**A Review of Hydrogels their Classifications, and Applications**

 **Deepti Chauhan, e-mail-** deeptichauhan2570@gmail.com

Department of Applied Chemistry, Delhi Technological University, Delhi, India

**Abstract**

A hydrogel is an insoluble network of polymers in three dimensions that has the ability to absorb biological fluids. Such a polymer network is produced by physical as well as chemical cross-linking processes. Covalent forces create chemical hydrogels, whereas weak secondary forces create physical hydrogels. Hydrogels can be prepared from a very wide range of natural and synthetic polymers. The swelling, mechanical, and biological capabilities of hydrogels are its most important features; these attributes all affect the hydrogel's morphology and structure. Hydrogel finds its application in several fields such as wound dressings, tissue engineering, contact lenses, adsorbents, sensors, and medicine owing to its property to absorb water and similarity in structural framework to extracellular matrix (ECM). This review covers hydrogels, their varieties, and their uses

.**1 Introduction**

**1.1 hydrogels**

Hydrogels have been defined differently by researchers over time. For example, they are large-scale hydrogel networks that hold onto a substantial amount of water in their structure despite being insoluble in it. The absorbance and water retention properties of a hydrogel are said to be caused by hydrophilic functional groups that are connected to the polymeric network. Conversely, the resistance of polymeric chains to dissolution can be due to the cross-links that exist between them. A hydrogel is characterized by the existence in a polymeric chain network of three dimensions of two or more parts. Networks of polymeric chain, or hydrophilic gels, are typically colloidal gels with water acting as a dispersion medium.1-2 The most frequent definition of hydrogels is a cross-linked polymeric chain that swells when exposed to water. And are produced by a straightforward reaction involving one or more monomers. Its ability to stay three-dimensional throughout the swelling phase is due to crosslinking.3. Hydrogels have garnered significant interest in the last fifty years due to their outstanding potential in a extensive range of applications.4. Hydrogels are capable to hold excess amounts of water and fluids, including bio- fluids that may imitate biological tissues, and as a result, their flexibility is extremely comparable to that of genuine tissue. This property has sparked a great interest in creating novel devices by adjusting their tunable physicochemical properties. Synthetic hydrogels, which have unique architectures and can produce variable functioning and degradation with further modification, have largely superseded natural hydrogels in recent times. Depending on the characteristics of the parts they can contain different amount of water in equilibrium based on the characteristics of the components used in the polymeric network and the density of the network joints.5.

Hydrogel synthesis can be accomplished through various chemical techniques, including one-step methods such as cross-linking and polymerization of multifunctional monomers, as well as methods of multiple-steps that entail the formation of polymeric chains with highly reactive functional groups, which are then cross-linked using an appropriate cross-linking agent. A polymer engineer is able to create polymeric networks with customized qualities such as mechanical capabilities, biological and chemical reaction to stimuli, biodegradation, and molecular-scale control over structure, including density of cross-linking.6

**1.2 Natural Gums based Hydrogels**

Because of their exceptional qualities, affordability, structural variety, and accessibility, natural gum polysaccharides have drawn the attention of researchers in a varied fields, such as the water, food, energy, medicine, and biotechnology industries. Natural gums, also known as polysaccharides7, are derived from a variety of tree species and have remarkable qualities such as being renewable, biodegradable, biocompatible, non-toxic, and easily chemically modifiable.7. When compared to synthetic origin, natural gum-based hydrogels or polysaccharides offer some advantageous features. Since the uncontrolled use of hydrogels manufactured of synthetic polymers has resulted in health, ecological, and environmental issues, they have seen notable progress as a fresh alternative in recent past years.8, 9, Consequently, there is a high demand for environmentally friendly materials. These hydrophilic polymeric networks have greater strength and elasticity and are insoluble in water.1, 10 They exhibit remarkable reactivity to changes in temperature, pH, electric field strength, solvent composition, pressure, and solvent composition.12, 13, These hydrated polymeric networks are becoming increasingly important in practice and are useful as biomimetic, intelligent, and intelligent materials. They find use as actuators and sensors, and they are frequently being researched as self-oscillating gels.14. Hydrogels known as "smart networks" react physiochemically significantly to even minute alterations in their environment. These are reversible changes, they can return back to their initial state if the trigger has been removed.15.

**1.3 Classification of Hydrogels**

 Depending on the source, they might have an artificial or natural origin. Natural polymers include gums, agarose-formed hydrogels, starch, cellulose, glucomannan, pectin, hemicellulose, and polysaccharides like alginate and proteins like collagen and gelatine. Chemical polymerization techniques are typically used to create synthetic polymers like hydrogel-formed polyethylene glycol (PEG), hydrogel-formed polyvinyl alcohol (PVA), hydrogel-formed polyacrylic acid (PAA), and hydrogel-formed polyacrylamide (PAM).2.

Depending on the synthesis or composition of polymers:

(I) The fundamental structural and functional unit of homopolymer hydrogel is made up of a only one kind of monomer within the polymeric network. based on the kind of monomer and the polymerization procedure, their skeletons could be cross-linked.

(II) Copolymeric hydrogels are derived from a variety of monomeric units with at least one hydrophilic component. The polymeric network chains can be arranged in a unorganised, block or alternating configuration. 17

(III) Multipolymer interpenetrating polymeric network (IPN) can be synthesized using two separate, cross-linked components of natural or synthetic polymers, confined in a network form. In the case of Semi-interpenetrating hydrogel, one polymer is cross-linked and the other polymeric component is non-cross-linked.18 One straight polymeric chain enters another crosslinked network, and they interact without any chemical bonding.19

Based on physical and chemical composition: (I) Non-crystalline (Amorphous) (II) Semicrystalline, a composite of amorphous and crystalline phases. (III) Crystalline.2

Based on cross-linked networks: Chemically cross-linked networks have permanent bonding involving covalent interaction while physical networks have transient junctions involving entanglements of polymeric chains involving hydrogen bonds, polar or ionic, hydrophobic type of physical interactions.2

(IV) Based on electrical charge: (I) Neutral (non-ionic), (II) Ionic (including anionic or cationic), (III) Amphoteric having both acidic and basic groups, (IV) Zwitterionic (polybetaines) possess both cationic and anionic functionality in each repeating unit.2

**1.4 Preparation of hydrogels**

Hydrogels can be produced employing natural, synthetic, and composites of both natural and synthetic polymeric materials. Hydrogels have been created by cross-linking polymer chains through chemical alteration, external cross-linking agents, exposure to high energy radiation, and polymerization grafting. In the hydrogel formation chemical cross-linking involve the formation of new covalent bond between polymeric chain in the hydrogel, where as physical cross-linking involves physical interactions between polymer chains.53 Both chemical and physical methods have their own advantages and disadvantages related to them. Conventional and controlled radical polymerization technique result in hydrogels along with various morphologies, sizes and compositions including hollow core-shells particles.54, 55 The most widely used mechanism is free radical polymerization to prepare hydrogels.56, 57 Usually in hydrogel preparation, the gel reactants react with a crosslinker (s) to generate 3D-crosslinked networks in the presence of radical initiators like potassium persulfate or ammonium persulfate. Free radical polymerization occurs in three main steps: initiation, propagation, and termination. In the initiation step, free radicals (R●) are produced when an initiator dissociates and then reacts with other molecules (M) to produce the first radicals M●. In the propagation step, highly reactive free radicals rapidly react with molecules of monomer resulting in the formation of macroradicals. Usually, termination occurs by the combination or disproportionation reaction of free radicals. Various shapes of hydrogels like bulk, sphere, and films can be obtained by selecting the appropriate preparation process, raw material, and polymerization condition.47

Bulk Hydrogels: Usually, they are smoothly obtained by solution or homogeneous polymerization wherein all the reactants i.e., the monomer (or polymer), initiator, and cross-linker are soluble in the medium. The resultant hydrogel generally takes up the shape of the container in which it has been polymerized and yields a relatively homogeneous hydrogel.59 However, due to the slow diffusion of solute to the adsorption sites within hydrogel it will take a long time to reach equilibrium during water treatment.60 Usually, bulk hydrogel is cut into small sized pieces manually or by using a food blender to produce small size hydrogel beads for better adsorption efficiency. On the other hand, occasionally a cutting or grinding step could produce hydrogel particles with a fractured morphology and polydispersity.61, 62

Spherical Hydrogels:  Spherical hydrogel does not require grinding or cutting and thus avoids further morphology destruction and energy consumption. Hydrogels bead is an example of spherical hydrogels with a millimetre diameter. Usually, the synthesis of spherical hydrogels involves dropping the monomer or polymer suspension using a syringe into a solution. Thus, the size of the resultant hydrogel beads typically depends on the syringe's diameter. Chitosan, a natural polysaccharide which is biodegradable, nontoxic, odourless, biocompatible and Hydrogel beads are often prepared using biopolymer. When it comes into contact with potassium and sodium cations, it can get crosslinked.63-67

Hydrogel Films: Hydrogel composite films appear to hold a lot of potential for practical use. They are simple to make and show robust and repeatable self-healing behavior in the aqueous medium. Numerous hydrogels have been used as an effective ion-exchange film to purify water. Recently, the direct synthesis of nanofiber hydrogel film has been achieved using electrospinning technology.38 Some extra components could be added to the hydrogel film either by grafting after polymerization or by combining additives with the hydrogel precursors before the polymerization to create a specific hydrogels composite with the required qualities.69 Hydrogel film is typically utilized as an active membrane in sensing applications, mainly to give a more hydrophilic surface that is less prone to contamination.65

**1.5 Characterization of Hydrogels**

Numerous characterization approaches have been utilized for knowing the hydrogel’s physical and chemical properties. The physical properties of polymeric hydrogel are determined by the volume fraction, effective molecular weight of the polymeric chains in between two crosslinking junctions and by the density of crosslinking.20 Hydrogels have many properties, such as absorption capacity, permeability, swelling behaviour, optical, surface, and mechanical properties. The nature of the polymer chains and the crosslinking present in the network structures play a significant function in the result of the properties of the hydrogel. All these properties are responsible for making hydrogels are the important materials for a huge range of applications.21

Analysis of Fourier Transform Infrared Spectroscopy FTIR : This method provides reliable crosslinking data and gives a notion of the hydrogels' morphology.

Atomic Force Microscopy (AFM): This technique helps to examine hydrogels' surface morphology. It uses a multimode atomic force microscope.

Network Pore Size: Various techniques, for instance, mercury porosimetry, quasi-elastic laser light scattering, equilibrium swelling, electron microscopy, and rubber elasticity measurements experiments are employed to find out the network pore size of hydrogel. This is an important technique for hydrogel characterisation.

 X-ray Diffraction: X-ray diffraction analysis enables one to understand the crystalline and amorphous nature of hydrogels, whether the crystallinity is maintained or was distorted while synthesizing.

Swelling Behaviour: To study the potential use as a hydrogel, specific swelling data studies are employed and it has been successfully studied by numerous researchers.

Crosslinking and the Mechanical Strength: The crosslinking density inside the network structure of hydrogel determines its mechanical strength. Generally, with increasing crosslinker concentration the mechanical strength of the hydrogel also increases.

Rheology: It based on the kind of interaction (entanglement, association, and crosslinks) present in the polymeric network among polymer chains.

All these characterization methods provide important information about the desired crosslinking results, formation of hydrogel. Which can be useful further for various applications.3

**2 Applications of Hydrogel**

Among the salient characteristics of hydrogels are biodegradability, hydrophilicity, biocompatibility, less toxicity, high flexibility, and easy modification. They have good transport properties and the capacity to adapt to changes in the environment, such as those in pH, temperature, or metabolite concentration. As a result of their extraordinary properties, hydrogels can be used in many fields, including drug delivery, wound dressing, agriculture, tissue engineering, water purification, hygiene applications, etc.3,7. Hydrogels are widely used in biomedical fields for a number of reasons, including drug delivery22-25, gene vectors, tissue engineering26, 27 and biosensors28, 29. Hydrogels meet both material and biological requirements because they have unique characteristics like desired functionality, reversibility, and biocompatibility. They are frequently employed for cell-laden, tissue regeneration, drug delivery, and biosensors.

soft contact lenses: As a result of their biocompatibility and mechanical properties, soft contact lenses remain one of the most popular applications for hydrogels.

 By dissolving the lens' water, hydrogels can be adjusted to match the curvature of the entire eye, allowing atmospheric oxygen to reach the cornea. As a favorable and ideal candidate for the manufacture of contact lenses, polyhydroxyethylmethacrylate (PHEMA) was first established by Wichterle and Lim (1960).3

Tissue Regeneration and Tissue Engineering: A severe disease or accident causing the loss of organ function necessitates the need for tissue and organ transplantation. It has become more difficult due to fewer donors available and because of societal, legal, and other norms.31 Tissue engineering has raised hopes for creating a perfect living replacement that mimics the way living tissues perform in the human body.3 Scaffolds act as 3-D artificial templates in which the rebuilding of targeted tissues is cultured to grow. The extremely porosity of hydrogels enables the diffusion of cells during migration, transfer of nutrients and excludes unwanted products outside of cellular membranes.32 Hydrogels, both natural and synthetic, are utilized as scaffolds in numerous tissue engineering applications, such as the restoration of blood arteries, skin, heart valves, cartilage, and tendons.33 They have been used in a number of biomedical applications, including fillers for scar cosmetic repair7, bladder34, cartilage35, orthopedic applications36,

Skin37 and bone38. Polysaccharides-based hydrogels that exhibit biocompatibility with tissues which increases their significance in tissue engineering and biomedical applications.

Wound healing: Injured skin is covered to avoid bleeding and to protect the wound from environmental infections. Wound dressings are non-toxic, antiseptic, permeable to oxygen, preserve wound moisture, cause minimal damage, eliminate excess exudates and thus fasten the healing process while directly interacting with the wound. A great advantage of gum-based hydrogels in wound dressings is that they can easily be applied or removed without interfering with the wound beds.39, 40 Compared to the traditional bandages, pads, or gauzes, the mechanical characteristics of hydrogel increases their elasticity and flexibility to adapt to wounds and provide patients with immediate pain relief. They act as a coolant to localized wounds in case of burn and also reduce the pain and recover from resultant damage.41, 42 The non-adhesive nature and hydrophilic surface of hydrogels do not allow it to attach with cells therefore causes less pain and discomfort to the patient. Hydrogel transparency has a benefit over traditional bandages as it causes less discomfort when peeling it off. Various hydrogels for wound dressings are available, like amorphous gels, gel-impregnated gauzes, plasters or sheets. The development of hydrogel formulations to address various aspects of wound healing and management such as easy dressing, reduction in infection is attaining new heights.43, 3

Drug Delivery: Hydrogels' porous structure can act as a matrix for the loading or distribution of pharmaceuticals while also shielding them from harsh environments. Hydrogel targets specific sites like the colon as a drug delivery agent and releases drugs or other nutrients timely. In addition to this hydrogel interacts very less with the drug and other loaded solutes hence sustained and prolonged release occurs in a larger fraction comparative to conventional drug delivery systems.7 Because of their special ability to retain large volumes of water, hydrogels are valuable in drug delivery applications that regulate the release of solute over a predetermined length of time. This trait is known as hydrophilicity. Many biomaterials that function through two mechanisms have been investigated for this aim. (1) By adjusting the crosslinker dosage and keeping an eye on the proportion of hydrophilic to hydrophobic monomers, a controlled release of the medication can be accomplished. (2) Hydrogel releases a big fraction of active drug molecule (protein and peptides) because its interaction with the drug is very less. Drug delivery that is targeted and controlled would help with healing and lessen unwanted side effects. Drugs release from hydrogels are expressed by a number of processes, including diffusion, chemical control, deswelling, and environmentally responsive release. 3

Agricultural Applications: One significant step in achieving sustainable development and growth in agriculture is water management. Superabsorbent polymeric hydrogels (SPH) derived from natural polysaccharides have gained significance in agriculture owing to their remarkable capacity to hold and retain large amounts of water. In dry and semi-arid regions, SPH can be added to the soil to prolong longer moisture retention, enabling crops to tolerate arid weather. In dry and semi-arid soil, hydrogels act as "mini liquid tanks," releasing water into the soil along with the targeted amount of loaded nutrients. Modification in hydrogel properties as required gives fertile physical properties of soil.45 The usage of natural polysaccharides based SPH is flourishing owing to their biodegradability, durability, high water holding ability, avoid loss of nutrients, nontoxic, and their sustainability compared to synthetic polymer based hydrogel.46 Hydrogels have been used for the prevention of soil erosion over a decade by reduction in soil erosion, increasing water holding capacity, enhancing permeability of finely textured soils, enhance water infiltration among fine-textured agricultural soil. The water-soluble polyacrylamide (PAM) hydrogels form a thin film covering soil surface and are very efficient in preventing soil erosion. This film protects the soil surface from washing away during irrigation and retains the optimum water content within the soil system, so that irrigation water can permeate easily.3

Hydrogel as an adsorbent:  As we all know emerging contaminantsincluding pharmaceuticals, pesticides, industrial chemicals, metal ions, surfactants, and personal care products have elevated worldwide concern for their noteworthy hazard to human health and marine ecosystems. Many of them have no regulatory standard on the effects of chronic exposure due to the lack of information.70 These contaminants are stable under a variety of circumstances such as aerobic digestion, heat and light thus they have the potential to build up and harm ecosystems. Therefore, the adsorption method has been greatly adopted to treat emerging contaminates as it is really efficient and affordable.71

The use of hydrogel as an adsorbent in pollution management applications is becoming more and more popular. Both the hydrogel adsorbents and the type of adsorbate have a significant impact on the adsorption process. The Freundlich and Langmuir models provide a good interpretation for the adsorption data of emerging contaminants on hydrogel; the kinetic model is often pseudo-second-order. Because of the several interactions that occur between the adsorbate and the adsorbent, such as hydrophobic interaction, hydrogen bonding, ionic or electrostatic interaction, and π–π interaction, hydrogel adsorbents have a great affinity for pollutants. This fluctuates depending on several factors, including pH, the ionic strength of the solution, the chemical makeup of the adsorbent and adsorbate, and more.

The surface of the adsorbent will have an ionic charge when the pH of the solution differs from the hydrogel adsorbents' isoelectric point. Ionic adsorbates undergo simultaneous protonation and deprotonation at varying pH levels, leading to electrostatic interactions between them. Hence, pH is an important factor responsible for the adsorption mechanism.47, 3 Many solid and liquid phase removal trials remain tracked for the elimination of pollutants from liquid such as coagulation, biochemical precipitation, adsorption, photodegradation, ion exchange, flocculation, electrochemical treatment, and membrane percolation.48-51 Of all these many methods, adsorption is seen to be superior due to its high efficiency, low effort, and ease of use. Hydrogels are thought to be special for adsorption-based water refining because of their high absorption capacity, low crystallinity, abundance of functional groups, and porous structure. Due to the several significant functional groups that polysaccharides (Gum) include in their structure, hydrogels based on them and graft copolymers are thoroughly investigated as adsorbents for the removal of contaminants from aqueous environments, including heavy metal ion and organic dyes. The chief advantage of using natural gum-based hydrogel as adsorbents is their biocompatibility. Their structure can be easily tailored according to the nature of the pollutants.52 Although hydrogels are found to be superior candidates for the elimination of several aqueous contaminants, including heavy metals, dyes and other emerging contaminates, selective adsorption of contaminates is hardly explored. Therefore, research attempts are required to prepare hydrogels with desired properties, sensitivity, and selectivity for a specific contaminant. Many hydrogels have been developed with desirable strength and adsorption capacity, but their chemical and biological stability is always ignored which needs to be considered for the sustainability and economic viability of wastewater treatment.47

Hydrogel as a sensor of heavy metal ions in environmental and biological samples: Nonbiodegradable heavy metal ions' widespread existence in water is potentially threatening to the ecosystem and living organisms. Hydrogels have been functionalized with many biomolecules, including DNA, to form stimuli-responsive sensors and materials72,73 However, for sensing applications, most of them rely on hydrogel phase transition or volume change. Because of their high sensor loading capacity, excellent biocompatibility, and extremely low optical background, hydrogels are perfect for optical sensor immobilization. Moreover, hydrogels backbone properties such as charge and hydrophobicity can be modified by mixing with different monomers, allowing further control of sensor performance.73

As a transducer material, the stimuli-responsive hydrogel can be utilized to convert a recognition unit's reaction into a physical signal that can be detected by, e.g., quantifying the change in optical length with an optical fibre, observing the resulting change in swelling pressure under isochoric conditions or by measuring the diffracted wavelength of a polymerized crystalline colloidal array.

Host-guest interactions in sensing applications have been proven to be a powerful tool. Usually, macrocyclic polyethers, i.e., crown ethers have been proved to be promising candidates in combination with hydrogel facilitated by the generation of highly selective and reversible host-guest complexes with specific alkali and heavy metal cations. Notably, the colorimetric sensing approach has garnered a lot of interest due to its direct visual perception, affordability, speed, and ease of use. Most colorimetric sensor is dispersed in sample solution for full contact with the target chemical to increase sensitivity; however, an uneven and unstable dispersion of the sensors might occasionally result in unsteady detection findings. Chemo sensors can be constructed on solid substrates to circumvent this issue. The choice of a solid substrate is crucial since it has a significant impact on the sensor's sensitivity. In sensor studies, a colorimetric chemo sensor can be formed by the design of molecules that change their color in sample solution owing to an alteration in their molecular structures in the presence of target ions.74 In aqueous conditions, the designed sensor molecule's solubility is crucial. The fact that the sensors cannot dissolve directly in water, although pollutant species, such as anion or cation, are soluble in water, is one of the most significant problems in this research. Additionally, the soluble sensor is meant to be used just once. To deal with such issues, researchers have opted to polymerize molecules that have sensing properties. According to this perspective, the sensor must be easily extracted from the sample solution and insoluble to be utilized again. Hydrogel is the best illustration of a solid support or polymer that is readily extracted from the sample solution through filtration. They are important for various sensing applications as they can be prepared in good yield, have swelling in water, are reusable and stimuli responsive.74,75

**3 Conclusion**

The presented review deals the literature relating the classification of hydrogels, their properties, and applications. Hydrogels can be integrated into systems and changed into different configurations due to their biocompatibility, sensitivity to external stimuli, and physical and chemical structure. Hydrogel-based chemical and biosensors have advanced significantly in the past several years across a huge range of application areas. Hydrogels have proven beneficial in a variety of disciplines, including, environmental remediation, energy, soft robotics, humidity sensing, medicine, and health monitoring, due to their versatile composition, innate properties, and ability to adjust numerous physicochemical parameters.

**Acknowledgment**

D.C thanks to Delhi Technological University for the research facilities.

**References**

1. Ahmed, E. M.; Aggor, F. S.; Awad, A. M.; El-Aref, A. T. An Innovative Method for Preparation of Nanometal Hydroxide Superabsorbent Hydrogel. Carbohydr. Polym. 2013, 91 (2), 693–698. https://doi.org/10.1016/j.carbpol.2012.08.056.
2. Ahmed, E. M. Hydrogel: Preparation, Characterization, and Applications: A Review. J. Adv. Res. 2015, 6 (2), 105–121. https://doi.org/10.1016/j.jare.2013.07.006.
3. Mishra, S.; Rani, P.; Sen, G.; Dey, K. P. Preparation, Properties and Application of Hydrogels: A Review; Springer Singapore, 2018. https://doi.org/10.1007/978-981-10-6077-9\_6.
4. Li, Y.; Huang, G.; Zhang, X.; Li, B.; Chen, Y.; Lu, T.; Lu, T. J.; Xu, F. Magnetic Hydrogels and Their Potential Biomedical Applications. Adv. Funct. Mater. 2013, 23 (6), 660–672. https://doi.org/10.1002/adfm.201201708.
5. 5) Ali, M.; Husain, Q. Guar Gum Blended Alginate/Agarose Hydrogel as a Promising Support for the Entrapment of Peroxidase: Stability and Reusability Studies for the Treatment of Textile Effluent. Int. J. Biol. Macromol. 2018, 116, 463–471. <https://doi.org/10.1016/j.ijbiomac.2018.05.037>.
6. (6) Burkert, S.; Schmidt, T.; Gohs, U.; Dorschner, H.; Arndt, K. F. Cross-Linking of Poly(N-Vinyl Pyrrolidone) Films by Electron Beam Irradiation. Radiat. Phys. Chem. 2007, 76 (8–9), 1324–1328. https://doi.org/10.1016/j.radphyschem.2007.02.024.
7. Ahmad, S.; Ahmad, M.; Manzoor, K.; Purwar, R.; Ikram, S. A Review on Latest Innovations in Natural Gums Based Hydrogels: Preparations & Applications. Int. J. Biol. Macromol. 2019, 136, 870–890. https://doi.org/10.1016/j.ijbiomac.2019.06.113.
8. Saravanan, S.; Vimalraj, S.; Thanikaivelan, P.; Banudevi, S.; Manivasagam, G. A Review on Injectable Chitosan/Beta Glycerophosphate Hydrogels for Bone Tissue Regeneration. Int. J. Biol. Macromol. 2019, 121, 38–54. https://doi.org/10.1016/j.ijbiomac.2018.10.014.
9. Graham, S.; Marina, P. F.; Blencowe, A. Thermoresponsive Polysaccharides and Their Thermoreversible Physical Hydrogel Networks. Carbohydr. Polym. 2019, 207, 143–159. https://doi.org/10.1016/j.carbpol.2018.11.053.
10. Jonker, A. M.; Löwik, D. W. P. M.; Van Hest, J. C. M. Peptide- and Protein-Based Hydrogels. Chem. Mater. 2012, 24 (5), 759–773. https://doi.org/10.1021/cm202640w.
11. Mogoşanu, G. D.; Grumezescu, A. M. Natural and Synthetic Polymers for Wounds and Burns Dressing. Int. J. Pharm. 2014, 463 (2), 127–136. https://doi.org/10.1016/j.ijpharm.2013.12.015.
12. Buwalda, S. J.; Boere, K. W. M.; Dijkstra, P. J.; Feijen, J.; Vermonden, T.; Hennink, W. E. Hydrogels in a Historical Perspective: From Simple Networks to Smart Materials. J. Control. Release 2014, 190, 254–273. https://doi.org/10.1016/j.jconrel.2014.03.052.
13. Vermonden, T.; Klumperman, B. The Past, Present and Future of Hydrogels. Eur. Polym. J. 2015, 72 , 341–343. https://doi.org/10.1016/j.eurpolymj.2015.08.032.
14. Ikram, S.; Kumari, M.; Gupta, B. Thermosensitive Membranes by Radiation-Induced Graft Polymerization of N-Isopropyl Acrylamide/Acrylic Acid on Polypropylene Nonwoven Fabric. Radiat. Phys. Chem. 2011, 80 (1), 50–56. https://doi.org/10.1016/j.radphyschem.2010.08.013.
15. Noreen, A.; Nazli, Z. i. H.; Akram, J.; Rasul, I.; Mansha, A.; Yaqoob, N.; Iqbal, R.; Tabasum, S.; Zuber, M.; Zia, K. M. Pectins Functionalized Biomaterials; a New Viable Approach for Biomedical Applications: A Review. Int. J. Biol. Macromol. 2017, 101, 254–272. <https://doi.org/10.1016/j.ijbiomac.2017.03.029>.
16. Yang, Z.; Peng, H.; Wang, W.; Liu, T. Crystallization Behavior of Poly(ε-Caprolactone)/Layered Double Hydroxide Nanocomposites. J. Appl. Polym. Sci. 2010, 116 (5), 2658–2667. https://doi.org/10.1002/app.
17. Yang, L.; Chu, J. S.; Fix, J. A. Colon-Specific Drug Delivery: New Approaches and in Vitro/in Vivo Evaluation. Int. J. Pharm. 2002, 235 (1–2), 1–15. https://doi.org/10.1016/S0378-5173(02)00004-2.
18. Maolin, Z.; Jun, L.; Min, Y.; Hongfei, H. The Swelling Behavior of Radiation Prepared Semi-Interpenetrating Polymer Networks Composed of PolyNIPAAm and Hydrophilic Polymers. Radiat. Phys. Chem. 2000, 58 (4), 397–400. https://doi.org/10.1016/S0969-806X(99)00491-0.
19. Zhang, J. T.; Bhat, R.; Jandt, K. D. Temperature-Sensitive PVA/PNIPAAm Semi-IPN Hydrogels with Enhanced Responsive Properties. Acta Biomater. 2009, 5 (1), 488–497. https://doi.org/10.1016/j.actbio.2008.06.012.
20. (20) Lin, C. C.; Metters, A. T. Hydrogels in Controlled Release Formulations: Network Design and Mathematical Modeling. Adv. Drug Deliv. Rev. 2006, 58 (12–13), 1379–1408. https://doi.org/10.1016/j.addr.2006.09.004.
21. (21) Peppas, N. A.; Hilt, J. Z.; Khademhosseini, A.; Langer, R. Hydrogels in Biology and Medicine: From Molecular Principles to Bionanotechnology. Adv. Mater. 2006, 18 (11), 1345–1360. https://doi.org/10.1002/adma.200501612.
22. (22) Tønnesen, H. H.; Karlsen, J. Alginate in Drug Delivery Systems. Drug Dev. Ind. Pharm. 2002, 28 (6), 621–630. https://doi.org/10.1081/DDC-120003853.
23. Xian, C.; Yuan, Q.; Bao, Z.; Liu, G.; Wu, J. Progress on Intelligent Hydrogels Based on RAFT Polymerization: Design Strategy, Fabrication and the Applications for Controlled Drug Delivery. Chinese Chem. Lett. 2020, 31 (1), 19–27. https://doi.org/10.1016/j.cclet.2019.03.052.
24. (24) Carter, P.; Narasimhan, B.; Wang, Q. Biocompatible Nanoparticles and Vesicular Systems in Transdermal Drug Delivery for Various Skin Diseases. Int. J. Pharm. 2019, 555, 49–62. https://doi.org/10.1016/j.ijpharm.2018.11.032.
25. (25) Wei, X.; Liao, J.; Davoudi, Z.; Zheng, H.; Chen, J.; Li, D.; Xiong, X.; Yin, Y.; Yu, X.; Xiong, J.; Wang, Q. Folate Receptor-Targeted and Gsh-Responsive Carboxymethyl Chitosan Nanoparticles Containing Covalently Entrapped 6-Mercaptopurine for Enhanced Intracellular Drug Delivery in Leukemia. Mar. Drugs 2018, 16 (11). https://doi.org/10.3390/md16110439.
26. Li, Z.; Ramay, H. R.; Hauch, K. D.; Xiao, D.; Zhang, M. Chitosan-Alginate Hybrid Scaffolds for Bone Tissue Engineering. Biomaterials 2005, 26 (18), 3919–3928. <https://doi.org/10.1016/j.biomaterials.2004.09.062>.
27. Huang, K.; Wu, J.; Gu, Z. Black Phosphorus Hydrogel Scaffolds Enhance Bone Regeneration via a Sustained Supply of Calcium-Free Phosphorus. ACS Appl. Mater. Interfaces 2019, 11 (3), 2908–2916. https://doi.org/10.1021/acsami.8b21179.
28. Brown, J. Q.; Srivastava, R.; McShane, M. J. Encapsulation of Glucose Oxidase and an Oxygen-Quenched Fluorophore in Polyelectrolyte-Coated Calcium Alginate Microspheres as Optical Glucose Sensor Systems. Biosens. Bioelectron. 2005, 21 (1), 212–216. <https://doi.org/10.1016/j.bios.2004.08.020>.
29. Whitchurch, C. B.; Alm, R. A.; Mattick, J. S. The Alginate Regulator AlgR and an Associated Sensor FimS Are Required for Twitching Motility in Pseudomonas Aeruginosa. Proc. Natl. Acad. Sci. U. S. A. 1996, 93 (18), 9839–9843. <https://doi.org/10.1073/pnas.93.18.9839>.
30. (30) Lum, E.; Golebiowski, B.; Gunn, R.; Babhoota, M.; Swarbrick, H. Corneal Sensitivity with Contact Lenses of Different Mechanical Properties. Optom. Vis. Sci. 2013, 90 (9), 954–960. https://doi.org/10.1097/OPX.0000000000000016.
31. Lee, K. Y.; Mooney, D. J. Hydrogels for Tissue Engineering. Chem. Rev. 2001, 101 (7), 1869–1879. https://doi.org/10.1021/cr000108x.
32. Loh, Q. L.; Choong, C. Three-Dimensional Scaffolds for Tissue Engineering Applications: Role of Porosity and Pore Size. Tissue Eng. - Part B Rev. 2013, 19 (6), 485–502. https://doi.org/10.1089/ten.teb.2012.0437.
33. Ma, P. X. Scaffolds for Tissue Fabrication. Mater. Today 2004, 7 (5), 30–40. https://doi.org/10.1016/S1369-7021(04)00233-0.
34. Sloff, M.; Simaioforidis, V.; De Vries, R.; Oosterwijk, E.; Feitz, W. Tissue Engineering of the Bladder - Reality or Myth? A Systematic Review. J. Urol. 2014, 192 (4), 1035–1042. https://doi.org/10.1016/j.juro.2014.03.116.
35. Makris, E. A.; Gomoll, A. H.; Malizos, K. N.; Hu, J. C.; Athanasiou, K. A. Repair and Tissue Engineering Techniques for Articular Cartilage. Nat. Rev. Rheumatol. 2015, 11 (1), 21–34. https://doi.org/10.1038/nrrheum.2014.157.
36. Naahidi, S.; Jafari, M.; Logan, M.; Wang, Y.; Yuan, Y.; Bae, H.; Dixon, B.; Chen, P. Biocompatibility of Hydrogel-Based Scaffolds for Tissue Engineering Applications. Biotechnol. Adv. 2017, 35 (5), 530–544. https://doi.org/10.1016/j.biotechadv.2017.05.006.
37. Jeong, K. H.; Park, D.; Lee, Y. C. Polymer-Based Hydrogel Scaffolds for Skin Tissue Engineering Applications: A Mini-Review. J. Polym. Res. 2017, 24 (7). https://doi.org/10.1007/s10965-017-1278-4.
38. Liu, Y.; Lim, J.; Teoh, S. H. Review: Development of Clinically Relevant Scaffolds for Vascularised Bone Tissue Engineering. Biotechnol. Adv. 2013, 31 (5), 688–705. https://doi.org/10.1016/j.biotechadv.2012.10.003.
39. Purwar, R.; Rajput, P.; Srivastava, C. M. Composite Wound Dressing for Drug Release. Fibers Polym. 2014, 15 (7), 1422–1428. https://doi.org/10.1007/s12221-014-1422-2.
40. Fonder, M. A.; Lazarus, G. S.; Cowan, D. A.; Aronson-Cook, B.; Kohli, A. R.; Mamelak, A. J. Treating the Chronic Wound: A Practical Approach to the Care of Nonhealing Wounds and Wound Care Dressings. J. Am. Acad. Dermatol. 2008, 58 (2), 185–206. https://doi.org/10.1016/j.jaad.2007.08.048.
41. Cuttle, L.; Pearn, J.; McMillan, J. R.; Kimble, R. M. A Review of First Aid Treatments for Burn Injuries. Burns 2009, 35 (6), 768–775. https://doi.org/10.1016/j.burns.2008.10.011.
42. (42) Coats, T. J.; Edwards, C.; Newton, R.; Staun, E. The Effect of Gel Burns Dressings on Skin Temperature. Emerg. Med. J. 2002, 19 (3), 224–225. https://doi.org/10.1136/emj.19.3.224.
43. Grippaudo, F. R.; Carini, L.; Baldini, R. Procutase® versus 1% Silver Sulphadiazine in the Treatment of Minor Burns. Burns 2010, 36 (6), 871–875. https://doi.org/10.1016/j.burns.2009.10.021.
44. Shahid, S. A.; Qidwai, A. A.; Anwar, F.; Ullah, I.; Rashid, U. Effects of a Novel Poly (AA-Co-AAm)/AlZnFe 2O 4/ Potassium Humate Superabsorbent Hydrogel Nanocomposite on Water Retention of Sandy Loam Soil and Wheat Seedling Growth. Molecules 2012, 17 (11), 12587–12602. https://doi.org/10.3390/molecules171112587.
45. Silberbush, M.; Adar, E.; De Malach, Y. Use of an Hydrophilic Polymer to Improve Water Storage and Availability to Crops Grown in Sand Dunes I. Corn Irrigated by Trickling. Agric. Water Manag. 1993, 23 (4), 303–313. https://doi.org/10.1016/0378-3774(93)90042-9.
46. Zonatto, F.; Muniz, E. C.; Tambourgi, E. B.; Paulino, A. T. Adsorption and Controlled Release of Potassium, Phosphate and Ammonia from Modified Arabic Gum-Based Hydrogel. Int. J. Biol. Macromol. 2017, 105, 363–369. https://doi.org/10.1016/j.ijbiomac.2017.07.051.
47. Du, H.; Shi, S.; Liu, W.; Teng, H.; Piao, M. Processing and Modification of Hydrogel and Its Application in Emerging Contaminant Adsorption and in Catalyst Immobilization: A Review. Environ. Sci. Pollut. Res. 2020, 27 (12), 12967–12994. https://doi.org/10.1007/s11356-020-08096-6.
48. (48) Ahmad, M.; Manzoor, K.; Chaudhuri, R. R.; Ikram, S. Thiocarbohydrazide Cross-Linked Oxidized Chitosan and Poly(Vinyl Alcohol): A Green Framework as Efficient Cu(II), Pb(II), and Hg(II) Adsorbent. J. Chem. Eng. Data 2017, 62 (7), 2044–2055. https://doi.org/10.1021/acs.jced.7b00088.
49. Ahmad, M.; Ahmed, S.; Swami, B. L.; Ikram, S. Preparation and Characterization of Antibacterial Thiosemicarbazide Chitosan as Efficient Cu(II) Adsorbent. Carbohydr. Polym. 2015, 132 (Ii), 164–172. https://doi.org/10.1016/j.carbpol.2015.06.034.
50. (50) Oussalah, A.; Boukerroui, A.; Aichour, A.; Djellouli, B. Cationic and Anionic Dyes Removal by Low-Cost Hybrid Alginate/Natural Bentonite Composite Beads: Adsorption and Reusability Studies. Int. J. Biol. Macromol. 2019, 124, 854–862. https://doi.org/10.1016/j.ijbiomac.2018.11.197.
51. (51) Sharma, G.; Kumar, A.; Naushad, M.; García-Peñas, A.; Al-Muhtaseb, A. H.; Ghfar, A. A.; Sharma, V.; Ahamad, T.; Stadler, F. J. Fabrication and Characterization of Gum Arabic-Cl-Poly(Acrylamide) Nanohydrogel for Effective Adsorption of Crystal Violet Dye. Carbohydr. Polym. 2018, 202, 444–453. <https://doi.org/10.1016/j.carbpol.2018.09.004>
52. (52) Naushad, M.; Sharma, G.; Kumar, A.; Sharma, S.; Ghfar, A. A.; Bhatnagar, A.; Stadler, F. J.; Khan, M. R. Efficient Removal of Toxic Phosphate Anions from Aqueous Environment Using Pectin Based Quaternary Amino Anion Exchanger. Int. J. Biol. Macromol. 2018, 106, 1–10. https://doi.org/10.1016/j.ijbiomac.2017.07.169.
53. (53) Hoare, T. R.; Kohane, D. S. Hydrogels in Drug Delivery: Progress and Challenges. Polymer (Guildf). 2008, 49 (8), 1993–2007. https://doi.org/10.1016/j.polymer.2008.01.027.
54. Chiang, W. H.; Ho, V. T.; Huang, W. C.; Huang, Y. F.; Chern, C. S.; Chiu, H. C. Dual Stimuli-Responsive Polymeric Hollow Nanogels Designed as Carriers for Intracellular Triggered Drug Release. Langmuir 2012, 28 (42), 15056–15064. https://doi.org/10.1021/la302903v.
55. Oishi, M.; Nagasaki, Y. Stimuli-Responsive Smart Nanogels for Cancer Diagnostics and Therapy. Nanomedicine 2010, 5 (3), 451–468. https://doi.org/10.2217/nnm.10.18.
56. Shariatinia, Z.; Jalali, A. M. Chitosan-Based Hydrogels: Preparation, Properties and Applications. Int. J. Biol. Macromol. 2018, 115, 194–220. https://doi.org/10.1016/j.ijbiomac.2018.04.034.
57. Ullah, F.; Othman, M. B. H.; Javed, F.; Ahmad, Z.; Akil, H. M. Classification, Processing and Application of Hydrogels: A Review. Mater. Sci. Eng. C 2015, 57, 414–433. https://doi.org/10.1016/j.msec.2015.07.053.
58. Khan, M.; Lo, I. M. C. A Holistic Review of Hydrogel Applications in the Adsorptive Removal of Aqueous Pollutants: Recent Progress, Challenges, and Perspectives. Water Res. 2016, 106, 259–271. https://doi.org/10.1016/j.watres.2016.10.008.
59. Qi, X.; Li, Z.; Shen, L.; Qin, T.; Qian, Y.; Zhao, S.; Liu, M.; Zeng, Q.; Shen, J. Highly Efficient Dye Decontamination via Microbial Salecan Polysaccharide-Based Gels. Carbohydr. Polym. 2019, 219 (January), 1–11. https://doi.org/10.1016/j.carbpol.2019.05.021.
60. (60) Tang, S. C. N.; Wang, P.; Yin, K.; Lo, I. M. C. Synthesis and Application of Magnetic Hydrogel for Cr(VI) Removal from Contaminated Water. Environ. Eng. Sci. 2010, 27 (11), 947–954. https://doi.org/10.1089/ees.2010.0112.
61. (61) Shah, L. A.; Khan, M.; Javed, R.; Sayed, M.; Khan, M. S.; Khan, A.; Ullah, M. Superabsorbent Polymer Hydrogels with Good Thermal and Mechanical Properties for Removal of Selected Heavy Metal Ions. J. Clean. Prod. 2018, 201, 78–87. https://doi.org/10.1016/j.jclepro.2018.08.035.
62. Thompson, B. R.; Horozov, T. S.; Stoyanov, S. D.; Paunov, V. N. Hierarchically Porous Composites Fabricated by Hydrogel Templating and Viscous Trapping Techniques. Mater. Des. 2018, 137, 384–393. https://doi.org/10.1016/j.matdes.2017.10.046.
63. Afzal, M. Z.; Yue, R.; Sun, X. F.; Song, C.; Wang, S. G. Enhanced Removal of Ciprofloxacin Using Humic Acid Modified Hydrogel Beads. J. Colloid Interface Sci. 2019, 543, 76–83. https://doi.org/10.1016/j.jcis.2019.01.083.
64. (64) Kluczka, J.; Gnus, M.; Kazek-Kęsik, A.; Dudek, G. Zirconium-Chitosan Hydrogel Beads for Removal of Boron from Aqueous Solutions. Polymer (Guildf). 2018, 150, 109–118. https://doi.org/10.1016/j.polymer.2018.07.010.
65. Bilal, M.; Jing, Z.; Zhao, Y.; Iqbal, H. M. N. Immobilization of Fungal Laccase on Glutaraldehyde Cross-Linked Chitosan Beads and Its Bio-Catalytic Potential to Degrade Bisphenol A. Biocatal. Agric. Biotechnol. 2019, 19 (March). <https://doi.org/10.1016/j.bcab.2019.101174>.
66. Gogoi, N.; Barooah, M.; Majumdar, G.; Chowdhury, D. Carbon Dots Rooted Agarose Hydrogel Hybrid Platform for Optical Detection and Separation of Heavy Metal Ions. ACS Appl. Mater. Interfaces 2015, 7 (5), 3058–3067. <https://doi.org/10.1021/am506558d>.
67. Yin, S.; Ma, Z. “Smart” Sensing Interface for the Improvement of Electrochemical Immunosensor Based on Enzyme-Fenton Reaction Triggered Destruction of Fe3+ Cross-Linked Alginate Hydrogel. Sensors Actuators, B Chem. 2019, 281 (May 2018), 857–863. https://doi.org/10.1016/j.snb.2018.11.030.
68. Zhang, C.; Li, H.; Yu, Q.; Jia, L.; Wan, L. Y. Poly(Aspartic Acid) Electrospun Nanofiber Hydrogel Membrane-Based Reusable Colorimetric Sensor for Cu(II) and Fe(III) Detection. ACS Omega 2019. https://doi.org/10.1021/acsomega.9b02109.
69. Zhang, W.; Cheng, W.; Ziemann, E.; Be’er, A.; Lu, X.; Elimelech, M.; Bernstein, R. Functionalization of Ultrafiltration Membrane with Polyampholyte Hydrogel and Graphene Oxide to Achieve Dual Antifouling and Antibacterial Properties. J. Memb. Sci. 2018, 565, 293–302. https://doi.org/10.1016/j.memsci.2018.08.017.
70. Wang, H.; Liu, Z. hua; Zhang, J.; Huang, R. ping; Yin, H.; Dang, Z.; Wu, P. xiao; Liu, Y. Insights into Removal Mechanisms of Bisphenol A and Its Analogues in Municipal Wastewater Treatment Plants. Sci. Total Environ. 2019, 692, 107–116. https://doi.org/10.1016/j.scitotenv.2019.07.134.
71. (71) Zhao, L.; Deng, J.; Sun, P.; Liu, J.; Ji, Y.; Nakada, N.; Qiao, Z.; Tanaka, H.; Yang, Y. Nanomaterials for Treating Emerging Contaminants in Water by Adsorption and Photocatalysis: Systematic Review and Bibliometric Analysis. Sci. Total Environ. 2018, 627, 1253–1263. <https://doi.org/10.1016/j.scitotenv.2018.02.006>.
72. Zhang, C.; Li, H.; Yu, Q.; JLA, L.; Wan, LY. Poly (aspartic acid) Electrospun Nanofiber Hydrogel Membrane-Based Reusable Colorimetric Sensor for Cu(II) and Fe(III) Detection. ACS Omega.  2019 4 (11), 14633-14639 DOI: 10.1021/acsomega.9b02109
73. [Büning](https://pubs.rsc.org/en/results?searchtext=Author%3ADominic%20B%C3%BCning), D.;  [Roth](https://pubs.rsc.org/en/results?searchtext=Author%3AFranka%20Ennen-Roth),FE.;   [Walter](https://pubs.rsc.org/en/results?searchtext=Author%3ASarah%20Verena%20Walter),SV.;    [Hennecke](https://pubs.rsc.org/en/results?searchtext=Author%3ATobias%20Hennecke), T.;  [Ulbricht](https://pubs.rsc.org/en/results?searchtext=Author%3AMathias%20Ulbricht),M. Potassium-sensitive poly(N-isopropylacrylamide)-based hydrogels for sensor applications. **Polym. Chem.** 2018 ,**9**, 3600-3614 https://doi.org/10.1039/C8PY00490K
74. (74) Ozay, H.; Ozay, O. Rhodamine based reusable and colorimetric naked-eye hydrogel sensors for Fe3+ ion. Chemical Engineering Journal. 2013, 232,364-371, https://doi.org/10.1016/j.cej.2013.07.111.
75. Joseph, KA.; Dave, N.; Liu, J. Electrostatically Directed Visual Fluorescence Response of DNA-Functionalized Monolithic Hydrogels for Highly Sensitive Hg2+ Detection. ACS Applied Materials & Interfaces. 2011 3 (3), 733-739 DOI: 10.1021/am101068c