.

As a nanoparticle carrier, has been created by the combination of mesoporous silica and carboxymethylcellulose. Tetracycline and methylene blue, both antibacterial medications, were administered into the system, and the results indicated that they had quite distinct releases [39]. Tetracycline is an antibiotic with a wide range of activity that is used to treat a variety of skin and soft tissue conditions, as well as wounds. Tetracycline used topically was shown to be a very efficient therapy for bacterial skin infections [39]. Methylene blue is a cationic dye with antiseptic qualities that is used to treat poisoning, kidney stones, methemoglobin, and cyanide in humans. Methylene blue is also known as blue methylene. In addition to this, it is used on a large scale as a light-sensitive material in photodynamic therapy, which is a developing method of combating germs that are resistant to antibacterial drugs [39,40]..

Drug Release:

By using ultrasound, Abdullahi and colleagues were able to successfully make a hydrogel that was loaded with fluoxamine. This demonstrated the controlled release of the medication in an environment that was modelled like the inside of the body. They believe that the mechanism of drug release from the hydrogel is dependent on a number of factors including the composition of the hydrogel, the geometric structure of the hydrogel, the method of preparation, the type of drug, and the environmental conditions during the release period, with pH being one of the most important factors [41]. In a different experiment, Ganji and colleagues were successful in slowly releasing pyridostigmine bromide utilizing injectable hydro-gel, which is sensitive to the temperature of the chitosan in vitro. They believe that the addition of glycerol phosphate salt caused the solution to become darker, in comparison to the chitosan solution that did not include any salt. Throughout the course of time, turbidity shifts were seen in solutions of chitosan and chitosan/glycerol phosphate. These shifts were observed in solutions that included 8% by weight/volume of salt. At a temperature of 37 degrees Celsius, the turbidity of the chitosan solution did not vary much during the course of the experiment. Hence, it is possible to draw the conclusion that chitosan solution without glycerol phosphate salt is not affected by temperature and continues to be the same at 37 degrees for a considerable amount of time.

At 37 degrees Celsius, however, a chitosan and glycerol phosphate solution showed a slow but steady rise in turbidity throughout the course of the experiment. When nine minutes had passed, there was an abrupt onset of darkness. The point of gel formation is determined by the rapid appearance of an increase in opaqueness throughout the process. The results of this experiment demonstrated that the addition of glycerol phosphate salt to the chitosan solution decreased the stability of the chitosan solution when it was heated to 37 degrees Celsius and caused a rapid phase transition from the solution state to the gel state [42].

Bakhshashi et al. were successful in their attempt to create a Baghdadit-vancomycin nanostructured scaffold with drug release capacity, anti-bacterial activity, and biocompatibility. The drug release was

evaluated on a net basis. Under the context of their research, the incorporation of vancomycin into the Baghdad scaffold served as a drug model to investigate the behaviour of drug release [43]. After being submerged in phosphate-buffered saline solution, the process of drug release from the scaffold was seen both explosively and in a controlled way (PBS). Specifically, an explosive release was detected for the first six hours, and then a stable release was observed after a period of time; nonetheless, 45 to 75% of the drug was released from the scaffold after 36 hours for all drug compounds. The discharge of vancomycin proved successful in killing S. aureus and preventing the bacteria from reproducing on the scaffold. They observed that 35% of the medicine remained in the scaffold and was not eliminated; hence, it is possible to suggest that bacterial infection in the early phases of bone infection may be managed using a Baghdadit / vancomycin scaffold [43-45].

Conclusion

This article is a review that discusses the many forms of hydrogels, as well as their properties, the process behind their creation, and the medicinal applications of hydrogels. When it comes to the process behind the production of hydrogel, there are a few distinct ways that the structure may be crosslinked. In the field of tissue engineering, physically networked hydrogels have been employed as a substrate for a range of medicinal applications, including the release of bioactive chemicals and the confinement of cells, among others. The fact that these networks don't need the usage of organic solvents is one of their many benefits. The swelling of the structure is the primary mechanism responsible for the release of medicinal drugs from hydrogels. In recent years, there has been a rise in interest in hydrogels that respond to external stimuli. The regulated release of pharmacological substances from the hydrogel network is dependent on the medications as well as environmental factors such as temperature and pH. Because of their ability to absorb water, their gentle structure, their biocompatibility, and their resemblance to extracellular matrix (ECM), hydrogels are seen as a promising candidate for use in a variety of medical applications.

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