International Journal of Academic Health and Medical Research (IJAHMR)
ISSN: 2643-9824
Vol. 8 Issue 6 June - 2024, Pages: 25-29

Hydrogel Technology: Insight into Hydrogel Structure, Classification, and Biomedical Applications.

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Abstract*: Background:** *Hydrogels are polymeric networks with a high water absorption capacity. It has other properties like flexibility, porosity, stimuli-responsiveness, soft structure, and its resemblance to living tissue.* ***Objectives: *The current review aims to highlight on structure, classification, and biomedical applications of hydrogel.* ***Methods:*** *In this investigation, a review of the literature was used. Using the keywords hydrogel technology, biomedicine, and drug delivery, PubMed was searched for publications and papers published between 2010 and 2023. A total of 116 publications were found; the focus was on free-access English-language papers that focused on the uses of hydrogel technology in medicine, particularly drug delivery. The benefits of hydrogels include their soft structure, stimuli-responsiveness, flexibility, and adaptability. It is categorized according to its physical qualities, responsiveness, ionic charge, cross-linking, source, and preparation. Hydrogels find application in diverse domains such as biosensors, agriculture, the food industry, and medicine. Hydrogels are employed in many different industries because of their biocompatibility, biodegradability, and resemblance to living tissue.* ***Conclusion:*** *Hydrogel, a three-dimensional structured polymer with the capacity to absorb water, is categorized according to its source, charge, cross-links, and physical properties. It finds application in biomedical fields such as tissue engineering, 3D cell cultures, wound dressings, and drug delivery.*

Keywords: Hydrogel technology, Hydrogel structure**,** Biomedical Applications.

Introduction

Hydrogels are hydrophilic polymers, with a three-dimensional network structure that can absorb a large volume of water due to the presence of hydrophilic moieties [1]. It has other properties like flexibility, porosity, stimuli-responsive, soft structure, and its resemblance to living tissue [2]. The hydrogel can be processed as solid, semi-solid, and liquid [3]

Methods

A literature review was used in this study. PubMed® was searched for articles and papers published between 2010 and 2023 using the keywords hydrogel technology, biomedicine, and drug delivery. A total of 116 publications were identified, emphasis was on papers published in English with free access and focusing on applications of hydrogel technology in medicine, especially drug delivery.

Structure of hydrogel

The solid form of a hydrogel is a network structure of cross-linked polymer chains [4]. The mesh size and the molecular weight of the polymer chain between the cross-links are the most crucial parameters to define the hydrogel structure (Figure 1) [5]. Hydrogels can be cross-linked through physical (hydrogen bonding entanglement) or chemical (covalent) cross-linking. The diffusion of water into a hydrogel is the primary factor that determines its swelling [6].

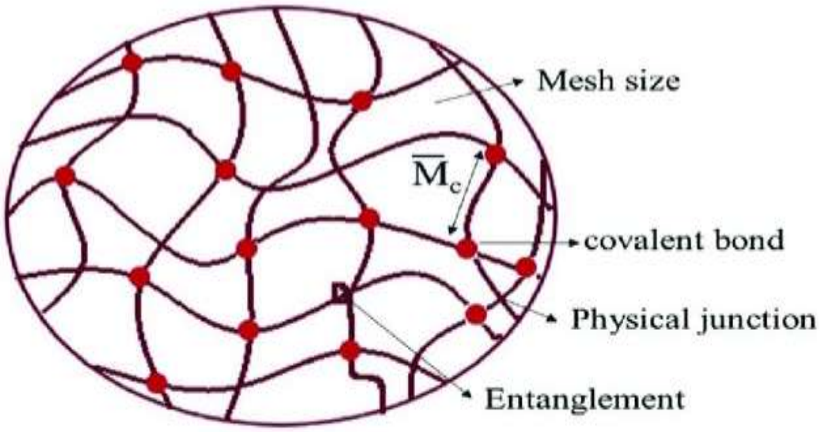

Figure 1. Structure of hydrogel at the molecular level [5].

Classification of hydrogels

Hydrogels are classified based on their source, preparation, ionic, charge, response, cross-linking, and physical properties [1]. Its further classification is given in a schematic representation in Figure 2 [7].

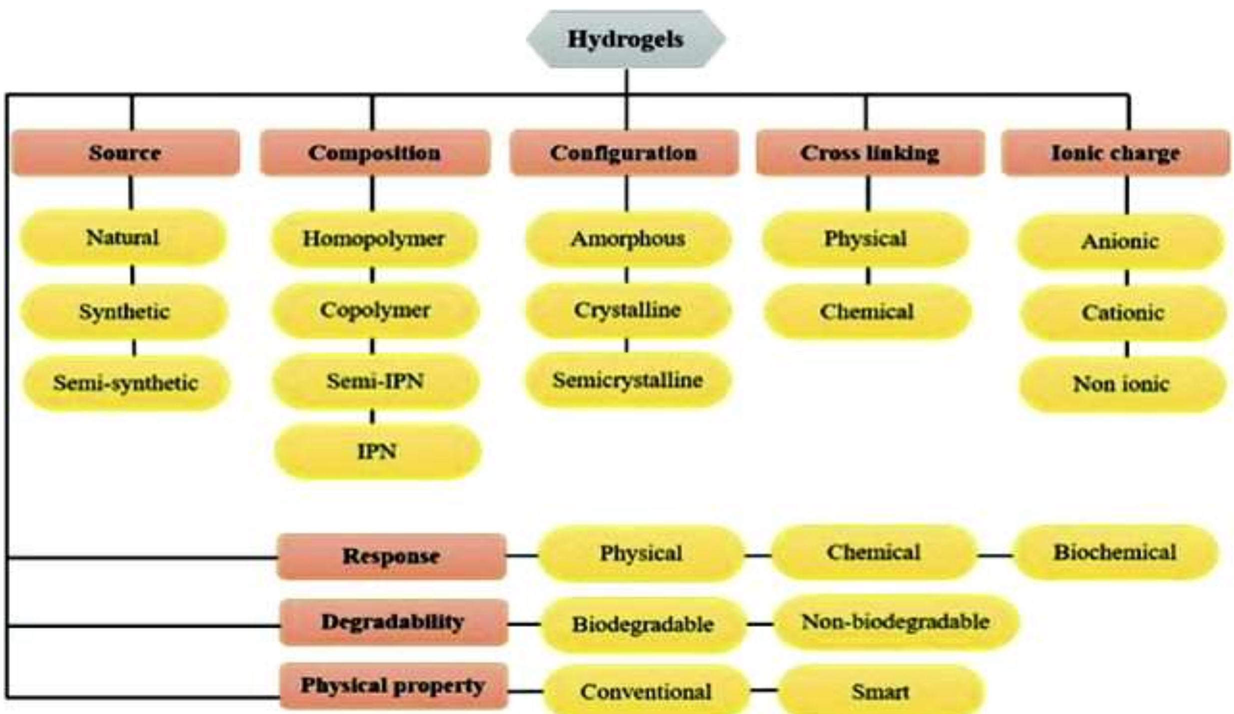

Figure 2. Schematic representation of classification of hydrogels [7].

Biomedical Applications
Wound dressings
Hydrogels can eliminate extra exudates and provide a physical barrier. Additionally, they offer a moist atmosphere that aids in the healing of wounds. Hydrogels can also be used as an injectable or sprayable wound dressing, which can help to fill up wounds with

uneven shapes [8-10]. The objective of tissue engineering is to create a scaffold that resembles the extracellular matrix found in vivo to facilitate tissue regeneration.[11]

Tissue Engineering

Because of their mechanical strength, biocompatibility, biodegradability, and similarity to the extracellular matrix found in vivo, hydrogels have attracted a lot of attention in the field of tissue engineering [12]. For the regeneration of bone, cartilage, nerves, and heart tissue, a hydrogel scaffold may be helpful. For instance, 3D printing collagen-chitosan can enhance nerve fiber regeneration and reduce the creation of cavities and scars [13].

3D Cell Cultures

Cells can develop in vitro in all directions on a helpful platform offered by three-dimensional cell cultures. It is possible to establish 3D cell culture by cultivating the cells on a 3D scaffold. The extracellular matrix (ECM) surrounds the cells in the in vivo 3D cell structures, forming a three-dimensional structure[14].

Drug delivery

The stimuli-responsive characteristics of polymeric moieties in hydrogels have led to increased interest in smart hydrogels. The ability to respond to stimuli can facilitate the development of innovative targeted pharmaceuticals and regulate drug release via non-intravenous delivery. The primary benefit is that a smart hydrogel can adapt to its environment, including temperature, pH, electromagnetic fields, radiation, magnetic fields, and biological factors, by changing its mechanical properties, swelling capacity, hydrophilicity, or permeability of bioactive molecules.[15]

Table 1. shows the application of those synthetic smart hydrogels for drug delivery.[15-26]

Hydrogels	Drug	Materials	Sustained-Release Time	Proposed Applications
Thermoresponsive hydrogel	Dexamethasone	HPMA	More than 30 days	Osteoarthritis and rheumatoid arthritis
	Topotecan	Poloxamer 407 and poloxamer 188	28 days	Colorectal cancer
	Lamivudine and zidovudine	Pluronic® F-127	168 h	AIDS
	Antibody	PEGMA	13 days	Enhance the efficacy of antibody treatment
pH-responsive hydrogel	Bortezomib	mPEG-LUT	50 h	Colorectal cancer
	Amifostine (S-2(3-aminopropylamino) ethyl phosphorothioate	MAC-g-PCL	6 h	Acute radiation syndrome
Photoresponsive hydrogel	Doxycycline	SPCOOH modified-silicone-hydrogel (poly(HEMA-co-PEGMEA))	42 h	Inflammation disease
	Insulin	BP, pNIPAM, PEG, and ETPTA	Not detected	Diabetic disease
Daul-responsive hydrogel				
pH/thermo	Doxorubicin chemosensitizer curcumin	poly (NIPAAm-co-DMAEMA)	168 h	Colon cancer
	Methotrexate		50 h	Breast cancer
pH/redox	Magnesium ions	poly (NIPAAm-co-DMAEMA) PLP-CDE	6 h	Ionic therapeutics

Conclusion

Hydrogel, a three-dimensional structured polymer with the capacity to absorb water, is categorized according to its source, charge, cross-links, and physical properties. It finds application in biomedical fields such as tissue engineering, 3D cell cultures, wound dressings, and drug delivery.

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