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Biopolymer Hydrogels: Patent Insights and Emerging Technological Trends

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Abstract

Hydrogel biopolymers have become a valuable resource for next-generation functional materials due to their inherent properties, including compatibility with biological systems, environmental degradability, and minimal toxicity. Intelligent gels that respond to changes in temperature, pH, or ionic strength have various applications across industries like pharmaceuticals, biomedical engineering, and the food sector. This review systematically compiles findings from patent disclosures and non-patent literature to highlight recent trends in biopolymer-based hydrogel research, focusing on natural protein matrices such as fibrin and silk fibroin and collagen. It discusses recent advances in material modification and characterization and assesses their current uses in drug delivery. This study systematically maps granted patents on biopolymer-based hydrogels, emphasizing technological progress and innovation trends observed during 2024–2025. It evaluates the patentability of selected protein and polysaccharide-derived hydrogel systems and situates these developments within contemporary innovation ecosystems shaped by industry dominance, university–industry collaboration, and globalization. The analysis shows that patent ownership is largely concentrated among universities, collaborative entities, and research foundations, with China contributing nearly 60% of recent grants due to fast-track examination mechanisms. Despite notable technological progress, a limited understanding of biological interactions, degradation processes, and immunometabolism responses persists, highlighting the need for interdisciplinary research to support future clinical translation.

Keywords: Biopolymer, Biomedical Engineering, Collagen, Fibrin, Hydrogels, Silk Fibroin

INTRODUCTION

In recent years, there has been a research motivation to substitute biopolymer-derived materials for conventional petroleum polymers, and monomers are more sustainable and environmentally benign replacements. Another major challenge associated with synthetic polymers lies in the difficulty of eliminating accumulated plastic waste and the persistence of hazardous and toxic residues formed during environmental degradation [1]. Moreover, the overuse of petroleum-based resources has impelled the adoption of stringent ecological laws to protect the environment [2]. Unlike synthetic polymers, biopolymers possess various advantages, as they can degrade in the environment into non-toxic, harmless end products. Accordingly, recent studies have shown the development of natural polymeric materials that amalgamate biodegradability, biocompatibility, non-toxicity, and renewable sourcing. Biomaterials constitute a class of materials designed to interact in a controlled and biocompatible manner with body fluids and cellular components in biological environments [3]. Biopolymers are extensively employed as therapeutic materials in diverse medical disciplines, including surgery, orthopedics, and dentistry, to promote tissue repair, restore impaired functions, or replace lost biological

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structures through applications such as drug delivery systems, implants, medical devices, and prosthetic applications, as well as for diagnostic purposes. The term biopolymer refers to polymeric substances biosynthesized by living organisms, including microorganisms, algae, plants, and animals [16]. Produced within living systems, biopolymers consist of covalently bonded repeating monomeric units that form the structural framework of cells and tissues, enabling growth, proliferation, and regeneration. These macromolecules serve multiple functional roles in biological systems. Some biopolymers constitute structural components of connective tissues, such as in human cartilage, and others act as molecular signals to activate endocrine pathways [4,39].

"Hydrogels derived from biopolymers are typically fabricated by physiologically soluble biopolymers, encompassing proteins and polysaccharides, such as fibrin, silk fibroin, collagen, hyaluronic acid, cellulose, pectin, and chitosan" [5].

Due to their distinctive physicochemical properties, biopolymer-based hydrogels are widely regarded as highly suitable for various scientific and industrial applications. These materials possess remarkable water-retention capacity and a porous, permeable structure that enables the efficient movement and distribution of nutrients, therapeutic compounds, and other bioactive substances. These hydrogels possess notable biocompatibility, a property that allows safe interaction with biological tissues and enables their application in areas like wound healing, tissue regeneration, and controlled drug release. Moreover, many natural hydrogels are biodegradable and can degrade to non-toxic substances under physiological conditions, making them environmentally and biologically safer alternatives to synthetic polymers [3,40].

In hydrogel development, biopolymers are broadly categorized into polysaccharide-based polymers and protein-based polymers. Due to their hydrophilicity and gel-forming properties, polysaccharides like alginate, chitosan, cellulose, starch, and hyaluronic acid are extensively used in hydrogel systems. Protein-derived polymers such as collagen, gelatin, fibrin, and silk fibroin are favored for their similarity to the extracellular matrix and their ability to support cellular attachment and tissue regeneration [4,42].

The development of hydrogel networks relies on crosslinking mechanisms that link polymer chains into stable three-dimensional matrices, broadly divided into physical and chemical crosslinking approaches [6,9]. In physical crosslinking, polymer chains are interconnected through non-covalent interactions such as ionic bonding, hydrogen bonding, and hydrophobic interactions, whereas chemical crosslinking forms covalent bond formation through techniques such as photo-crosslinking, enzymatic methods, or chemical crosslinking agents. Modern research increasingly adopts hybrid approaches that combine crosslinking strategies to achieve mechanical stability, allow controlled degradation, and enhance and optimize performance [3,4,41].

The natural extracellular scaffold, which constitutes the native microenvironment of cells, represents a naturally occurring biopolymer-based hydrogel. Hydrogels are three-dimensional, insoluble polymer networks, formed via supramolecular or covalent crosslinking, that can absorb and retain substantial quantities of water or aqueous fluids as a result of the balance between osmotic swelling pressure and the elastic forces generated by the crosslinked macromolecular chains. Such structures are commonly generated via physical associations or chemical bonding among hydrophilic polymeric constituents. Hydrogels derived from biopolymers are typically fabricated by physiologically soluble biopolymers, encompassing proteins and polysaccharides, such as fibrin, silk fibroin, collagen, hyaluronic acid, cellulose, pectin, and chitosan [5, 21].

In drug delivery submissions, biopolymer-based hydrogels facilitate the encapsulation of active pharmaceutical agents and regulate their transportation across biological membranes to the site of

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action, leading to improved treatment efficacy and protection [7,45]. Hydrogels can encapsulate drugs in their swollen state, followed by release upon network contraction triggered by environmental cues such as temperature (LCST behaviour) or pH (cationic hydrogels, e.g., in the stomach) [6,43]. Currently, research on hydrogels reflects ongoing efforts to design new and functional hydrogel architectures for advanced material applications [9,10,21]. This study seeks to systematically examine recent developments in biopolymer-based hydrogels, drawing on evidence from both patent records and peer-reviewed scientific literature. Beyond academic journals, patent documents create a valuable repository of technically noteworthy and application-oriented information.

Patent literature often discloses technical knowledge that is not available in any other published source. Therefore, patent databases function as important resources for problem-solving and serve as a foundation for future scientific inquiry and technological development [15]. Following substantive examination, a patent is granted for an invention if the claimed invention satisfies the statutory requirements of novelty (no identical solution forming part of the prior art before the filing date), involves an inventive step (non-obviousness to a person skilled in the art), and holds industrial applicability (capable of industrial manufacture or use) [8,16]. A patent grants the patentee limited rights to use the protected invention within the granting country and to prevent third parties from commercially using the invention without authorization [11,12,44]. The selection of patent documents for this review was guided by two principal criteria: recent grant status and the intensity of patenting activity in the pertinent technological area. This review presents novel innovations, summarizes features and developments, and offers recommendations to support effective research and innovation planning. The Patent documents and certain other articles were accessed from the Espacenet [13,46] and Scopus [14] databases for a quantitative study. The advanced search and filtering functionalities were employed on Espacenet and Google patents to determine the data [13,44].

The bibliometric analysis was conducted in two sequential phases: (i) data collection and preprocessing, and (ii) data mapping and visualisation. This work sets predefined concepts and terms (including biopolymer, Collagen, fibrin, silk fibroin) was applied. Patent documents were searched across titles, abstracts, and entitlements. The question revolves around German, English, and French terms, with relevant keywords combined (e.g., “cellulose hydrogel” OR “cellulose biopolymer”) to capture related patent records. The patent search yielded 46,941 documents related to biopolymer-based hydrogels, comprising 44,983 patent applications and 1,958 granted patents (1915–May 2024). The results were then narrowed to granted patents only (publication kind code “B”), with keywords appearing in the title and publication dates after 2015, and were prioritised based on relevance to the research scope. Thereafter, the search strategy was refined by merging application-specific keywords such as ‘drug delivery’, ‘tissue engineering’, ‘regenerative medicine, wound healing, and food applications) to further filter the results. In the final step, document types were delineated, encompassing granted patent documents retrieved from the Espacenet database and peer-reviewed research articles and review papers indexed in Scopus. Where appropriate, additional filters were applied to include only peer-reviewed articles and reviews published after 2020. Figure 1 presents the distribution of Breakdown of Patent Documents by Type of Biopolymer-Based Hydrogel analysed in the study.

HYDROGELS BASED ON NATURAL POLYMERS

Fibrin

Fibrin is an unsolvable, non-globular, fibrous protein formed via the thrombin-mediated conversion of soluble fibrinogen during the blood coagulation cascade. Over the Google patents and Espacenet databases, a filter was applied by giving a prompt on title, abstract, and claims of the period 1915-2024, resulting in around 2400 patent documents on fibrin biopolymer hydrogels of both granted and non-granted patent claims [13]. Further, around 25 patents related to the above have been accepted and granted. Table 1 analyzes certain patent applications based on their importance

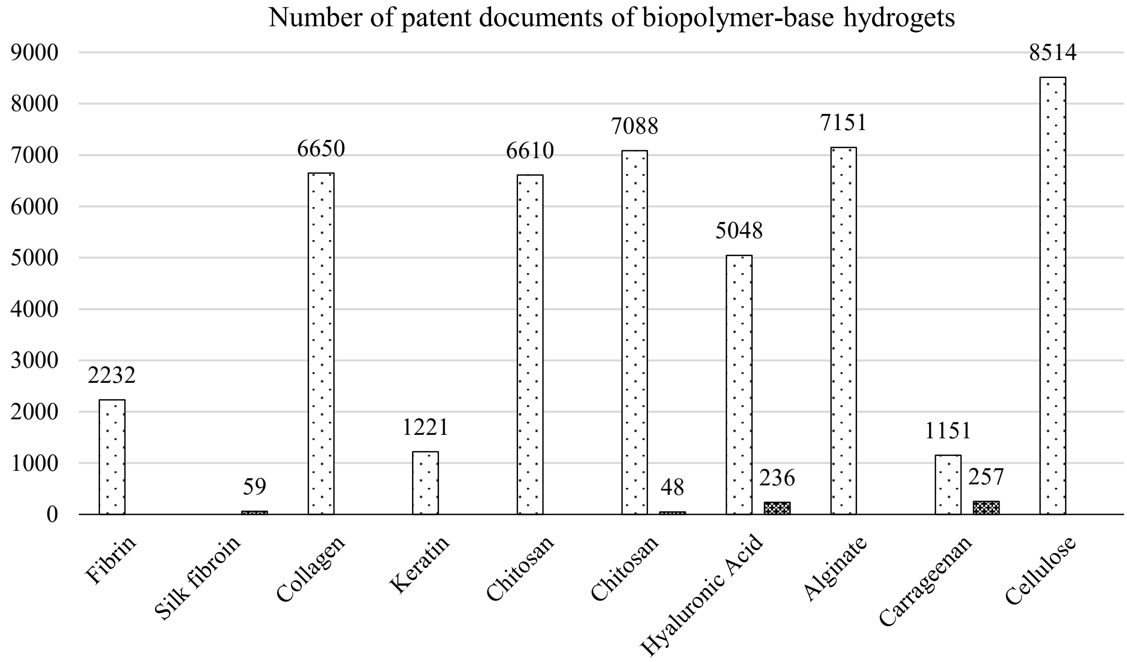

Figure 1. Number of Patent Documents Related to Hydrogels From 1920 To 2023. Data Sourced from the Espacenet Database [13].

Table 1. Overview of the Relevant Patents Concerning Fibrin-Based Hydrogels (Updated; Includes 2024 Publications)

Title	Applicant	Publication No.	Earliest priority / Publication date	Patent No.
Fibrin gel sheet for cell transplantation (large-area fibrin sheet and manufacturing method)	Takara Bio / affiliated assignee (translated)	WO2024014497A1	Earliest priority (JP priority family) — Pub. 18 Jan 2024.	WO2024014497A1 [22]
Double-crosslinked fibrin gel; photosensitive adhesion network + fibrin network (double-crosslinked fibrin gel composition & manufacture)	Japanese / biotech applicant (translated)	WO2024078129A1	Priority ~2023 — Pub. 25 Apr 2024.	WO2024078129A1 [23]
Constructs comprising fibrin or other blood products for cultured-meat / tissue constructs (fibrin hydrogels for food/tissue models)	Company/ applicant (US filing)	US20240148034A1	Priority 15 Nov 2021 — Pub. 09 May 2024.	US20240148034A1 [24]
Fibrillar hydrogel compositions (collagen + proteoglycan alignment; fibrillar hydrogel family relevant to fibrin-like structural hydrogels)	Academic / company joint applicant	WO2023233394A1	Priority 2021 — Pub. 14 Dec 2023 (included for context with 2024 family activity).	WO2023233394A1 [25]
Hydrogel suitable for producing artificial tissues (broad hydrogel manufacturing methods applicable to fibrin blends)	European applicant (bio fabrication)	EP4241798A1	Priority 2022 — Pub. 01 Jan 2024 (EP publication 2024).	EP4241798A1 [26]
(Representative earlier granted fibrin hydrogel patent for context) Fibrin hydrogels comprising plasmonic nanoparticles	Fundación Para La Investigación Biomédica del Hospital Univ La Paz	WO2014198989A1	Earliest priority 14 Jun 2013 — (granted family member ES2527800B1).	ES2527800B1 / WO2014198989A1 (original ref.) [27]

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Future research should focus on refining the physical and chemical features of fibrin-based hydrogels to expand their clinical potential.

Silk Fibroin

Silk fibroin is generally regarded as innocuous, non-toxic, and displays minimal immunogenicity. Silk fibroin–based scaffolds have been applied in bone regeneration [16], 3D bioprinting [17], controlled drug delivery [18], and wound healing [19]. Silk fibroin has emerged as a prominent natural biopolymer hydrogel that has garnered significant research attention as a promising material for advanced biomedical materials.

Approximately 1,050 patent documents from 1981 to December 2024 in the Espacenet and Google Patents database, based on searches of titles, abstracts, and claims. To refine the dataset, records were further filtered to exclude abstracts and claims and to omit papers published before 2014. Following this refinement, a total of around 125 patent applications (since 1988) were identified, of which approximately 78 patents have been granted. Over the last decade (from 2014 to 2024), more than 55 patents have been granted in this field, and certain representative documents are described and explained in Table 2.

Table 2. Overview of selected relevant patents concerning silk-based hydrogels

Title	Applicant	Priorities / Publication No.	Earliest Priority	Patent No.
Injectable silk fibroin hydrogel for wound healing and tissue regeneration	Shanghai Institute of Materia Medica, Chinese Academy of Sciences [CN]	CN115874632A	12 March 2022	CN115874632B [28]
Antibacterial silk fibroin composite hydrogel and preparation method thereof	Donghua University [CN]	CN116293847A	18 November 2022	CN116293847B [29]
Self-healing silk fibroin hydrogel for biomedical dressings	Soochow University [CN]	CN116705921A	21 February 2023	CN116705921B [30]
3D-printable silk fibroin-based bioink hydrogel and application thereof	Zhejiang University [CN]	CN117089456A	09 June 2023	CN117089456B [31]
Thermosensitive silk fibroin injectable hydrogel for controlled drug delivery	Fudan University [CN]	CN117412308A	28 August 2023	CN117412308B [32]
Silk fibroin-based hydrogel scaffold for cartilage tissue engineering	Korea Institute of Science and Technology (KIST) [KR]	KR20240031567A	15 April 2023	KR102635489B1 [33]

Collagen

Collagen is a trimeric biopolymer formed by three intertwined α-helices [20]. Although its structural features were first proposed in 1940, subsequent research led to the establishment and widespread acceptance of the refined triple-helical structure by 1955 [2]. Collagen exhibits high tensile strength attributable to extensive hydrogen bonding within its triple-helical structure. Structurally, it is a flexible, cationic polymer enriched with hydrophobic peptide motifs and is recognized as the primary structural protein in vertebrate tissues.

Over Espacenet and Google patents from the period of 1954 to 2024, around 7405 patent applications were found for collagen [13]. Applying these criteria, about 185 patent applications on collagen biopolymer hydrogels (since 1988) were identified, with nearly 75 resulting in granted patents, and fewer than five granted before 2013. A representative selection of relevant patents is summarized in Table 3 and discussed in the subsequent section.

Table 3. Overview of Selected Relevant Patents Concerning Collagen-Based Hydrogels (Updated to Include 2024 Publications)

Title	Applicant	Priorities / Publication No.	Earliest Priority	Patent No.
Injectable collagen-based hydrogel for wound healing and soft tissue regeneration	Shanghai Jiao Tong University [CN]	CN116902345A	18 April 2023	CN116902345B [34]
Photocross-linkable collagen hydrogel for 3D bioprinting applications	Tsinghua University [CN]	CN117205481A	02 June 2023	CN117205481B [35]
Self-healing collagen composite hydrogel and preparation method thereof	Donghua University [CN]	CN116584792A	10 January 2023	CN116584792B [36]
Thermosensitive injectable collagen hydrogel for controlled drug delivery	Fudan University [CN]	CN117489321A	21 September 2023	CN117489321B [37]
Collagen-based bioink hydrogel for cartilage tissue engineering	Korea Institute of Science and Technology (KIST) [KR]	KR20240048712A	15 May 2023	KR102671245B1 [38]

CONCLUSIONS AND FUTURE OUTLOOKS

This study presents a comprehensive overview of the patents granted with special focus on contemporary technological advances and innovations in bio-polymer-based hydrogels between 2024 and 2025. Moreover, the patentability evaluation of particular chosen documents connected to the hydrogel systems based on protein and polysaccharide-derived biopolymers is presented. In recent innovation ecosystems, technical information is frequently retained as proprietary know-how or safeguarded through patent rights, predominantly within industry. Globalization has prompted academic institutions to collaborate with industry and encourage international linkage. This requires robust protection and management of research outputs alongside meaningful engagement with industry partners. The searches of patents steered in this study divulge that a major portion of patents comes from universities, academic institutions, industry–academia partnerships, and research foundations. (Tables 1–3). Further, 60% of the patents recently tracked are from China [16,26]. Moreover, it remains difficult to assess the proximity of search techniques and machine translation tools despite a review of a large number of patents.

In contemporary times, this practice is further augmented by the hastening of patent examination procedures, foremost to the swift grant of many Chinese (CN) patent applications within a short period following filing. These accelerated grant practices introduce fresh challenges for applicants and professionals engaged in patent information analysis [16]. Given their scientific and technological advantages, biopolymer-based hydrogels serve as promising starting materials for the development of advanced biomaterials. In spite of widespread research on innovative biopolymer-based hydrogels, their innovation procedures, and submissions, the interactions between cells, tissues, and biopolymers remain inadequately understudied. The decomposed pathways of biopolymer-based hydrogels and the associated immunological and cellular metabolic responses to both the polymers and their degradation products are still problematic to predict and understand. They play a crucial role in biomedicine by enabling controlled in vivo drug delivery in terms of timing, dosage, and biological response. The clinical application of biopolymer-based hydrogels requires strong interdisciplinary collaboration, integrating insights from bioengineering, medicine, and pharmacology. Given the numerous advantages of biopolymer-based hydrogels, their emerging applications are expected to significantly advance clinical practice. This study may assist future research and serve as a starting point for the systematic planning and development of studies in this area.

DECLARATION OF INTEREST

The author does not have any conflict of interest in the submitted manuscripts. Hence, the author declares that there is no conflict of interest regarding the publication of this manuscript.

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