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Review Article

Exploration: Nanoparticles in the Diagnosis and Treatment of Retinal Diseases

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In recent years, research on nanoparticles (NPs) has brought a new phase in the development of medicine. The term "NPs" refers to nanoscale particles, typically between 10 and 1,000 nm in size, that are within the range of cellular and molecular structures. Compared with traditional ophthalmic drugs, NPs can carry drugs to overcome obstacles, target drug delivery, prolong drug release, reduce drug toxicity, and can be used in gene therapy. After a brief introduction to the classification of NPs, we will focus on the potential applications of different NPs in the diagnosis and treatment of different retinal diseases and introduce innovative methods derived from NPs.

1. Introduction

Nanoscale particles in the size range of cellular and molecular structures, often referred to as nanoparticles (NPs), typically range in size from 10 to 1,000 nm [1]. Depending on their structure, NPs can be categorized as liposomes [2], nanospheres [3], dendrimers [4], hydrogels [5], and nanoemulsions [6, 7]. In general, the pharmacokinetics and pharmacodynamics of bioactive molecules or medications can be altered by being adsorbed, encapsulated, captured, or covalently coupled to NPs [8]. Cell absorption, drug delivery, and diffusion of NPs are all impacted by both their aspect ratio and surface characteristics [9]. NPs have many advantages, such as controlled release, drug targeting, and improved bioavailability [10, 11]. The development of nanotechnology has brought innovation to medicine [12]. Today, research on NPs is widely conducted and used for the diagnosis and treatment of retinal diseases [13]. In the following sections, we will review the application of NPs in the diagnosis and treatment of retinal diseases.

2. NPs for Diagnosis of Retinal Diseases

NPs have recently been developed as agents that improve contrast in a variety of imaging modalities, such as fluoroscopy, X-ray, and CT [14–17]. Indocyanine green (ICG), an amphiphilic cyanine dye, was authorized for clinical use by the Food and Drug Administration (FDA) in 1954 [18]. However, ICG has significant drawbacks, such as a short half-life, low photostability, and poor hydrolytic stability, which limit its future use in the detection of retinal disorders [19]. Incorporating ICG into NP systems appears to be a potential solution to circumvent these constraints. ICG encapsulated in NPs can be used for near-infrared (NIR) imaging and photoacoustic (PA) imaging to improve contrast [20]. Because optical coherence tomography (OCT) can acquire structural information based on tissue reflectance, it is primarily used for imaging in the diagnosis of retinal diseases [21]. Gold NPs (Au NPs) have been investigated as a promising contrast agent in recent years because of their ability to absorb NIR radiation for selective visualization of target structures with minimal background noise [22]. Au NPs have enabled improvements in OCT imaging [23, 24]. According to research by Gordon et al. [25], mice's retinas were injected with Au NPs, which increased contrast and dramatically boosted the clarity of scanned lesions. Chemla et al. [26] used Au NPs to improve tracking of transplanted photoreceptor precursors (PRPs) and no adverse reactions occurred within 1 month. Nguyen et al. [27] presented chain-like

Au NPs and resulted in up to 176% increase in OCT signal. Tang et al. [28] designed a peptide-functionalized silicon nanoparticles (SiNPs) that not only label angiogenesis but also inhibit neovascularization, which has a dual effect.

RPE cell transplantation produced from human embryonic stem cells (hESC) or induced pluripotent stem cells (iPSC) has proven ground-breaking success in the treatment of retinal disorders [29]. A better understanding of the survival and biodistribution of transplanted cells is necessary to enhance the functional benefits of cell therapy [30]. Magnetic NPs (MNPs), mainly iron oxide NPs, can target label photoreceptor precursors for up to 12 weeks with magnetic resonance imaging (MRI) tracking, and the ability of photoreceptor precursors to proliferate, remain viable, or differentiate is unaffected by this labeling [31]. Zou et al. [32] developed the first multifunctional magnetic carbon CMT NPs for dual-mode imaging-guided laser/immunotherapy. The carbonized CM and CMT NPs exhibited stable magnetic properties and carbon material characteristics, enabling the NPs to simultaneously achieve PA/MR imaging. MNPs can also carry drugs into the body via multiple routes, such as topical administration and intravenous infusion, and direct MNPs to specific targets in the body via magnetic fields [33, 34]. One study has covalently coupled nerve growth factors to MNPs and delivered MNPs complexes to the retina by controlled magnetic fields [35]. Another study attempted to deliver the growth inhibitor analog octreotide to the retina via MNPs for DR [36].

It has been demonstrated that poly(3,4-ethylenedioxythiophene) (PEDOT)/Au NP composites can be used as a reproducible and sensitive tool for measuring VEGF concentrations. Kim et al. [37] synthesized a PEDOT/Au NP composite that improves the binding of PEDOT to antibodies and found that the charge transfer resistance (Rct) was linearly correlated with the VEGF concentration in the analyte over a range. In this way, the concentration of VEGF in the patient's retina can be measured to aid in disease diagnosis and to precisely control the dose and frequency of IVT injections of anti-VEGF drugs. Accurate measurement of VEGF concentrations can greatly reduce the financial burden on patients as well as reduce the side effects associated with anti-VEGF drug overdose.

3. NPs for Treatment of Retinal Diseases

3.1. Retinal Neovascularization Diseases. The broad category of retinal neovascularization includes diabetic retinopathy (DR), retinal vascular obstruction (RVO), exudative age-related macular degeneration (AMD), and even choroidal neovascularization (CNV) [38]. The aberrant angiogenesis that results in bleeding and exudation in the retina or subretina is a common hallmark of these conditions [39]. When it comes to neovascular diseases, it is inevitable to discuss vascular endothelial growth factor (VEGF). A vital factor in encouraging endothelial cell development and vascular permeability is the endothelial mitogen VEGF [40]. Numerous retinal cell types, including vascular endothelial cells and retinal pigment epithelial (RPE) cells, release VEGF [41]. Currently, anti-VEGF drugs are the most advanced drugs that have been developed to treat neovascular diseases, such as aflibercept and ranibizumab [42, 43].

3.1.1. Topical Drug Delivery. The gold standard of treatment for neovascular diseases is now intravitreal (IVT) injection of anti-VEGF drugs, but there is a risk of pain, bleeding, retinal detachment, cataracts, and intraocular infections, and they are expensive [44]. Drug delivery to the posterior portion of the eye is still difficult since the bioavailability of medications applied topically to this area is just 5% [45]. Targeted drug delivery is made possible by ocular drug delivery devices in the nanoscale range, which also shield the drug from external degradation and increase its bioavailability there [46, 47]. For the treatment of diabetic retinopathy, one study created topical delivery of hyaluronic acid (HA) NPs loaded with apatinibc (Apa) to obtain better delivery to retinal cells [48]. Apa, a brand-new VEGF receptor 2 selective inhibitor, has recently been demonstrated to have anticancer properties by blocking the VEGF signaling pathway [49]. HA is a biodegradable, nonimmunogenic biopolymer with the ability to interact with multiple retinal cell surface differentiation (CD44) receptor clusters [50]. It is frequently utilized to safely and effectively administer therapeutic medicines locally to the retina and retinal pigment epithelium [51]. Their data suggest that HA-BSA-NPs may be a safe alternative to invasive vitreous cavity therapy by targeting the posterior eye via a local route with few complications and high patient compliance. Another study using NPs carrying disulfiram was found to attenuate the deterioration of electroretinograms (ERGs) in rats and to restore the decline in retinal function [52]. Additionally, a number of NPs, including poly(lactic-co-glycolic acid) (PLGA) NPs [53, 54] and peptide (PENE) NPs [55], can transport medications to the retina through topical application. Some of these NPs may even simultaneously cure anterior and posterior segment eye diseases [56].

3.1.2. Subconjunctival Drug Delivery. The subconjunctival (SC) delivery system associated with SC injections may also serve as a potential method of targeting posterior ocular tissues and may improve bioavailability in the retina [57, 58]. In one study, chitosan (CS)-coated PLGA NPs of bevacizumab were developed and optimized for sustained and efficient delivery to posterior ocular tissues [59]. It was demonstrated that the optimized CS-coated NPs' in vitro drug-release profile could be maintained and under control for longer than 72 hr. The team also found that CS-PLGA NPs treated by the SC injection route reduced VEGF levels in the retina more than topical and IVT administration in the retinopathy model [60]. Tsai et al. [61] compared the efficiency of topical and SC injections of hyaluronic acid-coated NPs into the posterior eye. It was found that all types of NPs reaching the posterior ocular region (choroid/retina) were exceeded by topical administration (eye drops), with SC injections being more efficient than topical administration (14.55% vs. 6.89%). It is worth mentioning that a team in search of an effective insulin slow-release system for DR developed NPs to deliver insulin to the retina via SC injection with sufficient

neuroprotective effect to attenuate retinal microstructural changes and reduce retinal cell apoptosis [62].

3.1.3. Intravitreal Injections. Delivery of drugs with polymeric NPs could reduce the cytotoxicity of drugs and potentially bring more drugs into clinical treatment. Adriamycin (DOX), a HIF-1a inhibitor, has previously been used to treat cancers such as leukemia, breast, and ovarian cancer [63]. Iwase et al. [64] found that IVT injection of DOX improved choroidal neovascularization in mice. However, DOX treatment has been identified to be risky due to its nonspecific cytotoxicity [65]. One study using polymeric NPs encapsulated with DOX proved to reduce this cytotoxicity and provide sustained drug release [66]. The findings imply that nanoprecipitation (NPC) NPs may be the most efficient NP agents for DOX nanodelivery. Sustained-release anti-VEGF delivery systems associated with NPs can also extend drug half-life, control drug release, reduce dosing frequency, and reduce associated risks. Itraconazole (ITZ) was previously used as an antifungal drug, but it is also an effective anti-angiogenic drug by inhibiting the proliferation of vascular endothelial cells [67]. One study developed ITZ-loaded PLGA NPs coupled to R5K peptide and found that R5K-ITZ-NPs have the twin effects of ITZ-controlled release and antiangiogenesis, which may open up new therapeutic options for neovascular AMD [68].

It has also been reported that PLGA NPs loaded with IL-12, a chemokine with strong antiangiogenic effects, restored retinal thickness and reduced neovascularization in DR mice [69]. HA NPs were used to load Cx43 mimetic peptide, a sequence of a widely present gap junction protein prevalent in the retina, to treat retinal ischemia [70]. Polydopamine (PDA) NPs exhibit excellent performance in eliminating reactive oxygen species (ROS), thereby reducing retinal ganglion cell degeneration and restoring visual function after RVO [71].

Additionally, it has been demonstrated that IVT injection of NPs made of cerium oxide, gold, and silica inhibits neovascularization and promotes disease improvement. Cerium oxide NPs are believed to mimic superoxide dismutase action and limit the overproduction of VEGF and reactive oxygen species via reducing reactive oxygen species (ROS) [72]. Cerium oxide NPs may also counteract lipofuscin deposits accumulation in the retina and may be targeted to treat AMD [73]. Au NPs inhibit VEGF-2 by blocking the activation of extracellular signal-regulated kinases 1/2 (ERK1/2) and ameliorate retinal inflammation by transrepression of nuclear factor kappa B (NF-κB) [74–76]. Even intravenous injection of Au NPs has been reported to inhibit CNV [77]. Silica NPs can also inhibit VEGF-induced neovascularization [78].

3.1.4. Gene Therapy. Gene therapy combined with nanotechnology is also a promising strategy for the treatment of retinal neovascularization diseases [79]. Small interfering RNAs (siRNAs) are small RNA molecules that can specifically downregulate target gene expression following transcription and "silence" target mRNAs in a sequence-specific way [80]. However, naked RNAs are susceptible to nuclease degradation [81]. Wang et al. [82] encapsulated VEGF siRNA in bioreducible lipid-like NPs and discovered that these NPs could successfully suppress retinal neovascularization and decrease the expression of VEGF mRNA and protein. Small noncoding RNA molecules known as microRNAs (miRNAs) are a family of naturally occurring molecules. More than 60% of human proteins are regulated by miRNAs, which are essential regulators of cell differentiation, death, and proliferation [83]. By suppressing VEGF, the powerful antiangiogenic factor miR200-b prevents the development of new blood vessels [84]. Mitra et al. [85] discovered that miR200-b dose negatively regulated VEGFR-2 expression in type 1 diabetes and demonstrated phenotypic improvement at 3 months after IVT injection. They also discovered that by downregulating VEGFR-2 expression, NP-mediated mir200-b delivery could shield the retina from retinal neovascularization. Thus, nanotechnology may provide a potential gene therapy option for VEGF-mediated neovascularization (Figure 1).

3.2. Inherited Retinal Diseases. Inherited retinal diseases (IRDs) mainly include retinitis pigmentosa (RP), Leber congenital amaurosis (LCA), and Stargardt disease [86]. There is now no effective treatment for these illnesses, although gene therapy offers enormous potential to help patients [87]. The use of NPs for gene therapy in a variety of medical research fields has grown in popularity in recent years.

3.2.1. Retinitis Pigmentosa. RP is a hereditary retinal neurodegenerative disease characterized by progressive photoreceptor cell loss and RPE atrophy, initially manifesting as night vision, followed by persistent vision loss until blindness [88]. The prevalence of RP is between 1/7,000 and 1/3,000 worldwide, with a heritability of 5%–20%, and symptoms tend to start at age 10 and worsen significantly at age 40–50 [89]. Binder et al. [90] and Weber [91] composed peptide (POD) with 10 Kd polyethylene glycol (PEG) to form a homogeneous PEGPOD DNA NP of ~150 nm in size, which may avoid the limitations of adeno-associated virus (AAV) as a vector and has potential as a new retinal gene delivery vector. They found that at 77 days postinjection, the thickness of the outer nuclear layer (ONL) of the retina recovered by 76%, and at 37 days postinjection, we observed that A and B wave electroretinography (ERG) amplitudes recovered by 53% and 55%, respectively, and ONL recovered by 60%. NPs are gradually replacing viruses as new gene delivery platforms [92]. Mitra et al. [93] incorporated pDNA into GCS NPs and discovered that, upon subretinal distribution, it promoted gene expression in the RPE, indicating that it might offer a different therapy option for genetic illnesses connected to the RPE. Trigueros et al. [94] used DNA-Au NPs for successful in vitro gene delivery on human RPE cells in culture and found faster expression of reporter genes compared with DNA–liposome complexes. There are also many studies trying to deliver genetic material to the retina using different NPs, which have been expected to treat RP [95–97]. Neurotrophic agents have been proven to reduce the course of retinal degeneration in earlier research [98, 99]. Among these factors, ciliary neurotrophic factor (CNTF), expressed by Muller and RPE cells, has shown a good ability to promote the survival of photoreceptors and retinal ganglion cells (RGCs) in multiple animal models [100]. Yang et al. [101] suggested that NPs

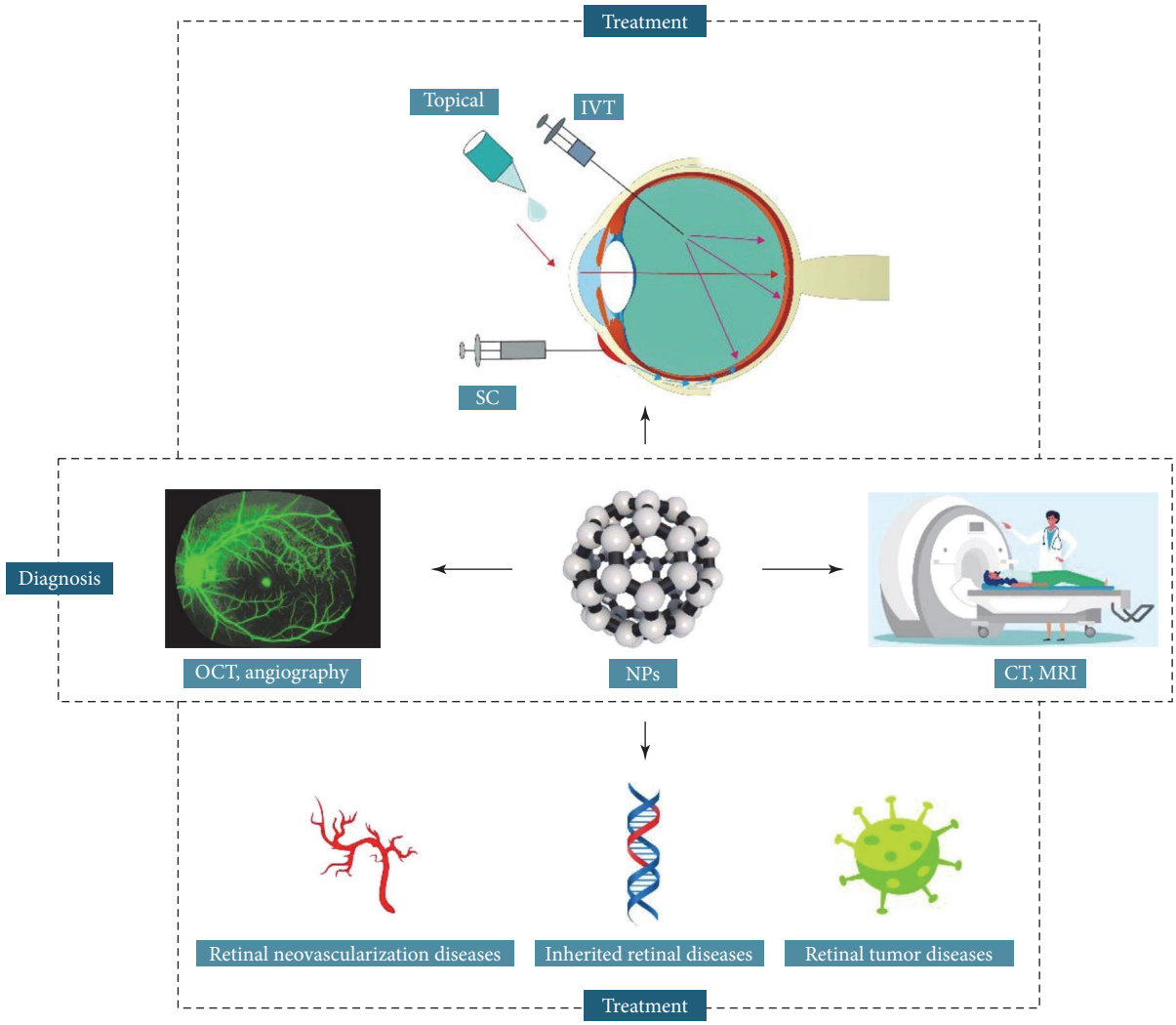

Figure 1: Schematic diagram of NPs for diagnosis and treatment of retinal diseases. The diagnosis of retinal diseases by NPs is mainly reflected in imaging, such as optical coherence tomography (OCT), angiography, CT, and MRI. The treatment of retinal diseases with NPs mainly includes topical administration, subconjunctival (SC) administration, and intravitreal (IVT) injection. The drug-delivery routes of different drug-delivery methods are shown in the figure. Retinal neovascularization diseases, inherited retinal diseases (IRDs), and retinal tumor diseases can be treated with targeted.

could continuously deliver ciliary neurotrophic factor to provide long-term protection to the retina.

3.2.2. Leber Congenital Amaurosis. LCA is an autosomal recessive disorder that affects 1 in every 81,000 births and for which there is no effective treatment. Mutations in the RPE-specific allosteric hydrolase RPE65 account for 5%–10% of all patients with LCA [102]. Without the action of RPE65, retinyl esters would continue to build up in the RPE and prevent the visual recycling and regeneration of the chromophore 11-cis-retinal [103]. The RPE gradually deteriorates and retinal cone and optic rod cells die as a result of the buildup of this toxic intermediate [104]. After a series of studies, Koirala et al. [105, 106] found that scaffold/matrix attachment region (S/mar)-containing DNA NPs promote sustained, long-term gene expression and improvement of RPE65-associated LCA, and showed that DNA NPs have a nontoxic payload capacity, expanding the range of treatments that can be used for ocular gene therapy. Another study focused on the delivery of mRNA to the retina with liposomal NPs to treat monogenic genetic disorders [107]. The mRNA-based gene delivery can eliminate unexpected genomic integration and associated safety concerns and can promote protein synthesis more efficiently compared with DNA due to the translation machinery in the cytoplasm [108, 109]. They found that this approach is mostly expressed in RPE, with limited expression in Muller cells.

3.2.3. Stargardt Disease. Stargardt illness, sometimes referred to as fundus yellow spot disease, manifests as delayed dark adaptation and severe macular vision loss in addition to the normal fundus alterations, such as the buildup of lipofuscin granules in the RPE and pigment disorders in the macula [110]. Mutations in the photoreceptor-specific flippase ABCA4 (ATP-binding cassette, subfamily A, member 4) are usually associated with Stargardt disease [111]. Previously, ABCA4

gene therapy was performed based on AAV, but the gene was too large to be successfully expressed [112, 113]. Thus, Han et al. [114] created DNA NP-based vectors to deliver ABCA4 to the subretina. They concluded that DNA NPs offer several advantages, including safety, efficacy, and high expression, and can accommodate large genes. Also to promote ABCA4 expression, Sun et al. [115, 116] developed NPs self-assembled from a multifunctional pH-sensitive aminolipid (ECO) and a therapeutic ABCA4 plasmid-induced ABCA4-specific expression for at least 8 months, with an average 35% reduction in A2E (loss of function of ABCA4 leads to the accumulation of substances) accumulation and delayed Stargardt disease progression for at least 6 months.

3.2.4. Best Vitelliform Macular Dystrophy. Best vitelliform macular dystrophy (BVMD), a rare autosomal dominant condition that largely results from mutations in the BEST1 gene, is characterized by a juvenile-onset form of retinal macular degeneration that can induce macular degeneration and loss of central visual acuity [117]. Curcumin has been found to have multiple pharmacological activities and has previously been shown to improve macular degeneration by reducing light and oxidative stress-induced cell death in RPE cells [118]. Lin et al. [119] showed that curcumin-loaded PLGA NPs could be efficiently absorbed by RPE and boosted BEST1 expression.

3.3. Retinal Tumor Diseases. Retinoblastoma (Rb) is a common intraocular cancer that frequently goes undetected in the early stages in children. In advanced stages, Rb can invade the brain backward and lead to high mortality [120]. Rb accounts for 2% of all childhood malignancies in children, 90% of which are under 5 years of age [121]. The main treatments for retinoblastoma today include retinal condensation, retinal laser, and even eye removal [122]. IVT injections of chemotherapeutic drugs have the potential to treat retinoblastoma, but the drugs often do not reach an effective concentration in the cancerous tissue [123]. Topotecan is a chemotherapeutic drug that has a short half-life in vivo in glass [124]. TCs-NPs are small in size and have an appropriate surface charge to cross the biological barrier and deliver the drug to the lesion [125]. By encapsulating topotecan in TCs-NPs, topotecan can remain undissociated during administration and immediately after injection, extending the therapeutic window of the drug in vivo and potentially reducing the number of IVT injections [126]. Another study used thiolated and methylated chitosan carboxymethyl dextran NPs (CMD-TCs-NPs and CMD-TMC-NPs) to deliver drugs to the posterior segment of the eye in retinoblastoma-induced rat eyes [127]. Photodynamic therapy (PDT) is increasingly being used in the field of ocular oncology [128]. PDT involves the injection of a photosensitizer (PS) followed by irradiation of the tumor at a specific wavelength. In the presence of oxygen, excitation of PS leads to the formation of reactive oxygen species (ROS), which induces cell death [129]. However, PSs are not yet effective enough because their limited intracellular penetration leads to a suboptimal accumulation of specificity in RB cells. N'Diaye et al. [130] designed biodegradable lipid NPs (LNPs) consisting of a poly(D,L)-lactide (PDLLA) NP coated with a phospholipid bilayer. An anticancer drug, laparone (β-Lap), and a PS, m-THPC, were coencapsulated for the combination of chemotherapy and PDT. However, it did not show a clear synergistic effect and was cytotoxic. Another study was conducted on new NPs assembled by liposomes and indocyanine green (ICG) for the treatment of retinoblastoma, which overcame the ICG's easy self-aggregation and instability, and also enabled image-guided photothermal therapy [131].

3.4. Endophthalmitis. Endophthalmitis is a serious intraocular inflammation caused by an exogenous or endogenous microbial infection that often leads to loss of vision [132]. IVT antibiotic injections are the mainstay of current treatment plans; however, they can result in surgical complications [133]. Noninvasive therapeutic strategies with NPs simultaneously loaded with azithromycin or triamcinolone acetonide have been developed [134]. The delivery system showed that the drugs can be released continuously for 300 hr, have antibacterial effects against Gram-positive and Gram-negative bacteria, and the two drugs can act synergistically. Delivery of PS with Ag NPs to finish PDT to treat endophthalmitis has also been reported [135] (Table 1).

4. New Technologies Derived from NPs Development

The development and optimization of artificial retina provide a new possibility for the treatment of retinal degeneration and irreversible damage caused by various causes [136–138]. Due to the biological characteristics of nanomaterials, they are increasingly used in various structures and links involved in retinal light signal conversion, in order to develop more sensitive, durable, and stable artificial retina [139–141]. NPs can be used to form artificial photoreceptors in the artificial retina. Bacteriorhodopsin (bR) has been suggested recently as an efficient photoconversion component for the building of different optoelectronic devices, particularly artificial retinas, due to its capacity to convert light energy into electrical energy and outstanding chemical/thermal stability [142]. Npconversion NPs (UCNPs), mainly composed of lanthanides, can accelerate the bR photocycle to generate stable photocurrents, and together with bR form photoreceptors [143]. The involvement of Au NPs in the composition of artificial photoreceptors is also being investigated [144].

The inner limiting membrane (ILM) is the main bottleneck preventing effective drug delivery to the retina after vitreous cavity injection [145, 146]. Clerck et al. [147] attempted to perforate the ILM with ICG-loaded NPs thereby facilitating drug uptake by the retina. After the injection of ICG NPs, they irradiated the bovine retina with high-intensity laser pulses and subsequently generated vapor nanobubbles (VNBs), and when these VNBs collapse, the mechanical effect can disrupt ILM. This technology resulted in enhanced retinal delivery of 120 nm sized model NPs and may boosted the efficacy of NPs within the retina by a factor of 5 [148]. VNBs can also safely dissolve vitreous opacity in vivo under laser induction [149].

Table 1: Some NPs for the treatment of retinal diseases.

Disease classification	Treatment mode/disease name	NPs	References
Retinal neovascularization diseases	Topical drug delivery	HA-BSA-NPs	[48]
		PLGA-NPs	[53, 54]
		PENE-NPs	[55]
	Subconjunctival drug delivery (SC)	CS-PLGA-NPs	[59, 60]
		HA-EGCG-NPs	[61]
		PLGA-PEG-NPs	[62]
	Intravitreal injections (IVT)	DXR-PSA-PEG-NPs	[64]
		NPC-NPs	[66]
		R5K-ITZ-NPs	[68]
		PLGA-NPs	[69]
		HA-Cx43 MP-NPs	[70]
		PDA-NPs	[71]
		Cerium oxide NPs	[72, 73]
		Au NPs	[74–77]
		Silica NPs	[78]
	Gene therapy	VEGF-siRNA-NPs	[82]
		miRNA-NPs	[85]
Inherited retinal diseases (IRDs)	Retinitis pigmentosa (RP)	PEGPOD-DNA-NPs	[90, 91]
		GCS-DNA-NPs	[93]
		DNA-Au NPs	[94]
		PEG-PLGA-PLL-siRNA-NPs	[95]
	Leber congenital amaurosis (LCA)	S/Mar DNA-NPs	[105, 106]
		Mrna-NPs	[107]
	Stargardt disease	ABCA4 DNA-NPs	[114]
		ECO/pRHO-ABCA4-NPs	[115, 116]
	Best vitelliform macular dystrophy (BVMD)	Cur-PLGA-NPs	[119]
Retinal tumor diseases	Retinoblastoma (Rb)	TPH-TCs-NPs	[126]
		CMD-TCs-NPs	[127]
		PDLLA-NPs	[130]
		ICG-NPs	[131]
Endophthalmitis		PLA-CHI NPs	[134]
		PS-Ag-NPs	[135]

5. Challenges and Conclusion

Entering the 21st century, nanotechnology has ushered in a phase of rapid development. However, most of the research on nanoparticles stays in the experimental stage, and very few of them enter the clinic. It is important to pay attention to the hazards of NPs, such as the potential toxicity of some NPs, which may be harmful to the retina. With the deepening of the research on NPs, the use of NPs is becoming more and more extensive, and NPs can also be used to treat proliferative vitreoretinopathy (PVR), retinal inflammation caused by autoimmune uveitis [150, 151]. With the development of nanotechnology, many new fields have also been derived, such as biomimetic nanosponges [152].

In summary, NPs may provide new diagnostic and therapeutic approaches, alter traditional drug delivery, prolong drug release, improve retinal bioavailability, reduce drug cytotoxicity, and provide assistance for gene therapy. NPs are a powerful tool, and their research opens new avenues for the diagnosis and treatment of most retinal diseases. However, research on NPs is still mainly at the experimental stage and few of them enter the clinic, so there are still many challenges to be solved. For example, some NPs have dose-dependent cytotoxicity or size-dependent cytotoxicity that limits their use in retinal diseases, such as titanium dioxide NPs, silica NPs, zinc sulfide NPs, and silver NPs [153–156]. It is important to be aware of the hazards of NPs, such as the potential toxicity of some nanoparticles, which may be harmful to the retina. In conclusion, further research will enrich the future of NPs, and nanomaterials have good prospects for applications in the retina.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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