Materials Today Bio 26 (2024) 101082

Contents lists available at ScienceDirect

Materials Today Bio

journal homepage: www.journals.elsevier.com/materials-today-bio

Research progress of photo-crosslink hydrogels in ophthalmology: A comprehensive review focus on the applications

Qinghe Zhang [a], Ke Yan [a], Xiaoqin Zheng [a], Qiuping Liu [a], Yi Han [a,*], Zuguo Liu [a,b,**]

[a] Department of Ophthalmology, The First Affiliated Hospital of University of South China, Hengyang Medical School, University of South China, Hengyang Hunan 421001, China

[b] Xiamen University Affiliated Xiamen Eye Center, Fujian Provincial Key Laboratory of Ophthalmology and Visual Science, Fujian Engineering and Research Center of Eye Regenerative Medicine, Eye Institute of Xiamen University, School of Medicine, Xiamen University, Xiamen Fujian 361005, China

ARTICLE INFO

Keywords:
Photo-crosslink hydrogels
Ophthalmology
Tissue engineering
Drug delivery
3D printing

ABSTRACT

Hydrogel presents a three-dimensional polymer network with high water content. Over the past decade, hydrogel has developed from static material to intelligent material with controllable response. Various stimuli are involved in the formation of hydrogel network, among which photo-stimulation has attracted wide attention due to the advantages of controllable conditions, which has a good application prospect in the treatment of ophthalmic diseases. This paper reviews the application of photo-crosslink hydrogels in ophthalmology, focusing on the types of photo-crosslink hydrogels and their applications in ophthalmology, including drug delivery, tissue engineering and 3D printing. In addition, the limitations and future prospects of photo-crosslink hydrogels are also provided.

1. Introduction

Ocular diseases significantly impact patients' quality of life, drawing considerable attention from researchers in ophthalmology therapeutics. Currently, ophthalmic innovation therapeutic products are mainly concentrated in the field of ocular surface and fundus. The generalized ocular surface includes cornea, conjunctival and lacrimal glands, accessory lacrimal glands, meibomian glands, and related eyelid structures; Fundus refers to the bottom of the posterior segment of the eye, including retinal, choroid, optic nerve head, macula, arteriae and venae centralis retinae, among others [1,2]. The homeostasis of the ocular surface depends on the ocular surface structural and functional integrity, and the destruction of its integrity leads to various symptoms and diseases, such as dry eye, pterygium, keratoconjunctivitis [3,4]. The cornea acts as the transparent tissue on the ocular surface that forms the lateral wall of the eyeball, accounting for about one-sixth of the wall of the eye and providing about two-thirds of the refractive power [5,6]. The fundus is responsible for the light-sensitive function of the eye, and any lesion in the fundus will cause visual impairment [7,8]. The eyeball, exposed to the external environment, aimed to reduce the influence of external factors on the eye, there are multiple barriers on eye, such as cornea, conjunctival and blood-eye barrier formed by the blood-aqueous barrier and the blood-retinal barrier [1,9,10]. These barriers protect the eye from damage, while they also reduce the concentration and delivery efficiency of therapeutic drugs, thus, it is important to develop new dosage forms that can be consistently administered and can reach specific sites through the eye barrier [11]. Predominantly, the current eye treatment drugs mainly focus on the eye drops, while it exists some limitations, such as little absorption of ocular surface, blinking or tear flushing causing the rapid removal of eye drops from the ocular surface, resulting in low bioavailability of drug [12]. In addition, as the presence of the eye barrier, eye drops are difficult to reach the posterior part of the eye [13]. Vitreous injection is a commonly used fundus treatment, however it present the disadvantages of increasing the risk of infection and endophthalmitis caused by frequent injection and poor patient compliance [14]. In order to solve these challenges, innovative smart materials have been developed in recent years, which plays an important role in the biomedical field, crucial to overcome the current defects of ophthalmic drug delivery, achieving efficient delivery and long-acting slow release of ophthalmic drugs, and improve the bioavailability of drugs [15,16]. Furthermore, as eye diseases advance, certain conditions inevitably reach end-stage, placing some patients at risk of eyeball removal. Consequently, the emergence of regenerative medicine has

* Corresponding author.
** Corresponding author. Department of Ophthalmology, The First Affiliated Hospital of University of South China, Hengyang Medical School, University of South China, Hengyang Hunan 421001, China.
E-mail addresses: hanyixmu@foxmail.com, hanyi@usc.edu.cn (Y. Han), zuguoliu@xmu.edu.cn (Z. Liu).

https://doi.org/10.1016/j.mtbio.2024.101082
Received 27 January 2024; Received in revised form 19 April 2024; Accepted 3 May 2024
Available online 6 May 2024

Abbreviations

3D	Three-dimensional
HA	Hyaluronic acid
ECM	Extracellular matrix
GelMA	Methacrylate Gelatin
DS	The degree of substitution
GAG	Glycosaminoglycan
GlcNAc	D-*n*-acetylglucosamine
GlcUA	D-glucuronic acid
UV	Ultraviolet
pDCSM-G	Porcine-derived acellular corneal stroma hydrogel
SF	Silk fibroin
H	Heavy chain
L	Light chain
GA	Glycyrrhizic acid
SFMA	Methacrylate silk fibroin
NETs	Neutrophil extracellular traps
PEG	Polyethylene glycol
PAA	Polyacrylic acid
PVA	Polyvinyl alcohol
PDA	Polydopamine
PAM	Polyacrylamide
IPNs	Interpenetrate networks
PEGDA	Polyethylene glycol diacrylate
PVA-MA	PVA-methacrylate
FRPP	Free radical photopolymerization
FRP	Free radical polymerization
CRP	Controlled free radical polymerization
ATRP	Atom transfer radical polymerization
RAFT	Eversible addition-fragmentation chain transfer polymerization
Ce6	Chlorin e6
CAT	Catalase
PLGA	Poly lactic-hydroxyglycolic acid
PDT	Photodynamic therapy
FAD	Flavin adenine dinucleotide
FMN	Flavin mononucleotide
ODex	Oxyglucan
CXL	Corneal collagen crosslinking
COL I	I collagen
IOP	Intraocular pressure
NAGA	N-acrylylglyamide
CBAA	Carboxybetaine Acrylamide
PCO	Posterior capsule opacity
HAMI	HEMA-co-MAA-comma-co-HI
HEMA	Hydroxyethyl methacrylate
MMA	Methyl methacrylate
MAA	Methacrylate
HEMA-IND (HI)	Indomethacin methacrylate
AMD	Age-related macular degeneration
RP	Retinitis pigmentosa
RPE	Retinal pigment epithelium
2D	Two-dimensional
MeCTS	Methacrylate functionalized chitosan
CsA	Cyclosporin
PEGNB	O-nitrobenzyl alcohol-modified polyethylene glycol
HAMA	Methacrylate modified hyaluronic acid
ICG	Indocyanine green
Dex	Dexamethasone
TA	Triamcinolone
rASCs	Rabbit adipose-derived mesymal stem cells
CJSCs	Conjunctival stem cells
DLP	Digital light processing
PAH	Polyacrylamide acrylate hydrogel
IOL	Intraocular lens
LECs	Lens epithelial cells
PR	Photoreceptors
OLM	Outer limiting membrane
ONL	Outer nuclear layer
OPL	Outer plexiform layer
INL	Inner nuclear layer
IPL	Inner plexiform layer
GCL	Ganglion cells layer
NFL	Nerve fiber layer
TPMS	Three-period minimum surface
DLP	Digital light process
PNG	Poly-NAGA-GelMA
FBR	Foreign body reaction

become pivotal in addressing these challenges. Particularly, with the advancements in biomaterials science, the field of ophthalmic regenerative medicine has seen significant progress, especially with the promising application of intelligent response materials.

Photo-crosslink hydrogels composed of photo-crosslinked polymers, photo-initiators and other compounds. As a photosensitive system, they could be photo-crosslinked from solution to hydrogels under ultraviolet or visible light irradiation to achieve liquid-solid phase transition [17]. Through adjusting the light intensity and exposure time, the crosslinking state of hydrogels can be controlled, and then the properties of cured hydrogels can be affected [18]. Photo-crosslink hydrogels exhibit several advantages, such as good biocompatibility and less cytotoxicity, which supports cell proliferation and phenotypic maintenance [19,20]. Besides, the hydrophilic network structure inside the hydrogel provides scaffolds and spaces for cell adhesion and migration, as well as drug storage and release, hence it identified as a suitable cell carrier material or drug delivery system [17,21]. Thanks to the biocompatibility, reaction gentleness and condition controllability, photo-crosslink hydrogels have been widely studied and applied in tissue engineering, drug delivery and 3D bioprinting.

The following review delves into recent advancements in photo-crosslink hydrogels within ophthalmology. It primarily explores the progress made in the field of tissue engineering, encompassing corneal regeneration, vitreous substitutes, lens substitutes, retina regeneration. Additionally, it investigates developments in the drug delivery, specifically addressing concerns such as dry eyes, corneal inflammation, and retinal neovascularization. Furthermore, the review extends its focus to the realm of 3D printing, examining applications in corneal, conjunctival, crystalline lens, retina, orbital implant, and various ophthalmic devices.

2. Overview of photo-crosslink hydrogel

2.1. Hydrogel

Hydrogels identified as the crosslinked three-dimensional (3D) polymer networks with high water content formed by chemical monomers or polymer chains connected by covalent or non-covalent bonds [22,23]. The polymer chain is rich in groups, the hydrophilic functional groups on the main chain maintain the water absorption ability of the hydrogels, and the cross-linking between the polymer chains provides the resistance to dissolution, making them stable in the water environment [24,25]. In addition, hydrogels exhibit polymer network topology and three-dimensional water-containing pore space structure, enabling

them to provide delivery functions for the encapsulation of synthetic drugs or biological macromolecules such as oligonucleotides, peptides and proteins [26–28]. Due to the good biocompatibility and degradability, hydrogels also display a good application prospect in tissue engineering [29].

2.2. Photo-crosslink hydrogel

Over the past decade, hydrogels have evolved from static materials to intelligent materials with controllable response, and the properties can be changed by adjusting external physical and chemical stimuli [30]. Physical stimuli include temperature, electric or magnetic fields, light, mechanical pressure and sound, while chemical stimuli include pH, solvent composition, ionic strength and molecular species [25,31]. Notably, light-sensitive (light-responsive) hydrogels have received more attention due to their non-contact remote control and inherent spatio-temporal control capabilities [32].

Photo-crosslink hydrogels could be switched by photo-crosslinked and solidified into hydrogels to achieve sol-gel phase transition when exposed to ultraviolet or visible light [17]. Light irradiation is a convenient and non-invasive mode of controllable response, which undergo remotely control without direct contact, which produces corresponding stimulus, and it adjusted by the light source switch, light dose, light wavelength, exposure time and irradiation position, to achieve the formation of hydrogel time and space and various properties of regulation. The specific advantage presents: (1) By switching the light source, the remote non-contact control of hydrogel liquid-solid phase transition can be realized easily; (2) The properties of hydrogels (strength, viscosity, porosity, and degradation) precisely regulated by adjusting the light parameters (intensity, wavelength and exposure time of light); (3) The variable wavelength of the cured-light applied to different application scenarios; (4) The accessibility of the curing position is not limited by the external environment; (5) Involved in the regulation of material properties and cell states inside the encapsulated photo-crosslink hydrogels. The advantageous features of photo-crosslink hydrogels make them as promising materials in the biomedical field, particularly for ophthalmic applications, such as tissue engineering, drug delivery and as sources for 3D printing ink [33,34].

3. Types of photo-crosslink hydrogels

The main components of photo-crosslink hydrogels comprise water-soluble photo-crosslinked polymers, the main photopolymerization methods are chain polymerization reactions triggered by free radicals and biological orthogonal clicking reactions [33,34]. The former is the most commonly used reaction in the synthesis of hydrogels, usually based on methacrylate functionalized prepolymers, via a chain growth mechanism [35]. The latter, distinguished by high reactivity, good selectivity, and mild reaction conditions, facilitates the development of hydrogels with a consistent structure and stable contents encapsulation [34,36]. Naturally derived materials containing bioactive motifs for cell-matrix interactions, or synthetic compounds with controllable material properties such as elasticity and degradability, form photo-crosslink hydrogels. Representative photo-crosslink hydrogels derived from naturally materials include collagen, hyaluronic acid, chitosan, fibroin and gelatin. Sources of synthetic materials include polyvinyl alcohol, polyacrylic acid, polyethylene glycol and polyacrylamide (Fig. 1) [35].

3.1. Natural materials

Collagen, gelatin, hyaluronic acid (HA), chitosan, fibroin protein and other natural hydrogel materials are rich in sources, easy to obtain, which present good biocompatibility and biodegradability. Although natural hydrogels have poor mechanical properties such as rigidity and stretchability, the active groups (-COOH, –OH, $–NH_2$) on the hydrogel chain provide sites for the functional modification [22,37]. The physical properties of photo-crosslink hydrogels could be altered through grafting, multiple crosslinking and composite formation with other polymers [38].

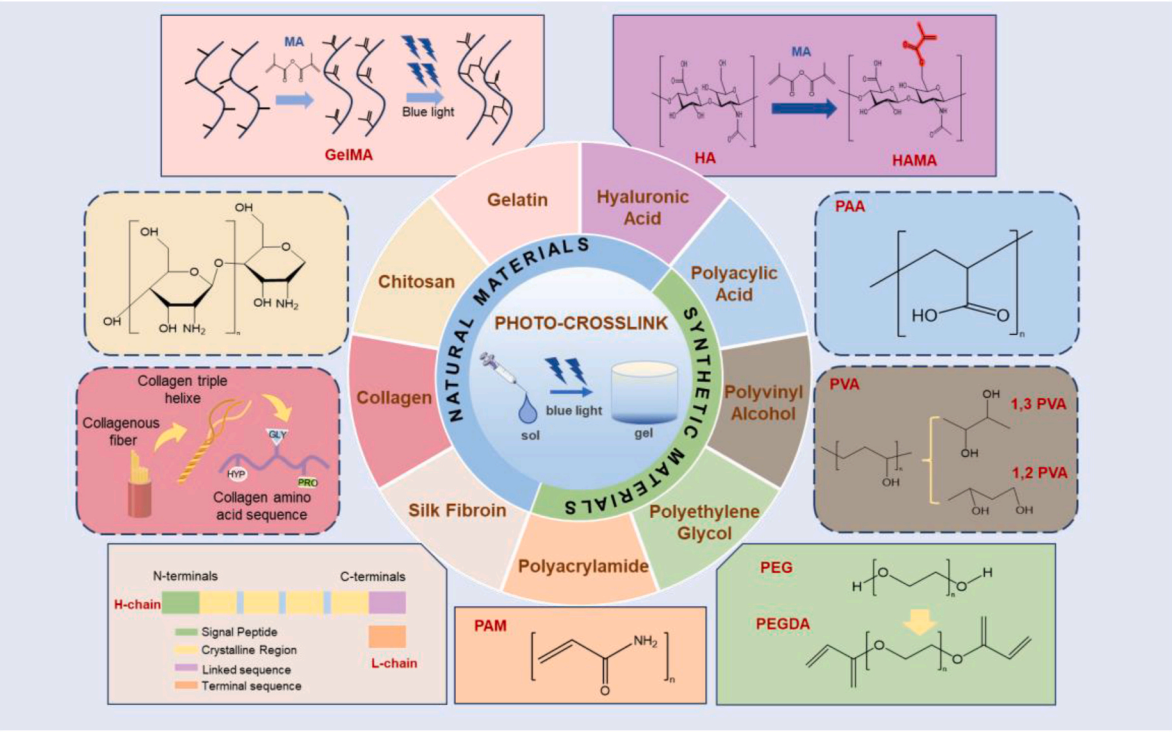


Fig. 1. Classification of photo-crosslink hydrogels: natural materials and synthetic materials.

3.1.1. Gelatin

Gelatin, derived from collagen, is a derivative of type I collagen. It is widely available and water solubility, temperature sensitivity, high biocompatibility, degradability and low antigenicity [39–41]. Besides, as the main components of the extracellular matrix (ECM), gelatin gains the function of enhancing cell adhesion and reshaping the cell microenvironment via the arginine-glycine-aspartic acid sequence [39,42]. However, natural gelatin hydrogels present poor mechanical properties, insufficient stability and fast degradation rates. In order to overcome the limitations, comprising enhance the mechanical properties, improve the stability and cytocompatibility, methacrylate is induced in the side chain of gelatin, synthetic Methacrylate Gelatin (GelMA) can be chain photopolymerized by ultraviolet and visible light. The elastic modulus of GelMA in the range of 3.3–110 kPa is determined by the degree of substitution (DS) of methacrylate and concentrations. Thus, the hydrogel with adjustable mechanical properties, good biocompatibility and low immunogenicity was formed [35,42–45]. Han et al. developed a photo-crosslink hydrogel based on GelMA, which owned excellent transparency and mechanical properties, as well as good biocompatibility, cell adhesion and slow degradation. Injecting it into corneal stroma which provided space for cell growth and migration, maintain corneal thickness, promote corneal stroma remodeling. It present a prospect in correcting refractive errors such as hyperopia and keratoconus [46]. Compared with the current photo-crosslink hydrogels, GelMA is more widely used and meets a variety of biological functions. Combining the advantages of natural and synthetic hydrogels, it becomes the most representative materials in the field of photo-crosslink hydrogels.

3.1.2. Hyaluronic acid

Hyaluronic acid (HA) is a hydrophilic, electronegative linear non-sulfated glycosaminoglycan (GAG), formed by alternating connections of D-*n*-acetylglucosamine (GlcNAc) and D-glucuronic acid (GlcUA) as basic disaccharide units [47]. As the main component of ECM, it exists in skin, cartilage, vitreous and other tissues and participates in inflammation and angiogenesis [48,49]. Due to its unique viscoelasticity, good biocompatibility, biodegradability and hydrophilicity, hyaluronic acid also displays great potential in regenerative medicine [50,51]. Typically, hydrogels composed of hyaluronic acid exhibit loose binding between side chains, leading to a soft structure and low strength, making them susceptible to hydrolysis and degradation [51,52]. However, the physical and chemical properties of hyaluronic acid changed by modifying the active groups such as hydroxyl group and carboxyl group on the molecule [50]. For example, after the methacrylate group is introduced to the hyaluronic acid chain, the hyaluronic acid chain can be photo-crosslinked under ultraviolet (UV) light irradiation, so as to form a hyaluronic acid hydrogel with higher strength that supports other bioactive factors, called HAMA hydrogel [53]. In addition, the cell adhesion of HAMA increased by grafting RGD peptide on HAMA or by introducing other types of hydrogels to construct multi-group hydrogels. Shen et al. constructed a double-cross-linked double-network composite hydrogel based on porcine-derived acellular corneal stroma hydrogel (pDCSM-G) and HAMA. The hydrogel improved the poor cell adhesion of HAMA, showing good pro-regenerative biological activity, adhesion and mechanical properties. It quickly sealed corneal defects of different shapes and sizes without suture, effectively support the survival and proliferation of corneal cells, promoting corneal re-epithelialization and stroma regeneration, inhibit scar formation, and reconstruct transparent cornea [54].

3.1.3. Collagen

Collagen identified a stable triple helix structure, and the polypeptide chain is composed of a tripeptide $(GlyX\text{-}Y)_n$ repeat domain, where X and Y are usually proline (Pro) and hydroxyproline (Hyp), besides the collagen length is about 300 nm, which presents high biomechanical properties [55]. In addition, triple helix collagen has a certain protease resistance, while collagenase can degrade it by removing terminal peptides from its structure, disrupting the interconnect between cross-linked trivalent ions [56–59]. Among all collagen proteins, type I, II and III account for more than 90 % of the total collagen protein. They are the most important extracellular matrix proteins, which can serve as cell scaffolds to support cell growth and are the main structural components of connective tissues [57,60,61]. Collagen is one of the most widely used natural biomaterials as to its good biocompatibility, physical, mechanical properties and low immunogenicity [55]. Enhancing the specific strength and toughness of collagen is achievable by modifying it with different crosslinking agents as well as conditions [62]. Chemically modifying photo-crosslinked functional groups, such as methacrylate and epoxy propyl methacrylate, on the side chains of collagen allows collagen derivatives to produce hydrogels with stronger mechanical properties and greater biological stability by exposing to the visible or ultraviolet light [63]. Photo-crosslink collagen hydrogels are suitable for a variety of biomedical application scenarios, including tissue engineering, regenerative medicine, drug delivery and biosensing [61,64,65].

3.1.4. Silk fibroin

Silk fibroin (SF) is a common fibrous protein of which composition and structure are similar to extracellular matrix [31]. SF protein is a natural amphiphilic block copolymer, consisting of a hydrophobic heavy chain (H) and a relatively elastic hydrophilic light chain (L) composed of Gly-Ala-Gly-Ala-Gly-Ser and Gly-Ala/Ser/Tyr repeated polypeptide sequences, which are connected by disulfide bonds, with certain flexibility and stability [20,66,67]. SF protein shows excellent biocompatibility, biodegradability and mechanical properties, has good water vapor permeability and bactericidal properties, which results in reducing inflammation and promoting wound healing [68–70]. As a semi-crystalline structural protein, SF hydrogel owns excellent mechanical properties, porous structure and controllable drug delivery ability. Thanks to its properties, SF becomes a smart polymer biomaterial, extensively employed in the fields of suture and wound repair, controlled drug delivery and tissue engineering [31,66,67,71]. The properties of SF changed by chemical modification intervention according to the need, so that it obtain good mechanical, biological effects and better performance [67,72,73]. Qian et al. built a polymer hybrid hydrogel based on inorganic Zn^{2+} induced self-assembly glycyrrhizic acid (GA) and SF photo-crosslinked methacrylate silk fibroin (SFMA). Possessing the ability for rapid *in situ* photo-crosslinking, strong tissue adhesion, good injection performance and mechanical strength, which facilitates the regulation of macrophage response in the inflammatory microenvironment. The stimulation leads to the polarization of macrophages to the M2 phenotype, elimination of reactive oxygen species in the wound, and the swift healing of the injured site. It is well-suited for use in wound dressings [74]. Mei et al. developed a photo-crosslink hydrogel system, called M@M -Ag-Sil-MA, which was assembled by a methylpropylene oxyated silk protein hydrogel (Sil-MA) system with metformin supported mesoporous silica microspheres (MET@MSNs) and silver nanoparticles (AgNPs). In the hydrogel system, Sil-MA endows the hydrogel system with *in situ* photo-crosslink ability and controls the release of silver NPs, thus inhibiting bacterial aggregation and creating a sterile microenvironment. M@M-Ag-Sil-MA promotes wound healing by inhibiting the formation of neutrophil extracellular traps (NETs), reducing the release of pro-inflammatory factors and promoting fibroblast migration and endothelial angiogenesis by modulating the immune microenvironment *in vivo* [75].

3.1.5. Chitosan

Chitosan is a positive linear polysaccharide copolymer composed of glucosamine (2-amino-2-deoxyd-glucose) and n-acetylglucosamine (2-acetylamino-2-deoxyd-glucose) units via (β-1-4) glucoside bonds, mainly derived from Marine crustaceans, produced by deacetylation of chitin. With biocompatibility, antibacterial ability and mucosal

adhesion, it is usually involved in biomedical fields such as wound dressing and tissue engineering [76–78]. The active functional groups of chitosan side chains, such as amino and hydroxyl, can be crosslinked with different crosslinkers or other polymers at the molecular level to improve the physical and chemical properties and functions of chitosan [79]. Through the combination of chitosan with photosensitive groups like methacrylate and the induction of a photo-initiator to generate free radicals via ultraviolet or blue light irradiation, covalent crosslinking between chitosan polymers is achieved. It leads to the formation of photo-crosslink hydrogels with adjustable concentration-dependent mechanical properties and structural morphology, showcasing favorable physical and chemical characteristics [79–82]. Owing to their unique electrical properties, hydrophilicity, biocompatibility, non-toxicity and diverse biological activities, such as broad-spectrum antibacterial, anti-tumor and anti-oxidation effects, glycan hydrogels attracte significant attention in the fields of drug delivery and tissue engineering [80,83].

3.2. Synthetic material

Synthetic hydrogels such as polyethylene glycol (PEG), polyacrylic acid (PAA), polyvinyl alcohol (PVA) and polyacrylamide (PAM) are chemically cross-linked. Compared with natural polymers, synthetic polymers identified modifiable structure, higher mechanical strength and controllable biodegradation rate, nevertheless there are still some shortcomings exists. Such as poor biocompatibility, risk of biological toxicity and wound immune rejection, or lack of biological activity which may cause the necessary reaction in the body. The aim of preparing new copolymer hydrogels is to simulate the structure of natural polymers and enrich the functions of polymers [38]. Composite hydrogels are developed, which appears as copolymers with main-chain crosslinks, or as poly interpenetrating networks (IPNs), where copolymers consist of two or more different monomers arranged in random, block or alternating configurations along the polymer network chain. Poly interpenetrating polymer hydrogels consist of two independently cross-linked synthetic and/or natural polymers in a network form. In this way, hydrogels precisely modified to highlight the best properties of each of their constituent components, allowing for a greater degree of control over their properties [25,37].

3.2.1. Polyethylene glycol

Polyethylene Glycol (PEG) is a polymer composed of repeated glycol units, which is safe, non-toxic, flexible, biocompatible and highly hydrating [84,85]. Polyethylene glycol can be used alone or in combination with polymers [86]. It exists rich side chain active groups on PEG. To optimize the pharmacokinetic and pharmacodynamic outcomes of drugs, PEG chemically modified or combined with proteins or drugs to achieve pegylation. The approach enhances biocompatibility, reduces immune reactions, diminishes uptake by the reticuloendothelial system and lowers the drug degradation rate. Thereby extending the biological half-life of circulation in the body [85,87–89]. Therefore, Polyethylene glycol and its derivatives are widely used in a variety of biomedical applications, such as coating medical devices to control host immune responses, or as molecular biological carriers to carry drugs or bioactive molecules to penetrate barriers in and reduce degradation *in vivo*, besides, it manipulated to form various hydrogels for cell culture and stem cell differentiation [52,86,90]. PEG chemically modified with acrylate groups to produce a photopolymerizable polyethylene glycol diacrylate (PEGDA) [91]. Originating from PEG, the photo-crosslink hydrogel rapidly encapsulates cells or drugs, demonstrating controllable mechanical properties, adhesion, high controlled release ability, antibacterial effects and antioxidant properties, applied span tissue engineering, drug delivery and other fields [92–94].

3.2.2. Polyvinyl alcohol

Polyvinyl alcohol (PVA) consists of vinyl acetate by polymerization and alcoholysis, containing alcohol groups, easily soluble in water, and form hydrogen bonds with water. PVA is a biodegradable semi-crystalline synthetic polymer, with excellent properties such as biocompatibility, adhesion, high mechanical properties [95–98]. PVA is widely used in wound dressing and drug delivery as its excellent physical, chemical properties, non-toxicity and biodegradability [96,98]. Compared with other polymers, simple polyvinyl alcohol present limited water resistance, biological activity, lack of exudate absorption and drug delivery ability, hence there are still some shortcomings when used as wound dressings alone [99,100]. By chemically modifying PVA with acrylate groups, a copolymer with photopolymerization ability formed. The polyvinyl methacrylate for wound dressing displays good biocompatibility, biodegradability, antibacterial activity and provides necessary moist environment, so as to improve the wound healing rate [101]. PVA mixes with other organic or inorganic compounds, such as blending UV-curable PVA-methacrylate (PVA-MA) with RGD polypeptide polymer, enhances cell adhesion and explores its potential application in soft tissue engineering [102].

3.2.3. Polyacrylic acid

Polyacrylic acid polymerized by acrylic monomer via covalent bond, the molecular formula is $C_3H_4O_2$, the structural formula contains a *cis*-double bond and carboxyl group, is a water-soluble chain polymer, including shell polymerization, star and interpenetrating network series, with low-toxic, dry adhesion and hemostatic ability [103]. The underwater bonding polyacrylic acid (PAAc) hydrogel coating formed by chemical modification of polyacrylic acid with methacrylic acid gives inert materials the ability to bond underwater, hence it attracts much attention in the field of wound dressings [104]. Polyacrylic acid changes its properties and applications by introducing different side chains and crosslinks, offering the possibility of hydrogen bond formation, thus allowing it to react with other polymers that forms hydrogen bonds [105]. When polymers such as polyacrylic acid and polyacrylamide come into combined, they cause a liquid to solid transformation of the polymer under light irradiation, with targeted drug delivery to specific organs as well as tissues, in the meanwhile sustained drug release [105,106].

3.2.4. Polyacrylamide

Polyacrylamide (PAM) is a neutral polymer formed by copolymerization of acrylamide homopolymer or other monomers. As a linear polymer, PAM displays good thermal stability [107]. Moreover, the abundance of amide groups in the structural unit of polypropylene diluted amide facilitates the formation of hydrogen bonding, resulting in excellent water solubility and chemical activity, consequently, it finds extensive applications in the medical and various other industries [105]. Polyacrylamide (PAM) exhibits poor cell adhesion, while it owns good mechanical properties, hence it is usually used in combination with natural hydrogels to maximize functionality [108]. Li et al. designed a dressing, PAM/DA-HA-EPL, for the light-triggered, *in situ* formation of an antimicrobial memory hydrogel, it based on acrylamide (AM) and dopamine-hyaluronic acid-ε-poly(L-lysine) (DA-HAEPL), underwent rapid transformation from liquid to solid under blue light, and conformed to the wound morphology, effectively isolating the wound through adhesion, thereby enhancing biocompatibility and accelerating the healing of infected wounds [109]. Han et al. prepared a GelMA/PAM biohybrid hydrogel based on gelatin methacrylate (GelMA) and acrylamide (AM) under ultraviolet light irradiation, which combined the biocompatibility of GelMA hydrogel with the physical properties of flexible PAM, and repaired the cartilage defects in rabbit knee joints, which identified a broad prospect in the field of articular cartilage tissue engineering [110].

4. Reactions in photo-crosslink hydrogels

Hydrogels feature polymeric networks in which crosslinking plays an

important role in the formation and degradation of polymers. There are two main forms of cross-linking, covalent cross-linking including Schiff base reaction and free radical polymerization, and non-covalent cross-linking including hydrogen bonding and hydrophobic interaction. According to the different crosslinking methods, hydrogels were divided into chemical hydrogels and physical hydrogels [111–113]. Physical cross-linking is widely used in self-healing hydrogels due to the absence of cross-linking agents and reversible cross-linking, which owns the prominent advantage of safety and injectable [114,115]. The formation of irreversible covalent bonds in chemically crosslinked hydrogels is usually mediated by crosslinking agents [114]. In comparison to physical cross-linking, hydrogels formed through chemical cross-linking are typically more stable and have diverse biomedical applications, such as 3D printing, specifically, photo-crosslink hydrogels were produced mainly through free radical photopolymerization (FRPP), facilitating a macroscopic transition from liquid to solid states (Fig. 2).

4.1. Photo-crosslink mechanism of hydrogels

Free Radical Polymerization (FRP) is known as a polymerization reaction initiated by free radicals that results in the growth of chain-growing radicals, also free radical polymerization [116]. Free radical polymerization consists of four basic steps: i) Chain initiation, that is, the formation of active center free radical, and free radical initiator monomer. ii) Chain growth (Propagation), active monomer free radicals form macromolecular free groups through chain addition with alkene monomers. iii) Chain termination, the disappearance of active free radicals, including single-base termination and double-base termination, which usually occurs through bimolecular binding or (and) disproportionation. iv) Chain transfer, chain radicals terminate stably by snatching atoms from other molecules, while molecules that lose atoms new free radicals [117]. In comparison to other polymerization techniques, the reaction conditions of free radical polymerization are mild and easy to operate. Controlled free radical polymerization (CRP) provides enhanced control over the molecular weight, distribution, functionality, and composition of polymers. The method is suitable for developing polymers with specific composition and properties, besides it combined with various vinyl monomers to create polymers tailored for different purposes [118–120]. CRP technologies including photoinduced CRP, electrochemically regulated CRP and ultrasound-regulated CRP, among which photoinduced CRP includes photo-regulated atom transfer radical polymerization (ATRP) and photo-regulated reversible addition-fragmentation chain transfer polymerization (RAFT) [119]. Free radical graft copolymerization of hydrogels usually requires the presence of an initiator, and the properties of hydrogels adjusted by the type and dose of the initiator. The photoinitiated radical-mediated thiol-alkene reaction serves as a "click" polymerization method, offering high efficiency, simplicity, and the absence of by-products typical of traditional "click" reactions, and primarily utilized for cross-linking thiomers and olefins, it presents significant advantages in polymer synthesis [121]. The reaction initiates with photochemical cleavage induced by UV or visible light irradiation, generating a reactive mercapto radical. This radical subsequently reacts with an olefin, resulting in the formation of a new carbon radical, following this, another thiol substrate reacts with the carbon radical, regenerating a mercapto radical, thus initiating a propagation cycle [122,123]. Meng et al. combined the photosensitizer Chlorin e6 (Ce6) with catalase (CAT) by forming an amide bond to obtain a composite photosensitizer (Ce6-CAT), and in the case of imiquimod (R837)-loaded poly lactic-hydroxyglycolic acid (PLGA) nanoparticles (RPNPs) as immunoadjuvant, Ce6-CAT and polyethylene glycol diacrylate (PEGDA), as well as RPNPs were blended to obtain an injectable hydrogel precursor, which could form hydrogels *in situ* based on free radical polymerization reaction under light exposure (Fig. 3A). Besides, the free radicals generated by Ce6 also had a strong injurious effect on tumor cells, which led to the long term retention of drugs and multiple rounds of photodynamic therapy (PDT) [124]. Hu et al. constructed a light-enzyme coupling system based on flavinase/flavin adenine dinucleotide (FAD)/flavin mononucleotide (FMN) with high efficiency and controllability of light-enzyme activity, and realized a light-enzyme coupled hydrogel platform for enzyme immobilization with spatio-temporally controllable hydrogel network by stimulating the enzyme to initiate

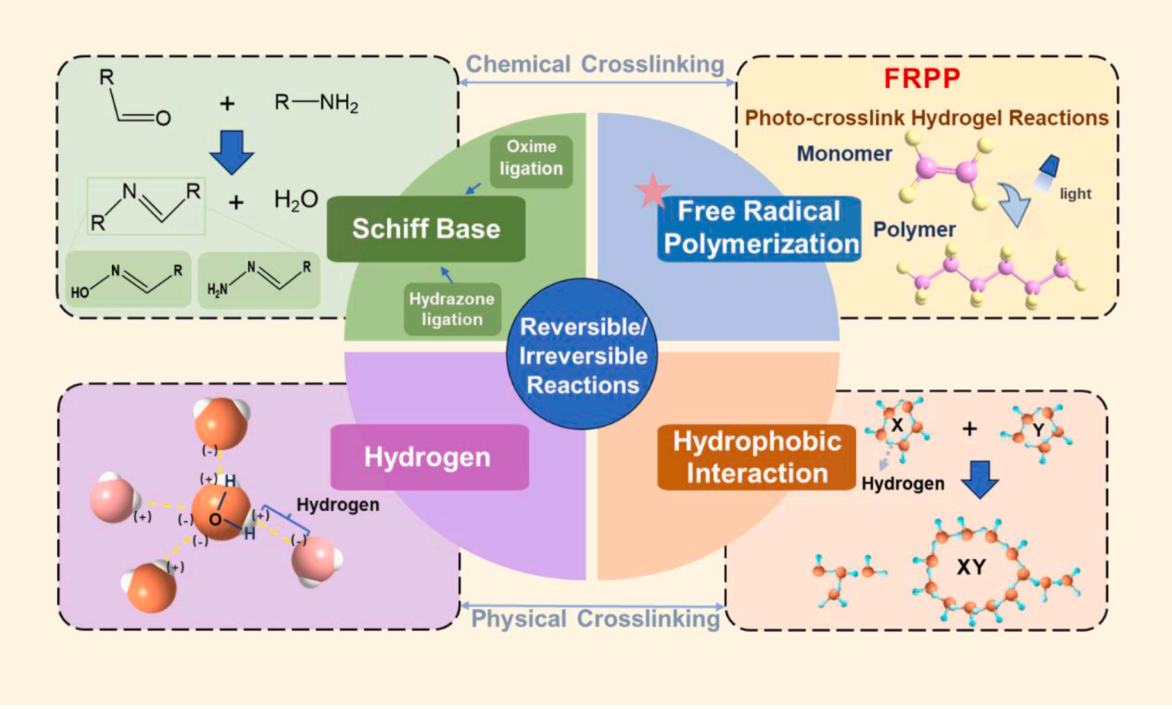


Fig. 2. Classification of hydrogel reactions: chemical crosslinking and physical crosslinking (★Red star represents the main reaction in the photo-crosslink hydrogels). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

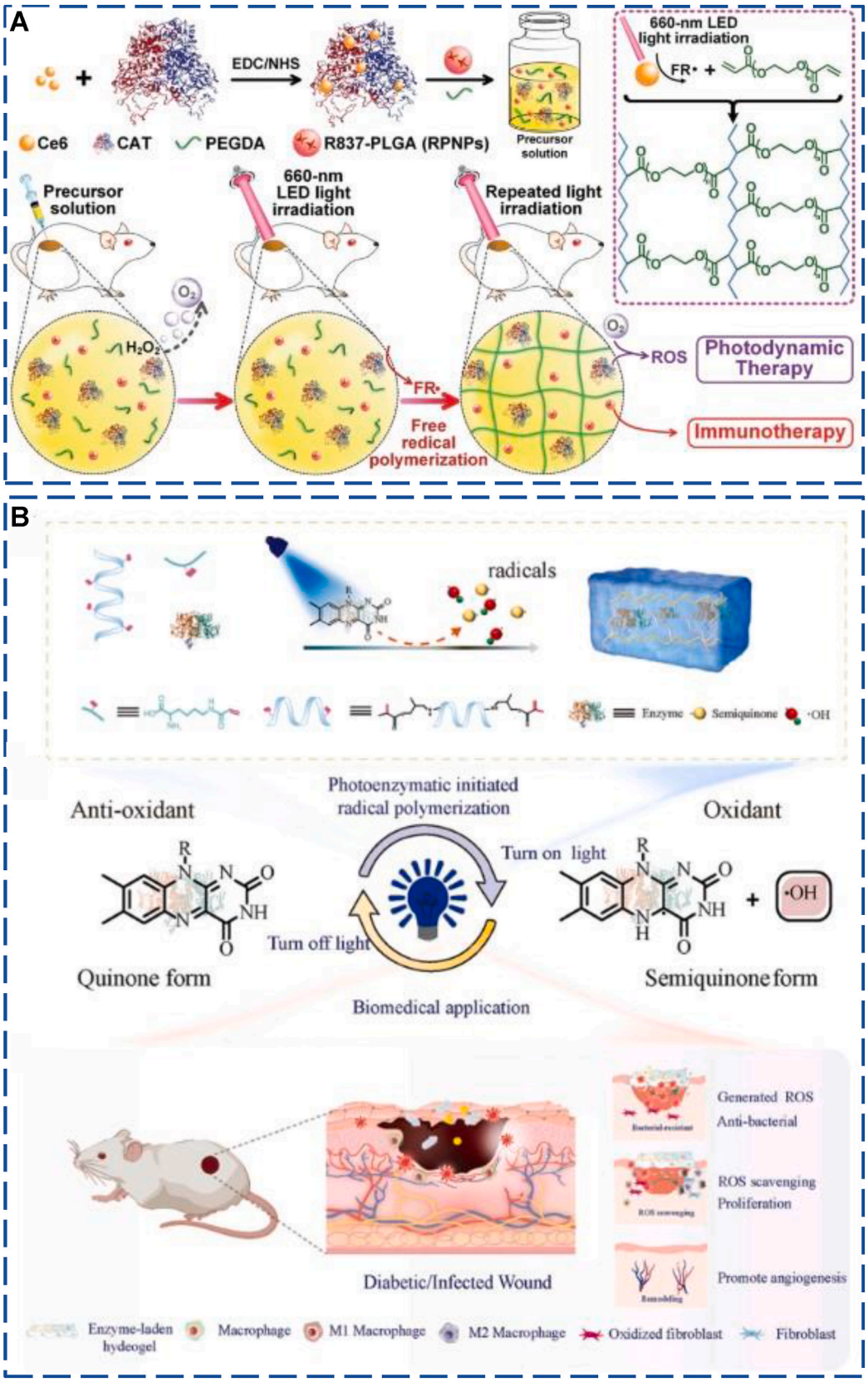


Fig. 3. Illustration of photo-triggered radical polymerization hydrogel. (**A**) Photo triggers formation maps of Ce6-CAT/PEGDA hydrogels. Reproduced with permission from Ref. [124]. Copyright 2019 WILEY. (**B**) Construction of a hydrogel platform based on photo-enzymatic coupling and its use for wound healing regulation. Reproduced with permission from Ref. [125]. Copyright 2023 Elsevier.

the polymerization of free radicals in the light condition (Fig. 3B). By switching the light on/off, the hydrogel further inhibits the bacterial infection of diabetic wounds and reduce the oxidative stress in the microenvironment, thus promoting wound healing [125].

In addition to the common gelling strategies induced by FRP, there are also some special and novel crosslinking strategies based on free radicals. Zhu et al. proposed a new "photocoupling reaction" PTPC reaction crosslinking strategy, which photo-triggered instantaneous free radical and persistent free radical coupling reaction. During the reaction, highly cross-linked HAMA particles are formed through 395 nm light irradiation, inducing the cross-linking of HAMA particles. Concurrently, nitroso groups are generated from NB groups located at the end of PEG under the acceleration of LAP. These nitroso groups promptly capture free radicals, generating long-lasting nitrogen oxides. Subsequently, the carbon central free radicals couple with the HAMA particles. Thus, the covalent interface bonding between HAMA particles and PEG matrix is realized, and the gelation process is completed. The PTPC reaction achieves the establishment of a micro-phase separation structure at the interface of both photo-crosslinking and biomimetic materials. This facilitates the preparation of composite gels with ultra-high toughness and excellent tensile strength, thereby advancing the development of soft materials and 3D printing technology [126].

Free radicals derived mainly from the breaking of covalent bonds in molecules. When the covalent bond is broken, the shared electron pair divided into two atoms or groups, resulting in the formation of an unpaired electron atom or group is a free radical [127]. Photoinduced radical polymerization is typically achieved by activating a suitable photo-initiator with ultraviolet light. During this process, photons and molecules transition to their excited states, leading to rapid decomposition and the formation of free radicals or ions [128,129]. Previous studies proved that in the biological body, free radical ROS regulated cell behavior and closely related to various diseases. As a substance lacking electrons, ROS competes for electrons in the human body, resulting in the circulation of electron transfer [130]. In chemical reactions, however, free radicals usually exist as intermediates, while two free radicals combine with each other to form a molecule, the free radical reaction is thus terminated [131,132]. The free radicals present a low concentration and retention time during the overall reaction process. In the process of photoinitiated radical polymerization, the photopolymerization stops when the light source is removed. Based on the background above, curing of hydrogels without free radicals is proposed by photodimerization. Photodimerization refers to the process whereby two identical organic compound molecules are polymerized into the dimer form of the molecule by cross-linking through covalent bonds in the presence of light [133]. During the process, light-induced photons are initially absorbed by the photoreceptors, inducing conformational changes and increasing the affinity of the partner. By introducing styrene pyridine into the polyvinyl alcohol chain, Li et al. overcame the problem that PVA-based hydrogels lack photocuring functional groups and were difficult to customize, making it possible to achieve photocuring 3D printing in the absence of a matt initiator through photodimerization crosslinking [134]. Zhu et al. prepared hydrogels with coumarin monomer and acrylic acid in an aqueous solution of cetyltrimethylammonium chloride (CTAC) micelles through hydrophobic interactions as well as ionic interactions, and the hydrogels were phase-transformed by efficient photodimerization of coumarin under 365 nm light irradiation [135]. Rizzo et al. proposed a free radical-free (RF) photo-crosslinking strategy based on hydrophilic coumarin and 4-armed poly(ethylene glycol)-thiols (PEG4SH), which provided temporal and spatial control over the michael addition reaction in the alkali-catalyzed thiol-enclick reaction by light irradiation of the hydrophilic coumarin photocages (PCs) that underwent a photodissociation reaction that in turn exposes the reactive compounds or functional groups of the PEG4SH, leading to the formation of a hydrogel [136].

4.2. The factors affect the forming of photo-crosslink hydrogels

The photo-initiator plays a pivotal role in light-curing hydrogel systems, influencing both the curing speed and the ultimate performance of the polymer, when selecting the photo-initiator, several factors must be taken into account, including spectral matching, initiation efficiency, solubility, and others [137,138]. Depending on the reaction mechanism, photo-initiators categorized into free radicals and cations [138]. Among these, free radical photo-initiators can be categorized into cleavage photo-initiators and hydrogen-capture photo-initiators, depending on the mechanisms involved in generating free radicals. In the free radical polymerization process, oxygen blocking polymerization is the most common external factor affecting the rate of light curing. Oxygen molecules produce peroxyl radicals by competitively combining with free radicals, thus reducing the efficiency of light curing [139–141]. The above problems effectively improved by increasing the concentration of photo-initiator, light intensity and monomer concentration which make the number of initial free radicals exceed the concentration of dissolved oxygen, accelerating the light curing process, hindering the diffusion of oxygen to the deeper layers, reducing the competitive reaction between oxygen and radical polymerization, hence decreasing the unevenness of the deeper layers of curing [142,143]. Diverse light intensities and wavelengths exert varying effects on the polymerization characteristics of light-curing materials. The choice of photo-initiator determines the required UV or visible light excitation wavelength. Notably, visible light-based Ru/SPS photo-initiators demonstrate accelerated polymerization rates and enhanced penetration depths, enabling more uniform curing in deeper material layers, and these factors contribute to the distinct properties observed in the resulting hydrogel [137,143]. Therefore, according to different application scenarios, different light intensity and light wavelength should be selected [129]. He et al. proposed the Effective Double Bond Conversion (EDBC), which reflects the proportion of double bonds converted to cross-linking bonds. In this process, light intensity directly influences the formation state of the light-curing hydrogel. Under the same exposure dose, higher light intensity accelerates the generation of free radicals, resulting in faster cross-linking of the hydrogel. Conversely, lower exposure intensity leads to slower cross-linking, albeit with more intensive cross-linking and higher mechanical strength, accompanied by a reduced swelling rate [18]. In addition, free radical polymerization in light-curing hydrogels is also affected by other factors, such as monomer type, monomer photosensitive group substitution, by adjusting the above factors that the structure of the photo-crosslinked network and crosslinking density altered. Monomer photosensitive groups are the key factors in the formation of light-curing hydrogels, and their degree of substitution, molecular weight, and molecular structure affect the various mechanical properties of hydrogels. The reaction of combining appropriate side chains or groups on a chemically bonded preformed main chain is called grafting, which can be divided into chemical grafting and radiation grafting according to the type of initiator [144–147]. Acrylic grafting is one of the most common types of chemical grafting. Gelatin further activated by substituting amino and hydroxyl groups on gelatin with grafted methacrylic anhydride (MA) to produce methacrylated gelatin (GelMA) [17]. The higher the degree of MA substitution in GelMA, the more chemical cross-linking reactions the polymer is capable of generating, resulting in a denser network structure. Generally, the higher the degree of cross-linking of the polymer network, the higher the mechanical strength and the shorter the degradation time [148]. Both natural and synthetic hydrogels exhibit drawbacks when composed of a single component. For instance, natural hydrogels often lack robust physical properties, while synthetic hydrogels may lack optimal biocompatibility. Utilizing multi-component material monomers, modified to offer enhanced chemical or physical crosslinking potential, allows for the copolymerization and formation of multi-component interpenetrating or semi-interpenetrating double or multi-network hydrogels, and the approach enables a more

comprehensive optimization of the physicochemical properties of the hydrogels [149,150].

5. Application of photo-crosslink hydrogels in ophthalmology

Ocular drug delivery systems, tissue engineering and 3D printing based on photo-crosslink hydrogels are important research priorities. Photo-crosslink hydrogels as water-swollen degradable polymer networks that achieve a liquid solution-solid hydrogel phase transition under UV or visible light irradiation. It boasts high biocompatibility, offers convenient and controllable light regulation, and contains high water content. The drug loaded into the hydrogel pore network with high efficiency via light curing, which overcomes the defects of current ophthalmic drug delivery and achieve efficient delivery and long-term sustained release of drugs. As a smart material, light-cured hydrogel demonstrates the capacity to encapsulate highly viable cells in three dimensions and regulate physicochemical properties *in vitro*. This characteristic enables the promotion of cell growth or intraocular tissue replacement using photo-crosslink hydrogel materials, offering promising prospects in the field of tissue engineering. Leveraging the sensitivity and accuracy of light, 3D printing facilitates the precise simulation of individual tissue structures. This capability allows for comprehensive disease treatment and advances regenerative medicine by transforming corresponding models from tissue engineering into reality through 3D printing.

5.1. Tissue engineering

In the development of tissue engineering, biological materials must interact with the body to induce tissue regeneration, reshape the tissue, and undergo complete degradation. Thanks to its spatiotemporal controllability, mechanical adaptability and biocompatibility, photo-crosslink hydrogels not only enable the three-dimensional encapsulation of highly viable cells within the hydrogel polymer network but also allow for the on-demand adjustment of the hydrogel's physical and chemical properties. It is widely used in various biological applications and present an application prospect in the field of tissue engineering [151] (Table 1).

5.1.1. Corneal regeneration

The application of photo-crosslink hydrogels in ophthalmology reaches the hot research field in recent years, mainly focusing on tissue engineered cornea and vitreous body substitutes. The tissue-engineered corneal stroma constructed by photo-crosslink hydrogels attracted the attention of researchers. Li et al. designed a hydrogel GEcAA/GEcSH that realized rapid photo-crosslinking using thiodiene chemistry, which present good biocompatibility and transparency (Fig. 4A). *In vivo* experiments conducted on rabbit models of corneal injury showed that GEcAA/GEcSH identified good repair effects and accelerated the rate of corneal epithelialization. Effectively reduced corneal mist and scar and promoted the regeneration of new tissue under the corneal wound more quickly [152]. Zhao et al. devised a dual-network photo-crosslink hydrogel comprising methacrylate gelatin (GelMA) and oxyglucan (ODex). The hydrogel demonstrates high light transmission, exceptional biocompatibility, resistance to enzymatic degradation, and superior adhesive strength compared to commercial adhesives like fibrin glue. It enables long-term effective adhesion to the cornea and facilitates rapid re-epithelialization of the cornea (Fig. 4B). The double-network photo-crosslink hydrogel used as an alternative to keratoplasty and other corneal surgical sutures, presenting a novel approach to tissue fixation in ophthalmology and surgery with considerable clinical application value [153]. Yazdanpanah et al. synthesized a photo-crosslink corneal stroma (LC-CO Matrix), a functional hydrogel derived from acellular porcine corneal extracellular stroma containing undenatured collagen and sulfosaminoglycan. This hydrogel exhibits good swelling behavior, biodegradation, and viscosity. Following photo-crosslinking, the biomechanical strength, stability, and adhesion are further enhanced (Fig. 4C). *In vitro*, it also demonstrated good adhesion to the human cornea, serving as a potential replacement for the natural corneal stroma, and it effectively closes whole-layer corneal perforations and tissue defects, offering broad prospects in corneal and ophthalmic surgery [154]. Deriving from the clinical application of UV-riboflavin corneal collagen crosslinking (CXL), Li et al. developed a multi-cross-linked photo-crosslink hydrogel based on GelMA, F127DA & AF127 co-assembled bifocal micelles and type I collagen (COL I) that was used with CXL applications (Fig. 4D). The hydrogels present the characteristics of transparency, epithelium & stroma generation, suturelessness, toughness (T. E. S. T). In addition, the hydrogel owned stable properties, slow degradation, strong ability to withstand pressure and deformation. In the rabbit models of deep corneal stromal defect, the hydrogel gelled *in situ* at the cornea stromal defect under ultraviolet irradiation, and seamlessly filled and supported the regeneration of corneal epithelium and stroma, which identified as a good prospect in the treatment of keratoconus and other corneal disease [155]. The construction of tissue-engineered corneas using photo-crosslink hydrogels represents an innovative research area focused on developing novel biomaterials and technologies. It aims to facilitate the repair of corneal injuries through non-invasive and sutureless methods. By leveraging material innovation and technology applications, it offers new ideas and methods for corneal injury repair and regeneration, as well as for tissue regeneration in ophthalmology and other surgical procedures, thus presenting a wide range of clinical applications.

5.1.2. Vitreous substitutes

Vitreous substitutes applied for treatment of retinal detachment and retinal injury. Currently, most vitreous substitutes involve the use of gas or silicone oil, but both methods have drawbacks, for instance, silicone oil implants cannot undergo degradation and necessitate a second operation for later removal, while gas implants exhibit poor stability due to their easy diffusion [162]. Thanks to its advantages such as photo-control, high transparency, suitable toughness and good biocompatibility, photo-crosslink hydrogels can be injected into the vitreous cavity

Table 1
Photo-crosslink hydrogels for tissue engineering applications.

Direction	Application	Materials	Curative Effect	Ref.
Tissue Engineering	Corneal Regeneration	GEcAA/GEcSH	Effectively reduce corneal haze and accelerate corneal epithelialization	[152]
		GelMA-Odex	Higher bond strength than commercial adhesives for long-term corneal adhesion	[153]
		LC-COMatrix	Effective closure of full corneal perforations and tissue defects	[154]
		GelMA/F127DA/AF127	Seamlessly fills and supports the regeneration of the corneal stroma and epithelium	[155]
	Vitreous Substitutes	HA	Restores normal eye shape and intraocular pressure	[156]
		PNAGA-PCBAA	Vitreous cavity gelation at body temperature after *in vitro* UV pre-crosslinking	[157]
	Crystal Substitute	HEMA-co-MAA-comma-co-HI (HAMI)	Treats eye inflammation, prevents clouding of the posterior chamber, filters out harmful blue light	[158]
		PEGDA	Good injectability and shape of the crosslinked polymer solution	[159]
	Retinal Regeneration	MeCTS	Attachable induced pluripotent stem cells and promotes stem cell differentiation towards neuronal phenotypes	[160]
		Agarose/HA	Controlled spatial position curing of biomolecules in 3D hydrogels	[161]

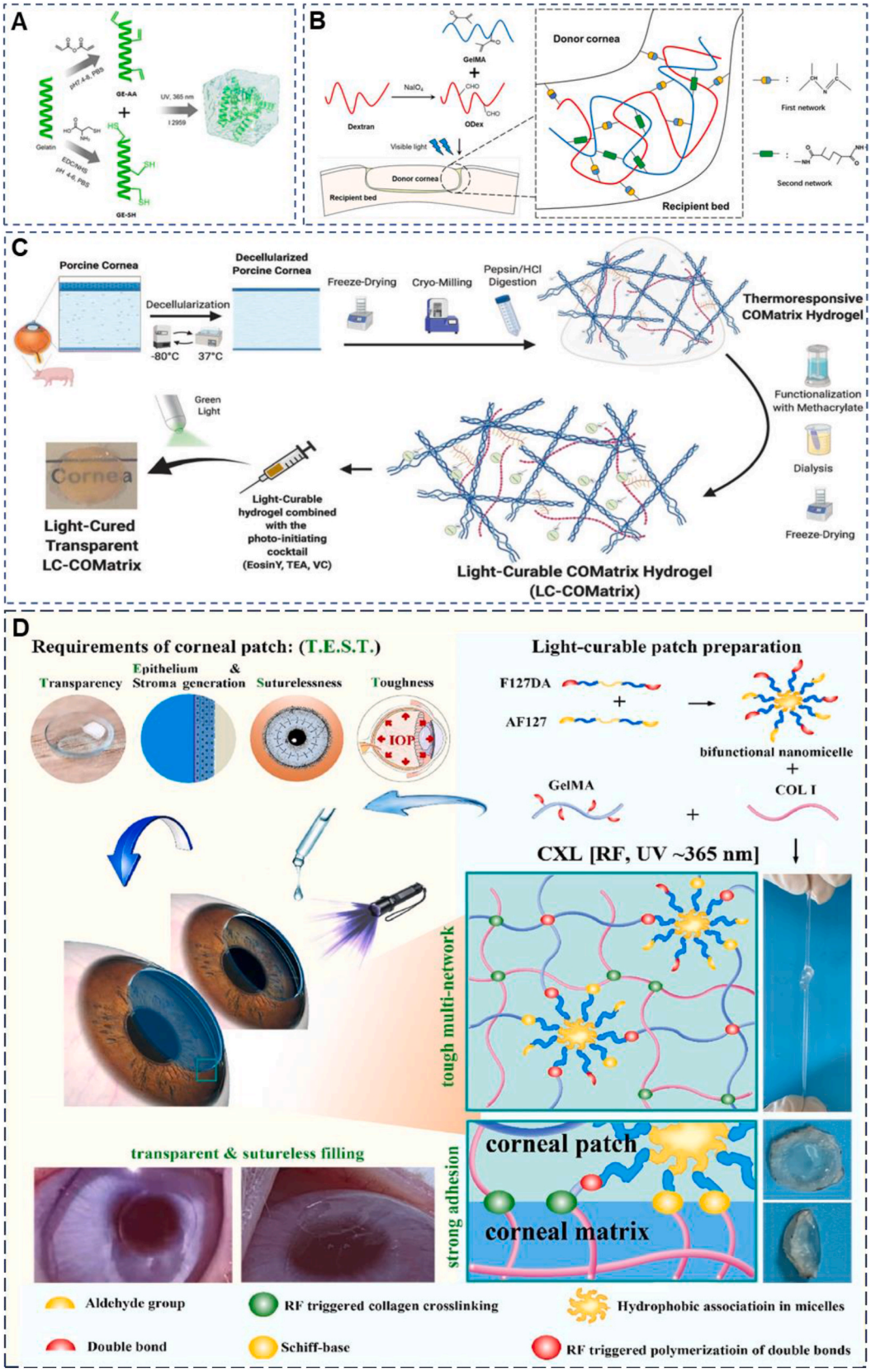


Fig. 4. Representative diagram of photo-crosslink hydrogels applied for cornea regeneration. (**A**) Schematic synthesis of GE-AA, GE-SH and Schematic description of the mechanism of network formation between GE-AA and GE-SH. Reproduced with permission from Ref. [152]. Copyright 2018 American Chemical Society. (**B**) Fabrication and observation of adhesive hydrogels with different ratios of GelMA to ODex. Reproduced with permission from Ref. [153]. Copyright 2022 Elsevier. (**C**) The fabrication process of photo-crosslink LC-COMatrix hydrogel. Reproduced with permission from Ref. [154]. Copyright 2022 Wiley-VCH. (**D**) Fabrication and application, as well as networks illustration of photo-crosslink adhesive corneal hydrogel patch. Reproduced with permission from Ref. [155]. Copyright 2023 Elsevier.

in situ to form a vitreous substitute [163]. Raia et al. designed and synthesized enzymic crosslinked silk-hyaluronic acid (HA) hydrogels characterized by horseradish peroxidase and H_2O_2. By adjusting the polymer ratio and crosslinking density, the hydrogel has a wide range of mechanical and expansive properties, which better maintain intraocular pressure (IOP) and retinal location. *In vivo* experiments on vitreous removal models of live pig eyes also showed that photo-crosslink hydrogel implantation restored the normal shape of the eye and IOP, which present potential clinical application value as a substitute for vitreous body [156]. Wang et al. prepared a supramolecular bipolymer photo-crosslink hydrogel called PNAGA-PCBAA based on N-acryl-ylglyamide (NAGA) and Carboxybetaine Acrylamide (CBAA) (Fig. 5A). The hydrogel possesses not only shear-thinning, temperature compressibility, and self-healing properties but also exhibits fast network recovery. Besides, it identified similar parameters to human vitreous body, such as transmittance, refractive index and stability. After UV pre-crosslinking *in vitro* and shear dilution injection with a 22G needle, the hydrogel rapidly underwent intra-vitreous gelation at body temperature. It maintained high transparency, stability, self-regulation, and exhibited an ultra-low fibrosis reaction. There were no post-operative adverse reactions, and it did not impact other intraocular tissue structures. These findings indicated that the hydrogel served as an ideal vitreous substitute with promising prospects in the field of ophthalmology [157]. Due to its excellent biocompatibility, capacity to maintain retinal function, and simplicity of surgical procedure, photo-crosslink hydrogels serve as a vitreous replacement, reducing surgical risks and providing a new solution for ophthalmic surgery. While photo-crosslink hydrogels have made scientific progress in

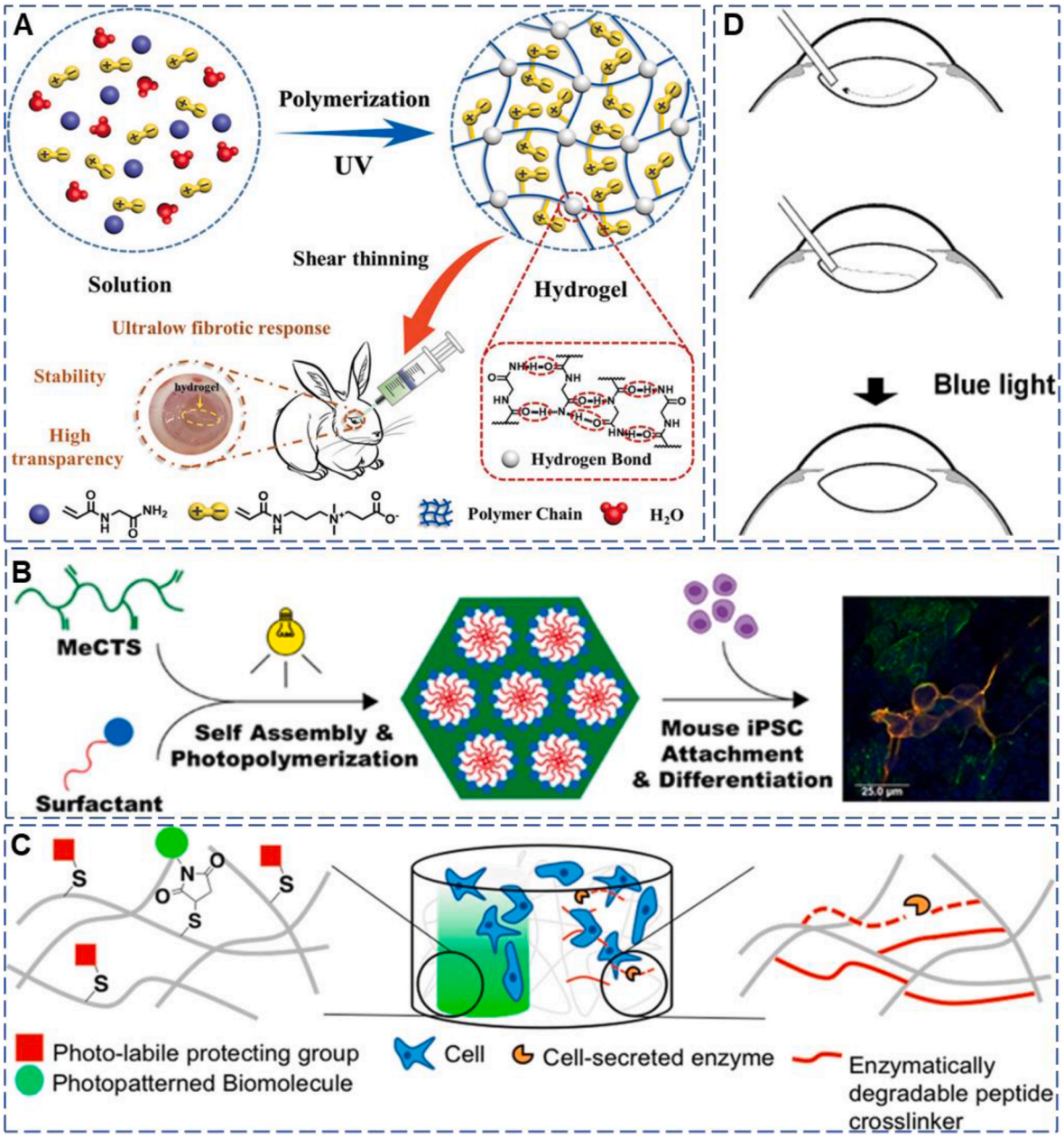


Fig. 5. Representative diagram of photo-crosslink hydrogels applied for vitreous, crystal and retinal substitutes. (**A**) Schematic illustration of the molecular structure of PNAGA-PCBAA binary copolymer. Reproduced with permission from Ref. [157]. Copyright 2018 WILEY-VCH. (**B**) Diagram of hydrogel crystal formation. Reproduced with permission from Ref. [159]. Copyright 2001 ACS. (**C**) Schematic of surfactant templating and stem cell differentiation facilitating used to create chitosan hydrogels. Reproduced with permission from Ref. [160]. Copyright 2016 ACS. (**D**) Schematic illustration of the molecular structure of the 3D photosensitive hydrogel. Reproduced with permission from Ref. [161]. Copyright 2017 ACS.

vitreous replacement engineering, they still face limitations. Precision in the preparation and processing of light-cured hydrogels may hinder their widespread clinical use, and their transparency might not always meet the requirements for high vitreous body transparency in patients. Moreover, the mechanical strength and long-term stability of photo-crosslink hydrogels necessitate further long-term experimental investigation to prevent deformation or damage during prolonged clinical application. Addressing these challenges, including mechanical strength, transparency, processing difficulty, and long-term effects, could promote the broad clinical application of photo-crosslink hydrogels.

5.1.3. Crystal substitute

Cataracts are the leading cause of vision impairment and blindness worldwide, manifested primarily as a degenerative opacity of the lens [164]. The light fails to pass through the lens to cast in retinal entirety because of the opaque lens [165]. By far, the primary treatment for cataracts involves surgically implanting an artificial lens [166]. Although current foldable acrylic lens improves cataract patients to some extent, posterior capsule opacity (PCO, secondary cataract) remains a challenge [167]. Yang et al. developed the HEMA-co-MAA-comma-co-HI (HAMI) hydrogel based on 2-hydroxyethyl methacrylate (HEMA), methyl methacrylate (MMA), methacrylate (MAA) and indomethacin methacrylate (HEMA-IND) (HI) by free radical polymerization. The hydrogel present good biocompatibility, transparency, suitable mechanical strength, hydrophilicity and other necessary properties of intraocular lens. In addition, the hydrogel releases HI slowly, and HI treats ocular inflammation, prevents PCO and filters postoperative harmful blue light by inhibiting the collagen synthesis of lens epithelial cells and absorbing short-wavelength blue light. Therefore, HAMI hydrogel identified a good prospect in the field of intraocular lens biomaterials [158]. Groot et al. designed injectable photo-crosslink hydrogel lenses, which mainly consisted of low molecular weight PEGDA and high molecular weight acrylic modified copolymers of N-vinylpyrrolidone and vinyl alcohol. The copolymer of (4-vinyl-2, 6-dimethylbenzoyl) diphenylphosphine oxide and dimethylacrylamide was used as photoinitiator (Fig. 5B). In the case of blue light irradiation, the polymer solution underwent a liquid-solid phase transition, forming to hydrogel. The hydrogel exhibits good transparency and biocompatibility, with a refractive index close to that of the natural crystal. It exhibits an expansion rate of less than 1 % and demonstrates appropriate injectability and viscosity. The polymer solution was injected into the capsular band of the lens within the pig eyeball, it was found that the polymer solution kept *in situ* and present a suitable shape compared to the pre-crosslinked solution. The light intensity and time required for photo curing are also accepted within the range of retinal damage (0.33 W/cm^2) [159]. As a crucial component of the eye, the lens regulates ciliary muscle relaxation or contraction to achieve refractive adjustment, refracts light for focusing, and filters ultraviolet light to protect the retina. While replacing the lens with photo-crosslink hydrogel could simplify the surgical process and achieve some degree of personalization, it poses significant technical challenges in achieving the complex three-dimensional structure and precise functional gradient. Further research and technological innovation are needed to address these challenges and realize its potential for clinical application.

5.1.4. Retinal regeneration

As a typical neurodegenerative disease, age-related macular degeneration (AMD) and retinitis pigmentosa (RP) bring about visual impairment to millions of people around the world due to degenerative damage of retinal pigment epithelium(RPE)and photoreceptor [168–170]. However, even after denaturation of RPE and photoreceptor, cells remain intact, and transplant photoreceptors or RPE puts forward an important direction of therapeutic research [171]. Two-dimensional (2D) cell culture using biomimetic hydrogels emerged as an alternative strategy to reproduce natural cell growth *in vitro*. Worthington et al. formed a surfactant templated chitosan hydrogel using methacrylate functionalized chitosan (MeCTS) and surfactant to self-assemble under light irradiation (Fig. 5C). The surfactant template adjusted the water absorption and compression modulus of the photo-crosslinked chitosan hydrogel, and prevented the property fluctuation caused by the change of pH. In addition, after removing a certain amount of surfactant, MeCTS attached pluripotent stem cells and promoted the differentiation of stem cells into neuronal phenotype, providing new insights in retinal regeneration [160]. Compared with 2D culture, three-dimensional (3D) cell culture in hydrogel better simulates natural cell growth. Tam et al. developed a photosensitive hydrogel based on agarose and hyaluronic acid, which could solidify biomolecules in a controlled spatial position in a 3D hydrogel through single or two-photo irradiation,and further studied showed that the interaction effect on endothelial cell and retinal stem cells (Fig. 5D) [161]. Current research on the utilization of photo-crosslink hydrogels for retinal regeneration primarily focuses on the early stages in laboratory settings. While some positive results have been achieved in the laboratory, the clinical application of these materials still necessitates further safety and efficacy studies.

5.2. Drug delivery

Millions of individuals worldwide suffer from various types of ocular diseases. Presently, ophthalmic drugs are primarily administered locally, predominantly in the form of eye drops [172,173]. However, due to the secretion of tears and the mechanical movement of the eyelids, eye drops hardly retained on the ocular surface. Ocular barriers such as conjunctiva, sclera, blood-eye barrier (formed by blood-water barrier and blood-retinal barrier), results in the low bioavailability of drugs on the ocular surface and the delivery to the corresponding lesion sites of the fundus is challenging [174,175]. Further improving the efficiency of ophthalmic drug delivery is needed, a variety of delivery systems proposed, among which photo-crosslink hydrogels, as a degradable polymer network, efficiently load drugs into the hydrogel network, achieving controlled release and continuous drug delivery, which become the focus of research in recent years [176] (Table 2).

5.2.1. Dry eye

Dry eye is a multi-factor disease, its pathological mechanism includes tear film instability, high osmotic pressure of tears. Inflammation plays an important role in the occurrence and development of dry eye. Therefore, inhibiting ocular surface inflammation is one of the important and effective ways for dry eye [184]. Cyclosporin A (CsA) is a known immunosuppressant that present a significant effect on inhibiting inflammation, however, CsA is insoluble in water, which affects its efficacy [185]. Gong et al. constructed a drug loading system based on *o*-nitrobenzyl alcohol-modified polyethylene glycol (PEGNB) and methacrylate modified hyaluronic acid (HAMA), loaded with CsA and implanted into the lacrimal duct to form a stable drug loading and gradually slowly release photo-crosslink dual-network hydrogel. Through the construction of rabbit dry eye model, it was confirmed that photosensitive hydrogel CsA drug-loaded lacrimal plug increased tear secretion, inhibited ocular surface inflammation, and finally promoted the repair of ocular surface epithelial damage, providing a new treatment strategy for refractory dry eye [177]. Dai et al. designed and synthesized a hydrogel tear plug (SFMA/FTN) using methacrylate modified fibroin protein (SFMA) as a hydrogel scaffold and indocyanine green (ICG) nanoparticles (FTN) as a tracer (Fig. 6A). Following photo-crosslinking via free radical polymerization, the hydrogel exhibited excellent biocompatibility, biodegradability and mechanical properties. It withstood tissue pressure, enabled non-invasive detection under near-infrared light, and achieved optimal compatibility with irregular lacrimal passages. The model of dry eye in rabbits showed that it could completely block lacrimal duct, improved breakup time of tear film and increased the number of goblet cells, which appeared a high

Table 2
Photo-crosslink hydrogels for drug delivery applications.

Direction	Application	Materials	Curative Effect	Ref.
Drug Delivery	Dry Eye	PEGNB/HAMA	Increase tear secretion, inhibit ocular surface inflammation, promote epithelial damage repair	[177]
		SFMA/FTN	Matching irregular tear ducts, improving tear film breakup time, and increasing conjunctival cup cell count	[178]
	Corneal Inflammation	G4-PAMAM/HA	Targeting macrophages to reduce corneal neovascularization and inflammatory factors	[179]
		HA	Promoting corneal re-epithelialization and reducing neovascularization	[180]
		Acrylic gelatin	High drug carrier and long-lasting slow-release ability, effectively inhibiting corneal neovascularization	[181]
		Collagen	Maintaining corneal thickness and stromal morphology, reducing corneal epithelial inflammatory factors, and reducing corneal haze and vascular invasion	[182]
	Retinal Neovascularization	GelMA	With long-lasting drug slow-release effect, the whole layer of rabbit ocular transretinal tissue functioned normally after implantation	[183]

value in the treatment of dry eye [178]. Currently, the primary form of medication for treating dry eye is through eye drops. However, the absorption and utilization of eye drops are limited due to mechanical movements such as blinking. Photo-crosslink hydrogel, with its highly water-containing three-dimensional network, prolongs its residence time on the ocular surface when treating dry eye. This prolonged contact helps maintain continuous moisture in the eye and reduces the need for frequent eye drop usage. Additionally, the incorporation of drugs within the hydrogel's 3D network structure enables sustained drug release, further supporting the repair and regeneration of ocular tissues. The photo-crosslink hydrogel drug delivery system offers a novel approach to dry eye treatment and is poised to enhance the quality of life and therapeutic outcomes for patients with dry eye through its unique drug release mechanism and benefits.

5.2.2. Corneal inflammation

Corneal chemical burn is one of the serious emergency ocular diseases, among which severe ocular chemical burn is mostly caused by strong alkali, corneal inflammation caused by alkali burn and the subsequent corneal neovascularization are one of the reasons for corneal turbidity and even blindness. Timely intervention reduces the occurrence of [186]. Soiberman et al. designed a subconjunctival injection gel based on G4-PAMAM dendrimer, hyaluronic acid and dexamethasone (Dex) (Fig. 6B). After photo-crosslinking, the Dex bioavailability improved and the drug release can be sustained. By constructing a rat model of alkali burn, the hydrogel was selectively targeted and localized to macrophages. It showed that the central thickness of cornea decreased, the transparency increased, and the corneal neovasculation and inflammatory factors decreased after the use of the photo-crosslink hydrogel. Compared with free dexamethasone, the hydrogel has better anti-inflammatory effect, and may become a potential drug delivery platform for other inflammatory ocular surface diseases (dry eye et al.), and present a good application prospect [179]. Sun et al. synthesized photo-crosslinked *in situ* hyaluronic acid (HA) hydrogel by inducing the sulfhydryl reaction through blue light, and tested its therapeutic effect on the rat model of corneal alkali burn (Fig. 6C). The results showed that compared with the use of HA eye drops, the photo-crosslinked HA hydrogel had better pharmacological effects. It promoted corneal re-epithelialization and reduced neovascularization, making it a new effective treatment for corneal alkali burns [180]. Huang et al. designed a hydrogel composite material based on acrylic gelatin and methacrylate groups through photo-initiator free radical polymerization as triamcinolone cinolone (TA) carrier for the treatment of corneal neovasculature (Fig. 6D) [181]. Xeroudaki et al. utilized cellulose nanofibers to reinforce pig skin collagen, which was subsequently chemically and photo-crosslinked after being loaded with dexamethasone, resulting in the formation of a double-crosslinked hydrogel. The double-crosslinked hydrogel exhibited excellent optical transparency and mechanical strength while maintaining corneal thickness as well as corneal stromal morphology. In addition, the double-crosslinked hydrogel supported the continuous release of dexamethasone *in vitro* for 60 days, resulting in decreased production of pro-inflammatory cytokines in human corneal epithelial cells, decreased corneal haze and vascular invasion, providing new ideas for the treatment of corneal stromal diseases after corneal transplantation [182]. Chemical injuries to the cornea represent serious and urgent conditions in ophthalmology, with primary treatment focusing on the prompt removal of the causative agent and early medication administration. Leveraging photo-crosslink technology, hydrogels can be rapidly cured and bonded, facilitating immediate treatment of corneal inflammation and promoting epithelial regeneration, thereby expediting the repair of corneal damage.

5.2.3. Retinal neovascularization

The retinal neovascularization and choroid neovascularization are the two leading causes of retinal blindness. Intravitreal injection of *anti*-VEGF drugs which blocks the activity of VEGF and inhibits the formation of pathogenic angiogenesis in the eye, which is the most effective treatment for ocular neovascularization diseases [187,188]. However, intravitreal injection also has limitations, such as the increased incidence of endophthalmitis due to frequent injection. Long-term, slow release of intravitreal drugs through hydrogel-loaded formulations reduces the frequency of intravitreal injections, enhances patient compliance, and mitigates the risk of eye infection [189]. Shen et al. constructed an intraocular injection delivery system based on GelMA and TA,which has low toxicity and swelling rate, good biocompatibility and slower and longer release kinetics than TA suspension. The results of the photo-crosslink hydrogel implantation in rabbit eyes showed all layers of rabbit eye retinal tissue function is normal. Therefore, the use of photo-crosslink hydrogel as a biologic drug carrier holds promise in the treatment of posterior ocular diseases [183]. Currently, the main treatment modalities for retinal neovascularization include vitreous injection of *anti*-VEGF drugs, laser photocoagulation, and photodynamic therapy (PDT). Utilizing photo-crosslink hydrogels to construct carriers loaded with *anti*-VEGF drugs enables the inhibition of neovascularization formation and development through localized drug release. Additionally, retinal neovascularization is prone to rupture and bleeding, and the fibrous tissue formed after bleeding cessation can exert traction on the retina, increasing the risk of retinal detachment. By injecting photo-crosslink hydrogel loaded with *anti*-VEGF drugs into the vitreous cavity, not only can retinal neovascularization be inhibited through prolonged VEGF release, but it also acts as a vitreous substitute to facilitate retinal repositioning. Incorporating photo-responsive materials into the hydrogel enables remote control and stimulation of nerve cells, potentially playing a crucial role in treating nerve injuries or neurodegenerative diseases induced by retinal detachment.

5.3. 3D printing

3D printing is a technology that creates 3D physical substances from digital technology, identifies the digital technology by layers through computer software, and sends it to the machine in the form of instructions for layer-by-layer printing to fabricate 3D objects with

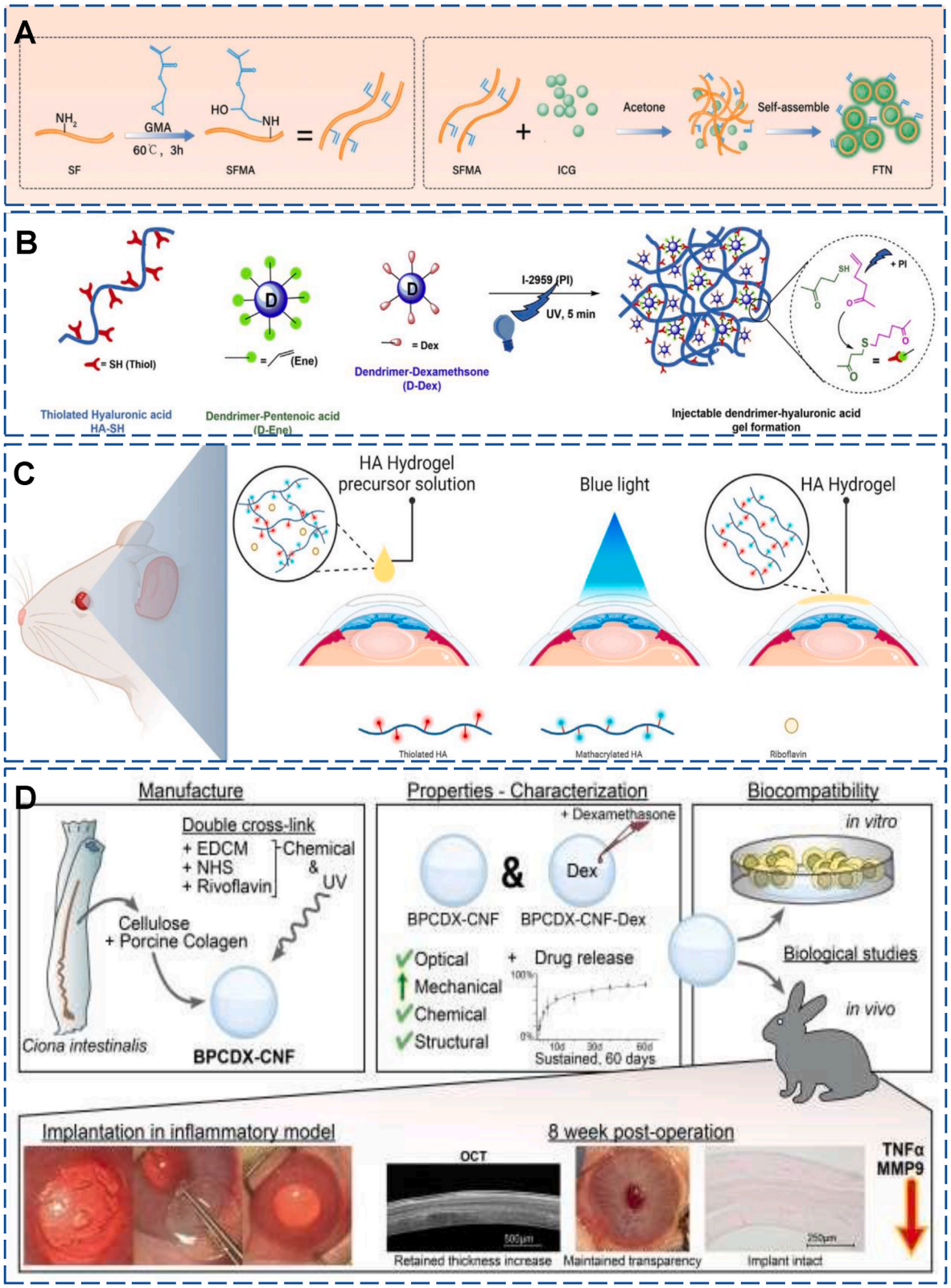


Fig. 6. Representative diagram of photo-crosslink hydrogels applied for dry eye and corneal inflammation. (**A**) Synthesis and application of SFMA/FTN hydrogel plugs. Reproduced with permission from Ref. [178]. Copyright 2022 WILEY-VCH. (**B**) A schematic representation of formation of D-Dex loaded injectable gel by thiol-ene click chemistry. Reproduced with permission from Ref. [179]. Copyright 2017 Elsevier. (**C**) Schematic images of hyaluronic acid (HA) hydrogel formation. Reproduced with permission from Ref. [180]. Copyright 2022 Elsevier. (**D**) Synthesis and application of the double-crosslinked hydrogel. Reproduced with permission from Ref. [181]. Copyright 2022 Elsevier.

predefined structures [190,191]. The most common bioprinting techniques are extrusion-based printing and light-based printing [192]. Light-based 3D bioprinting primarily encompasses DLP printing, SLA-based printing, and laser-assisted printing. Due to the precision and sensitivity of light, the method offers higher accuracy, printing resolution, and speed. The reaction conditions are also milder, making it suitable for printing cells with high vitality and achieving high resolution [193]. As an advanced biomanufacturing technology, 3D printing technology embedded with cyto-compatible materials to achieve accurate reproduction of tissue or organ structures to replace injured or diseased tissues, providing a new idea for the regeneration of complex tissues or organ systems [194,195] (Table 3).

5.3.1. Cornea

Corneal regeneration has always been a challenge due to the complex structure of the cornea which 3D printing appeared to tackle the problem. He et al. designed and synthesized a polyethylene glycol diacrylate (PEGDA)/GelMA hydrogel, and constructed a corneal scaffold loaded with rabbit corneal epithelial cells and rabbit adipose-derived mesymal stem cells (rASCs) using a photo-crosslink 3D bio-printer (BP8600), which has sufficient mechanical properties, high light transmittance and shape fidelity, suitable swelling degree and degradation rate. In addition, PEGDA/GelMA hydrogel present excellent cytocompatibility, which supported cell adhesion, proliferation and migration, and the embedded cells existed a high survival rate during the printing process (Fig. 7A). After the cell-encapsulated hydrogel was implanted *in vivo*, postoperative results demonstrated that the hydrogel accelerated epithelial healing and stromal regeneration, the dual function of corneal epithelial cells and stem cells provided the most effective regeneration environment for corneal stromal cells [196]. Corneal curvature plays an important role in the recovery and regeneration of corneal epithelium. The adhesion of natural corneal epithelium in different areas of the cornea is different, and the stability of tear film and epithelium on curved surface is higher than that on plane [205]. Xu et al. used collagen and photo-crosslinked GelMA hydrogel to prepare a smooth surface corneal repair material with curvature structure through temperature-controlled 3D printing technology, which is used to promote corneal stroma regeneration and corneal function recovery (Fig. 7B). 180 days after implantation *in vivo*, it was found that compared with the planar structure, the convex structure inhibited the formation of fibroblasts, and better promoted the epithelialization of corneal defects, cell adhesion and neuronal regeneration. The structure and function of the convex structure indicated that it had a good prospect in the field of corneal replacement [197]. As a transparent membrane exposed to the environment, the cornea is highly fragile, yet most blinding corneal diseases can be effectively treated with corneal transplants. However, the scarcity of donated corneas, coupled with the challenges associated with donation, has resulted in an extreme shortage of these resources. Through personalized design and 3D printing, corneal structures with higher precision can be fabricated, thus mitigating the global shortage of corneal resources to some extent. However, despite the progress made in 3D printing cornea technology, it still faces several challenges. These include determining how to implant artificial corneas and improving corneal structure while ensuring its refractive function. In summary, 3D printed cornea technology is experiencing rapid development, driving progress in the 3D printing industry and introducing new therapeutic approaches to ophthalmology. Nevertheless, addressing existing difficulties and challenges requires further innovative research.

5.3.2. Conjunctiva

The conjunctiva includes the palpebral conjunctiva, the fornix conjunctiva and the bulbar conjunctiva, and the non-keratinized epithelial region contains mucus-producing goblet cells [206]. As a component of the ocular surface, the conjunctiva plays a crucial role in protecting the ocular surface and maintaining the stability of the tear film. Its integrity is essential for a healthy ocular surface and clear vision [207]. Severe conjunctival defects resulting from immune diseases, trauma, chemical or thermal burns, or surgery involving the conjunctiva compromise the integrity of the ocular surface and impair visual function, therefore, conjunctival reconstruction is imperative in restoring ocular health and preserving vision [208]. Stem cell therapy based on conjunctival stem cells (CjSCs) has become one of the important strategies for conjunctival reconstruction. Zhong et al. developed a CjSCs expansion method *in vitro* based on bioprinting technology of digital light processing (DLP), that is, hydrogel for loaded delivery of CjSCs (Fig. 7C). The 3D printed hydrogel present adjustable mechanical properties and excellent cell compatibility, which maintained the high vitality of CjSCs while supporting their self-renewal ability. By constructing a rabbit subconjunctival injection model, the injectability and post-injection vitality of the hydrogel were further verified, providing a new minimally invasive treatment of 3D printed cell-supported hydrogel for ocular surface regeneration [198]. 3D printing technology holds significant promise in tissue reconstruction, and researchers are currently exploring suitable biocompatible materials to offer novel solutions for conjunctival reconstruction. Culturing Conjunctival Stem Cells (CjSCs) in 3D printing ink facilitates cell attachment and growth. While early experiments with 3D printed conjunctiva technology have shown promise, further scientific studies and clinical evaluations are necessary in the future to confirm its biocompatibility and long-term stability.

5.3.3. Crystalline lens

At present, the most effective way to treat cataract is intraocular lens implantation, however, uniform intraocular lens cannot meet people's increasingly personalized needs [192,209]. 3D printing holds significant potential in biomedical engineering research and ophthalmology applications, and it enables the design of personalized lenses through digital modeling, fitting into the lens sac and potentially addressing patients' refractive errors simultaneously [210]. Li et al. prepared polyacrylamide sodium acrylate hydrogel (PAH) intraocular lens (IOL)

Table 3
Photo-crosslink hydrogels for 3D printing applications.

Direction	Application	Materials	Curative Effect	Ref.
3D printing	Corneal	PEGDA/GelMA	Excellent cytocompatibility, supporting cell adhesion, proliferation and migration, accelerating epithelial healing and matrix regeneration	[196]
		GelMA	Promoting re-epithelialization of corneal defects, cell adhesion and neuronal regeneration	[197]
	Conjunctiva	GelMA	Loading delivery of CjSCs,as well as maintaining their vitality and dryness	[198]
	Crystalline Lens	PAH	With good transparency and cytocompatibility, no increase in inflammatory cells in the anterior chamber angle after implantation	[199]
	Retinal	HAMA	Construction of a multilayered tissue model with the same arrangement and localization as the natural retina and good cell viability of PR obtained by co-differentiation	[200]
	Orbital Implant	Ca_2–Zn–Si–O_7	Good cell adhesion, cell viability and angiogenic effects	[201]
	Corneal Contact Lens	Poly-NAGA-GelMA	Maintaining epithelial phenotype and avoiding its excessive transformation to keratinocytes-myofibroblasts; inhibiting inflammation and promoting tissue regeneration	[202]
	Lacrimal Plug	PEGDA/PEG400	Long-acting and sustained-release drug-loaded lacrimal plug with broad promise in dry eyes	[203]
	Biosensor	IP-VISIO	Extremely low response of the grafted foreign body, and can accurately sense and respond to physiological stimuli	[204]

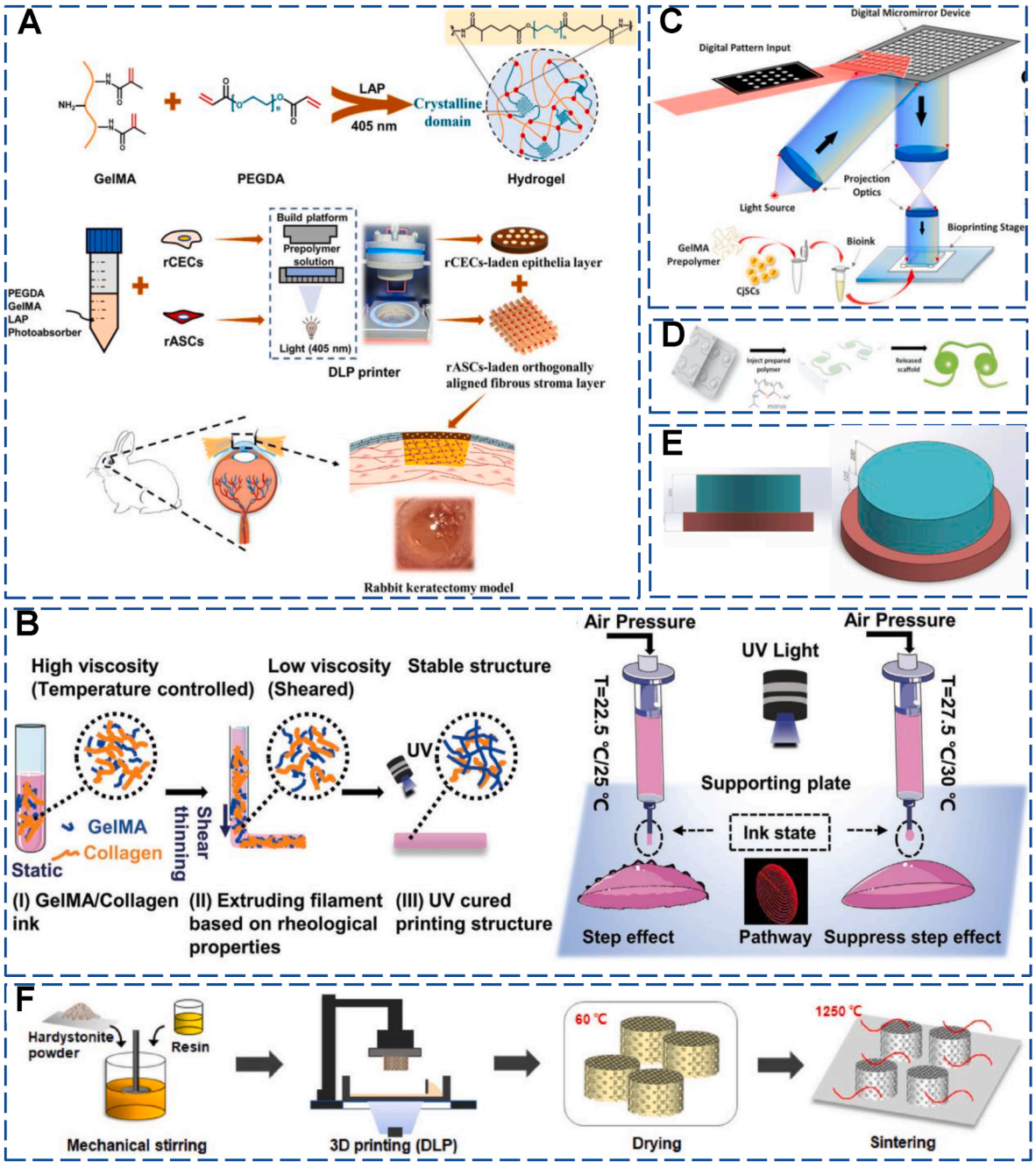


Fig. 7. Representative diagram of photo-curing hydrogels applied for 3D printing. (A) Components of ink and schematic illustration of network formation in PEGDA-GelMA hydrogel. Reproduced with permission from Ref. [196]. Copyright 2022 Elsevier. (B) Fabrication of 3D-printed convex cornea. Reproduced with permission from Ref. [197]. Copyright 2023 Wiley-VCH. (C) Bioprinting of CjSC-loaded Hydrogel Micro-constructs with Tunable Mechanical Properties. Reproduced with permission from Ref. [198]. Copyright 2021 Elsevier. (D) Synthesis of the PAH 3D-printed IOL. Reproduced with permission from Ref. [199]. Copyright 2020 IJO. (E) Bilayer printing of fluorescent labelled hydrogels. Reproduced with permission from Ref. [200]. Copyright 2018 Elsevier. (F) Scheme illustration of the preparation process for digital light processing 3D printed porous bio-ceramic scaffolds. Reproduced with permission from Ref. [201]. Copyright 2022 Elsevier.

material using 3D printing technology, which present good transparency and cell compatibility, and showed no significant changes in cell viability when co-cultured with human lens epithelial cells (LECs) or ARPE19 cells (Fig. 7D). In comparison to intraocular lens implantation, there was no significant difference observed in the number of inflammatory cells in the anterior chamber following the implantation of the hydrogel crystal material. This suggested that the preparation of hydrogel intraocular lenses using 3D printing technology holds potential clinical value [199]. Through computer-aided digital modeling, 3D printing technology achieves precise control over the shape and size of the lens on a microscopic scale, thereby optimizing material properties and meeting the personalized needs of patients. However, transitioning from a lens structure that is "shape-like" to one that functions with the precision of a "god-like" lens remains a significant challenge for the future.

5.3.4. Retina

The retina is a complex tissue responsible for collecting information about light from the external environment and transmitting it to the brain. It is divided into ten layers: retinal pigment epithelium (RPE), photoreceptors (PR), outer limiting membrane (OLM), outer nuclear layer (ONL), outer plexiform layer (OPL), inner nuclear layer (INL),

inner plexiform layer (IPL), ganglion cells layer (GCL), nerve fiber layer (NFL) and internal limiting membranes. Each layer structure has unique functions, and its functional and structural integrity is closely related to retinal functional integrity [211]. In human retina, cells with specific functions are embedded in the extracellular matrix (ECM) in a multi-layered structure, which is mainly composed of hyaluronic acid (HA), which has an important influence on the function and growth of photoreceptor cells [212,213]. Recently, 3D printed bio-simulated microstructures received a lot of attention in the retinal field. Wang et al. proposed a strategy that integrates physical and chemical signals by introducing methacrylate groups to form methacrylic hyaluronic acid (HAMA), changing its compression modulus to match retina (Fig. 7E). And the cells were encapsulated by HAMA and layered HAMA-RPE and HAMA-RPC were printed by 3D printing technology to guide cell differentiation through the regulation of nutrient and growth factor diffusion gradient. A multi-layer tissue model mirroring the natural arrangement of the retina was constructed, and cell experiments yielded promising results. Photoreceptor cells obtained through the co-differentiation of retinal pigment epithelium and retinal progenitor cells demonstrated robust cell viability [200]. The application of 3D printing technology in the field of the retina is expanding, and the integration of stem cells and 3D printing has facilitated the reconstruction of functional retinas. This technological advancement has significantly contributed to the development of ophthalmology and introduced new ideas and methods for researching and treating ophthalmic diseases. The fabrication of retinal organoids via 3D printing holds immense promise, although there have been fewer scientific breakthroughs in this area thus far. By constructing 3D retinal organoids, it becomes possible to overcome interspecies differences and simulate the normal growth and development of the human retina, thereby providing a foundational model for *in vitro* research in the field of retina.

5.3.5. Orbital implant

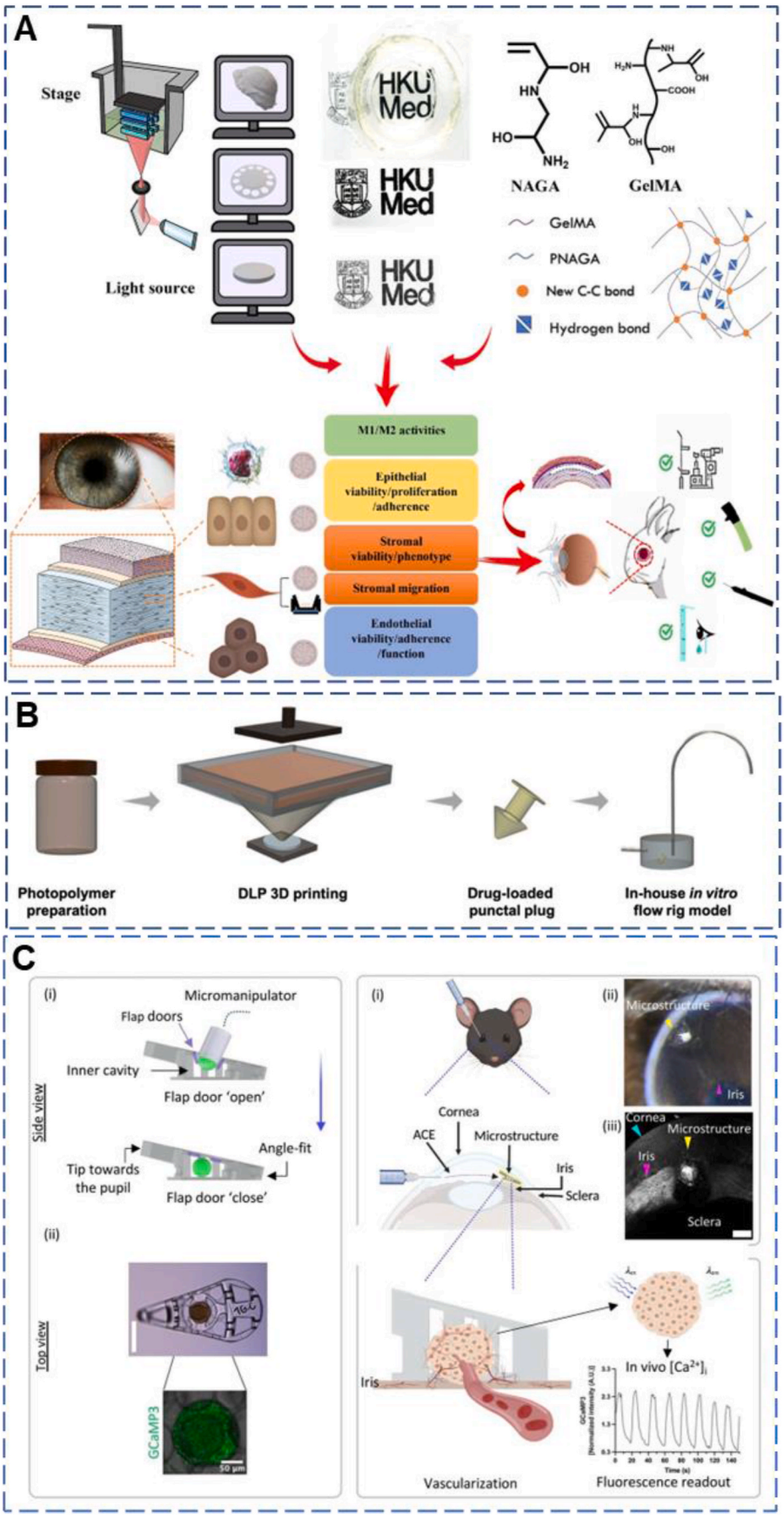
In some cases of severe ocular trauma or disease, the eyeball needs to be removed and an orbital implant inserted to achieve good visual results [214–216]. The existing orbital implants mainly include autologous materials, polymer implants, ceramic implants, magnetic implants, composite implants and other biological materials [215]. The utilization of 3D printing technology for preparing orbital implants can meet the demands of individual differences and achieve a more accurate restoration of the volume of individual eyeballs [217]. Wang et al. developed a novel multifunctional Ca–Zn-silicate bio-ceramic implants by fabricating a hierarchical porous hard calcite ($Ca_2ZnSi_2O_7$) scaffold with a three-period minimum surface (TPMS) based porous structure and a graded pore size distribution using projective photo curing 3D printing technology (Fig. 7F). The graded porous scaffolds exhibited controlled biolysis behavior and moderate mechanical strength compared to scaffolds with uniform pore size, and cell experiments demonstrated enhanced cell adhesion, cell viability, and angiogenesis. The new antibacterial hard quartz bio-ceramics with gradient pore design have great potential for application in orbital implants, and the pore-topological features offer the possibility of improving biological performance in orbital reconstruction [201]. Currently, the utilization of 3D printing technology in crafting artificial prosthetic eye technology has reached a relatively advanced stage. However, addressing individual variations in restoring the volume of a patient's eye while simultaneously restoring retinal function poses numerous challenges. One potential solution lies in leveraging 3D printing technology alongside diode or semiconductor technology to fabricate miniature light sensors. These sensors have the capability to swiftly capture subtle changes in light and convert external images into current signals that can be transmitted back to the brain. This innovative approach holds promise for restoring eyesight in patients and may represent a future solution to this complex issue.

5.3.6. Ophthalmic device

5.3.6.1. Corneal contact lens. Refractive error refers to the condition in which parallel light rays pass through the optical system of the eye without accurately landing on the retina. Uncorrected refractive errors stand as the second leading cause of blindness worldwide and addressing refractive errors significantly enhances the quality of life and yield socio-economic benefits [218]. 3D printing prepares specific contact lenses according to individual corneal needs. Jia et al. made hydrogel lenses through digital light processing (DLP)-bioprinting based on poly-NAGA-GelMA (PNG) bio-inks (Fig. 8A). It had good optical transparency, mechanical stability, hydrophilicity and biocompatibility. As a corneal stroma implants, the hydrogel lens adhered firmly to corneal epithelial cells and maintained their epithelial phenotype, avoiding excessive keratinating-myofibroblast transformation. In addition, the hydrogel lens activated type 2 immunity, promoted tissue regeneration, and suppressed inflammation. One month after implantation, there were no significant changes in IOP, corneal sensitivity, and tear production at postoperative follow-up, suggesting that DLP bio-printed PNG hydrogel lenses offer a potential therapeutic strategy for correcting refractive errors [202]. Photo-crosslink hydrogels, as water-swollen 3D polymer networks, hold significant potential in the market for corneal contact lenses. The research and development of 3D printed corneal contact lenses represent a crucial advancement in ophthalmology in recent years. Through the utilization of suitable biocompatible materials via 3D printing technology, highly customized production of corneal contact lenses can be achieved, thereby enhancing comfort and efficacy during wear. The potential value of these lenses in ophthalmology will be further elevated by enhancing printing accuracy, biocompatibility, long-term stability, and reducing production costs.

5.3.6.2. Lacrimal plug. Eye drops are a common treatment for the Dry Eye, but their effectiveness is limited [15,219]. In the study of Xu et al., dexamethasone-loaded lacrimal plug was prepared by 3D printing technology, which was composed of polyethylene glycol diacrylate (PEGDA) and polyethylene glycol 400 (PEG 400), which realized the loading of different concentrations of drugs by creating a semi-interpenetrating network (semi-IPN) (Fig. 8B). In addition, the researchers evaluated the release dynamics of lacrimal plugs *in vitro* by using an internal flow device model that mimics the subconjunctival space. The results indicated that dexamethasone achieved sustained release for up to 7 days in a lacrimal stopper made of 20 % w/w PEG 400/80 % w/w PEGDA. In contrast, the release time for the lacrimal stopper made of 100 % PEGDA exceeded 21 days. The study demonstrated that 3D printing technology could be used to manufacture drug-loaded lacrimal stopper with long-term slow-release effect, which has broad prospects in dry eye treatment [203]. Tear duct embolization represents an innovative approach to treating dry eye. The utilization of 3D printing in the preparation of tear duct embolization presents a novel avenue for ophthalmic treatment. Through precise computer-regulated design and fabrication, tear duct embolization can be tailored to individual specifications, enabling accurate blockage of the patient's tear ducts and facilitating tear aggregation on the eye's surface, thereby alleviating dry eye symptoms. By selecting different hydrogel materials, the time requirements for permanent or temporary embolization in different patients can be met, while the addition of drugs can prolong drug residence time and enhance drug efficacy. Although current 3D printing of tear duct embolization poses certain challenges, leveraging 3D printing for personalized medicine can better address the evolving therapeutic needs of the modern era.

5.3.6.3. Biosensor. Integrating biological cells with sensors, wherein living cells become part of a biosensing element, yields a sensor known as a biohybrid sensor, and the biohybrid sensor sensitively detect small physiological changes in the body [220]. The anterior chamber angle is



(caption on next page)

Fig. 8. Representative diagram of photo-crosslink hydrogels applied for ophthalmic device. (**A**) Schematic illustration of DLP-bioprinting poly-NAGA-GelMA-based hydrogel for correcting refractive errors. Reproduced with permission from Ref. [202]. Copyright 2023 IOP. (**B**) Schematic representation of the DLP 3D printing process for punctal plug. Reproduced with permission from Ref. [203]. Copyright 2021 MDPI. (**C**) Schematic overview of localization, transplantation, and application of pancreatic islet biohybrid microstructures. Reproduced with permission from Ref. [204]. Copyright 2023 WILEY-VCH.

possible for tissue engineering and hybridization because of its immune properties and transparency [221]. Kavand et al. utilized two-photon polymerization technology to conduct 3D printing based on islet microtissue, resulting in the development of a bio-hybrid sensor. This sensor was affixed at the angle of the anterior chamber using a photo-resin material (IP VISIO), renowned for its outstanding transparency. It demonstrated precise sensing and response to physiological stimuli while exhibiting commendable biocompatibility (Fig. 8C). The results of *in vivo* transplantation show that, it had the smallest foreign body reaction (FBR), and corneal transparency and tissue morphology were not affected after 20 W transplantation. In addition, it maintained the functional integrity of islet cells. After using the gene-encoded Ca^{2+} indicator GCaMP3, it was found that capillary buds and new blood vessels could be formed in the islets within 2–4 days after transplantation under the microscope [204]. The study establishes a foundation for future biological tissue engineering and biohybrid technology. It also introduces new ideas and methods for the potential treatment of eye diseases in the future. By incorporating functional materials, structures printed via 4D printing, which builds upon 3D printing technology, can undergo structural changes in response to external stimuli. This capability enables the simulation of unique functions observed in natural tissues, such as parasympathetic excitation leading to pupil constriction via acetylcholine release [222]. Through the application of 3D and 4D printing technology, the development of biosensors mimicking the photoreceptor function of the retina becomes feasible. This advancement facilitates personalized medicine by replicating the natural structure of eye tissues to achieve the precision of structural hierarchy and natural function of the retina. Such innovations hold immense promise in the field of ophthalmology for the future.

6. Conclusion and prospect

The eye, a vital organ in the human body, serves multiple functions, among which the sense of vision stands out as particularly crucial. Millions of people around the world suffer from ocular diseases, which are intricately linked to the destruction of the structural and functional integrity of the eye. As an organ exposed to the environment directly, the eye is highly susceptible to stimuli, although there are certain barriers within the body, such as the ocular surface barrier, this also affects the absorption and utilization of ocular drugs to a certain extent. Topical eye drops are currently the most common form of ophthalmic drugs, which contacts the ocular surface and reduces the obstruction of drugs by the blood-ocular barrier, but they are also subject to the effects of tear flushing and mechanical movements such as eye blinking, which bring about a decrease in the concentration and dosage of the drugs, thus causing a lack of bioavailability. More effective treatments are needed to ensure that the drug reaches the site of disease and works for a longer period of time. Simultaneously, the unique immune environment of the eye has fostered well-developed research in regenerative medicine within ophthalmology, particularly in the replacement of eye tissue using various biological materials. Regenerative medicine in ophthalmology has propelled the continuous advancement of tissue-engineered cornea, tissue-engineered retina, and other related fields. The emergence of 3D printing technology has expedited the application of biomaterials in ophthalmology. Photo-crosslink hydrogel in the field of ophthalmology is a research hotspot in recent years, as a widely used biomaterials which has the advantages of high biocompatibility, more convenient and controllable using light modulation, high water content, and a mesh structure for encapsulation of cells or drugs, so it has attracted a lot of attention in the fields of tissue engineering, drug delivery and 3D bioprinting.

Although some photo-crosslink hydrogels are not currently utilized in medical applications, they hold potential for future medical use. For instance, in a recent study conducted by Ekblad et al., polyethylene glycol (PEG)-based hydrogel coatings were prepared using 2-hydroxyethyl methacrylate (HEMA) and poly(ethylene glycol) methacrylate (PEGMA) via UV irradiation free radical polymerization. The coatings underwent a six-month evaluation in artificial seawater, revealing remarkable stability and exhibiting broad-spectrum antifouling properties. In addition, the hydrogel coating exhibited low adsorption for complex fluids such as proteins and plasma, and has the advantage of being simple to prepare and easy to quantify industrially [223]. As medical technology advances, the utilization of implantable medical devices has become widespread. However, there exists a risk of microorganisms, proteins and platelets adhering to these devices upon implantation within the body. This adherence can subsequently lead to inflammation and thrombosis at the implantation site. The introduction of Marine Antifouling Field antifouling film hydrogel coatings on implantable medical devices inhibits the adhesion and proliferation of microorganisms, proteins, and platelets on the surface of the device, thereby reducing the potential for inflammation, thrombosis, and the incidence of post-treatment side effects in patients, and increasing the lifespan of the implantable medical device. Hence, while the anti-fouling hydrogel developed for marine applications has not yet been utilized in the medical field, it holds significant promise for biomedical applications. This potential can be realized through enhancements in biocompatibility, control over degradation properties and mechanical characteristics, as well as increased adhesion to medical devices.

This review provides a comprehensive description of photo-crosslink hydrogels, encompassing their types, modes of action, and applications in ophthalmology, with a primary focus on tissue engineering, drug delivery and 3D printing. In general, photo-crosslink hydrogels regulate the physicochemical properties of hydrogels by adjusting the exposure intensity and time due to their photocontrol nature and the eye, as an external organ, has the accessibility of light regulation, which increases the possibility of research on photo-crosslink hydrogels in ophthalmology. Moreover, photo-crosslink hydrogels possess a hydrophilic porous structure with excellent cytocompatibility. They can encapsulate cells for tissue engineering regeneration or ocular structural substitution, and also encapsulate drugs for fundus medication delivery. Additionally, the fitness of hydrogels with individuals can be enhanced through 3D printing. So far, a variety of substances delivered to the eye through photo-crosslink hydrogels, including drugs, genes, bioactive molecules and stem cells. There are also a variety of structures that can be formed by 3D printing or photo-crosslink hydrogels for substitution, including corneal contact lenses and vitreous body. These advances are aimed at improving the effectiveness and safety of ophthalmic treatments, and providing a new strategy for precision ophthalmic treatments.

Currently, the diagnosis and treatment of ophthalmic diseases based on photo-crosslink hydrogels are primarily in the early stages in the laboratory. Although some positive results have been achieved in experiments, there are still challenges in translating these findings to clinical applications. Indeed, several factors contribute to this situation. First of all, one of the reasons for the low conversion is the disconnection between product development and application. The path of transformation of scientific and technological achievements is complicated, which requires professional evaluation standards for technical assessment of scientific and technological achievements, as well as specialized organizations and institutions to provide technical and theoretical

guidance services and financial guarantees. Moreover, one of the reasons for the low transformation rate is the insufficient technical capability of the transformation process itself. Before clinical application, a large number of researches are needed to prove its mechanism of action, drug distribution and metabolism, which is very important for whether the material itself plays an effective and safe role, furthermore, the current pre-laboratory research on animal experiments mainly focuses on the study of mice and rabbits, and seldom uses the monkey model, and the immune composition and physiological structure of animals are different from that of human beings. Moreover, the immune composition and physiological structure of animals are different from that of human beings, and the results of animals cannot replace the results of human beings. Enhancing the credibility of experimental results involves meticulous experimental design, rigorous methodologies, and robust statistical analyses. Establishing more reliable animal models requires a thorough understanding of the biological mechanisms involved and continuous refinement of the model parameters. For low-cost clinical trials, strategic planning, collaboration, and efficient resource utilization are essential to address challenges and optimize the trial design. Once the aforementioned challenges are addressed, there is the potential for the application of photo-crosslink hydrogels in the treatment of ophthalmic diseases.

CRediT authorship contribution statement

Qinghe Zhang: Writing – original draft, Visualization, Conceptualization. **Ke Yan:** Visualization. **Xiaoqin Zheng:** Visualization. **Qiuping Liu:** Supervision. **Yi Han:** Writing – review & editing, Supervision, Conceptualization. **Zuguo Liu:** Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare no conflict.

Data availability

No data was used for the research described in the article.

Acknowledgements

Authors would like to acknowledge the support provided by grants from the National Natural Science Foundation of China (No. 82271054, ZL), the China Postdoctoral Science Foundation (No. 2023M741608, YH).

References

[1] X. Zhang, V.J. M, Y. Qu, X. He, S. Ou, J. Bu, C. Jia, J. Wang, H. Wu, Z. Liu, W. Li, Dry eye management: targeting the ocular surface microenvironment, Int. J. Mol. Sci. 18 (2017) 1398, https://doi.org/10.3390/ijms18071398.
[2] D.R. Janagam, L. Wu, T.L. Lowe, Nanoparticles for drug delivery to the anterior segment of the eye, Adv. Drug Deliv. Rev. 122 (2017) 31–64, https://doi.org/10.1016/j.addr.2017.04.001.
[3] M. Alves, TFOS Lifestyle Report: Impact of Environmental Conditions on the Ocular Surface, (n.d.)..
[4] G.-B. Van Setten, Ocular surface allostasis—when homeostasis is lost: challenging coping potential, stress tolerance, and resilience, Biomolecules 13 (2023) 1246, https://doi.org/10.3390/biom13081246.
[5] M. Xuan, S. Wang, X. Liu, Y. He, Y. Li, Y. Zhang, Proteins of the corneal stroma: importance in visual function, Cell Tissue Res. 364 (2016) 9–16, https://doi.org/10.1007/s00441-016-2372-3.
[6] C.D. McTiernan, F.C. Simpson, M. Haagdorens, C. Samarawickrama, D. Hunter, O. Buznyk, P. Fagerholm, M.K. Ljunggren, P. Lewis, I. Pintelon, D. Olsen, E. Edin, M. Groleau, B.D. Allan, M. Griffith, LiQD Cornea: pro-regeneration collagen mimetics as patches and alternatives to corneal transplantation, Sci. Adv. 6 (2020) eaba2187, https://doi.org/10.1126/sciadv.aba2187.
[7] L. Yue, J.D. Weiland, B. Roska, M.S. Humayun, Retinal stimulation strategies to restore vision: fundamentals and systems, Prog. Retin. Eye Res. 53 (2016) 21–47, https://doi.org/10.1016/j.preteyeres.2016.05.002.
[8] B. Roska, J.-A. Sahel, Restoring vision, Nature 557 (2018) 359–367, https://doi.org/10.1038/s41586-018-0076-4.
[9] E.M. Del Amo, A.-K. Rimpelä, E. Heikkinen, O.K. Kari, E. Ramsay, T. Lajunen, M. Schmitt, L. Pelkonen, M. Bhattacharya, D. Richardson, A. Subrizi, T. Turunen, M. Reinisalo, J. Itkonen, E. Toropainen, M. Casteleijn, H. Kidron, M. Antopolsky, K.-S. Vellonen, M. Ruponen, A. Urtti, Pharmacokinetic aspects of retinal drug delivery, Prog. Retin. Eye Res. 57 (2017) 134–185, https://doi.org/10.1016/j.preteyeres.2016.12.001.
[10] J. Cunha-Vaz, R. Bernardes, C. Lobo, Blood-retinal barrier, Eur. J. Ophthalmol. 21 (2011) 3–9, https://doi.org/10.5301/EJO.2010.6049.
[11] V. Gote, S. Sikder, J. Sicotte, D. Pal, Ocular drug delivery: present innovations and future challenges, J. Pharmacol. Exp. Therapeut. 370 (2019) 602–624, https://doi.org/10.1124/jpet.119.256933.
[12] C. Jumelle, S. Gholizadeh, N. Annabi, R. Dana, Advances and limitations of drug delivery systems formulated as eye drops, J. Contr. Release 321 (2020) 1–22, https://doi.org/10.1016/j.jconrel.2020.01.057.
[13] F.J. Cabrera, D.C. Wang, K. Reddy, G. Acharya, C.S. Shin, Challenges and opportunities for drug delivery to the posterior of the eye, Drug Discov. Today 24 (2019) 1679–1684, https://doi.org/10.1016/j.drudis.2019.05.035.
[14] E. Moisseiev, A. Loewenstein, Drug delivery to the posterior segment of the eye, in: G. Coscas, A. Loewenstein, J. Cunha-Vaz, G. Soubrane (Eds.), Dev. Ophthalmol., S. Karger AG, 2017, pp. 87–101, https://doi.org/10.1159/000455276.
[15] N. Nagai, H. Otake, Novel drug delivery systems for the management of dry eye, Adv. Drug Deliv. Rev. 191 (2022) 114582, https://doi.org/10.1016/j.addr.2022.114582.
[16] G. Xie, S. Lin, F. Wu, J. Liu, Nanomaterial-based ophthalmic drug delivery, Adv. Drug Deliv. Rev. 200 (2023) 115004, https://doi.org/10.1016/j.addr.2023.115004.
[17] J. He, Y. Sun, Q. Gao, C. He, K. Yao, T. Wang, M. Xie, K. Yu, J. Nie, Y. Chen, Y. He, Gelatin methacryloyl hydrogel, from standardization, performance, to biomedical application, Adv. Healthcare Mater. 12 (2023) 2300395, https://doi.org/10.1002/adhm.202300395.
[18] C. He, Y. Sun, N. Liu, K. Yu, Y. Qian, Y. He, Formation theory and printability of photocurable hydrogel for 3D bioprinting, Adv. Funct. Mater. 33 (2023) 2301209, https://doi.org/10.1002/adfm.202301209.
[19] M. Wu, H. Liu, Y. Zhu, F. Chen, Z. Chen, L. Guo, P. Wu, G. Li, C. Zhang, R. Wei, L. Cai, Mild photothermal-stimulation based on injectable and photocurable hydrogels orchestrates immunomodulation and osteogenesis for high-performance bone regeneration, Small 19 (2023) 2300111, https://doi.org/10.1002/smll.202300111.
[20] S.H. Kim, H. Hong, O. Ajiteru, MdT. Sultan, Y.J. Lee, J.S. Lee, O.J. Lee, H. Lee, H. S. Park, K.Y. Choi, J.S. Lee, H.W. Ju, I.-S. Hong, C.H. Park, 3D bioprinted silk fibroin hydrogels for tissue engineering, Nat. Protoc. 16 (2021) 5484–5532, https://doi.org/10.1038/s41596-021-00622-1.
[21] D.M. Catori, L.C.E. Da Silva, M.F. De Oliveira, G.H. Nguyen, J.C. Moses, E. J. Brisbois, H. Handa, M.G. De Oliveira, In situ photo-crosslinkable hyaluronic acid/gelatin hydrogel for local nitric oxide delivery, ACS Appl. Mater. Interfaces 15 (2023) 48930–48944, https://doi.org/10.1021/acsami.3c10030.
[22] H. Cao, L. Duan, Y. Zhang, J. Cao, K. Zhang, Current hydrogel advances in physicochemical and biological response-driven biomedical application diversity, Signal Transduct. Targeted Ther. 6 (2021) 426, https://doi.org/10.1038/s41392-021-00830-x.
[23] Y. Wang, Programmable hydrogels, Biomaterials 178 (2018) 663–680, https://doi.org/10.1016/j.biomaterials.2018.03.008.
[24] A.M. Gutierrez, E.M. Frazar, M.V.X. Klaus, P. Paul, J.Z. Hilt, Hydrogels and hydrogel nanocomposites: enhancing healthcare through human and environmental treatment, Adv. Healthcare Mater. 11 (2022) 2101820, https://doi.org/10.1002/adhm.202101820.
[25] E.M. Ahmed, Hydrogel: preparation, characterization, and applications: a review, J. Adv. Res. 6 (2015) 105–121, https://doi.org/10.1016/j.jare.2013.07.006.
[26] J. Mercado-Montijo, D.M. Anstine, S.J. Rukmani, C.M. Colina, J.S. Andrew, PEGDA hydrogel structure from semi-dilute concentrations: insights from experiments and molecular simulations, Soft Matter 18 (2022) 3565–3574, https://doi.org/10.1039/D1SM01708J.
[27] M. Hamidi, A. Azadi, P. Rafiei, Hydrogel nanoparticles in drug delivery, Adv. Drug Deliv. Rev. 60 (2008) 1638–1649, https://doi.org/10.1016/j.addr.2008.08.002.
[28] Z. Feng, Y. Zhang, C. Yang, X. Liu, Y. Huangfu, C. Zhang, P. Huang, A. Dong, J. Liu, J. Liu, D. Kong, W. Wang, Bioinspired and inflammation-modulatory glycopeptide hydrogels for radiation-induced chronic skin injury repair, Adv. Healthcare Mater. 12 (2023) 2201671, https://doi.org/10.1002/adhm.202201671.
[29] M. Qasim, D.S. Chae, N.Y. Lee, Advancements and frontiers in nano-based 3D and 4D scaffolds for bone and cartilage tissue engineering, Int. J. Nanomed. 14 (2019) 4333–4351, https://doi.org/10.2147/IJN.S209431.
[30] Z. Zhu, Y. Liu, J. Chen, Z. He, P. Tan, Y. He, X. Pei, J. Wang, L. Tan, Q. Wan, Structural-functional pluralistic modification of silk fibroin via MOF bridging for advanced wound care, Adv. Sci. 9 (2022) 2204553, https://doi.org/10.1002/advs.202204553.
[31] W. Sun, D.A. Gregory, M.A. Tomeh, X. Zhao, Silk fibroin as a functional biomaterial for tissue engineering, Int. J. Mol. Sci. 22 (2021) 1499, https://doi.org/10.3390/ijms22031499.
[32] L. Li, J.M. Scheiger, P.A. Levkin, Design and applications of photoresponsive hydrogels, Adv. Mater. 31 (2019) 1807333, https://doi.org/10.1002/adma.201807333.

[33] J.R. Choi, K.W. Yong, J.Y. Choi, A.C. Cowie, Recent advances in photo-crosslinkable hydrogels for biomedical applications, Biotechniques 66 (2019) 40–53, https://doi.org/10.2144/btn-2018-0083.
[34] R.F. Pereira, C.C. Barrias, P.J. Bártolo, P.L. Granja, Cell-instructive pectin hydrogels crosslinked via thiol-norbornene photo-click chemistry for skin tissue engineering, Acta Biomater. 66 (2018) 282–293, https://doi.org/10.1016/j.actbio.2017.11.016.
[35] C.-C. Lin, C.S. Ki, H. Shih, Thiol-norbornene photoclick hydrogels for tissue engineering applications, J. Appl. Polym. Sci. 132 (2015), https://doi.org/10.1002/app.41563 n/a-n/a.
[36] Y. Jiang, J. Chen, C. Deng, E.J. Suuronen, Z. Zhong, Click hydrogels, microgels and nanogels: emerging platforms for drug delivery and tissue engineering, Biomaterials 35 (2014) 4969–4985, https://doi.org/10.1016/j.biomaterials.2014.03.001.
[37] R. Dimatteo, N.J. Darling, T. Segura, In situ forming injectable hydrogels for drug delivery and wound repair, Adv. Drug Deliv. Rev. 127 (2018) 167–184, https://doi.org/10.1016/j.addr.2018.03.007.
[38] L. Qi, C. Zhang, B. Wang, J. Yin, S. Yan, Progress in hydrogels for skin wound repair, Macromol. Biosci. 22 (2022) 2100475, https://doi.org/10.1002/mabi.202100475.
[39] Y.H. Choi, S.-H. Kim, I.-S. Kim, K. Kim, S.K. Kwon, N.S. Hwang, Gelatin-based micro-hydrogel carrying genetically engineered human endothelial cells for neovascularization, Acta Biomater. 95 (2019) 285–296, https://doi.org/10.1016/j.actbio.2019.01.057.
[40] A.B. Bello, D. Kim, D. Kim, H. Park, S.-H. Lee, Engineering and functionalization of gelatin biomaterials: from cell culture to medical applications, Tissue Eng., Part B 26 (2020) 164–180, https://doi.org/10.1089/ten.teb.2019.0256.
[41] A. Gaspar-Pintiliescu, A.-M. Stanciuc, O. Craciunescu, Natural composite dressings based on collagen, gelatin and plant bioactive compounds for wound healing: a review, Int. J. Biol. Macromol. 138 (2019) 854–865, https://doi.org/10.1016/j.ijbiomac.2019.07.155.
[42] P. Hassanzadeh, M. Kazemzadeh-Narbat, R. Rosenzweig, X. Zhang, A. Khademhosseini, N. Annabi, M. Rolandi, Ultrastrong and flexible hybrid hydrogels based on solution self-assembly of chitin nanofibers in gelatin methacryloyl (GelMA), J. Mater. Chem. B 4 (2016) 2539–2543, https://doi.org/10.1039/C6TB00021E.
[43] L.-J. Yang, Y.-C. Ou, The micro patterning of glutaraldehyde (GA)-crosslinked gelatin and its application to cell-culture, Lab Chip 5 (2005) 979, https://doi.org/10.1039/b505193b.
[44] J.-H. Wang, C.-W. Tsai, N.-Y. Tsai, C.-Y. Chiang, R.-S. Lin, R.F. Pereira, Y.-C.E. Li, An injectable, dual crosslinkable hybrid pectin methacrylate (PECMA)/gelatin methacryloyl (GelMA) hydrogel for skin hemostasis applications, Int. J. Biol. Macromol. 185 (2021) 441–450, https://doi.org/10.1016/j.ijbiomac.2021.06.162.
[45] S. Ding, S. He, K. Ye, X. Shao, Q. Yang, G. Yang, Photopolymerizable, immunomodulatory hydrogels of gelatin methacryloyl and carboxymethyl chitosan as all-in-one strategic dressing for wound healing, Int. J. Biol. Macromol. (2023) 127151, https://doi.org/10.1016/j.ijbiomac.2023.127151.
[46] Y. Han, L. Zheng, Y. Wang, K. Fan, S. Guo, H. Kang, J. Lin, Y. Xue, Z. Liu, C. Li, Corneal stromal filler injection of gelatin-based photocurable hydrogels for maintaining the corneal thickness and reconstruction of corneal stroma, Composites, Part B 266 (2023) 111004, https://doi.org/10.1016/j.compositesb.2023.111004.
[47] Y. Qiu, Y. Ma, Y. Huang, S. Li, H. Xu, E. Su, Current advances in the biosynthesis of hyaluronic acid with variable molecular weights, Carbohydr. Polym. 269 (2021) 118320, https://doi.org/10.1016/j.carbpol.2021.118320.
[48] S.L. Fenn, R. Floreani, Visible light crosslinking of methacrylated hyaluronan hydrogels for injectable tissue repair, J. Biomed. Mater. Res. B Appl. Biomater. 104 (2016) 1229–1236, https://doi.org/10.1002/jbm.b.33476.
[49] F. Chen, P. Le, G.M. Fernandes-Cunha, S.C. Heilshorn, D. Myung, Bio-orthogonally crosslinked hyaluronate-collagen hydrogel for suture-free corneal defect repair, Biomaterials 255 (2020) 120176, https://doi.org/10.1016/j.biomaterials.2020.120176.
[50] J. Zheng, Y. Wang, Y. Wang, R. Duan, L. Liu, Gelatin/hyaluronic acid photocrosslinked double network hydrogel with nano-hydroxyapatite composite for potential application in bone repair, Gels 9 (2023) 742, https://doi.org/10.3390/gels9090742.
[51] M.F.P. Graça, S.P. Miguel, C.S.D. Cabral, I.J. Correia, Hyaluronic acid—based wound dressings: a review, Carbohydr. Polym. 241 (2020) 116364, https://doi.org/10.1016/j.carbpol.2020.116364.
[52] A. Skardal, A. Atala, Biomaterials for integration with 3-D bioprinting, Ann. Biomed. Eng. 43 (2015) 730–746, https://doi.org/10.1007/s10439-014-1207-1.
[53] H. Lin, J. Liu, K. Zhang, Y. Fan, X. Zhang, Dynamic mechanical and swelling properties of maleated hyaluronic acid hydrogels, Carbohydr. Polym. 123 (2015) 381–389, https://doi.org/10.1016/j.carbpol.2015.01.047.
[54] X. Shen, S. Li, X. Zhao, J. Han, J. Chen, Z. Rao, K. Zhang, D. Quan, J. Yuan, Y. Bai, Dual-crosslinked regenerative hydrogel for sutureless long-term repair of corneal defect, Bioact. Mater. 20 (2023) 434–448, https://doi.org/10.1016/j.bioactmat.2022.06.006.
[55] N. Zhou, Y.-D. Liu, Y. Zhang, T.-W. Gu, L.-H. Peng, Pharmacological functions, synthesis, and delivery progress for collagen as biodrug and biomaterial, Pharmaceutics 15 (2023) 1443, https://doi.org/10.3390/pharmaceutics15051443.
[56] S. Varma, J.P.R.O. Orgel, J.D. Schieber, Nanomechanics of type I collagen, Biophys. J. 111 (2016) 50–56, https://doi.org/10.1016/j.bpj.2016.05.038.
[57] K. Gelse, Collagens—structure, function, and biosynthesis, Adv. Drug Deliv. Rev. 55 (2003) 1531–1546, https://doi.org/10.1016/j.addr.2003.08.002.
[58] S. Takahashi, D. Geenen, E. Nieves, T. Iwazumi, Collagenase degrades collagen in vivo in the ischemic heart, Biochim. Biophys. Acta BBA - Gen. Subj. 1428 (1999) 251–259, https://doi.org/10.1016/S0304-4165(99)00090-2.
[59] R. Naomi, J. Ratanavaraporn, M.B. Fauzi, Comprehensive review of hybrid collagen and silk fibroin for cutaneous wound healing, Materials 13 (2020) 3097, https://doi.org/10.3390/ma13143097.
[60] B.N. Brown, S.F. Badylak, Extracellular matrix as an inductive scaffold for functional tissue reconstruction, Transl. Res. 163 (2014) 268–285, https://doi.org/10.1016/j.trsl.2013.11.003.
[61] A. Sorushanova, L.M. Delgado, Z. Wu, N. Shologu, A. Kshirsagar, R. Raghunath, A.M. Mullen, Y. Bayon, A. Pandit, M. Raghunath, D.I. Zeugolis, The collagen suprafamily: from biosynthesis to advanced biomaterial development, Adv. Mater. 31 (2019) 1801651, https://doi.org/10.1002/adma.201801651.
[62] S. Hao, C. Tian, Y. Bai, L. Wu, L. Hao, Y. Kuang, S. Yang, H. Mao, Z. Gu, Photo-crosslinkable hyaluronic acid microgels with reactive oxygen species scavenging capacity for mesenchymal stem cell encapsulation, Int. J. Biol. Macromol. 243 (2023) 124971, https://doi.org/10.1016/j.ijbiomac.2023.124971.
[63] K.E. Drzewiecki, A.S. Parmar, I.D. Gaudet, J.R. Branch, D.H. Pike, V. Nanda, D. I. Shreiber, Methacrylation induces rapid, temperature-dependent, reversible self-assembly of type-I collagen, Langmuir 30 (2014) 11204–11211, https://doi.org/10.1021/la502418s.
[64] L. Gu, T. Shan, Y. Ma, F.R. Tay, L. Niu, Novel biomedical applications of crosslinked collagen, Trends Biotechnol. 37 (2019) 464–491, https://doi.org/10.1016/j.tibtech.2018.10.007.
[65] D. Olsen, Recombinant collagen and gelatin for drug delivery, Adv. Drug Deliv. Rev. 55 (2003) 1547–1567, https://doi.org/10.1016/j.addr.2003.08.008.
[66] S.U.D. Wani, S.P. Gautam, Z.L. Qadrie, H.V. Gangadharappa, Silk fibroin as a natural polymeric based bio-material for tissue engineering and drug delivery systems-A review, Int. J. Biol. Macromol. 163 (2020) 2145–2161, https://doi.org/10.1016/j.ijbiomac.2020.09.057.
[67] B. Kundu, R. Rajkhowa, S.C. Kundu, X. Wang, Silk fibroin biomaterials for tissue regenerations, Adv. Drug Deliv. Rev. 65 (2013) 457–470, https://doi.org/10.1016/j.addr.2012.09.043.
[68] Ł. Mazurek, M. Szudzik, M. Rybka, M. Konop, Silk fibroin biomaterials and their beneficial role in skin wound healing, Biomolecules 12 (2022) 1852, https://doi.org/10.3390/biom12121852.
[69] M. Gholipourmalekabadi, S. Sapru, A. Samadikuchaksaraei, R.L. Reis, D. L. Kaplan, S.C. Kundu, Silk fibroin for skin injury repair: where do things stand? Adv. Drug Deliv. Rev. 153 (2020) 28–53, https://doi.org/10.1016/j.addr.2019.09.003.
[70] P.P. Patil, M.R. Reagan, R.A. Bohara, Silk fibroin and silk-based biomaterial derivatives for ideal wound dressings, Int. J. Biol. Macromol. 164 (2020) 4613–4627, https://doi.org/10.1016/j.ijbiomac.2020.08.041.
[71] T. Asakura, M.P. Williamson, A review on the structure of Bombyx mori silk fibroin fiber studied using solid-state NMR: an antipolar lamella with an 8-residue repeat, Int. J. Biol. Macromol. 245 (2023) 125537, https://doi.org/10.1016/j.ijbiomac.2023.125537.
[72] X. Wu, M. Zhou, F. Jiang, S. Yin, S. Lin, G. Yang, Y. Lu, W. Zhang, X. Jiang, Marginal sealing around integral bilayer scaffolds for repairing osteochondral defects based on photocurable silk hydrogels, Bioact. Mater. 6 (2021) 3976–3986, https://doi.org/10.1016/j.bioactmat.2021.04.005.
[73] S.H. Kim, Y.K. Yeon, J.M. Lee, J.R. Chao, Y.J. Lee, Y.B. Seo, MdT. Sultan, O.J. Lee, J.S. Lee, S. Yoon, I.-S. Hong, G. Khang, S.J. Lee, J.J. Yoo, C.H. Park, Precisely printable and biocompatible silk fibroin bioink for digital light processing 3D printing, Nat. Commun. 9 (2018) 1620, https://doi.org/10.1038/s41467-018-03759-y.
[74] Y. Qian, Y. Zheng, J. Jin, X. Wu, K. Xu, M. Dai, Q. Niu, H. Zheng, X. He, J. Shen, Immunoregulation in diabetic wound repair with a photoenhanced glycyrrhizic acid hydrogel scaffold, Adv. Mater. 34 (2022) 2200521, https://doi.org/10.1002/adma.202200521.
[75] J. Mei, J. Zhou, L. Kong, Y. Dai, X. Zhang, W. Song, C. Zhu, An injectable photo-cross-linking silk hydrogel system augments diabetic wound healing in orthopaedic surgery through spatiotemporal immunomodulation, J. Nanobiotechnol. 20 (2022) 232, https://doi.org/10.1186/s12951-022-01414-9.
[76] L. Elviri, A. Bianchera, C. Bergonzi, R. Bettini, Controlled local drug delivery strategies from chitosan hydrogels for wound healing, Expet Opin. Drug Deliv. 14 (2017) 897–908, https://doi.org/10.1080/17425247.2017.1247803.
[77] Z. Shariatinia, A.M. Jalali, Chitosan-based hydrogels: preparation, properties and applications, Int. J. Biol. Macromol. 115 (2018) 194–220, https://doi.org/10.1016/j.ijbiomac.2018.04.034.
[78] M. Aghbashlo, H. Amiri, S.M. Moosavi Basri, H. Rastegari, S.S. Lam, J. Pan, V. K. Gupta, M. Tabatabaei, Tuning chitosan's chemical structure for enhanced biological functions, Trends Biotechnol. 41 (2023) 785–797, https://doi.org/10.1016/j.tibtech.2022.11.009.
[79] S. Peers, A. Montembault, C. Ladavière, Chitosan hydrogels for sustained drug delivery, J. Contr. Release 326 (2020) 150–163, https://doi.org/10.1016/j.jconrel.2020.06.012.
[80] M.A.S. Abourehab, S. Pramanik, M.A. Abdelgawad, B.M. Abualsoud, A. Kadi, M. J. Ansari, A. Deepak, Recent advances of chitosan formulations in biomedical applications, Int. J. Mol. Sci. 23 (2022) 10975, https://doi.org/10.3390/ijms231810975.

[81] Y. Shen, H. Tang, X. Huang, R. Hang, X. Zhang, Y. Wang, X. Yao, DLP printing photocurable chitosan to build bio-constructs for tissue engineering, Carbohydr. Polym. 235 (2020) 115970, https://doi.org/10.1016/j.carbpol.2020.115970.
[82] H.S. Ko, D.H. Yang, A. Kim, J.H. Wie, S.H. Kim, G.-J. Jeong, H. Hyun, J.C. Shin, H. J. Chun, Visible light-curable methacrylated glycol chitosan hydrogel patches for prenatal closure of fetal myelomeningocele, Carbohydr. Polym. 311 (2023) 120620, https://doi.org/10.1016/j.carbpol.2023.120620.
[83] M.E. Abd El-Hack, M.T. El-Saadony, M.E. Shafi, N.M. Zabermawi, M. Arif, G. E. Batiha, A.F. Khafaga, Y.M. Abd El-Hakim, A.A. Al-Sagheer, Antimicrobial and antioxidant properties of chitosan and its derivatives and their applications: a review, Int. J. Biol. Macromol. 164 (2020) 2726–2744, https://doi.org/10.1016/j.ijbiomac.2020.08.153.
[84] A.A. D'souza, R. Shegokar, Polyethylene glycol (PEG): a versatile polymer for pharmaceutical applications, Expet Opin. Drug Deliv. 13 (2016) 1257–1275, https://doi.org/10.1080/17425247.2016.1182485.
[85] A. Kolate, D. Baradia, S. Patil, I. Vhora, G. Kore, A. Misra, Peg — a versatile conjugating ligand for drugs and drug delivery systems, J. Contr. Release 192 (2014) 67–81, https://doi.org/10.1016/j.jconrel.2014.06.046.
[86] X. Kong, Q. Tang, X. Chen, Y. Tu, S. Sun, Z. Sun, Polyethylene glycol as a promising synthetic material for repair of spinal cord injury, Neural Regen. Res. 12 (2017) 1003, https://doi.org/10.4103/1673-5374.208597.
[87] J.-Z. Wang, M.-L. You, Z.-Q. Ding, W.-B. Ye, A review of emerging bone tissue engineering via PEG conjugated biodegradable amphiphilic copolymers, Mater. Sci. Eng. C 97 (2019) 1021–1035, https://doi.org/10.1016/j.msec.2019.01.057.
[88] Z. Chen, Y. Zeng, N. Chen, M. Zhang, Y. Wang, Z. Pan, J. Yuan, Z. Ye, X. Li, W. Bian, H. Li, K. Zhang, Y. He, X. Liu, A facile and universal method for preparing polyethylene glycol-metal hybrid nanoparticles and their application in tumor theranostics, Adv. Healthcare Mater. 11 (2022) 2200044, https://doi.org/10.1002/adhm.202200044.
[89] S. Parveen, S.K. Sahoo, Nanomedicine: clinical applications of polyethylene glycol conjugated proteins and drugs, Clin. Pharmacokinet. 45 (2006) 965–988, https://doi.org/10.2165/00003088-200645100-00002.
[90] X. Du, L. Wu, H. Yan, L. Qu, L. Wang, X. Wang, S. Ren, D. Kong, L. Wang, Multifunctional hydrogel patch with toughness, tissue adhesiveness, and antibacterial activity for sutureless wound closure, ACS Biomater. Sci. Eng. 5 (2019) 2610–2620, https://doi.org/10.1021/acsbiomaterials.9b00130.
[91] K. Krutkramelis, B. Xia, J. Oakey, Monodisperse polyethylene glycol diacrylate hydrogel microsphere formation by oxygen-controlled photopolymerization in a microfluidic device, Lab Chip 16 (2016) 1457–1465, https://doi.org/10.1039/C6LC00254D.
[92] S. Yao, J. Chi, Y. Wang, Y. Zhao, Y. Luo, Y. Wang, Zn-MOF encapsulated antibacterial and degradable microneedles array for promoting wound healing, Adv. Healthcare Mater. 10 (2021) 2100056, https://doi.org/10.1002/adhm.202100056.
[93] N. Rekowska, M. Teske, D. Arbeiter, A. Brietzke, J. Konasch, A. Riess, R. Mau, T. Eickner, H. Seitz, N. Grabow, Biocompatibility and thermodynamic properties of PEGDA and two of its copolymer, in: 2019 41st Annu. Int. Conf. IEEE Eng. Med. Biol. Soc. EMBC, IEEE, Berlin, Germany, 2019, pp. 1093–1096, https://doi.org/10.1109/EMBC.2019.8857503.
[94] M. Singh, J. Zhang, K. Bethel, Y. Liu, E.M. Davis, H. Zeng, Z. Kong, B.N. Johnson, Closed-loop controlled photopolymerization of hydrogels, ACS Appl. Mater. Interfaces 13 (2021) 40365–40378, https://doi.org/10.1021/acsami.1c11779.
[95] F. Kawai, X. Hu, Biochemistry of microbial polyvinyl alcohol degradation, Appl. Microbiol. Biotechnol. 84 (2009) 227–237, https://doi.org/10.1007/s00253-009-2113-6.
[96] E.A. Kamoun, S.A. Loutfy, Y. Hussein, E.-R.S. Kenawy, Recent advances in PVA-polysaccharide based hydrogels and electrospun nanofibers in biomedical applications: a review, Int. J. Biol. Macromol. 187 (2021) 755–768, https://doi.org/10.1016/j.ijbiomac.2021.08.002.
[97] C.B. Barros Araújo, I.L. Da Silva Soares, D.P. Da Silva Lima, R.M. Barros, B.P. G. De Lima Damasceno, J.A. Oshiro-Junior, Polyvinyl alcohol nanofibers blends as drug delivery system in TissueRegeneration, Curr. Pharmaceut. Des. 29 (2023) 1149–1162, https://doi.org/10.2174/1381612829666230508144912.
[98] S.P. Gherman, G. Biliuță, A. Bele, A.M. Ipate, R.I. Baron, L. Ochiuz, A.F. Șpac, D. E. Zavastin, Biomaterials based on chitosan and polyvinyl alcohol as a drug delivery system with wound-healing effects, Gels 9 (2023) 122, https://doi.org/10.3390/gels9020122.
[99] S. Van Nguyen, B.-K. Lee, Polyvinyl alcohol/cellulose nanocrystals/alkyl ketene dimer nanocomposite as a novel biodegradable food packing material, Int. J. Biol. Macromol. 207 (2022) 31–39, https://doi.org/10.1016/j.ijbiomac.2022.02.184.
[100] S.G. Jin, Production and application of biomaterials based on polyvinyl alcohol (PVA) as wound dressing, Chem. Asian J. 17 (2022) e202200595, https://doi.org/10.1002/asia.202200595.
[101] H.-T. Hsieh, H.-M. Chang, W.-J. Lin, Y.-T. Hsu, F.-D. Mai, Poly-methyl methacrylate/polyvinyl alcohol copolymer agents applied on diabetic wound dressing, Sci. Rep. 7 (2017) 9531, https://doi.org/10.1038/s41598-017-10193-5.
[102] M. Goldvaser, E. Epstein, O. Rosen, A. Jayson, N. Natan, T. Ben-Shalom, S. Saphier, S. Katalan, O. Shoseyov, Poly(vinyl alcohol)-methacrylate with CRGD peptide: a photocurable biocompatible hydrogel, J. Tissue Eng. Regen. Med. 16 (2022) 140–150, https://doi.org/10.1002/term.3265.
[103] L. Wang, L. Duan, G. Liu, J. Sun, M. Shahbazi, S.C. Kundu, R.L. Reis, B. Xiao, X. Yang, Bioinspired polyacrylic acid-based dressing: wet adhesive, self-healing, and multi-biofunctional coacervate hydrogel accelerates wound healing, Adv. Sci. 10 (2023) 2207352, https://doi.org/10.1002/advs.202207352.
[104] J. Liu, N. Hu, Y. Xie, P. Wang, J. Chen, Q. Kan, Polyacrylic acid hydrogel coating for underwater adhesion: preparation and characterization, Gels 9 (2023) 616, https://doi.org/10.3390/gels9080616.
[105] M. Simeonov, B. Kostova, E. Vassileva, Interpenetrating polymer networks of polyacrylamide with polyacrylicand polymethacrylic acids and their application for modified DrugDelivery - a flash review, Pharm. Nanotechnol. 11 (2023) 25–33, https://doi.org/10.2174/2211738510666220919103514.
[106] Y. Onuki, M. Nishikawa, M. Morishita, K. Takayama, Development of photocrosslinked polyacrylic acid hydrogel as an adhesive for dermatological patches: involvement of formulation factors in physical properties and pharmacological effects, Int. J. Pharm. 349 (2008) 47–52, https://doi.org/10.1016/j.ijpharm.2007.07.021.
[107] T. Shimamoto, T. Nakakubo, T. Noji, S. Koeda, K. Kawakami, N. Kamiya, T. Mizuno, Design of PG-surfactants bearing polyacrylamide polymer chain to solubilize membrane proteins in a surfactant-free buffer, Int. J. Mol. Sci. 22 (2021) 1524, https://doi.org/10.3390/ijms22041524.
[108] A. Wolfel, M. Jin, J.I. Paez, Current strategies for ligand bioconjugation to poly (acrylamide) gels for 2D cell culture: balancing chemo-selectivity, biofunctionality, and user-friendliness, Front. Chem. 10 (2022) 1012443, https://doi.org/10.3389/fchem.2022.1012443.
[109] J. Li, J. Shen, B. Zhuang, M. Wei, Y. Liu, D. Liu, W. Yan, X. Jia, Y. Jin, Light-triggered on-site rapid formation of antibacterial hydrogel dressings for accelerated healing of infected wounds, Biomater. Adv. 136 (2022) 212784, https://doi.org/10.1016/j.bioadv.2022.212784.
[110] L. Han, J. Xu, X. Lu, D. Gan, Z. Wang, K. Wang, H. Zhang, H. Yuan, J. Weng, Biohybrid methacrylated gelatin/polyacrylamide hydrogels for cartilage repair, J. Mater. Chem. B 5 (2017) 731–741, https://doi.org/10.1039/C6TB02348G.
[111] L. Lu, S. Yuan, J. Wang, Y. Shen, S. Deng, L. Xie, Q. Yang, The Formation mechanism of hydrogels, Curr. Stem Cell Res. Ther. 13 (2018) 490–496, https://doi.org/10.2174/1574888X12666170612102706.
[112] B.D. Fairbanks, L.J. Macdougall, S. Mavila, J. Sinha, B.E. Kirkpatrick, K.S. Anseth, C.N. Bowman, Photoclick chemistry: a bright idea, Chem. Rev. 121 (2021) 6915–6990, https://doi.org/10.1021/acs.chemrev.0c01212.
[113] V.M. Lechner, M. Nappi, P.J. Deneny, S. Folliet, J.C.K. Chu, M.J. Gaunt, Visible-light-mediated modification and manipulation of biomacromolecules, Chem. Rev. 122 (2022) 1752–1829, https://doi.org/10.1021/acs.chemrev.1c00357.
[114] A.C. Alavarse, E.C.G. Frachini, R.L.C.G. Da Silva, V.H. Lima, A. Shavandi, D.F. S. Petri, Crosslinkers for polysaccharides and proteins: synthesis conditions, mechanisms, and crosslinking efficiency, a review, Int. J. Biol. Macromol. 202 (2022) 558–596, https://doi.org/10.1016/j.ijbiomac.2022.01.029.
[115] W. Hu, Z. Wang, Y. Xiao, S. Zhang, J. Wang, Advances in crosslinking strategies of biomedical hydrogels, Biomater. Sci. 7 (2019) 843–855, https://doi.org/10.1039/C8BM01246F.
[116] A. Reyhani, T.G. McKenzie, Q. Fu, G.G. Qiao, Fenton-chemistry-mediated radical polymerization, macromol, Rapid Commun. 40 (2019) 1900220, https://doi.org/10.1002/marc.201900220.
[117] J. Zhu, Y. Zhu, Z. Li, Z. Yu, X. Guan, R. Liu, Y. Yagci, Chemiluminescence-induced free radical–promoted cationic polymerization, Macromol. Rapid Commun. 41 (2020) 2000004, https://doi.org/10.1002/marc.202000004.
[118] S. Zhu, X. Wang, Y. Cong, L. Liu, L. Li, Free radical polymerization of gold nanoclusters and hydrogels for cell capture and light-controlled release, ACS Appl. Mater. Interfaces 13 (2021) 19360–19368, https://doi.org/10.1021/acsami.1c03587.
[119] C. Aydogan, G. Yilmaz, A. Shegiwal, D.M. Haddleton, Y. Yagci, Photoinduced controlled/living polymerizations, Angew. Chem. Int. Ed. 61 (2022) e202117377, https://doi.org/10.1002/anie.202117377.
[120] D. Das, T.T.H. Pham, I. Noh, Characterizations of hyaluronate-based terpolymeric hydrogel synthesized via free radical polymerization mechanism for biomedical applications, Colloids Surf. B Biointerfaces 170 (2018) 64–75, https://doi.org/10.1016/j.colsurfb.2018.05.059.
[121] C.E. Hoyle, C.N. Bowman, Thiol–ene click chemistry, Angew. Chem. Int. Ed. 49 (2010) 1540–1573, https://doi.org/10.1002/anie.200903924.
[122] S. Summonte, G.F. Racaniello, A. Lopedota, N. Denora, A. Bernkop-Schnürch, Thiolated polymeric hydrogels for biomedical application: cross-linking mechanisms, J. Contr. Release 330 (2021) 470–482, https://doi.org/10.1016/j.jconrel.2020.12.037.
[123] H. Liang, D. Yin, L. Shi, Y. Liu, X. Hu, N. Zhu, K. Guo, Surface modification of cellulose via photo-induced click reaction, Carbohydr. Polym. 301 (2023) 120321, https://doi.org/10.1016/j.carbpol.2022.120321.
[124] Z. Meng, X. Zhou, J. Xu, X. Han, Z. Dong, H. Wang, Y. Zhang, J. She, L. Xu, C. Wang, Z. Liu, Light-triggered in situ gelation to enable robust photodynamic-immunotherapy by repeated stimulations, Adv. Mater. 31 (2019) 1900927, https://doi.org/10.1002/adma.201900927.
[125] M. Hu, X. Wang, Y. Tang, X. He, H. Shen, H. Pan, Y. Shang, D. Wu, S. Zheng, Q. Wang, Photo-enzyme-polymerized hydrogel platform exhibits photo-switchable redox reversibility for diabetic wound healing, Nano Today 53 (2023) 102028, https://doi.org/10.1016/j.nantod.2023.102028.
[126] B. Bao, Q. Zeng, K. Li, J. Wen, Y. Zhang, Y. Zheng, R. Zhou, C. Shi, T. Chen, C. Xiao, B. Chen, T. Wang, K. Yu, Y. Sun, Q. Lin, Y. He, S. Tu, L. Zhu, Rapid fabrication of physically robust hydrogels, Nat. Mater. 22 (2023) 1253–1260, https://doi.org/10.1038/s41563-023-01648-4.
[127] X. Chen, D. Sun-Waterhouse, W. Yao, X. Li, M. Zhao, L. You, Free radical-mediated degradation of polysaccharides: mechanism of free radical formation and degradation, influence factors and product properties, Food Chem. 365 (2021) 130524, https://doi.org/10.1016/j.foodchem.2021.130524.

[128] Y. Yang, J. Wang, J. Yang, L. Tong, D. Li, Y. Yang, M. Fang, Z. Li, Photo-response with radical afterglow by regulation of spin populations and hole-electron distributions, Angew. Chem. Int. Ed. 62 (2023) e202218994, https://doi.org/10.1002/anie.202218994.
[129] Y. Zhu, D. Xu, Y. Zhang, Y. Zhou, Y. Yagci, R. Liu, Phenacyl phenothiazinium salt as a new broad-wavelength-absorbing photoinitiator for cationic and free radical polymerizations, Angew. Chem. Int. Ed. 60 (2021) 16917–16921, https://doi.org/10.1002/anie.202104531.
[130] W. Buckel, Radical and electron recycling in catalysis, Angew. Chem. Int. Ed. 48 (2009) 6779–6787, https://doi.org/10.1002/anie.200900771.
[131] B.M. Rosen, V. Percec, Single-electron transfer and single-electron transfer degenerative chain transfer living radical polymerization, Chem. Rev. 109 (2009) 5069–5119, https://doi.org/10.1021/cr900024j.
[132] N. Ballard, S. Hamzehlou, F. Ruipérez, J.M. Asua, On the termination mechanism in the radical polymerization of acrylates, macromol, Rapid Commun. 37 (2016) 1364–1368, https://doi.org/10.1002/marc.201600278.
[133] S. Amirthalingam, A.K. Rajendran, Y.G. Moon, N.S. Hwang, Stimuli-responsive dynamic hydrogels: design, properties and tissue engineering applications, Mater. Horiz. 10 (2023) 3325–3350, https://doi.org/10.1039/D3MH00399J.
[134] C. Li, G. Lu, G. Wang, B. Liu, T. Xue, H. Yuan, J. Nie, X. Zhu, Initiator-free photocuring 3D-printable PVA-based hydrogel with tunable mechanical properties and cell compatibility, macromol, Rapid Commun. 44 (2023) 2300214, https://doi.org/10.1002/marc.202300214.
[135] C.N. Zhu, C.Y. Li, H. Wang, W. Hong, F. Huang, Q. Zheng, Z.L. Wu, Reconstructable gradient structures and reprogrammable 3D deformations of hydrogels with coumarin units as the photolabile crosslinks, Adv. Mater. 33 (2021) 2008057, https://doi.org/10.1002/adma.202008057.
[136] R. Rizzo, N. Petelinšek, A. Bonato, M. Zenobi-Wong, From free-radical to radical-free: a paradigm shift in light-mediated biofabrication, Adv. Sci. 10 (2023) 2205302, https://doi.org/10.1002/advs.202205302.
[137] K.-H. Yang, G. Lindberg, B. Soliman, K. Lim, T. Woodfield, R.J. Narayan, Effect of photoinitiator on precursory stability and curing depth of thiol-ene clickable gelatin, Polymers 13 (2021) 1877, https://doi.org/10.3390/polym13111877.
[138] W. Tomal, J. Ortyl, Water-soluble photoinitiators in biomedical applications, Polymers 12 (2020) 1073, https://doi.org/10.3390/polym12051073.
[139] G. Szczepaniak, L. Fu, H. Jafari, K. Kapil, K. Matyjaszewski, Making ATRP more practical: oxygen tolerance, Acc. Chem. Res. 54 (2021) 1779–1790, https://doi.org/10.1021/acs.accounts.1c00032.
[140] M.K. Aromaa, P.K. Vallittu, Delayed post-curing stage and oxygen inhibition of free-radical polymerization of dimethacrylate resin, Dent. Mater. 34 (2018) 1247–1252, https://doi.org/10.1016/j.dental.2018.06.019.
[141] R. Simič, J. Mandal, K. Zhang, N.D. Spencer, Oxygen inhibition of free-radical polymerization is the dominant mechanism behind the "mold effect" on hydrogels, Soft Matter 17 (2021) 6394–6403, https://doi.org/10.1039/D1SM00395J.
[142] E.A. Kamoun, A. El-Betany, H. Menzel, X. Chen, Influence of photoinitiator concentration and irradiation time on the crosslinking performance of visible-light activated pullulan-HEMA hydrogels, Int. J. Biol. Macromol. 120 (2018) 1884–1892, https://doi.org/10.1016/j.ijbiomac.2018.10.011.
[143] K.S. Lim, B.S. Schon, N.V. Mekhileri, G.C.J. Brown, C.M. Chia, S. Prabakar, G. J. Hooper, T.B.F. Woodfield, New visible-light photoinitiating system for improved print fidelity in gelatin-based bioinks, ACS Biomater. Sci. Eng. 2 (2016) 1752–1762, https://doi.org/10.1021/acsbiomaterials.6b00149.
[144] C. Zhao, L. Zhou, M. Chiao, W. Yang, Antibacterial hydrogel coating: strategies in surface chemistry, Adv. Colloid Interface Sci. 285 (2020) 102280, https://doi.org/10.1016/j.cis.2020.102280.
[145] A. Concheiro, C. Alvarez-Lorenzo, Chemically cross-linked and grafted cyclodextrin hydrogels: from nanostructures to drug-eluting medical devices, Adv. Drug Deliv. Rev. 65 (2013) 1188–1203, https://doi.org/10.1016/j.addr.2013.04.015.
[146] B. Singh, A. Kumar, Hydrogel formation by radiation induced crosslinked copolymerization of acrylamide onto moringa gum for use in drug delivery applications, Carbohydr. Polym. 200 (2018) 262–270, https://doi.org/10.1016/j.carbpol.2018.08.018.
[147] Z. Dong, Y. Wang, D. Wen, J. Peng, L. Zhao, M. Zhai, Recent progress in environmental applications of functional adsorbent prepared by radiation techniques: a review, J. Hazard Mater. 424 (2022) 126887, https://doi.org/10.1016/j.jhazmat.2021.126887.
[148] K.S. Lim, J.H. Galarraga, X. Cui, G.C.J. Lindberg, J.A. Burdick, T.B.F. Woodfield, Fundamentals and applications of photo-cross-linking in bioprinting, Chem. Rev. 120 (2020) 10662–10694, https://doi.org/10.1021/acs.chemrev.9b00812.
[149] J.M. Dodda, M.G. Azar, R. Sadiku, Crosslinking trends in multicomponent hydrogels for biomedical applications, Macromol. Biosci. 21 (2021) 2100232, https://doi.org/10.1002/mabi.202100232.
[150] X. Yu, C. Weng, H. Zhang, Z. Qin, Y. Miao, H. Wang, S. Xiong, J. Rong, Y. Hu, 'Multiple and short-range' cross-linking of dialdehyde carboxymethyl cellulose contributes to regulating the physicochemical property of collagen fibril, Int. J. Biol. Macromol. 219 (2022) 21–30, https://doi.org/10.1016/j.ijbiomac.2022.07.142.
[151] G. Ferracci, M. Zhu, M.S. Ibrahim, G. Ma, T.F. Fan, B.H. Lee, N.-J. Cho, Photocurable albumin methacryloyl hydrogels as a versatile platform for tissue engineering, ACS Appl. Bio Mater. 3 (2020) 920–934, https://doi.org/10.1021/acsabm.9b00984.
[152] L. Li, C. Lu, L. Wang, M. Chen, J.F. White, X. Hao, K.M. McLean, H. Chen, T. C. Hughes, Gelatin-based photo curable hydrogels for corneal wound repair, ACS Appl. Mater. Interfaces 10 (2018) 13283–13292, https://doi.org/10.1021/acsami.7b17054.
[153] X. Zhao, S. Li, X. Du, W. Li, Q. Wang, D. He, J. Yuan, Natural polymer-derived photocurable bioadhesive hydrogels for sutureless keratoplasty, Bioact. Mater. 8 (2022) 196–209, https://doi.org/10.1016/j.bioactmat.2021.07.001.
[154] G. Yazdanpanah, X. Shen, T. Nguyen, K.N. Anwar, O. Jeon, Y. Jiang, M. Pachenari, Y. Pan, T. Shokuhfar, M.I. Rosenblatt, E. Alsberg, A.R. Djalilian, A light-curable and tunable extracellular matrix hydrogel for in situ suture-free corneal repair, Adv. Funct. Mater. 32 (2022) 2113383, https://doi.org/10.1002/adfm.202113383.
[155] M. Li, R. Wei, C. Liu, H. Fang, W. Yang, Y. Wang, Y. Xian, K. Zhang, Y. He, X. Zhou, A "T.E.S.T." hydrogel bioadhesive assisted by corneal cross-linking for in situ sutureless corneal repair, Bioact. Mater. 25 (2023) 333–346, https://doi.org/10.1016/j.bioactmat.2023.02.006.
[156] N.R. Raia, D. Jia, C.E. Ghezzi, M. Muthukumar, D.L. Kaplan, Characterization of silk-hyaluronic acid composite hydrogels towards vitreous humor substitutes, Biomaterials 233 (2020) 119729, https://doi.org/10.1016/j.biomaterials.2019.119729.
[157] H. Wang, Y. Wu, C. Cui, J. Yang, W. Liu, Antifouling super water absorbent supramolecular polymer hydrogel as an artificial vitreous body, Adv. Sci. 5 (2018) 1800711, https://doi.org/10.1002/advs.201800711.
[158] Y. Xiang, M. Zou, Y. Zhang, R. Jin, Y. Nie, Drug-loaded and blue-ray filtered hydrogel as a potential intraocular lens for cataract treatment, Pharm. Nanotechnol. 8 (2020) 302–312, https://doi.org/10.2174/2211738508666200313144112.
[159] J.H. De Groot, F.J. Van Beijma, H.J. Haitjema, K.A. Dillingham, K.A. Hodd, S. A. Koopmans, S. Norrby, Injectable intraocular lens materials based upon hydrogels, Biomacromolecules 2 (2001) 628–634, https://doi.org/10.1021/bm005622r.
[160] K.S. Worthington, B.J. Green, M. Rethwisch, L.A. Wiley, B.A. Tucker, C. A. Guymon, A.K. Salem, Neuronal differentiation of induced pluripotent stem cells on surfactant templated chitosan hydrogels, Biomacromolecules 17 (2016) 1684–1695, https://doi.org/10.1021/acs.biomac.6b00098.
[161] R.Y. Tam, L.J. Smith, M.S. Shoichet, Engineering cellular microenvironments with photo- and enzymatically responsive hydrogels: toward biomimetic 3D cell culture models, Acc. Chem. Res. 50 (2017) 703–713, https://doi.org/10.1021/acs.accounts.6b00543.
[162] B. He, J. Yang, Y. Liu, X. Xie, H. Hao, X. Xing, W. Liu, An in situ-forming polyzwitterion hydrogel: towards vitreous substitute application, Bioact. Mater. 6 (2021) 3085–3096, https://doi.org/10.1016/j.bioactmat.2021.02.029.
[163] Q. Lin, J.Y.C. Lim, K. Xue, X. Su, X.J. Loh, Polymeric hydrogels as a vitreous replacement strategy in the eye, Biomaterials 268 (2021) 120547, https://doi.org/10.1016/j.biomaterials.2020.120547.
[164] J.D. Steinmetz, R.R.A. Bourne, P.S. Briant, S.R. Flaxman, H.R.B. Taylor, J. B. Jonas, A.A. Abdoli, W.A. Abrha, A. Abualhasan, E.G. Abu-Gharbieh, T.G. Adal, A. Afshin, H. Ahmadieh, W. Alemayehu, S.A.S. Alemzadeh, A.S. Alfaar, V. Alipour, S. Androudi, J. Arabloo, A.B. Arditi, B.B. Aregawi, A. Arrigo, C. Ashbaugh, E.D. Ashrafi, D.D. Atnafu, E.A. Bagli, A.A.W. Baig, T. W. Bärnighausen, M. Battaglia Parodi, M.S. Beheshti, A.S. Bhagavathula, N. Bhardwaj, P. Bhardwaj, K. Bhattacharyya, A. Bijani, M. Bikbov, M. Bottone, T. M. Braithwaite, A.M. Bron, S.A. Burugina Nagaraja, Z.A. Butt, F.L.L. Caetano Dos Santos, V.L.J. Carneiro, R.J. Casson, C.-Y.J. Cheng, J.-Y.J. Choi, D.-T. Chu, M.V. M. Cicinelli, J.M.G. Coelho, N.G.A. Congdon, R.A.A. Couto, E.A.M. Cromwell, S. M. Dahlawi, X. Dai, R. Dana, L. Dandona, R.A. Dandona, M.A. Del Monte, M. Derbew Molla, N.A. Dervenis, A.A.P. Desta, J.P. Deva, D. Diaz, S.E. Djalalinia, J.R. Ehrlich, R.R. Elayedath, H.R.B. Elhabashy, L.B. Ellwein, M.H. Emamian, S. Eskandarieh, F.G. Farzadfar, A.G. Fernandes, F.S. Fischer, D.S.M. Friedman, J. M. Furtado, S. Gaidhane, G. Gazzard, B. Gebremichael, R. George, A. Ghashghaee, S.A. Gilani, M. Golechha, S.R. Hamidi, B.R.R. Hammond, M.E.R.K. Hartnett, R. K. Hartono, A.I. Hashi, S.I. Hay, K. Hayat, G. Heidari, H.C. Ho, R. Holla, M. J. Househ, J.J.E. Huang, S.E.M. Ibitoye, I.M.D. Ilic, M.D.D. Ilic, A.D.N. Ingram, S. S.N. Irvani, S.M.S. Islam, R. Itumalla, S.P. Jayaram, R.P. Jha, R. Kahloun, R. Kalhor, H. Kandel, A.S. Kasa, T.A. Kavetskyy, G.A.H. Kayode, J.H. Kempen, M. Khairallah, R.A. Khalilov, E.A.C. Khan, R.C. Khanna, M.N.A. Khatib, T.A. E. Khoja, J.E. Kim, Y.J. Kim, G.R. Kim, S. Kisa, A. Kisa, S. Kosen, A. Koyanagi, B. Kucuk Bicer, V.P. Kulkarni, O.P. Kurmi, I.C. Landires, V.C.L. Lansingh, J.L. E. Leasher, K.E. LeGrand, N. Leveziel, H. Limburg, X. Liu, S. Madhava Kunjathur, S. Maleki, N. Manafi, K. Mansouri, C.G. McAlinden, G.G.M. Meles, A.M. Mersha, I. M.R. Michalek, T.R. Miller, S. Misra, Y. Mohammad, S.F.A. Mohammadi, J.A. H. Mohammed, A.H. Mokdad, M.A.A. Moni, A.A.R. Montasir, A.R.F. Morse, G.F. C. Mulaw, M. Naderi, H.S. Naderifar, K.S. Naidoo, M.D. Naimzada, V. Nangia, S. M. Narasimha Swamy, D.M. Naveed, H.L. Negash, H.L. Nguyen, V.A. Nunez-Samudio, F.A. Ogbo, K.T. Ogundimu, A.T.E. Olagunju, O.E. Onwujekwe, N. O. Otstavnov, M.O. Owolabi, K. Pakshir, S. Panda-Jonas, U. Parekh, E.-C. Park, M. Pasovic, S. Pawar, K. Pesudovs, T.Q. Peto, H.Q. Pham, M. Pinheiro, V. Podder, V. Rahimi-Movaghar, M.H.U.Y. Rahman, P.Y. Ramulu, P. Rathi, S.L. Rawaf, D. L. Rawaf, L. Rawal, N.M. Reinig, A.M. Renzaho, A.L. Rezapour, A.L. Robin, L. Rossetti, S. Sabour, S. Safi, A. Sahebkar, M.A.M. Sahraian, A.M. Samy, B. Sathian, G.K. Saya, M.A. Saylan, A.A.A. Shaheen, M.A.T. Shaikh, T.T. Shen, K. S. Shibuya, W.S. Shiferaw, M. Shigematsu, J.I. Shin, J.C. Silva, A.A. Silvester, J. A. Singh, D.S. Singhal, R.S. Sitorus, E.Y. Skiadaresi, V.Y.A. Skryabin, A. A. Skryabina, A.B. Soheili, M.B.A.R.C. Sorrie, R.A.R.C.T. Sousa, C. T. Sreeramareddy, D.G. Stambolian, E.G. Tadesse, N.I. Tahhan, M.I. Tareque, F. X. Topouzis, B.X. Tran, G.K. Tsegaye, M.K. Tsilimbaris, R. Varma, G. Virgili, A. T. Vongpradith, G.T. Vu, Y.X. Wang, N.H. Wang, A.H.K. Weldemariam, S.K. G. West, T.G.Y. Wondmeneh, T.Y. Wong, M. Yaseri, N. Yonemoto, C.S. Yu, M.

S. Zastrozhin, Z.-J.R. Zhang, S.R. Zimsen, S. Resnikoff, T. Vos, Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the Right to Sight: an analysis for the Global Burden of Disease Study, Lancet Global Health 9 (2021) e144–e160, https://doi.org/10.1016/S2214-109X(20)30489-7.
[165] J.C. Lim, M. Caballero Arredondo, A.J. Braakhuis, P.J. Donaldson, Vitamin C and the lens: new insights into delaying the onset of cataract, Nutrients 12 (2020) 3142, https://doi.org/10.3390/nu12103142.
[166] Y.-C. Liu, M. Wilkins, T. Kim, B. Malyugin, J.S. Mehta, Cataracts, Lancet 390 (2017) 600–612, https://doi.org/10.1016/S0140-6736(17)30544-5.
[167] R.C. Cooper, H. Yang, Hydrogel-based ocular drug delivery systems: emerging fabrication strategies, applications, and bench-to-bedside manufacturing considerations, J. Contr. Release 306 (2019) 29–39, https://doi.org/10.1016/j.jconrel.2019.05.034.
[168] Z. Tang, Y. Zhang, Y. Wang, D. Zhang, B. Shen, M. Luo, P. Gu, Progress of stem/progenitor cell-based therapy for retinal degeneration, J. Transl. Med. 15 (2017) 99, https://doi.org/10.1186/s12967-017-1183-y.
[169] H.A. Alsaeedi, C. Lam, A.E.-H. Koh, S.W. Teh, P.L. Mok, A. Higuchi, K.Y. Then, M.-L.C. Bastion, B. Alzahrani, A. Farhana, B.S. Muthuvenkatachalam, A.V. Samrot, K. B. Swamy, N. Marraiki, A.M. Elgorban, S.K. Subbiah, Looking into dental pulp stem cells in the therapy of photoreceptors and retinal degenerative disorders, J. Photochem. Photobiol., B 203 (2020) 111727, https://doi.org/10.1016/j.jphotobiol.2019.111727.
[170] A.H. Kashani, Stem cell-derived retinal pigment epithelium transplantation in age-related macular degeneration: recent advances and challenges, Curr. Opin. Ophthalmol. 33 (2022) 211–218, https://doi.org/10.1097/ICU.0000000000000838.
[171] N. Mitrousis, S. Hacibekiroglu, M.T. Ho, Y. Sauvé, A. Nagy, D. Van Der Kooy, M. S. Shoichet, Hydrogel-mediated co-transplantation of retinal pigmented epithelium and photoreceptors restores vision in an animal model of advanced retinal degeneration, Biomaterials 257 (2020) 120233, https://doi.org/10.1016/j.biomaterials.2020.120233.
[172] A. Vaneev, V. Tikhomirova, N. Chesnokova, E. Popova, O. Beznos, O. Kost, N. Klyachko, Nanotechnology for topical drug delivery to the anterior segment of the eye, Int. J. Mol. Sci. 22 (2021) 12368, https://doi.org/10.3390/ijms222212368.
[173] S. Awwad, A.H.A. Mohamed Ahmed, G. Sharma, J.S. Heng, P.T. Khaw, S. Brocchini, A. Lockwood, Principles of pharmacology in the eye, Br. J. Pharmacol. 174 (2017) 4205–4223, https://doi.org/10.1111/bph.14024.
[174] C. Wang, Y. Pang, Nano-based eye drop: topical and noninvasive therapy for ocular diseases, Adv. Drug Deliv. Rev. 194 (2023) 114721, https://doi.org/10.1016/j.addr.2023.114721.
[175] X. Wang, F. Luan, H. Yue, C. Song, S. Wang, J. Feng, X. Zhang, W. Yang, Y. Li, W. Wei, Y. Tao, Recent advances of smart materials for ocular drug delivery, Adv. Drug Deliv. Rev. 200 (2023) 115006, https://doi.org/10.1016/j.addr.2023.115006.
[176] J. Pan, H. Liao, G. Gong, Y. He, Q. Wang, L. Qin, Y. Zhang, H. Ejima, B.L. Tardy, J. J. Richardson, J. Shang, O.J. Rojas, Y. Zeng, J. Guo, Supramolecular nanoarchitectonics of phenolic-based nanofiller for controlled diffusion of versatile drugs in hydrogels, J. Contr. Release 360 (2023) 433–446, https://doi.org/10.1016/j.jconrel.2023.07.003.
[177] T. Lin, W. Wang, T. Chen, B. Bao, T. Liu, H. Zhao, C. Feng, Q. Lin, L. Zhu, L. Gong, A lacrimal duct drug delivery system based on photo-induced hydrogel for dry eye and allergic conjunctivitis therapy, Composites, Part B 266 (2023) 111014, https://doi.org/10.1016/j.compositesb.2023.111014.
[178] M. Dai, K. Xu, D. Xiao, Y. Zheng, Q. Zheng, J. Shen, Y. Qian, W. Chen, In situ forming hydrogel as a tracer and degradable lacrimal plug for dry eye treatment, Adv. Healthcare Mater. 11 (2022) 2200678, https://doi.org/10.1002/adhm.202200678.
[179] U. Soiberman, S.P. Kambhampati, T. Wu, M.K. Mishra, Y. Oh, R. Sharma, J. Wang, A.E. Al Towerki, S. Yiu, W.J. Stark, R.M. Kannan, Subconjunctival injectable dendrimer-dexamethasone gel for the treatment of corneal inflammation, Biomaterials 125 (2017) 38–53, https://doi.org/10.1016/j.biomaterials.2017.02.016.
[180] S.K. Park, M. Ha, E.J. Kim, Y.A. Seo, H.J. Lee, D. Myung, H.-S. Kim, K.-S. Na, Hyaluronic acid hydrogels crosslinked via blue light-induced thiol-ene reaction for the treatment of rat corneal alkali burn, Regen. Ther. 20 (2022) 51–60, https://doi.org/10.1016/j.reth.2022.03.005.
[181] C. Huang, X. Qi, H. Chen, W. Chao, X. Qi, H. Wang, H. Gao, Monolith/Hydrogel composites as triamcinolone acetonide carriers for curing corneal neovascularization in mice by inhibiting the fibrinolytic system, Drug Deliv. 29 (2022) 18–30, https://doi.org/10.1080/10717544.2021.2014603.
[182] M. Xeroudaki, M. Rafat, P. Moustardas, A. Mukwaya, S. Tabe, M. Bellisario, B. Peebo, N. Lagali, A double-crosslinked nanocellulose-reinforced dexamethasone-loaded collagen hydrogel for corneal application and sustained anti-inflammatory activity, Acta Biomater. (2023), https://doi.org/10.1016/j.actbio.2023.10.020. S1742706123006207.
[183] C. Shen, X. Zhao, Z. Ren, B. Yang, X. Wang, A. Hu, J. Hu, In situ formation of injectable gelatin methacryloyl (GelMA) hydrogels for effective intraocular delivery of triamcinolone acetonide, Int. J. Mol. Sci. 24 (2023) 4957, https://doi.org/10.3390/ijms24054957.
[184] Y. Han, L. Jiang, H. Shi, C. Xu, M. Liu, Q. Li, L. Zheng, H. Chi, M. Wang, Z. Liu, M. You, X.J. Loh, Y.-L. Wu, Z. Li, C. Li, Effectiveness of an ocular adhesive polyhedral oligomeric silsesquioxane hybrid thermo-responsive FK506 hydrogel in a murine model of dry eye, Bioact. Mater. 9 (2022) 77–91, https://doi.org/10.1016/j.bioactmat.2021.07.027.
[185] C. Luschmann, W. Herrmann, O. Strauß, K. Luschmann, A. Goepferich, Ocular delivery systems for poorly soluble drugs: an in-vivo evaluation, Int. J. Pharm. 455 (2013) 331–337, https://doi.org/10.1016/j.ijpharm.2013.07.002.
[186] J. Yu, Y. Shen, J. Luo, J. Jin, P. Li, P. Feng, H. Guan, Upadacitinib inhibits corneal inflammation and neovascularization by suppressing M1 macrophage infiltration in the corneal alkali burn model, Int. Immunopharm. 116 (2023) 109680, https://doi.org/10.1016/j.intimp.2023.109680.
[187] S. Rezzola, M. Belleri, G. Gariano, D. Ribatti, C. Costagliola, F. Semeraro, M. Presta, In vitro and ex vivo retina angiogenesis assays, Angiogenesis 17 (2014) 429–442, https://doi.org/10.1007/s10456-013-9398-x.
[188] H.E. Grossniklaus, S.J. Kang, L. Berglin, Animal models of choroidal and retinal neovascularization, Prog. Retin. Eye Res. 29 (2010) 500–519, https://doi.org/10.1016/j.preteyeres.2010.05.003.
[189] D. Patel, S.N. Patel, V. Chaudhary, S.J. Garg, Complications of intravitreal injections: 2022, Curr. Opin. Ophthalmol. 33 (2022) 137–146, https://doi.org/10.1097/ICU.0000000000000850.
[190] J. Norman, R.D. Madurawe, C.M.V. Moore, M.A. Khan, A. Khairuzzaman, A new chapter in pharmaceutical manufacturing: 3D-printed drug products, Adv. Drug Deliv. Rev. 108 (2017) 39–50, https://doi.org/10.1016/j.addr.2016.03.001.
[191] W. Huang, X. Zhang, 3D printing: print the future of ophthalmology, Investig. Opthalmology Vis. Sci. 55 (2014) 5380, https://doi.org/10.1167/iovs.14-15231.
[192] A.A. Al-Kinani, G. Zidan, N. Elsaid, A. Seyfoddin, A.W.G. Alani, R.G. Alany, Ophthalmic gels: past, present and future, Adv. Drug Deliv. Rev. 126 (2018) 113–126, https://doi.org/10.1016/j.addr.2017.12.017.
[193] W. Li, M. Wang, H. Ma, F.A. Chapa-Villarreal, A.O. Lobo, Y.S. Zhang, Stereolithography apparatus and digital light processing-based 3D bioprinting for tissue fabrication, iScience 26 (2023) 106039, https://doi.org/10.1016/j.isci.2023.106039.
[194] I. Matai, G. Kaur, A. Seyedsalehi, A. McClinton, C.T. Laurencin, Progress in 3D bioprinting technology for tissue/organ regenerative engineering, Biomaterials 226 (2020) 119536, https://doi.org/10.1016/j.biomaterials.2019.119536.
[195] P.S. Gungor-Ozkerim, I. Inci, Y.S. Zhang, A. Khademhosseini, M.R. Dokmeci, Bioinks for 3D bioprinting: an overview, Biomater. Sci. 6 (2018) 915–946, https://doi.org/10.1039/C7BM00765E.
[196] B. He, J. Wang, M. Xie, M. Xu, Y. Zhang, H. Hao, X. Xing, W. Lu, Q. Han, W. Liu, 3D printed biomimetic epithelium/stroma bilayer hydrogel implant for corneal regeneration, Bioact. Mater. 17 (2022) 234–247, https://doi.org/10.1016/j.bioactmat.2022.01.034.
[197] Y. Xu, J. Liu, W. Song, Q. Wang, X. Sun, Q. Zhao, Y. Huang, H. Li, Y. Peng, J. Yuan, B. Ji, L. Ren, Biomimetic convex implant for corneal regeneration through 3D printing, Adv. Sci. 10 (2023) 2205878, https://doi.org/10.1002/advs.202205878.
[198] Z. Zhong, X. Deng, P. Wang, C. Yu, W. Kiratitanaporn, X. Wu, J. Schimelman, M. Tang, A. Balayan, E. Yao, J. Tian, L. Chen, K. Zhang, S. Chen, Rapid bioprinting of conjunctival stem cell micro-constructs for subconjunctival ocular injection, Biomaterials 267 (2021) 120462, https://doi.org/10.1016/j.biomaterials.2020.120462.
[199] J.-W. Li, Biosafety of a 3D-printed intraocular lens made of a poly(acrylamide-co-sodium acrylate) hydrogel in vitro and in vivo, Int. J. Ophthalmol. 13 (2020) 1521–1530, https://doi.org/10.18240/ijo.2020.10.03.
[200] P. Wang, X. Li, W. Zhu, Z. Zhong, A. Moran, W. Wang, K. Zhang, S. Chen, 3D bioprinting of hydrogels for retina cell culturing, Bioprinting 12 (2018) e00029, https://doi.org/10.1016/j.bprint.2018.e00029.
[201] J. Wang, Y. Peng, M. Chen, X. Dai, L. Lou, C. Wang, Z. Bao, X. Yang, Z. Gou, J. Ye, Next-generation finely controlled graded porous antibacterial bioceramics for high-efficiency vascularization in orbital reconstruction, Bioact. Mater. 16 (2022) 334–345, https://doi.org/10.1016/j.bioactmat.2021.12.028.
[202] S. Jia, J. Yang, A.D.-S. Lau, F. Chen, Y. Bu, E. Cai, H. Wang, H.-E. Chieng, T. Sun, Z. Zhou, C. Ruan, W. Weijia Lu, J.C.-H. Chan, Digital light processing-bioprinted poly-NAGA-GelMA-based hydrogel lenticule for precise refractive errors correction, Biofabrication 15 (2023) 035011, https://doi.org/10.1088/1758-5090/accaab.
[203] X. Xu, S. Awwad, L. Diaz-Gomez, C. Alvarez-Lorenzo, S. Brocchini, S. Gaisford, A. Goyanes, A.W. Basit, 3D printed punctal plugs for controlled ocular drug delivery, Pharmaceutics 13 (2021) 1421, https://doi.org/10.3390/pharmaceutics13091421.
[204] H. Kavand, M. Visa, M. Köhler, W. Van Der Wijngaart, P. Berggren, A. Herland, 3D-Printed biohybrid microstructures enable transplantation and vascularization of microtissues in the anterior chamber of the eye, Adv. Mater. (2023) 2306686, https://doi.org/10.1002/adma.202306686.
[205] S. Park, W.-H. Jung, M. Pittman, J. Chen, Y. Chen, The effects of stiffness, fluid viscosity, and geometry of microenvironment in homeostasis, aging, and diseases: a brief review, J. Biomech. Eng. 142 (2020) 100804, https://doi.org/10.1115/1.4048110.
[206] P. Nguyen, S. Khashabi, S. C, Ocular surface reconstitution, in: A. Carpi (Ed.), Prog. Mol. Environ. Bioeng. - Anal. Model. Technol. Appl., InTech, 2011, https://doi.org/10.5772/22879.
[207] L. Zhao, Y. Jia, C. Zhao, H. Li, F. Wang, M. Dong, T. Liu, S. Zhang, Q. Zhou, W. Shi, Ocular surface repair using decellularized porcine conjunctiva, Acta Biomater. 101 (2020) 344–356, https://doi.org/10.1016/j.actbio.2019.11.006.
[208] J. Witt, S. Mertsch, M. Borrelli, J. Dietrich, G. Geerling, S. Schrader, K. Spaniol, Decellularised conjunctiva for ocular surface reconstruction, Acta Biomater. 67 (2018) 259–269, https://doi.org/10.1016/j.actbio.2017.11.054.
[209] H. Lin, H. Ouyang, J. Zhu, S. Huang, Z. Liu, S. Chen, G. Cao, G. Li, R.A.J. Signer, Y. Xu, C. Chung, Y. Zhang, D. Lin, S. Patel, F. Wu, H. Cai, J. Hou, C. Wen, M. Jafari, X. Liu, L. Luo, J. Zhu, A. Qiu, R. Hou, B. Chen, J. Chen, D. Granet,

C. Heichel, F. Shang, X. Li, M. Krawczyk, D. Skowronska-Krawczyk, Y. Wang, W. Shi, D. Chen, Z. Zhong, S. Zhong, L. Zhang, S. Chen, S.J. Morrison, R.L. Maas, K. Zhang, Y. Liu, Lens regeneration using endogenous stem cells with gain of visual function, Nature 531 (2016) 323–328, https://doi.org/10.1038/nature17181.

[210] G. Debellemanière, M. Flores, M. Montard, B. Delbosc, M. Saleh, Three-dimensional printing of optical lenses and ophthalmic surgery: challenges and perspectives, J. Refract. Surg. 32 (2016) 201–204, https://doi.org/10.3928/1081597X-20160121-05.

[211] A. Rattner, J. Nathans, Macular degeneration: recent advances and therapeutic opportunities, Nat. Rev. Neurosci. 7 (2006) 860–872, https://doi.org/10.1038/nrn2007.

[212] M. Eiraku, N. Takata, H. Ishibashi, M. Kawada, E. Sakakura, S. Okuda, K. Sekiguchi, T. Adachi, Y. Sasai, Self-organizing optic-cup morphogenesis in three-dimensional culture, Nature 472 (2011) 51–56, https://doi.org/10.1038/nature09941.

[213] B.G. Ballios, M.J. Cooke, L. Donaldson, B.L.K. Coles, C.M. Morshead, D. Van der Kooy, M.S. Shoichet, A hyaluronan-based injectable hydrogel improves the survival and integration of stem cell progeny following transplantation, Stem Cell Rep. 4 (2015) 1031–1045, https://doi.org/10.1016/j.stemcr.2015.04.008.

[214] R. Chalasani, L. Poole-Warren, R.M. Conway, B. Ben-Nissan, Porous orbital implants in enucleation: a systematic review, Surv. Ophthalmol. 52 (2007) 145–155, https://doi.org/10.1016/j.survophthal.2006.12.007.

[215] F. Baino, I. Potestio, Orbital implants: state-of-the-art review with emphasis on biomaterials and recent advances, Mater. Sci. Eng. C 69 (2016) 1410–1428, https://doi.org/10.1016/j.msec.2016.08.003.

[216] Y. Fang, F. Chen, H. Wu, B. Chen, Progress in the application of 3D printing technology in ophthalmology, Graefes Arch. Clin. Exp. Ophthalmol. 261 (2023) 903–912, https://doi.org/10.1007/s00417-022-05908-y.

[217] E.M. Bratton, V.D. Durairaj, Orbital implants for fracture repair, Curr. Opin. Ophthalmol. 22 (2011) 400–406, https://doi.org/10.1097/ICU.0b013e3283499409.

[218] E.N. Harb, C.F. Wildsoet, Origins of refractive errors: environmental and genetic factors, Annu. Rev. Vis. Sci. 5 (2019) 47–72, https://doi.org/10.1146/annurev-vision-091718-015027.

[219] L.-C. Liu, Y.-H. Chen, D.-W. Lu, Overview of recent advances in nano-based ocular drug delivery, Int. J. Mol. Sci. 24 (2023) 15352, https://doi.org/10.3390/ijms242015352.

[220] C. Wang, Z. Zhang, J. Wang, Q. Wang, L. Shang, Biohybrid materials: structure design and biomedical applications, Mater. Today Bio 16 (2022) 100352, https://doi.org/10.1016/j.mtbio.2022.100352.

[221] J.W. Streilein, Unraveling immune privilege, Science 270 (1995), https://doi.org/10.1126/science.270.5239.1158, 1158–1158.

[222] M.A. Heinrich, W. Liu, A. Jimenez, J. Yang, A. Akpek, X. Liu, Q. Pi, X. Mu, N. Hu, R.M. Schiffelers, J. Prakash, J. Xie, Y.S. Zhang, 3D bioprinting: from benches to translational applications, Small 15 (2019) 1805510, https://doi.org/10.1002/smll.201805510.

[223] T. Ekblad, G. Bergström, T. Ederth, S.L. Conlan, R. Mutton, A.S. Clare, S. Wang, Y. Liu, Q. Zhao, F. D'Souza, G.T. Donnelly, P.R. Willemsen, M.E. Pettitt, M. E. Callow, J.A. Callow, B. Liedberg, Poly(ethylene glycol)-containing hydrogel surfaces for antifouling applications in marine and freshwater environments, Biomacromolecules 9 (2008) 2775–2783, https://doi.org/10.1021/bm800547m.