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Review on formulation of cellulose-based hydrogels and their biomedical applications

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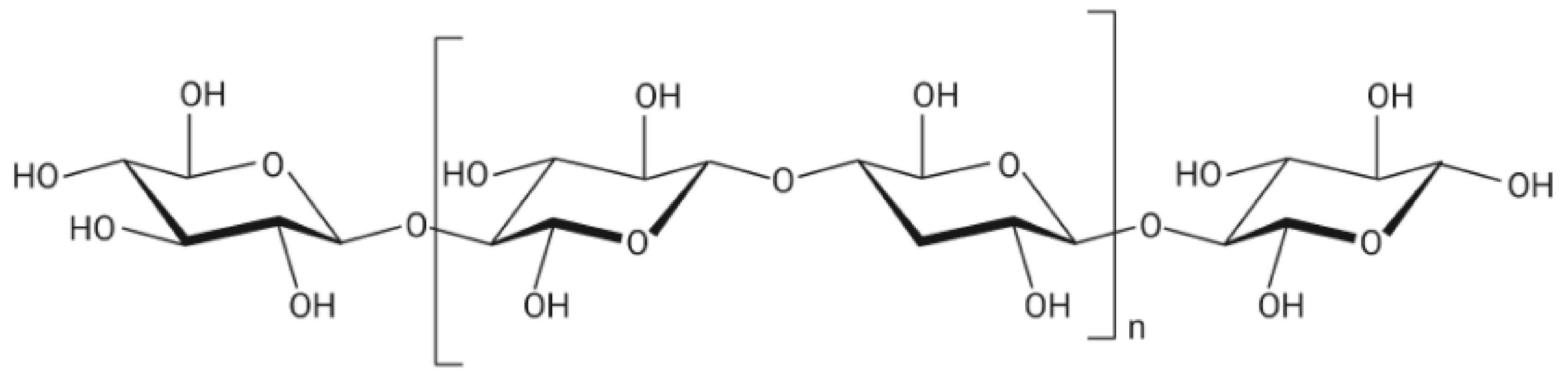
INTRODUCTION

- Cellulose, a biopolymer composed of D-glucose units, is the most abundant natural polymer on Earth. It can be extracted from a wide variety of sources, including plants, specific bacterial strains, and marine organisms, highlighting its versatility and making it a valuable material for various applications [1].



- Cellulose stands out as an ideal material for hydrogel preparation due to its exceptional properties, positioning it as one of the safest and most versatile options in biomedical applications, including [2]:
  - Biocompatibility;
  - Biodegradability;
  - Renewability;
  - Robust mechanical strength;
  - Environmental sustainability,

CELLULOSE DERIVATIVES

- Cellulose's limitations stem from its poor solubility, which is attributed to the presence of inter- and intramolecular hydrogen bonds, as well as van-der-Waals forces. However, these challenges can be mitigated through chemical modifications.
- The numerous active hydroxyl groups in cellulose allow for the development of various derivatives with customizable properties via processes such as oxidation, esterification, etherification, cross-linking [3].

CELLULOSE BASED HYDROGELS

- Cellulose-based hydrogels are prepared through physical or chemical cross-linking, utilizing the hydroxyl groups of cellulose and its derivatives to form an interconnected network structure through various interaction [2].
  - Physical crosslinking hydrogels involve non-covalent interactions,
  - Chemical crosslinking hydrogels are formed through covalent bonding mechanisms.

BIOMEDICAL APPLICATIONS OF CELLULOSE BASED HYDROGELS

The unique properties of cellulose and its derivatives position them as promising candidates for biomedical applications, with different formulations exhibiting potential in tissue engineering, wound healing, drug delivery, and 3D printing [4-6].

Biomedical applications	Cellulose hydrogels	Preparation
Drug delivery	CMC/Chitosan	Dissolving anionic CMC in dilute HCl solutions, followed by the addition of quaternized chitosan to form complexes through phase separation and subsequent neutralization.
	chitosan/hydroxy propyl methylcellulose (HPMC)/glycerol	Blending chitosan and HPMC powders in 0.1 M acetic acid, adjusting the pH to 6.8, and adding glycerol to prepare sample solutions.
	hydroxyethyl cellulose (HEC)/ hyaluronic acid (HA)	HA-HEC hydrogels were prepared by dissolving HA and HEC in NaOH, adding a cross-linker, incubating for 24 hours, and soaking in distilled water for neutralization.
Wound healing	hydroxyethyl cellulose (HEC)/tungsten oxide	HEC hydrogel membranes were prepared by dissolving HEC in water, crosslinking with citric acid, adding WO_3, and drying the mixture in Petri dishes.
	cellulose nanofiber (CNF)/quercetin (QT)	QT was dissolved in ethanol solutions, mixed with CNF suspension, homogenized, and then filtered and freeze-dried.
Tissue engineering	cellulose acetate (CA)/chitosan	Chitosan was dissolved in acetic acid, mixed with CA nanofibers, frozen, lyophilized, neutralized with NaOH, washed, and freeze-dried for scaffold preparation.
	bacterial cellulose (BC)/ collagen	The BC-collagen composites were prepared by incorporating collagen into BC hydrogels via esterification with Fmoc-glycine, followed by crosslinking with collagen and EDC, and drying and sterilization by gamma radiation.
3D bioprinting	carboxymethyl cellulose (CMC) / alginate	Scaffolds were prepared by mixing alginate and carboxymethyl cellulose (CMC) solutions, followed by a gelation process to form a stable network.
	nanofibrillated cellulose (NFC)/ alginate	Hydrogel prepared by concentrating NFC through centrifugation, mixing it with alginate, and then cross-linking the mixture with calcium chloride ($CaCl_2$).

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