

Review

Functional Liposomal Nanocarriers for the Treatment of Antimicrobial-Resistant and Biofilm-Associated Ocular Infections

Paula Stefana Pintilei ¹, Roya Binaymotlagh ¹ , Farid Hajareh Haghighi ¹ , Laura Chronopoulou ^{1,2} 
and Cleofe Palocci ^{1,2,*}

¹ Department of Chemistry, Sapienza University of Rome, Piazzale Aldo Moro 5, 00185 Rome, Italy

² Research Center for Applied Sciences to the Safeguard of Environment and Cultural Heritage (CIABC), Sapienza University of Rome, Piazzale Aldo Moro 5, 00185 Rome, Italy

* Correspondence: cleofe.palocci@uniroma1.it; Tel.: +39-06-4991-3317

Abstract

Nanomedicine-based liposomal delivery systems are gaining increasing attention as advanced therapeutic platforms for managing ocular infections associated with antimicrobial resistance (AMR) and biofilm formation. The primary objective of this review is to critically evaluate the potential of liposomal drug delivery systems for improving the treatment of antimicrobial-resistant and biofilm-associated ocular infections by integrating current knowledge on antimicrobial resistance mechanisms, biofilm-targeted therapeutic strategies, and advances in liposomal formulations, while also identifying the major limitations, translational challenges, and knowledge gaps in this rapidly evolving field. Traditional ocular antimicrobial treatments are frequently limited by poor drug penetration, short precorneal residence time, low bioavailability, systemic side effects, and inadequate activity against resistant microorganisms and biofilm-embedded pathogens. This review provides a comprehensive overview of different liposomal systems, including conventional, cationic, polyethylene glycol (PEG)-modified, deformable, and stimulus-responsive liposomes, and discusses their advantages in ophthalmic drug delivery, such as enhanced corneal permeation, prolonged drug retention, controlled release, improved biocompatibility, and reduced ocular toxicity. The review further examines the mechanisms through which liposomes help overcome AMR, including improved epithelial transport, membrane disruption, intracellular drug delivery, efflux pump evasion, and enhanced antimicrobial efficacy. In addition, liposomal approaches targeting ocular biofilms are explored, focusing on improved biofilm penetration and the delivery of anti-biofilm agents such as antibiotics, enzymes, quorum-sensing inhibitors, and antimicrobial peptides. Current evidence from in vitro and in vivo ocular infection models is summarized together with disease-specific applications in keratitis, endophthalmitis, and contact lens-related infections. The article also compares liposomes with other ocular nanocarriers and addresses important considerations related to safety, stability, sterilization, large-scale production, and regulatory translation. In addition to highlighting recent advances, this review critically discusses the current limitations of liposomal formulations, the major barriers to clinical translation, and the key knowledge gaps that should be addressed to facilitate the future development and successful clinical application of these systems. Finally, emerging directions including ligand-targeted and stimulus-responsive liposomes, AI-driven formulation development, personalized nanotherapy, and gene therapy combinations are discussed as promising future strategies for combating resistant ocular infections.



Academic Editor: Giuseppe Cavallaro

Received: 15 June 2026

Revised: 24 July 2026

Accepted: 28 July 2026

Published: 31 July 2026

Copyright: © 2026 by the authors.

Licensee MDPI, Basel, Switzerland.

This article is an open access article distributed under the terms and

conditions of the [Creative Commons](https://creativecommons.org/licenses/by/4.0/)

[Attribution \(CC BY\)](https://creativecommons.org/licenses/by/4.0/) license.

Keywords: liposomes; ocular drug delivery; antimicrobial resistance; ocular infections; biofilms; nanomedicine; keratitis; sustained release; ophthalmic nanocarriers

1. Liposomes as Ocular Drug Delivery Systems

Liposomes are highly versatile vesicular nanocarriers widely investigated for ocular drug delivery because of their biocompatibility, biodegradability, and structural similarity to biological membranes [1]. These systems consist of one or multiple concentric phospholipid bilayers surrounding an aqueous core, enabling the simultaneous encapsulation of hydrophilic drugs within the aqueous compartment and lipophilic compounds within the lipid bilayer [2]. Their physicochemical characteristics, including particle size, lamellarity, surface charge, lipid composition, membrane rigidity, and surface functionalization, can be precisely engineered to influence drug loading, stability, ocular retention, tissue interaction, and therapeutic performance [3]. Unlike conventional formulations, liposomes offer additional opportunities to address the specific challenges of antimicrobial-resistant (AMR) ocular infections [4]. Importantly, liposomes do not directly eliminate genetically encoded antimicrobial resistance mechanisms; rather, they may improve therapeutic outcomes by modifying drug exposure at the infection site, increasing local antimicrobial concentrations, enhancing penetration through complex ocular barriers, protecting unstable drugs from degradation, and facilitating delivery to pathogen-associated microenvironments [5]. In biofilm-associated infections, these properties may improve antimicrobial access by promoting interactions with extracellular polymeric substances (EPSs), increasing residence time at the infection site, and potentially reducing the impact of physiological barriers associated with biofilm tolerance [6] (Figure 1).

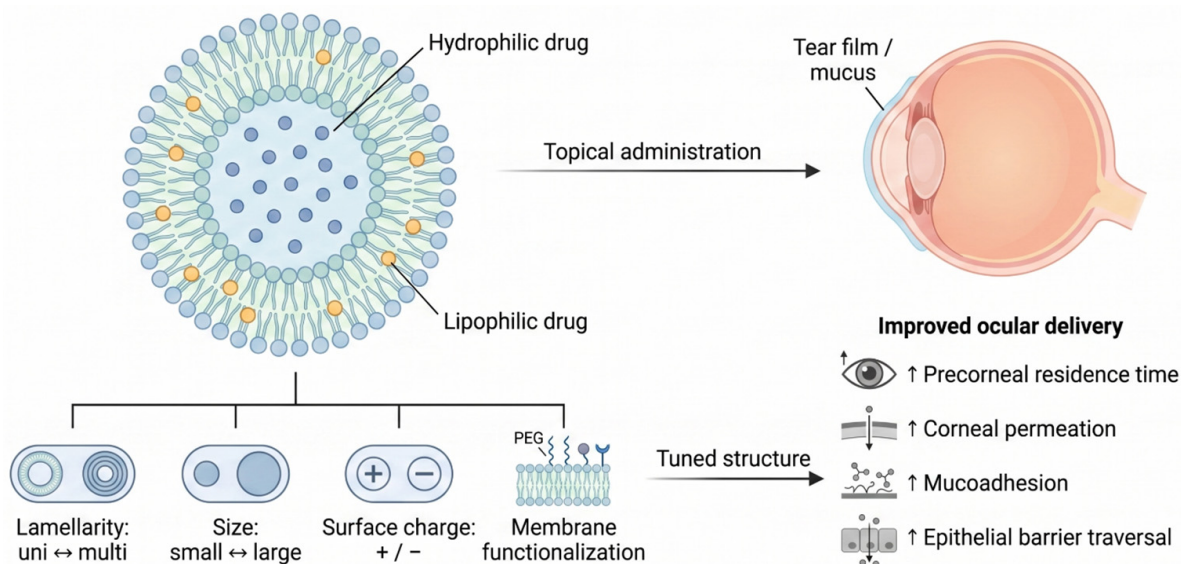


Figure 1. Engineered liposomes for ocular drug delivery. Schematic representation of multifunctional liposomes capable of co-encapsulating hydrophilic drugs within the aqueous core and lipophilic drugs in the lipid bilayer. Following topical administration, liposome properties including lamellarity, particle size, surface charge, and membrane functionalization (e.g., PEGylation or ligand attachment) can be tailored to optimize tear film interaction, mucoadhesion, corneal permeation, epithelial transport, and precorneal residence time for enhanced ocular drug delivery. Created in BioRender. Hajareh Haghighi, F. (2026) <https://BioRender.com/ik6lg1k> (accessed on 7 June 2026).

Unlike conventional formulations, liposomes offer additional opportunities to address the specific challenges of antimicrobial-resistant (AMR) ocular infections [7]. Importantly, liposomes do not directly eliminate genetically encoded antimicrobial resistance mechanisms; rather, they may improve therapeutic outcomes by modifying drug exposure at the infection site, increasing local antimicrobial concentrations, enhancing penetration through complex ocular barriers, protecting unstable drugs from degradation, and facilitating delivery to pathogen-associated microenvironments [8]. In biofilm-associated infections, these properties may improve antimicrobial access by promoting interactions with extracellular polymeric substances (EPSs), increasing residence time at the infection site, and potentially reducing the impact of physiological barriers associated with biofilm tolerance. However, the extent of these benefits remains highly dependent on liposome composition, pathogen characteristics, drug properties, and experimental model conditions.

Based on vesicle size and lamellarity, liposomes are generally classified into small unilamellar vesicles (SUVs), large unilamellar vesicles (LUVs), and multilamellar vesicles (MLVs) [9,10]. These structural variations influence drug loading capacity, release kinetics, membrane stability, corneal permeation, mucoadhesion, and precorneal residence time. In addition, surface modification and lipid engineering strategies have enabled the development of advanced liposomal systems with improved ocular performance and targeting potential [11,12]. Nevertheless, optimization of these parameters requires careful consideration because modifications that enhance one therapeutic property may negatively affect others. For example, increasing surface charge may improve mucosal interaction but can increase epithelial toxicity, whereas enhanced steric stabilization through PEGylation may improve colloidal stability but reduce cellular uptake [13].

Conventional liposomes represent the earliest and most extensively investigated liposomal systems for ocular drug delivery. They are typically composed of neutral or zwitterionic phospholipids, particularly phosphatidylcholine [14,15], combined with cholesterol to improve bilayer rigidity and stability [16]. Their biomimetic structure and ability to encapsulate both hydrophilic and lipophilic therapeutics have supported their application in the delivery of antibiotics, antifungal agents, antivirals, anti-inflammatory compounds, and glaucoma medications [17,18]. However, conventional liposomes frequently demonstrate limited clinical performance because of rapid precorneal clearance, weak interaction with ocular mucus, limited penetration across ocular barriers, formulation instability, and drug leakage during storage [19,20].

To overcome these limitations, engineered liposomal systems have been developed through modifications of lipid composition and surface characteristics. Cationic liposomes incorporate positively charged lipids such as DOTAP, DOTMA, or stearylamine, enhancing electrostatic interactions with negatively charged mucins and epithelial surfaces [21,22]. This property may increase precorneal retention and cellular uptake [23,24]; however, excessive positive charge can disrupt epithelial membranes, induce cytotoxicity, and promote vesicle aggregation [25,26]. PEGylated liposomes, also known as stealth liposomes, contain polyethylene glycol (PEG) chains attached to the vesicle surface, generating a hydrated steric barrier that reduces aggregation and protein adsorption [27]. PEGylation can improve physical stability and prolong ocular residence; however, excessive PEG density may decrease interactions with cellular membranes and reduce intracellular delivery [28]. This PEG-dependent balance between stability and biological interaction represents an important consideration for ocular applications.

Deformable liposomes, also referred to as elastic liposomes, incorporate edge activators such as Tween 80, Span 80, or sodium cholate to increase membrane flexibility and fluidity [29]. Their deformability may facilitate penetration across ocular barriers and improve drug deposition compared with rigid vesicles [1]. Nevertheless, excessive incorpo-

ration of edge activators can compromise membrane integrity, accelerate drug leakage, and negatively affect ocular tolerability. Thus, formulation optimization is essential to achieve an appropriate balance between flexibility, stability, and safety.

The ability of liposomes to enhance ocular drug absorption is attributed to several complementary mechanisms, including prolonged precorneal residence, interaction with tear film components, lipid exchange with biological membranes, improved solubilization of poorly water-soluble drugs, and enhanced epithelial transport [30]. Depending on formulation characteristics, liposomes may facilitate drug uptake through membrane fusion, endocytosis, or transient interaction with epithelial barriers. However, these mechanisms are not universal and vary considerably according to vesicle composition, drug physicochemical properties, and ocular tissue characteristics [31]. Therefore, improved ocular delivery should be interpreted as a formulation-dependent outcome rather than an inherent property of all liposomal systems.

More recently, stimulus-responsive liposomes have emerged as advanced delivery platforms designed to release therapeutic cargo in response to specific biological or externally applied triggers. These systems can be broadly categorized into endogenous and exogenous stimulus-responsive liposomes. Endogenous stimuli exploit pathological characteristics of ocular tissues, including acidic pH, disease-associated enzymes, and elevated reactive oxygen species (ROS) levels. Among these approaches, enzyme-responsive and ROS-responsive liposomes may have greater translational potential for ocular antimicrobial applications because they utilize local pathological conditions, such as infection-associated enzymatic activity and oxidative stress, without requiring additional external equipment. pH-responsive systems may also provide opportunities for controlled drug release in inflamed or infected microenvironments; however, their effectiveness depends on achieving sufficient differences between diseased and physiological ocular conditions [32].

In contrast, exogenous stimulus-responsive liposomes rely on externally applied triggers, including light, ultrasound, magnetic fields, or temperature changes [33], to achieve on-demand drug release [34]. Although these approaches provide precise temporal and spatial control, their clinical implementation in ophthalmology may be limited by the need for specialized equipment, potential effects on delicate ocular tissues, and challenges associated with treatment standardization. Light-responsive systems may be particularly attractive for anterior segment applications because of the accessibility of ocular tissues, whereas ultrasound- and magnetic-responsive systems may require further optimization for safety and practical clinical use [35]. Endogenous stimulus-responsive liposomes may currently appear more compatible with ocular infection therapy because they can exploit disease-specific biological signals while minimizing additional procedural requirements. Nevertheless, both endogenous and exogenous strategies remain largely at the experimental stage, and further studies are required to establish their long-term safety, manufacturing reproducibility, and regulatory feasibility [36,37]. The main structural characteristics, advantages, limitations, and ocular applications of conventional and engineered liposomal systems are summarized in Table 1.

It should be noted that the physicochemical characteristics of liposomes are not intrinsic properties of each class but are highly dependent on lipid composition, preparation techniques, drug loading, and surface modification strategies. Therefore, the values presented in Table 1 represent commonly reported ranges rather than fixed parameters.

Table 1. Representative physicochemical characteristics, ocular advantages, and translational limitations of conventional and engineered liposomal systems.

Liposomal Class	Representative Size Range (nm) *	Representative Zeta Potential Range (mV) *	Core Ocular Advantage	Translational/Safety Limitations	Ref.
Conventional liposomes	~80–300 nm	Approximately neutral (−10 to +10 mV)	High biocompatibility; suitable for encapsulation of hydrophilic and lipophilic drugs	Limited precorneal retention, rapid tear clearance, possible drug leakage	[38]
Cationic liposomes	~50–250 nm	Typically positive (+10 to +50 mV depending on lipid composition)	Enhanced interaction with negatively charged mucins and improved cellular uptake	Potential epithelial toxicity, irritation, aggregation at high charge density	[39]
PEGylated liposomes	~80–250 nm	Usually near neutral to mildly negative (−30 to 0 mV)	Improved colloidal stability, reduced aggregation, prolonged ocular residence	Reduced cellular uptake, possible interference with membrane fusion and drug release	[40]
Deformable/elastic liposomes	~80–300 nm	Variable, often neutral or negative	Enhanced membrane flexibility and improved corneal penetration	Structural instability, sensitivity to edge activator concentration, leakage risk	[41]
Stimulus-responsive liposomes	~100–300 nm	Highly formulation-dependent	Controlled and site-specific drug release in response to endogenous or external triggers	Increased formulation complexity, limited manufacturing standardization, regulatory uncertainty	[42]

* Representative values vary depending on lipid composition, preparation method, encapsulated drug, and surface modification strategy.

2. Benefits of Liposomal Systems for Ocular Drug Delivery

2.1. Increased Residence Time

Rapid percorneal elimination, driven by tear turnover, blinking, nasolacrimal drainage, and reflux lacrimation, continues to be the main obstacle for efficient ocular therapies, reducing drug bioavailability to less than 5% in standard eye drops [43]. Liposomes have emerged as one of the most effective strategies to reduce this limitation, as their vesicular architecture promotes better interaction with corneal and conjunctival epithelia and stabilizes adhesion to the tear film lipid layer, thereby mitigating rapid washout [44]. Surface engineering further amplifies these benefits: cationic and mucoadhesive liposomes exploit electrostatic and hydrogen-bonding interactions with mucin to achieve superior retention [45]. Sun and colleagues developed dual-modified liposomes functionalized with penetratin and hyaluronic acid, demonstrating markedly enhanced ocular surface residence and noninvasive posterior-segment delivery in neovascular AMD models due to the synergistic combination of HA-mediated mucoadhesion and CPP-mediated epithelial translocation [46], while Zhang et al. further advanced the field by designing mucin-targeting liposomes that not only prolonged retention through high-affinity MUC1/MUC16 binding but also modulated ferroptosis and inflammation in dry eye disease [47]. Huang et al. confirmed the therapeutic value of mucoadhesive designs by showing that their liposomal system improved retention and produced synergistic anti-inflammatory and antioxidant effects [48]. In glaucoma therapy, Brugnera et al. demonstrated that hyaluronic-acid-coated latanoprost liposomes provide long-term stability, enhanced corneal penetration, and significantly prolonged precorneal residence, translating into improved IOP-lowering performance in chronic models [49]. Bonechi et al. showed that citicoline encapsulation improves molecular stability and ocular bioavailability [50]; Yang et al. developed reactive-oxygen-species-responsive cyclosporine A liposomes that enhance corneal permeability

and retention in inflamed tissues [51]; and Wong et al. introduced a Cornea-SELEX aptamer-guided system that refines corneal targeting and adhesion through selective binding to ocular surface epitopes [52]. The adaptability of liposomes is further illustrated by Battista et al., who demonstrated that quinoline derivatives can be efficiently encapsulated within stable vesicles, supporting their suitability for diverse molecular structures [53] (see Figure 2). Despite these promising findings, the advantages of engineered liposomes for increasing ocular residence time should be interpreted within the limitations of current evidence. Most studies evaluating mucoadhesive, peptide-functionalized, or ligand-targeted liposomes have been performed in animal models or ex vivo systems, while direct clinical validation remains limited [54]. Furthermore, the magnitude of retention enhancement is highly dependent on formulation-specific parameters, including lipid composition, surface modification density, particle size, and the characteristics of the ocular disease model.

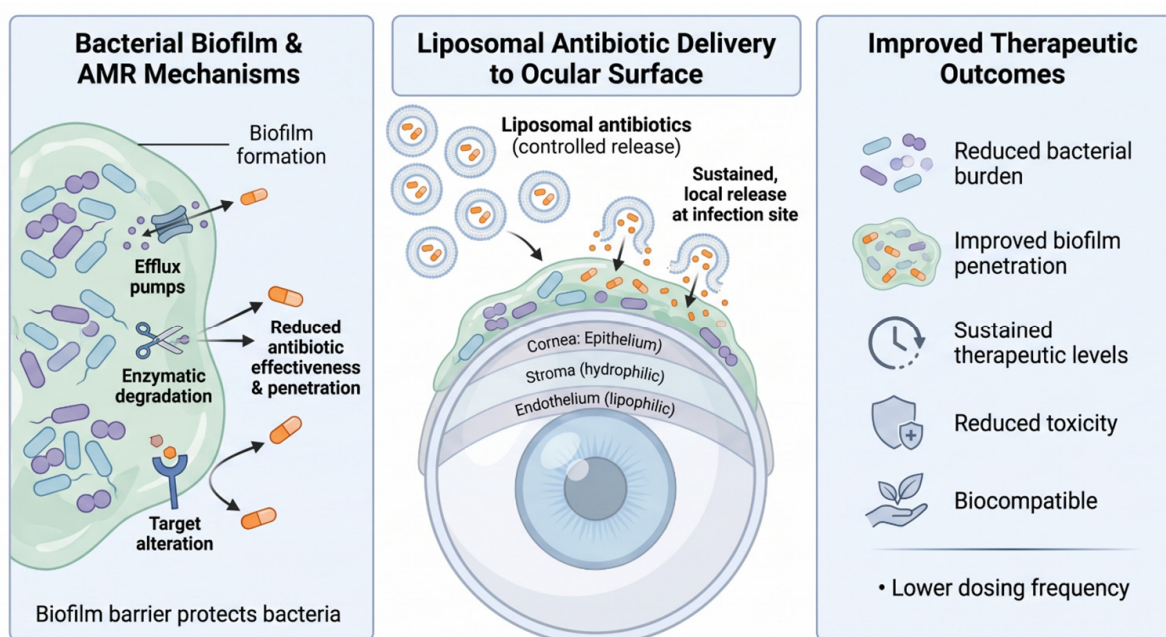


Figure 2. Biofilm formation, AMR mechanisms, and the local release of liposomal antibiotics. Created in BioRender. Hajareh Haghighi, F. (2026) <https://BioRender.com/ik6lg1k> (accessed on 7 June 2026).

2.2. Enhanced Corneal Penetration

The cornea represents a highly selective barrier to drug permeation due to its trilaminar organization, consisting of the lipophilic epithelium, hydrophilic stroma, and lipophilic endothelium. The biophasic architecture restricts the efficient transport of both hydrophilic and lipophilic molecules, posing a major challenge to achieving therapeutic intraocular concentrations. Liposomes have emerged as particularly effective in overcoming this constraint, utilizing their biomimetic phospholipid bilayer to fuse or adsorb onto epithelial membranes and promote transcellular transport, while their capacity to transiently modulate membrane fluidity further enhances penetration. Their dual aqueous-lipid compartments enable efficient encapsulation of drugs with diverse solubility profiles, and surface charge plays a decisive role: cationic liposomes interact strongly with the negatively charged corneal surface, improving adhesion and uptake [55]. At the molecular level, liposome-mediated corneal penetration occurs through multiple complementary mechanisms rather than a single transport pathway. Phospholipid bilayers can interact with epithelial membranes through adsorption, lipid exchange, and partial membrane fusion, facilitating transcellular transport of encapsulated drugs. Surface charge and ligand modification further influence interaction with the negatively charged glycocalyx and specific cellular receptors,

enhancing epithelial uptake [56]. In addition, deformable liposomal systems may improve penetration by transiently adapting their morphology and facilitating transport across restrictive ocular barriers. However, excessive membrane interaction or strong electrostatic effects may compromise epithelial integrity, highlighting the importance of balancing penetration enhancement with ocular safety. Huang et al. developed iRGD-decorated liposomes to exploit neuropilin-1-mediated translocation and demonstrated in New Zealand rabbits that iRGD functionalization increased corneal retention three-fold at 3 h and produced a six-fold higher drug level than AZOPT. In vitro and in vivo permeability assays showed that iRGD-PEG liposomes containing more than 10% iRGD enhanced corneal penetration by over three-fold, enabling deeper stromal entry and higher epithelial internalization than non-decorated controls, consistent with active receptor-mediated transport rather than passive diffusion [57]. Csorba et al. formulated ascorbic-acid-loaded liposomes to overcome the intrinsically poor corneal permeability of vitamin C and demonstrated on excised human corneas that liposomal encapsulation increased steady-state flux by approximately three-fold and significantly elevated cumulative permeation compared with free ascorbic acid, while simultaneously stabilizing the molecule against oxidation through markedly slower degradation kinetics; this enhancement was attributed to liposome-mediated transcellular transport and protection of ascorbic acid within the lipid bilayer [58]. Qiu et al. engineered dendritic oligoethylenimine-decorated liposomes (PL/TLPL) that exhibited prolonged precorneal retention, with FITC-PL fluorescence persisting on the ocular surface for at least 10 min compared with complete disappearance of free FITC by 5 min, and significantly enhanced corneal permeation, increasing timolol transport from 1.5% to 3% (two-fold) and latanoprost transport from 16.4% to 22% (1.4-fold) across rabbit corneas within 4 h. OEI decoration increased cellular uptake by approximately two-fold and induced tight-junction opening, with ZO-1 fluorescence reduced by more than 50%, enabling combined transcellular and paracellular penetration and supporting the sustained five-day intraocular-pressure-lowering effect observed in vivo [59]. Thanuja et al. developed fusogenic liposome-coated nanoparticles that rapidly merged with donor corneal endothelial membranes, with TEM showing direct bilayer fusion within minutes and uptake assays confirming immediate cytoplasmic entry without endocytic vesicles, demonstrating that fusogenic lipid compositions can bypass tight endothelial interfaces through membrane fusion rather than classical endocytosis [60]. Liao et al. applied a CNN-based analytical framework to evaluate insulin-loaded liposomes and showed that liposomal encapsulation improved corneal inflammatory responses, producing higher epithelial uptake, reduced epithelial thickening, and marked suppression of IL-1 β and TNF- α expression, confirming that liposomes stabilize insulin against tear-film degradation and enable therapeutically relevant peptide delivery to inflamed corneal tissues [61]. Moghimipour et al. demonstrated that pilocarpine-loaded liposomes increased transcorneal permeation two- to three-fold in Franz diffusion studies on excised rabbit corneas, with optimized vesicle size (120–212 nm), moderate negative charge, and enhanced bilayer fluidity collectively improving diffusion-driven transport of hydrophilic pilocarpine compared with the aqueous solution, highlighting the importance of liposomal membrane dynamics in corneal permeation [62]. Shimokawa et al. showed in a rat model of dry-eye disease that slightly cationic astaxanthin-loaded liposomes reduced corneal fluorescein scores from an average of 8.2 to 4.9, indicating substantial improvement in epithelial integrity, and increased tear volume from 3.5 μ L to 4.7 μ L, reflecting enhanced tear production. Molecular assays revealed a 30–50% downregulation of oxidative-stress markers, including reactive oxygen species and fluorescence markers such as p53, p21, and p16, confirming the antioxidative and cytoprotective effects of this delivery system. Fluorescence-tracking studies showed a 2.3-fold higher accumulation of cationic liposomes within corneal epithelial cells compared

with neutral liposomes, correlating with increased local bioavailability and improved therapeutic efficacy at lower doses [63]. Charge-mediated mechanisms are further elucidated by cationic tacrolimus liposomes, which inhibit neovascularization and inflammation in alkali burn models [64]. Although not liposomal, regenerative platforms such as growth-factor-loaded hydrogels [65] and exposome-based thermoresponsive matrices [66] contextualize the broader relevance of strategies designed to overcome corneal barriers. Beyond enhancing penetration, liposomes protect encapsulated drugs from enzymatic degradation in the tear film, ensuring that a greater proportion of the administered dose reaches the corneal surface intact. Experimental evidence demonstrates that liposomal formulations significantly increase drug permeation compared with conventional formulations. They have a better vesicle stability, release kinetics, and irradiation potential, which should be optimized to balance penetration efficiency with safety. Although numerous studies have demonstrated enhanced corneal penetration using engineered liposomes, the majority of evidence remains based on *in vitro* permeability assays, *ex vivo* corneal models, or small animal experiments. Differences in experimental design, liposome composition, and evaluation methods make direct comparison between formulations difficult [67]. In addition, increased penetration does not always correspond to improved clinical efficacy, as therapeutic success depends on achieving appropriate drug concentrations at the disease site while maintaining epithelial integrity and long-term tolerability.

2.3. Sustained Release

Sustained or controlled drug release is a central requirement in ocular therapeutics, as maintaining stable intraocular drug levels while reducing dosing frequency is essential for managing chronic diseases such as glaucoma, uveitis, and age-related macular degeneration [68,69]. Liposomes inherently support prolonged release owing to their compartmentalized architecture and the physicochemical interactions between encapsulated drugs and the lipid bilayer: hydrophilic molecules diffuse gradually from the aqueous core, whereas lipophilic compounds embedded within the membrane exhibit slower, membrane-regulated release governed by lipid phase behaviour and fluidity [70]. Release kinetics can be precisely tuned by modulating lipid composition, cholesterol content, vesicle size, and lamellarity. Cholesterol, for example, increases bilayer rigidity and reduces permeability, while multilamellar vesicles extend release duration relative to unilamellar systems. The clinical relevance of these mechanisms is well documented. Brugnara et al. developed latanoprost-loaded liposomes coated with a mucoadhesive polymer and demonstrated in a clinical-grade model that a single eye drop produced a longer-lasting hypotensive effect than the marketed formulation. Pharmacodynamic measurements showed a significant extension of IOP-lowering duration, attributed to both enhanced ocular surface retention and sustained release from the lipid bilayer [71]. Londhe and Sharma formulated a methazolamide liposomal *in-situ* gel for glaucoma therapy. Their optimized system exhibited prolonged intraocular residence, with *in vivo* rabbit studies showing higher and more sustained aqueous humor concentrations compared with free drug. The combination of liposomal encapsulation and gelation provided dual control over release and retention [72]. For posterior-segment delivery, Blazaki et al. introduced a Liposome Aggregate Platform (LAP)—a system in which liposomes self-assemble into larger aggregates after intravitreal injection. This architecture markedly slowed vitreous clearance, maintaining therapeutic drug levels for extended periods. Fluorescence tracking confirmed prolonged intravitreal retention, demonstrating the value of aggregate-forming liposomes for long-acting posterior delivery [73]. Several other studies highlight sustained release of prostaglandin analogues [74], long-acting intravitreal system for retinal neuroprotection [75], multivesicular liposomes for anti-VEGF therapy [76], and hybrid or implantable platforms designed

to overcome the limitations of conventional dosing strategies [77]. Despite the ability of liposomes to prolong drug exposure, sustained release alone does not necessarily guarantee superior therapeutic performance. Several formulation-dependent factors, including incomplete drug release, instability during storage, insufficient tissue penetration, and variability between experimental models, may limit clinical benefit.

2.4. Safety, Toxicity and Biocompatibility

Toxicity remains a central concern in ocular drug delivery due to the exceptional sensitivity of ocular tissues and their susceptibility to irritation and systemic exposure. Liposomes mitigate these risks through a combination of structural and physicochemical mechanisms that collectively reduce local toxicity while maintaining therapeutic efficacy. From a mechanistic perspective, the improved safety profile of liposomes is primarily attributed to drug encapsulation within phospholipid bilayers, which minimizes direct interaction between free drug molecules and ocular tissues. This is particularly important for compounds with narrow therapeutic indices or inherent irritancy. In addition, controlled and sustained release prevents abrupt peak concentrations that could induce cytotoxic responses, while reduced drainage through the nasolacrimal pathway limits systemic exposure [78]. Furthermore, the biomimetic nature of liposomes, composed of physiologically compatible phospholipids, enhances cellular compatibility by closely resembling natural biological membranes and undergoing enzymatic degradation into non-toxic metabolites [79]. At the formulation level, toxicity is strongly influenced by structural and surface properties. Surface charge plays a critical role, as highly cationic liposomes may increase membrane interactions and potentially induce irritation, whereas neutral or zwitterionic systems generally exhibit improved tolerability [80]. Similarly, excipients such as surfactants require careful optimization due to their potential membrane-disruptive effects at high concentrations. Surface modifications including PEGylation or polymer coating (e.g., chitosan) can further enhance safety by improving steric stabilization, reducing opsonization, and limiting non-specific cellular interactions, although excessive modification may alter membrane dynamics and drug release behavior [81]. Experimental evidence supports these mechanistic principles. Syama et al. demonstrated that phospholipid-based liposomes exhibit significantly lower cytotoxicity compared with non-lipid nanocarriers across multiple cell lines, as confirmed by membrane integrity and oxidative stress assays, highlighting the inherent biocompatibility of biomimetic bilayers [82]. Complementarily, Dymek and Sikora emphasized that enzymatic degradation of natural and zwitterionic lipids yields physiologically tolerated metabolites, reinforcing their low immunogenic and low-toxicity profile. In ocular models [83], Amalia et al. showed that liposomal amphotericin B maintains antifungal efficacy while significantly reducing corneal irritation and epithelial damage compared with conventional formulations, attributable to reduced free drug exposure and buffered release [84]. Similarly, studies on liposomal curcumin consistently demonstrate reduced oxidative stress and off-target toxicity, while maintaining or improving therapeutic efficacy through enhanced stability and controlled delivery.

3. Mechanisms by Which Liposomes Combat Antimicrobial Resistance

Antimicrobial resistance (AMR) represents a major challenge in the treatment of ocular infections, driven by the increasing prevalence of multidrug-resistant pathogens and the unique anatomical and physiological barriers that restrict effective antimicrobial delivery to ocular tissues [85]. Conventional antimicrobial therapies may fail to achieve sustained therapeutic concentrations at infected sites, particularly in the presence of biofilm formation, intracellular bacterial reservoirs [86], limited tissue penetration, and microbial resistance mechanisms such as reduced membrane permeability and active efflux

systems [87]. Liposomes have emerged as promising drug delivery platforms because their biomimetic phospholipid architecture, high drug-loading versatility, and tunable physicochemical properties allow them to address several delivery-related and resistance-associated barriers simultaneously [88,89]. However, the contribution of liposomal systems to overcoming AMR should be distinguished from their ability to simply improve pharmacokinetic performance. Enhanced ocular residence time, improved corneal penetration, and sustained drug release primarily represent pharmacokinetic advantages that increase antimicrobial exposure at the site of infection [90,91]. In contrast, resistance-modifying effects involve mechanisms such as bacterial membrane disruption, modulation of antimicrobial susceptibility, intracellular drug delivery, circumvention of microbial defense mechanisms, and synergistic co-delivery of antibiotics with resistance-modifying agents. Therefore, the therapeutic value of liposomes against resistant ocular pathogens depends not only on improved drug delivery but also on their ability to overcome specific biological mechanisms responsible for antimicrobial failure. The interaction between liposomal systems and antimicrobial-resistant pathogens is also influenced by pathogen-specific structural characteristics [92]. In Gram-positive bacteria, the exposed peptidoglycan-rich cell envelope allows relatively direct interaction with liposomal surfaces, and cationic or membrane-active liposomes may enhance antimicrobial accumulation through electrostatic interactions and membrane perturbation. In contrast, Gram-negative bacteria possess an additional outer membrane containing lipopolysaccharides (LPSs), which represents a major permeability barrier and contributes to intrinsic and acquired resistance. Liposomal systems may partially overcome this limitation by improving antibiotic delivery, increasing local concentration at bacterial surfaces, and facilitating membrane interaction; however, excessive membrane disruption may increase toxicity risks [93]. Fungal pathogens present distinct challenges because their eukaryotic cell structure, glucan/chitin-rich cell wall, and ergosterol-containing membranes differ substantially from bacterial targets. In these organisms, liposomes primarily improve antifungal delivery by enhancing drug solubility, protecting unstable compounds, increasing ocular retention, and reducing the exposure of host tissues to toxic free drug concentrations. The major mechanisms by which liposomal systems may enhance antimicrobial efficacy and counteract resistance-associated barriers are summarized in Table 2.

Although liposomal systems have demonstrated considerable potential in overcoming resistance-associated barriers, the strength of evidence supporting each proposed mechanism varies considerably. Many reported benefits, including enhanced penetration, increased intracellular accumulation, and improved antimicrobial activity, are primarily derived from *in vitro* studies or experimental infection models, and their contribution to clinically meaningful resistance reversal remains incompletely established [112]. Importantly, liposomes should not be considered direct inhibitors of antimicrobial resistance mechanisms in most cases; rather, they frequently enhance therapeutic efficacy by improving drug delivery, increasing local antimicrobial exposure, and facilitating interactions between antimicrobial agents and microbial targets. The effectiveness of these strategies is also highly dependent on formulation-related factors, including particle size, surface charge, lipid composition, encapsulation efficiency, and drug release characteristics, as well as pathogen-specific features such as membrane structure, biofilm formation capacity, and resistance phenotype [113].

Liposomes represent a multifunctional platform capable of integrating several strategies to improve antimicrobial performance against resistant ocular pathogens. A single liposomal formulation may simultaneously enhance ocular drug exposure, facilitate cellular uptake, promote localized antimicrobial delivery, and provide controlled release characteristics. However, the therapeutic impact of these combined functions is not solely determined

by the presence of a liposomal carrier, but rather by the optimization of formulation parameters and their compatibility with specific pathogens and infection environments. Factors such as lipid composition, particle size, surface charge, drug loading efficiency, and release kinetics can substantially influence antimicrobial outcomes, while differences in bacterial species, resistance mechanisms, and biofilm characteristics may affect the reproducibility of therapeutic effects [114]. Therefore, future studies should move beyond demonstrating enhanced antimicrobial activity and focus on establishing standardized comparative frameworks that identify the most effective liposomal designs for specific AMR-associated ocular infections. Such evidence will be essential for translating promising liposomal strategies from experimental models toward clinically applicable antimicrobial therapies.

Table 2. Mechanistic Basis, Evidence Level, and Limitations of Liposomal Strategies for Counteracting Antimicrobial Resistance in Ocular Pathogens.

Mechanism	How Liposomes Counter AMR	Representative Findings	Evidence Level	Key Limitations	Ref.
Improved penetration through ocular barriers	Biomimetic phospholipid bilayers promote membrane interaction, endocytosis, and enhanced transcorneal transport, increasing drug delivery to infected tissues.	pDrops achieved >6-fold higher posterior-segment drug levels; chitosan-coated and deformable liposomes improved epithelial uptake, corneal penetration, and retinal exposure.	Moderate–Strong	Enhanced penetration does not necessarily translate into improved antimicrobial activity, and outcomes are highly dependent on liposome composition, size, surface charge, and ocular infection model.	[94]
Electrostatic interaction with bacterial membranes	Positively charged liposomes preferentially bind negatively charged bacterial surfaces, increasing local drug concentration and facilitating antimicrobial action.	Enhanced ocular retention, cellular uptake, and antimicrobial efficacy observed with cationic and elastic liposomal systems.	Moderate	Excessive positive surface charge may improve bacterial interaction but can increase cytotoxicity and reduce ocular tolerability.	[95]
Bacterial membrane destabilization	Cationic lipids disrupt membrane integrity through pore formation, lipid mixing, and increased permeability, restoring susceptibility to antimicrobials.	Liposomal systems containing sesquiterpenes, methylglyoxal–tobramycin, essential oils, nitric oxide, and curcumin–nisin combinations enhanced bacterial killing and biofilm eradication.	Moderate	Membrane-disruptive strategies may show pathogen-dependent effects and require careful optimization to avoid toxicity toward host cells.	[96,97]
Enhanced intracellular antibiotic delivery	Endocytic uptake enables direct delivery of antibiotics into infected host cells, overcoming extracellular degradation and poor cellular penetration.	Targeted and peptide-functionalized liposomes improved intracellular accumulation and eradication of persistent pathogens.	Moderate	Most supporting evidence is derived from in vitro or intracellular infection models, while clinical relevance remains insufficiently validated.	[98,99]
Circumvention of host–cell efflux transporters	Liposomes enter cells via vesicular pathways, avoiding immediate recognition by membrane efflux pumps and improving intracellular drug retention.	Increased intracellular drug persistence and therapeutic efficacy in ocular tissues.	Limited–Moderate	Direct evidence demonstrating efflux pump avoidance by liposomal formulations in ocular pathogens remains limited.	[100,101]

Table 2. Cont.

Mechanism	How Liposomes Counter AMR	Representative Findings	Evidence Level	Key Limitations	Ref.
Overcoming microbial efflux-mediated resistance	Intracellular and localized drug release maintains concentrations above inhibitory levels, overwhelming bacterial efflux systems.	Liposomal antibiotics restored activity against multidrug-resistant pathogens and intracellular infections.	Limited–Moderate	Direct evidence of efflux pump inhibition or bypass in ocular pathogens remains scarce. Most studies are based on in vitro models, and the relative contribution of improved drug delivery versus true resistance reversal remains unclear.	[102,103]
Biofilm penetration and anti-biofilm activity	Liposomes penetrate extracellular polymeric matrices and deliver antimicrobials directly to biofilm-embedded cells.	Improved delivery of anti-biofilm agents and enhanced disruption of resistant microbial communities.	Moderate	Penetration efficiency depends strongly on biofilm maturity, extracellular polymeric substance composition, and pathogen species.	[104,105]
Membrane fusion and direct intracellular access	Fusogenic liposomes merge with bacterial membranes, enabling direct cytoplasmic delivery of antimicrobial agents.	Aptamer-loaded fusogenic liposomes significantly enhanced antibacterial activity against MRSA.	Limited	Fusogenic liposomes remain largely at experimental stages, with limited validation in clinically relevant ocular models.	[106,107]
Reduction in minimum inhibitory concentration (MIC)	Liposomal encapsulation increases drug accumulation at bacterial surfaces and improves antimicrobial potency.	Lower MIC values and restoration of antibiotic susceptibility in resistant strains.	Moderate	Reduced MIC values observed in vitro may not always predict improved therapeutic outcomes in vivo.	[108,109]
Co-delivery of synergistic therapeutics	Liposomes simultaneously transport antibiotics, adjuvants, and resistance-modifying agents to enhance antimicrobial efficacy.	Improved intracellular delivery and synergistic antimicrobial activity through combination therapies.	Moderate	Optimization of drug ratios, loading efficiency, and manufacturing complexity remains challenging.	[110,111]

4. Co-Delivery Strategies in Liposomal Ocular Therapy

Co-delivery strategies in liposomal systems for ocular therapy should be conceptualized based on therapeutic objectives rather than drug classes. In ocular infections and inflammatory diseases, co-encapsulation enables (A) simultaneous control of infection-associated inflammation [115,116]; (B) overcoming antimicrobial resistance through membrane-active mechanisms [117,118]; and (C) optimization of pharmacokinetic and pharmacodynamic synergy between multiple agents [119,120]. This functional classification provides a clearer mechanistic framework for understanding how liposomal platforms enhance therapeutic outcomes in complex ocular pathologies.

4.1. Infection Control with Anti-Inflammatory Synergy

Ocular infections are frequently accompanied by a pronounced inflammatory response that exacerbates epithelial damage, disrupts barrier integrity, and reduces antimicrobial penetration. Consequently, effective therapy requires simultaneous suppression of microbial growth and inflammatory cascades. Liposomal co-delivery systems enable synchronized administration of anti-infective and anti-inflammatory agents at the same pathological site, improving therapeutic efficiency while reducing dosing frequency and drug-induced toxicity [121]. The encapsulation of both drug classes within a single vesicular system ensures co-localized pharmacological action and improved ocular surface residence [122]. Chang et al. demonstrated that dexamethasone–moxifloxacin co-encapsulated liposomes

integrated into a hydrogel matrix provide synergistic antimicrobial and anti-inflammatory effects in infected corneal models. The hydrogel prolongs precorneal retention, while liposomes regulate release kinetics and enhance epithelial penetration, resulting in accelerated epithelial healing and reduced stromal inflammation [123]. Similarly, clinical and preclinical studies on liposomal anti-inflammatory agents, including cyclosporine-based formulations, confirm that modulation of immune responses significantly enhances infection resolution and tissue recovery in ocular surface disease [124].

4.2. Resistance-Breaking Strategies via Membrane-Active Agents

A major limitation in ocular antimicrobial therapy is the emergence of resistant strains and biofilm-associated infections, which significantly reduce drug susceptibility and therapeutic penetration. Membrane-active molecules such as antimicrobial peptides (AMPs) offer a powerful solution due to their ability to disrupt bacterial membranes, destabilize biofilms, and bypass classical resistance mechanisms [125].

When co-encapsulated in liposomal systems, AMPs act synergistically with antibiotics by increasing membrane permeability, enhancing intracellular drug accumulation, and facilitating biofilm penetration. Liposomes additionally protect AMPs from enzymatic degradation in the tear film, thereby prolonging their functional activity on the ocular surface. Silva et al. demonstrated that the AMP LyeTxI-b formulated as an ocular drop exhibits potent activity against resistant bacterial keratitis through direct membrane disruption and electrochemical collapse of bacterial cells [126]. van Gent et al. further showed that lipid-based delivery systems significantly enhance AMP stability and synergistic antibacterial efficacy when combined with conventional antibiotics, primarily by improving peptide–membrane interactions and prolonging residence time [127]. Beyond synthetic systems, endogenous antimicrobial peptides such as defensins also contribute to innate ocular immunity. Nanocarrier-based delivery strategies can amplify these natural defense mechanisms, enhancing both antimicrobial efficacy and epithelial protection [128]. Together, AMP-based co-delivery systems provide a robust strategy for overcoming biofilm-associated [129,130] resistance and improving treatment outcomes in refractory ocular infections [131].

4.3. Multi-Drug Synergy for Pharmacokinetic Optimization

Beyond infection control and resistance modulation, liposomal co-delivery systems can be engineered to optimize pharmacokinetics and synchronize drug exposure profiles. In this context, the primary objective is not necessarily mechanistic synergy at the microbial level but rather coordinated delivery, controlled release, and improved tissue exposure of multiple therapeutic agents [132].

Dual-drug liposomal systems enable precise control over drug ratios, co-localized tissue distribution, and temporally aligned release kinetics. These features are particularly relevant in polymicrobial infections, chronic ocular diseases, and conditions requiring multi-target pharmacological intervention [133]. Singh et al. demonstrated that co-delivery of antibiotics with quorum sensing inhibitors significantly disrupts *Pseudomonas aeruginosa* biofilm formation by simultaneously suppressing bacterial communication and growth pathways [134]. Similarly, azithromycin–nisin co-loaded liposomes have shown enhanced antimicrobial potency and reduced resistance development, highlighting the benefit of combining structurally and mechanistically distinct agents [135]. Further studies have extended this concept to hybrid therapeutic combinations, including natural compound–antibiotic systems (e.g., brazilin–streptomycin), where phytochemicals enhance membrane disruption and efflux pump inhibition [136]. In addition, dual-drug chemotherapeutic liposomes such as cytarabine–daunorubicin systems provide a well-established model for synchronized

intracellular drug release, reduced systemic toxicity, and optimized pharmacodynamic synergy, principles that are directly translatable to ocular drug delivery [137] (see Figure 3).

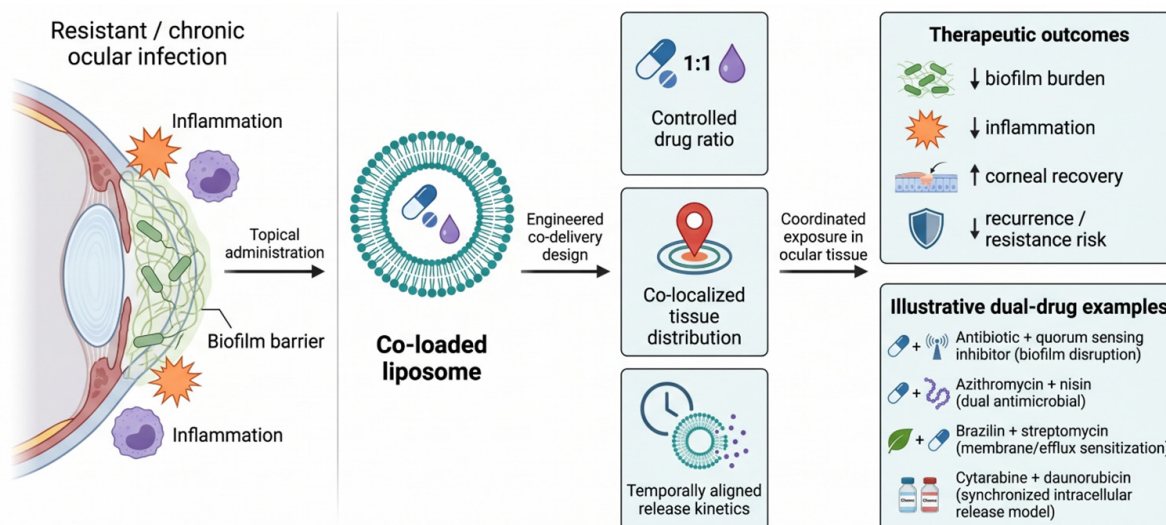


Figure 3. Liposomal co-delivery strategies to combat resistant ocular infections and associated inflammation. Topical administration of co-loaded liposomes carrying combination therapies (antibiotic + anti-inflammatory, antibiotic + AMP, or dual antimicrobials) to target biofilm-protected ocular infections. This multi-pronged approach exerts a synergistic effect that reduces bacterial load and inflammation, accelerates corneal healing, and mitigates the risk of drug resistance and infection recurrence. Created in BioRender. Hajareh Haghighi, F. (2026) <https://BioRender.com/ik6lg1k> (accessed on 7 June 2026).

5. Liposomes as a Strategy for Treating Biofilm-Associated Ocular Infections

Biofilms represent one of the most formidable barriers to effective antimicrobial therapy in ocular infections due to their highly organized extracellular polymeric substance (EPS) matrix and the profound physiological heterogeneity that develops within these microbial communities. The EPS barrier, composed of polysaccharides, extracellular DNA (eDNA), proteins, and lipids, forms a dense, hydrated, and negatively charged scaffold that anchors microorganisms to ocular surfaces, contact lenses, intraocular lenses, and damaged epithelium. Beyond providing structural integrity, the matrix actively regulates nutrient diffusion, waste exchange, and intercellular signaling, generating a dynamic microenvironment that promotes microbial survival under antimicrobial stress [138]. Importantly, this dense matrix creates significant diffusion resistance, physically impeding antimicrobial penetration while simultaneously binding, sequestering, or inactivating therapeutic agents before they can reach deeper biofilm layers.

Within the biofilm architecture, steep gradients of oxygen, nutrients, and pH produce pronounced phenotypic heterogeneity. Surface-associated cells remain metabolically active and proliferative, whereas cells embedded in deeper regions adopt dormant or slow-growing phenotypes that are intrinsically less susceptible to antibiotics targeting active cellular processes, including β -lactams and fluoroquinolones [139]. A defining component of this heterogeneity is the emergence of persister cells, dormant phenotypic variants capable of surviving extremely high antibiotic concentrations despite lacking heritable genetic resistance. Once antimicrobial pressure subsides, these persister populations can repopulate the biofilm, driving chronic, recurrent, and treatment-refractory ocular infections. In parallel, biofilm-associated efflux activity and enhanced horizontal gene transfer further amplify antimicrobial tolerance and facilitate the dissemination of resistance determinants.

Despite the central role of biofilms in antimicrobial tolerance and treatment failure, it is important to distinguish biofilm-associated tolerance from genetically mediated antimicrobial resistance. Biofilm formation can transiently reduce antimicrobial susceptibility through limited penetration, altered metabolic states, and the emergence of persister populations, whereas AMR involves heritable genetic adaptations such as target modification, enzymatic drug inactivation, and efflux-mediated resistance [140,141]. These mechanisms frequently coexist in ocular infections and may reinforce each other, creating complex therapeutic challenges. Therefore, successful liposomal strategies should not only improve antimicrobial penetration into biofilm structures but also be evaluated according to their ability to address specific resistance mechanisms, biofilm-associated physiological states, and pathogen-dependent barriers [142,143]. Quantitative comparisons from representative studies demonstrate that liposomal systems can substantially improve antimicrobial activity against biofilm-associated pathogens, although the magnitude of benefit varies depending on the pathogen, biofilm model, and liposomal design. For example, antibiotic-loaded liposomes have been reported to achieve several-fold increases in antimicrobial efficacy and greater biofilm reduction compared with free drugs [144,145], whereas surface-engineered systems such as chitosan-coated or cationic liposomes have demonstrated enhanced penetration and retention within biofilm matrices [146,147]. In fungal and bacterial biofilm models, liposomal or lipid-based nanocarriers have produced approximately 30–70% reductions in biofilm biomass and improved antimicrobial delivery [148,149]; however, direct comparison among studies remains challenging because of differences in biofilm maturity, experimental conditions, bacterial or fungal species, and outcome measurements.

Liposomal drug delivery systems offer a highly promising strategy for overcoming these interconnected barriers by enhancing penetration through the EPS matrix, protecting antimicrobials from inactivation, and sustaining therapeutic concentrations within the biofilm microenvironment. Owing to their nanoscale dimensions, tunable surface properties, and biomimetic lipid composition, liposomes can diffuse more effectively through hydrated biofilm matrices than free drugs [150]. Surface engineering approaches, including cationic and chitosan-coated liposomes, further improve interaction with negatively charged biofilm components and ocular tissues, enhancing retention and penetration into deeper microbial layers. Once internalized within the biofilm structure or microbial cells, liposomes provide controlled intracellular drug release, maintaining prolonged antimicrobial exposure capable of targeting both metabolically active bacteria and dormant persister populations. However, the extent of biofilm penetration and antimicrobial enhancement is highly dependent on liposomal characteristics, including particle size, surface charge, lipid composition, membrane rigidity, and drug release kinetics [151,152]. While cationic and deformable liposomes may improve interaction with negatively charged biofilm components, excessive adhesion to the outer biofilm layer can limit diffusion into deeper regions [153,154]. Similarly, enhanced penetration observed in simplified *in vitro* biofilm models may not fully represent the complex extracellular matrix composition and physiological conditions encountered in clinical ocular infections [155,156].

Recent studies highlight the translational significance of these approaches. Vicario de la Torre et al. demonstrated that liposomal formulations designed to mimic tear film components interact efficiently with ocular surface structures, emphasizing the importance of matrix-responsive carrier design for biofilm penetration [157]. Lu and colleagues showed that liposome–cyclodextrin nanocomposites preserve structural integrity throughout ocular transport, supporting their ability to withstand matrix-associated diffusion barriers [158]. Similarly, Gu et al. reported that chitosan-coated flexible liposomes significantly enhance ocular penetration and retention, illustrating how surface modification can overcome matrix-mediated resistance [159]. Gentili et al. further demonstrated that

ozonated oil liposome eye drops reduce biofilm formation and limit the emergence of antibiotic-resistant bacteria [160], while Obuobi et al. showed that peptide-based nanogels effectively penetrate biofilms and eradicate bacterial keratitis despite tolerance-associated barriers [161]. Additional studies on fungal biofilm resilience, resistome profiling of ocular pathogens, and nanocarrier-based ocular delivery systems further underscore the complexity of biofilm-associated tolerance and the necessity for advanced therapeutic platforms [162] (see Figure 4).

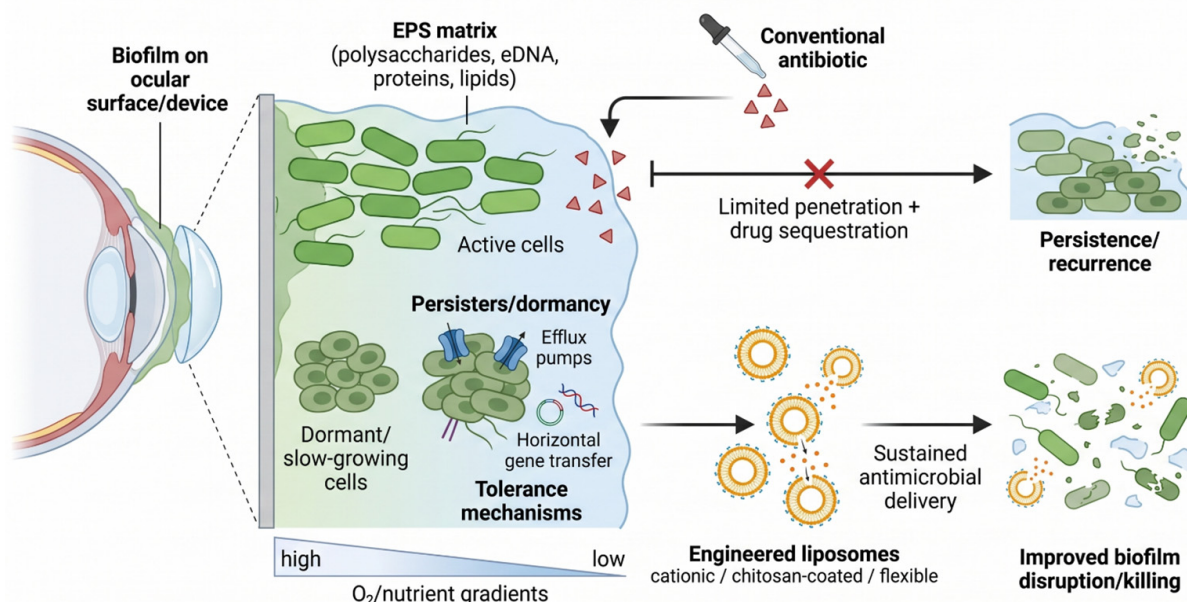


Figure 4. Comparison of conventional antibiotics and engineered liposomes against tolerant ocular biofilms. Microenvironment of an ocular biofilm showing the EPS matrix barrier and internal O₂ nutrient gradients that promote dormant persister cells. While conventional free therapies are halted by limited penetration and drug sequestration, engineered liposomal formulations (including cationic, chitosan-coated, or flexible variants) bypass these defensive structures to achieve sustained local drug delivery and enhanced biofilm killing. Created in BioRender. Hajareh Haghighi, F. (2026) <https://BioRender.com/ik6lg1k> (accessed on 7 June 2026).

5.1. Surface Modification Strategies

Surface engineering of liposomes represents a powerful strategy to enhance their penetration, distribution, and antimicrobial activity within ocular biofilms, enabling them to overcome the formidable physical and biochemical barriers imposed by the extracellular polymeric substance (EPS) matrix [163]. PEGylation is one of the most widely adopted approaches: polyethylene glycol (PEG) creates a hydrophilic steric barrier that reduces nonspecific binding to EPS components, minimizes protein corona formation, and improves nanoparticle mobility. Tavakoli et al. demonstrated that PEGylated lipid nanoparticles exhibit reduced protein adsorption and enhanced diffusion in vitreous-like environments, illustrating how steric stabilization supports deeper penetration into hydrated biological matrices [164]. In contrast, cationic surface modification enhances electrostatic interactions with negatively charged biofilm components and bacterial membranes, promoting strong initial adhesion and high local drug concentration; however, excessive positive charge can hinder deeper penetration due to strong binding at the biofilm periphery. Dai and colleagues showed that charge-governed essential-oil liposomes effectively disrupt *Listeria monocytogenes* biofilms, underscoring the importance of tuning surface charge to balance penetration and retention [165].

Although surface modification strategies substantially improve liposomal performance against biofilms, no single approach provides an optimal solution for all ocular infection scenarios. PEGylation primarily enhances colloidal stability and reduces nonspecific interactions, thereby improving diffusion through hydrated biological barriers [166,167]; however, excessive PEG density may reduce cellular uptake and decrease interactions with microbial surfaces. In contrast, cationic modification promotes strong electrostatic association with negatively charged bacterial membranes and biofilm components, increasing local drug accumulation [168,169], but excessive positive charge may induce cytotoxicity, accelerate clearance, or restrict penetration by trapping liposomes within superficial biofilm layers. Ligand-targeted systems offer improved pathogen specificity and reduced off-target interactions [170,171], yet their clinical translation may be limited by the availability of suitable targets, manufacturing complexity, and variability among bacterial species. Stimulus-responsive and enzyme-functionalized liposomes provide additional advantages by enabling site-specific activation or matrix degradation [172], although their effectiveness depends on the presence of appropriate biological triggers and remains largely validated in experimental models.

More advanced strategies include ligand-targeted liposomes, where lectins, antibodies, or bacterial-binding peptides are conjugated to the surface to promote selective accumulation at biofilm sites. Ogawa et al. developed *Staphylococcus aureus*-directed liposomes with enhanced affinity and antibacterial activity, demonstrating the potential of pathogen-specific targeting [173]. Enzyme-functionalized liposomes represent another innovative approach: DNase- or protease-decorated carriers degrade EPS components, facilitating deeper penetration and improving antimicrobial efficacy. Xia et al. reported that DNase-functionalized nanocarriers significantly enhance biofilm disruption and drug delivery against *Enterococcus faecalis* [174]. Stimulus-responsive systems further expand functional capabilities: pH-responsive or charge-reversal liposomes alter their surface properties upon encountering acidic or enzyme-rich biofilm microenvironments, improving penetration and enabling controlled drug release. Li et al. demonstrated that pH-responsive charge-reversal liposomes achieve superior penetration and multimodal synergistic therapy in bacterial infections [175]. Additional innovations include ultrasound-activated liposomes [176], mucoadhesive lignin-liposomes for targeting mucosal biofilms [177], and oxygen-supplying liposomes that enhance mechano-sonodynamic therapy [178].

Surface modification strategies significantly expand the functional capabilities of liposomes by improving their ability to interact with, penetrate, and respond to complex ocular biofilm environments. However, the clinical value of these approaches depends on achieving an appropriate balance between biofilm penetration, antimicrobial retention, ocular safety, and manufacturing feasibility. While engineered surfaces can overcome specific biological barriers, increased formulation complexity may introduce challenges related to reproducibility, stability, scalability, and regulatory approval [179,180]. Future studies should therefore focus not only on demonstrating enhanced biofilm disruption but also on identifying which surface engineering approaches provide consistent therapeutic advantages across clinically relevant ocular infection models.

5.2. Liposomal Delivery of Anti-Biofilm Agents

Liposomal anti-biofilm strategies can be broadly classified according to their therapeutic targets, including direct microbial killing, degradation of the biofilm matrix, interference with microbial communication, and enhancement of host–microbe interactions [181]. Antibiotic-loaded liposomes primarily aim to restore antimicrobial exposure within protected biofilm niches [182], whereas enzyme-based systems such as DNase-functionalized liposomes target the structural components of the extracellular polymeric substance (EPS).

Quorum sensing inhibitor (QSI)-loaded formulations act through anti-virulence mechanisms by preventing biofilm maturation and reducing pathogenic behavior [183], while antimicrobial peptide (AMP)-based systems provide membrane-active activity against tolerant microbial populations. However, the effectiveness of each approach depends on biofilm composition, pathogen species, infection stage, and the specific resistance mechanisms involved.

5.2.1. Antibiotics

Liposomal encapsulation of antibiotics represents one of the most established and effective strategies for treating biofilm-associated ocular infections, directly addressing the structural and physiological barriers that limit the efficacy of conventional therapies. By incorporating antimicrobial agents within lipid bilayers, liposomes enhance drug stability, protect antibiotics from enzymatic or chemical degradation, and improve their distribution throughout the dense extracellular polymeric substance (EPS) matrix [184]. Encapsulation enables higher local drug concentrations and sustained release, both of which are essential for overcoming biofilm-associated tolerance mechanisms such as restricted penetration, slow-growing subpopulations, and persister cells [185]. Importantly, liposomes can restore the activity of antibiotics that have become less effective due to resistance by facilitating their access to protected bacterial niches and increasing intracellular accumulation. Tufail et al. demonstrated that liposomal tobramycin and ceftazidime exhibit markedly enhanced activity against *Pseudomonas aeruginosa*, confirming that liposomal delivery improves penetration and potency against multidrug-resistant Gram-negative pathogens. The optimized liposomes increased antibacterial efficacy by 2–3-fold compared with free antibiotics, reducing viable *P. aeruginosa* counts by >3 log units in resistant clinical isolates. Time-kill assays showed sustained bactericidal activity for up to 24 h, whereas free drugs lost activity rapidly. The liposomal formulations also improved biofilm penetration, achieving 60–70% greater bacterial reduction within mature biofilms. These results validate liposomes as advanced nanocarriers capable of boosting antibiotic delivery and overcoming permeability-related resistance mechanisms in *P. aeruginosa* infections [186]. Although these findings demonstrate the potential of liposomal antibiotics to improve biofilm-associated antimicrobial activity, most available evidence remains based on laboratory or preclinical models [182]. Differences in biofilm maturation protocols, bacterial strains, infection severity, and outcome measurements make direct comparison between studies challenging and highlight the need for standardized evaluation frameworks. Ireland et al. showed that inhaled liposomal ciprofloxacin provides robust protection against lethal tularemia in the common marmoset, demonstrating how liposomal encapsulation enhances pharmacokinetics, tissue distribution, and therapeutic efficacy even at reduced doses. A single inhaled dose of liposomal ciprofloxacin achieved lung ciprofloxacin concentrations >100-fold higher than free drug and maintained therapeutic levels for over 24 h, reflecting markedly prolonged pulmonary retention. In the lethal *Francisella tularensis* challenge model, liposomal ciprofloxacin conferred 100% survival, whereas untreated controls succumbed rapidly and free ciprofloxacin offered only partial protection. These results confirm that liposomal delivery dramatically improves drug exposure and protective efficacy against intracellular respiratory pathogens, even when administered non-invasively [187]. Huo et al. reported that cationic liposome-fused endolysin Lys40 effectively overcomes the Gram-negative outer-membrane barrier and markedly improves survival outcomes in *Salmonella*-infected chicks. Fusion of Lys40 with cationic liposomes enhanced bactericidal activity by 2–3-fold compared with free endolysin, enabling efficient membrane permeabilization and rapid bacterial killing. In vivo, treatment with the liposomal Lys40 formulation increased survival to 80–90%, whereas untreated infected controls showed near-complete mortality. The formulation

also significantly reduced bacterial loads in intestinal and systemic tissues, confirming that liposomal fusion potentiates endolysin activity otherwise limited by the protective outer membrane of Gram-negative pathogens [188]. Supporting studies further demonstrate the versatility of liposomal antibiotic delivery, including cholesterol-modulated liposomes with improved stability under stress conditions [189], microneedle-mediated delivery of amikacin-liposomes for systemic infections [190], enzyme-responsive hydrogels that trigger antibiotic release at infected sites [191], and multifunctional liposomes that combine antimicrobial, antioxidant, and mucoadhesive properties for enhanced ocular retention [192]. Liposomal systems have also been applied to natural antimicrobials and immunoglobulins, broadening their utility beyond classical antibiotics [193,194].

5.2.2. Enzymes (DNase)

Enzymatic degradation of the biofilm matrix represents a highly effective strategy for overcoming the structural tolerance that protects microbial communities in ocular infections, and liposomal delivery systems provide an ideal platform for implementing this approach. Extracellular DNA (eDNA) is a critical structural component of the extracellular polymeric substance (EPS), contributing to adhesion, mechanical stability, and biofilm maturation [195,196]. DNase specifically targets and degrades eDNA, weakening the matrix architecture, increasing porosity, and enhancing the penetration of antimicrobial agents into deeper biofilm layers [197,198]. However, free DNase is rapidly inactivated by proteases, ionic conditions, and host-derived factors, limiting its therapeutic utility. Liposomal encapsulation protects DNase from degradation, prolongs its enzymatic activity, and enables controlled release directly within the biofilm microenvironment, ensuring that matrix disruption occurs precisely where it is most needed. Negari et al. demonstrated that DNase-functionalized nanocarriers significantly disrupt *Enterococcus faecalis* biofilms and enhance antimicrobial efficacy, validating enzyme-assisted matrix degradation as a synergistic therapeutic approach [199]; Liu et al. provided a biophysical perspective on targeted liposomal delivery, emphasizing how nanoscale carriers can be engineered to transport enzymes efficiently through dense biological barriers such as biofilms [171]; and Tavakoli et al. showed that nanoparticle surface properties, including protein corona formation, critically influence diffusion in ocular environments, underscoring the importance of stabilizing enzyme-loaded liposomes for effective penetration [164]. Supporting studies further illustrate the broader relevance of enzyme-enabled liposomal systems, including liposomes designed for nucleic-acid transport [200], CRISPR-loaded liposomes for targeted genome editing, and formulations engineered to enhance intracellular delivery or overcome complex biological barriers through surface modification [201]. This approach directly addresses the physical and biochemical barriers that underlie biofilm-associated tolerance in ocular infections and represents a key advancement in next-generation anti-biofilm therapy. However, the clinical applicability of DNase-loaded liposomal systems remains dependent on several unresolved factors, including enzyme stability during storage, preservation of catalytic activity after encapsulation, penetration into mature biofilms, and compatibility with ocular tissues [144]. Moreover, because extracellular DNA represents only one component of the EPS matrix, DNase treatment alone may be insufficient against highly organized biofilms containing polysaccharides, proteins, and other protective structures.

5.2.3. Quorum Sensing Inhibitors

Quorum sensing (QS) is a density-dependent communication system that orchestrates biofilm formation, virulence factor production, and antimicrobial tolerance in key ocular pathogens such as *Pseudomonas aeruginosa* and *Candida albicans*. Quorum sensing inhibitors (QSIs) are molecules that disrupt QS by blocking signal synthesis (e.g., inhibition

of AHL or AIP production), preventing signal binding to transcriptional regulators such as LasR, RhIR, or LuxR, degrading or sequestering signaling molecules, or interfering with downstream gene activation. Unlike antibiotics, QSIs do not kill bacteria directly; instead, they disarm pathogens by suppressing virulence and weakening biofilm architecture, making bacteria more susceptible to host immunity and antimicrobial therapy [202]. This anti-virulence mechanism reduces selective pressure for resistance and is therefore considered a promising next-generation strategy for combating chronic and resistant infections [203]. Liposomes provide an effective platform for delivering QSIs directly into the biofilm microenvironment, ensuring high local concentrations capable of interfering with signaling molecules such as acyl-homoserine lactones (AHLs) and autoinducing peptides (AIPs). By blocking QS, liposomal QSIs prevent biofilm maturation, suppress virulence, and potentiate the activity of co-administered antimicrobials, addressing a fundamental regulatory mechanism of biofilm-associated resistance. Hallan et al. showed that QSI-loaded nanosystems effectively modulate quorum-sensing pathways by delivering inhibitors to pericellular and intracellular sites of AHL/AIP accumulation. Their lipid nanocarriers achieved 70–80% encapsulation, reduced pyocyanin by 40–50%, and decreased biofilm biomass by 30–40%, with confocal imaging confirming intracellular uptake [204]. Bandara et al. extended this approach to fungi, demonstrating that QSI-infused liposomes suppressed *Candida albicans* biofilms by 55–70%, reduced hyphal density by 40%, and downregulated adhesion and morphogenesis genes by 50%, indicating improved QSI stability and penetration into dense hyphal networks [205]. Lu et al. further showed that polymeric QSI nanocarriers suppressed *P. aeruginosa* virulence, reducing pyocyanin by 50–60%, lowering biofilm biomass by 40%, and decreasing elastase activity, with combination therapy enhancing bacterial killing and reducing oxidative epithelial damage [206]. Tiwari et al. detailed how QS regulates efflux pumps, biofilm maturation, and metabolic dormancy in Gram-negative ocular pathogens, collectively reducing intracellular antibiotic levels and promoting persistence, and highlighted that QS disruption, particularly via nanocarrier-delivered inhibitors can restore antimicrobial susceptibility [207]. Natural-product-based QS inhibitors, such as *Hedera helix* saponins, have demonstrated anti-keratitis potential by simultaneously modulating PI3K/Akt and OPRL pathways, illustrating how plant-derived molecules can serve as dual-function anti-virulence and immunomodulatory agents [208]. Vetrivel et al. identified small-molecule LasR inhibitors that reduced biofilm biomass by 55–70%, decreased pyocyanin by 40–60%, and lowered elastase/protease activity by 35–50%, impairing biofilm maturation, reducing EPS accumulation, and weakening QS-driven tolerance mechanisms [209].

5.2.4. Antimicrobial Peptides

Antimicrobial peptides (AMPs) are components of the innate immune system and exhibit broad-spectrum activity against bacteria, including resistant strains. Their mechanism of action typically involves disruption of microbial membranes, making them particularly effective against biofilm-associated cells [210]. However, AMPs are often limited by instability and rapid degradation in biological environments. Liposomal encapsulation enhances their stability, protects them from enzymatic breakdown, and enables controlled delivery to the biofilm. When combined with antibiotics, AMPs can exert synergistic effects, further improving therapeutic outcomes (Figure 5).

The major liposomal anti-biofilm strategies discussed above target distinct but interconnected components of biofilm-associated tolerance, including microbial viability, extracellular matrix integrity, signaling pathways, and membrane stability. A comparative overview of these approaches, highlighting their therapeutic targets, advantages, limitations, and current developmental status, is provided in Table 3.

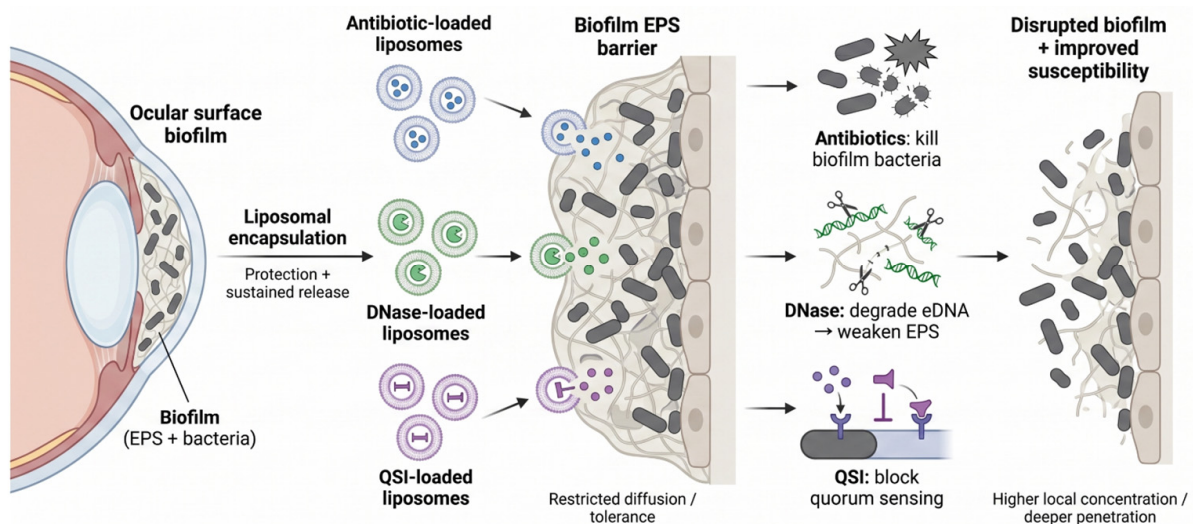


Figure 5. Liposomal encapsulation strategies targeting the ocular biofilm microenvironment. Overview of therapeutic approaches using liposomes to deliver antibiotics, DNase, and quorum sensing inhibitors (QSIs). Encapsulation protects these agents and facilitates their penetration past the EPS diffusion barrier, where they act to kill resident bacteria, degrade eDNA matrix components, and halt cell-to-cell signaling, ultimately disrupting the biofilm structure. Created in BioRender. Hajareh Haghighi, F. (2026) <https://BioRender.com/ik6lg1k> (accessed on 7 June 2026).

Table 3. Comparison of Liposomal Anti-Biofilm Strategies for Ocular Infections.

Strategy	Main Target	Major Advantages	Main Limitations	Development Stage	Ref.
Antibiotic-loaded liposomes	Bacterial cells and persisters	High local concentration, sustained release	Resistance may persist, limited deep penetration in mature biofilms	Preclinical	[145,146,182]
DNase-loaded liposomes	eDNA/EPS matrix	Improves matrix disruption and penetration	EPS contains multiple components beyond eDNA	Experimental	[144]
QSI-loaded liposomes	Biofilm signaling pathways	Reduces virulence without strong selective pressure	Limited clinical validation	Experimental	[184]
AMP-loaded liposomes	Microbial membrane	Broad-spectrum activity, potential against resistant strains	Stability and toxicity concerns	Preclinical	[150,211]
Combination systems	Multiple targets	Addresses several tolerance mechanisms simultaneously	Increased formulation complexity	Early development	[183,212]

6. Preclinical Validation

Preclinical evaluation of liposomal ocular drug delivery systems spans *in vitro*, *ex vivo*, and *in vivo* models, collectively demonstrating improved ocular retention, enhanced tissue penetration, and superior antimicrobial efficacy against both planktonic and biofilm-associated infections.

6.1. *In Vitro* and *Ex Vivo* Corneal Models

In vitro and *ex vivo* models consistently show that liposomal encapsulation enhances ocular drug performance by overcoming key anatomical and physiological barriers of the ocular surface. Rapid tear turnover and limited precorneal residence time significantly restrict conventional topical therapies; however, liposomes act as drug reservoirs that enable sustained release and prolonged retention within the tear film, thereby facilitating continuous diffusion into deeper ocular tissues [213].

Corneal permeability studies further confirm that the epithelium–stroma barrier significantly limits passive diffusion of free drugs due to its dual lipophilic and hydrophilic nature. Liposomal nanocarriers improve transcorneal transport by promoting membrane interaction and enhancing partitioning across epithelial layers. Surface-modified systems, including cationic, fusogenic, and mucoadhesive liposomes, further extend precorneal residence time and sustain concentration gradients that drive drug transport across epithelial tight junctions, resulting in increased intraocular tissue drug levels compared with conventional formulations. Importantly, the performance of liposomal formulations in corneal models is highly dependent on their physicochemical design. Conventional liposomes generally provide excellent biocompatibility and drug protection but often show limited retention and penetration compared with engineered systems [214]. Cationic liposomes typically demonstrate enhanced epithelial interaction and cellular uptake due to electrostatic attraction with negatively charged ocular surfaces [169]; however, excessive positive charge may increase cytotoxicity and reduce tolerability. Deformable and fusogenic liposomes can improve corneal penetration by increasing membrane flexibility or promoting direct lipid exchange with cellular membranes [215], although their structural instability and potential for drug leakage remain important limitations. PEGylated liposomes improve colloidal stability and prolong residence time by reducing aggregation and nonspecific interactions [168], but excessive PEG coverage may decrease cellular uptake and membrane fusion. Ex vivo models of ocular infection also demonstrate that liposomal systems interfere with early pathogenic events. By reducing bacterial adhesion to corneal epithelial surfaces, these systems limit the initiation of biofilm formation and early colonization, thereby attenuating disease progression at its earliest stages [216].

6.2. In Vivo Ocular Infection Models

The rabbit keratitis model remains the most widely used and clinically relevant pre-clinical in vivo system because of its anatomical and physiological similarities to the human eye. Across bacterial, fungal, and protozoal infection models, numerous liposomal formulations have demonstrated improved therapeutic outcomes compared with free-drug formulations [217]; however, the magnitude of benefit varies considerably depending on the pathogen, drug properties, liposomal composition, administration route, and infection model used. In bacterial keratitis, liposomal antibiotics such as ciprofloxacin and sustained-release norvancomycin formulations have been associated with reduced inflammatory responses, decreased stromal infiltration, and accelerated corneal epithelial healing. In fungal keratitis, liposomal amphotericin B and other lipid-based antifungal systems have shown enhanced suppression of fungal growth and reduced risk of corneal perforation in experimental models. Similarly, nucleic acid-based liposomal formulations, including siRNA-loaded systems, have demonstrated reduced protozoal burden in experimental *Acanthamoeba* keratitis, suggesting the versatility of liposomal platforms across multiple ocular pathogens [218]. Pharmacokinetic studies further indicate that liposomal encapsulation can prolong drug retention within corneal tissues while reducing systemic exposure and peak-related toxicity. Sustained intraocular drug concentrations have been reported following both topical and subconjunctival administration of formulations such as moxifloxacin liposomes and liposomal amphotericin B. Encapsulation efficiency, lipid composition, particle size, and surface characteristics all substantially influence drug release kinetics and therapeutic performance [219]. Nevertheless, improved pharmacokinetic behavior has not consistently translated into superior therapeutic efficacy in all preclinical studies. For example, Su et al. reported that although the liposomal formulation achieved prolonged ocular retention compared with the conventional formulation, the reduction in microbial burden and clinical keratitis scores was not significantly different [220]. Likewise, Kuang et al.

observed only modest improvements in corneal healing despite enhanced drug residence time, indicating that sustained drug exposure alone was insufficient to produce substantially greater antimicrobial efficacy. These findings suggest that therapeutic outcomes are influenced not only by ocular drug retention but also by factors such as drug penetration into infected stromal tissue, pathogen susceptibility, biofilm formation, host inflammatory responses, and the stage and severity of infection [221]. Furthermore, differences in animal species, inoculum size, microbial strain, disease severity, dosing regimen, treatment duration, and outcome assessment methods complicate direct comparison among studies and may account for the variability in reported efficacy. Additional translational challenges include formulation instability during storage, premature drug leakage, physicochemical changes following administration, sterilization difficulties, and the challenges associated with reproducible large-scale manufacturing, all of which remain important barriers to clinical translation [222].

7. Disease-Specific Applications

7.1. Bacterial Keratitis

Bacterial keratitis remains one of the most vision-threatening ocular infections worldwide, driven predominantly by *Pseudomonas aeruginosa*, *Staphylococcus aureus* (including MRSA), coagulase-negative staphylococci, and region-specific pathogens such as *Streptococcus pneumoniae* and Gram-negative Enterobacterales. Predisposing factors, including contact lens wear, trauma, ocular surface disease, and prior corticosteroid use, accelerate stromal necrosis and increase the risk of corneal perforation [223]. Rising antimicrobial resistance, reflected in increasing fluoroquinolone and cephalosporin MICs, global MRSA dissemination, and the emergence of multidrug-resistant *P. aeruginosa* (including carbapenem- and aminoglycoside-resistant strains), has eroded the reliability of empirical monotherapy and renewed reliance on fortified combination regimens. Within this therapeutic landscape, liposomal and liposome-like nanocarriers have gained prominence for their ability to enhance corneal penetration, prolong ocular residence, and modulate interactions with biofilms [224].

In vitro studies, including microtiter biofilm assays, confocal microscopy, viable cell counts, and contact-lens biofilm systems, consistently show that cationic, fusogenic, and antibiotic-loaded liposomes increase drug accumulation within biofilm matrices, reduce biomass, and suppress resistant subpopulations. Translational in vivo evidence from rabbit keratitis, the gold-standard model due to its anatomical similarity to the human cornea, reinforces these mechanistic insights. Feghhi et al. reported that liposomal ciprofloxacin achieves higher corneal concentrations, prolonged retention, and superior microbial eradication compared with free drug, resulting in faster epithelial closure and reduced stromal infiltration [225], while Al-Joufi and colleagues demonstrated that colloidal lipid-based ciprofloxacin carriers markedly enhance ocular bioavailability in post-surgical infection models [226]. Clinical translation is beginning to emerge: a 2025 prospective study by Aleksieieva and Sakovych showed that a liposomal ozone-based solution (LOBS), combined with adjunctive hyperbaric oxygenation, accelerated epithelial recovery, reduced inflammation, and improved visual acuity even in infections caused by fluoroquinolone-reduced-susceptibility strains [227], they also studied ozonated-oil liposomes, which exhibit potent antimicrobial, anti-adhesive, and anti-biofilm activity against *P. aeruginosa* and *S. aureus*, including strains with documented fluoroquinolone or macrolide resistance, decreasing bacterial adhesion to human corneal epithelial cells and interfering with early host–pathogen interactions [228].

Although not strictly liposomal, related nanocarrier systems, such as the nucleic-acid–peptide nanogels described by Chen et al., demonstrate enhanced activity against

drug-resistant *P. aeruginosa* and *S. aureus*, reduced corneal opacity, and lower bacterial burden in experimental keratitis, reinforcing the broader rationale for encapsulation-based strategies [229]. Collectively, these findings indicate that liposomal formulations are particularly promising in settings where resistance patterns limit the utility of conventional topical antibiotics. By tailoring lipid composition, surface charge, and deformability, liposomal systems can be engineered to interact with bacterial membranes and biofilms while sustaining therapeutic drug levels in the tear film and corneal tissue. Early clinical data with ozone-based liposomal eyedrops suggest improved outcomes and a potential role in mitigating the selection of resistant strains, although larger randomized trials directly comparing liposomal antibiotics or ozone-based systems with fortified regimens are still needed to define their optimal place in keratitis treatment algorithms.

7.2. Fungal Keratitis

Fungal keratitis is a severe, vision-threatening corneal infection most frequently caused by filamentous fungi such as *Fusarium* and *Aspergillus* in tropical and subtropical regions, whereas *Candida* species predominate in eyes with chronic surface disease, prior keratoplasty, or prolonged corticosteroid exposure. Classic risk factors, including trauma with vegetative matter, agricultural exposure, and delayed presentation, contribute to fulminant disease [230]. The pathogen profile is clinically decisive: filamentous fungi exhibit deep stromal invasion and respond poorly to conventional topical agents, with many *Fusarium* isolates demonstrating intrinsic or acquired azole resistance, while natamycin, despite being first-line therapy, shows limited corneal penetration and requires intensive dosing [231]. Yeast-like fungi such as *Candida albicans* and non-*albicans* species can form biofilm-like structures and display reduced susceptibility to fluconazole, voriconazole, and even amphotericin B. These pharmacodynamic and pharmacokinetic limitations have driven growing interest in liposomal antifungal formulations. Compared with conventional antifungal therapies, liposomal formulations provide several pharmacological advantages but also introduce important translational challenges. Conventional natamycin remains the current first-line treatment for filamentous fungal keratitis because of its established clinical efficacy and broad activity against *Fusarium* species; however, its poor aqueous solubility, limited stromal penetration, and requirement for frequent administration can reduce therapeutic efficiency in deep or severe infections. Similarly, conventional amphotericin B exhibits potent antifungal activity but is limited by poor ocular tolerability, formulation instability, and dose-related epithelial toxicity [232]. Liposomal encapsulation can improve drug solubility, protect antifungal molecules from degradation, enhance corneal retention, and reduce direct exposure of ocular tissues to toxic free drug concentrations. Nevertheless, liposomal antifungal systems have not consistently demonstrated superiority across all infection models, and most evidence remains derived from experimental studies rather than large clinical trials. Therefore, while liposomal formulations represent a promising strategy to overcome pharmacokinetic limitations of conventional antifungals, their clinical adoption will depend on demonstrating reproducible efficacy, long-term safety, manufacturing feasibility, and clear therapeutic advantages over established treatments.

Liposomal amphotericin B, long established in systemic mycoses, has been adapted for ocular use to enhance stromal penetration while reducing epithelial toxicity by shielding the ocular surface from the drug's detergent-like effects. Liposomal natamycin and voriconazole have also been developed to improve solubility, stromal penetration, and residence time. Sathe et al. demonstrated that nanomicelle-enabled natamycin significantly improved corneal penetration and antifungal efficacy across in vitro, ex vivo, and in vivo *Fusarium* keratitis models, outperforming conventional suspensions while maintaining epithelial safety [233]. Complementary work by Cai, Youssef, and Majumdar showed

that an optimized topical natamycin suspension achieved higher corneal drug levels and improved therapeutic outcomes in experimental fungal keratitis [234], while Velpandian and colleagues developed a water-soluble natamycin formulation (Natsol, Llanidloes, UK) that enhanced ocular bioavailability and reduced dosing burden [235]. Clinical relevance is further supported by Reddy et al., who found that combination therapy with natamycin and voriconazole improved outcomes in mild-to-moderate fungal keratitis compared with monotherapy [236].

Beyond azoles and polyenes, innovative nanocarrier systems continue to expand therapeutic possibilities. Rohita et al. demonstrated that a cell-penetrating-peptide natamycin conjugate markedly enhanced in vivo antifungal activity and reduced corneal opacity in experimental keratitis [237], while Ahmed and co-workers developed corneal-targeted fenticonazole-loaded novasomes that improved antifungal efficacy against ocular *Candida* infections [238]. Additional nanotechnology-based approaches, including microneedle-delivered fluconazole systems as in the research of Suriyaamporn et al. [239] and the comprehensive nanoformulations reviewed by Abd-Elmonem and colleagues [240], reinforce the translational potential of encapsulation strategies. Even alternative liposomal therapeutics, such as rapamycin-loaded liposomes evaluated by Zhang et al. for fungal keratitis in rats, demonstrate the versatility of lipid-based carriers in modulating corneal inflammation and fungal burden [241].

7.3. Viral Keratitis

Viral keratitis is dominated by a small group of DNA viruses, primarily herpes simplex virus type 1 (HSV-1), with varicella-zoster virus (VZV) and, less commonly, adenoviruses, whose clinical behavior is shaped more by latency, neurotropism, and host immune response than by species diversity. HSV-1 establishes lifelong latency in the trigeminal ganglion, leading to recurrent epithelial keratitis driven by viral reactivation and stromal keratitis mediated by immune responses to persistent antigens [242]. Antiviral resistance, although less common than in bacterial keratitis, is clinically significant: Boucher and colleagues describe how mutations in viral thymidine kinase or DNA polymerase reduce susceptibility to acyclovir, particularly in immunocompromised patients or those with prolonged antiviral exposure [243], while case series by De Clerck et al. highlight the growing recognition of acyclovir-resistant epithelial keratitis in real-world settings [244]. VZV keratitis may exhibit partial acyclovir refractoriness, though true resistance remains uncommon.

Within this therapeutic landscape, liposomal formulations have emerged as a promising strategy to enhance delivery of nucleoside analogues such as acyclovir and ganciclovir, improving corneal penetration, prolonging precorneal residence, and reducing dosing frequency compared with conventional gels or ointments. Pandey and co-workers provide a comprehensive overview of sustained-release antiviral systems, emphasizing how liposomes and related nanocarriers overcome rapid tear clearance and poor epithelial permeability, two major limitations of standard topical antivirals [245]. Deformable and cationic liposomes have been engineered to interact more effectively with the negatively charged corneal surface, facilitating intracellular uptake into epithelial cells, the primary site of HSV replication. More advanced approaches include the ganglioside-targeted liposomes developed by Shen et al., which deliver HSV-1 glycoprotein D to CD169⁺ macrophages, reducing viral load and clinical severity in murine keratitis while modulating local immune responses [246].

For adenoviral keratoconjunctivitis, liposomal cidofovir and siRNA-based antivirals have shown encouraging in vitro activity, limiting viral replication while mitigating the epithelial toxicity that has historically restricted topical cidofovir use. siRNA-loaded lipoplexes, such as those developed by Ribeiro and colleagues, demonstrate the feasibility of

nucleic-acid delivery to ocular tissues and highlight the potential for gene-silencing strategies in viral keratitis [247]. In the context of antiviral resistance, liposomal encapsulation may partially overcome reduced acyclovir susceptibility by achieving higher intracellular drug concentrations, although it cannot fully compensate for thymidine-kinase-negative mutants; for such strains, alternative agents such as foscarnet or cidofovir, potentially delivered in liposomal form, remain conceptually attractive due to their ability to bypass TK-dependent activation.

7.4. Endophthalmitis

Endophthalmitis is a fulminant intraocular infection of the vitreous and aqueous humors, most frequently caused by Gram-positive cocci, *Staphylococcus epidermidis*, *Staphylococcus aureus*, and *Streptococcus* spp., in the postoperative setting, whereas Gram-negative bacilli and filamentous fungi predominate in post-traumatic and endogenous cases. The pathogen profile is strongly shaped by the route of entry: coagulase-negative staphylococci dominate after cataract surgery or intravitreal injections, while *Bacillus* spp., *Pseudomonas aeruginosa*, and molds such as *Aspergillus* are more common following penetrating trauma; endogenous cases often involve *Candida* spp. [248]. Resistance patterns mirror systemic trends, including methicillin-resistant staphylococci, rising fluoroquinolone resistance across Gram-positive and Gram-negative isolates, and increasing vancomycin MICs in coagulase-negative staphylococci, while fungal pathogens may exhibit azole resistance in patients with prior systemic prophylaxis. Because endophthalmitis affects the vitreous cavity, topical therapy is ineffective and intravitreal injection of antibiotics or antifungals remains the standard of care [249].

Liposomal formulations have therefore been explored to improve intraocular pharmacokinetics, enhance antimicrobial efficacy, and reduce retinal toxicity. Liposomal vancomycin, ceftazidime, and amikacin consistently demonstrate prolonged intravitreal half-life, sustained therapeutic concentrations, and reduced peak retinal exposure in animal models, lowering the risk of retinal toxicity while maintaining bactericidal activity, as highlighted in the nanomedicine review by Fan and colleagues [250]. Tsoka et al. showed that a sustained-release liposomal moxifloxacin formulation significantly improved bacterial clearance and reduced inflammation in experimental endophthalmitis, underscoring the value of controlled intravitreal release systems [251]. Similarly, Youssef, Dudhipala, and Majumdar demonstrated that ciprofloxacin-loaded nanostructured lipid carriers incorporated into in-situ gels enhanced drug retention and therapeutic outcomes in bacterial endophthalmitis models [252]. Pharmacokinetic analyses by Luaces-Rodríguez et al. further emphasize the limitations of conventional intravitreal agents and the potential of liposomal systems to maintain therapeutic levels without repeated injections [253].

For fungal disease, liposomal amphotericin B, leveraging its established systemic safety advantages over amphotericin B deoxycholate, has shown effective fungal clearance with reduced retinal toxicity in experimental models, with Sakai et al. reporting successful use of multiple intravitreal injections in *Candida glabrata* endophthalmitis [254]. Beyond antimicrobials, liposomal delivery has also been applied to adjunctive therapies: Hammer and colleagues developed a methotrexate-loaded liposomal formulation capable of sustaining intraocular drug release for six weeks in a porcine model, demonstrating the feasibility of long-acting intravitreal liposomes for inflammatory and infectious indications [255]. Additional innovations include supramolecular hydrogels enabling sequential antimicrobial release, as shown by Yu et al., who achieved synergistic eradication of *S. aureus* endophthalmitis with reduced inflammation and improved retinal preservation [256].

7.5. Contact Lens-Associated Infections

Contact lens-associated infections represent a major subset of ocular infectious disease, dominated by bacterial keratitis caused by *Pseudomonas aeruginosa* and *Staphylococcus* spp., but also encompassing *Acanthamoeba* keratitis and, less frequently, fungal keratitis [257]. The pathogen profile is shaped by lens type, hygiene practices, and environmental exposure: *P. aeruginosa* readily forms dense biofilms on lens surfaces and within storage cases, while *Acanthamoeba* trophozoites and cysts persist in contaminated solutions and tap water, contributing to recalcitrant infections. Resistance patterns in these organisms are clinically significant; *P. aeruginosa* isolates from contact lens-related keratitis frequently demonstrate elevated fluoroquinolone MICs and multidrug resistance, while *Acanthamoeba* cysts show marked resistance to conventional disinfectants [258]. Molecular diagnostic work by Oraibi et al. underscores the diversity of bacterial species colonizing worn lenses and highlights the need for improved disinfection strategies [259], while Rathee and colleagues demonstrated that targeted hygiene education significantly reduces bacterial growth in contact lens users, emphasizing the behavioral dimension of infection risk [260].

Liposomal formulations have therefore been explored both as therapeutic eyedrops and as components of lens-care systems to address the intersecting challenges of biofilm biology, antimicrobial resistance, and patient adherence [261]. Among the most relevant advances, ozonated oil encapsulated in liposomes has shown broad-spectrum antimicrobial and anti-adhesive activity, reducing biofilm formation and bacterial adhesion to human corneal epithelial cells, including clinical isolates of *P. aeruginosa* and *Staphylococcus* spp. implicated in contact lens-associated keratitis [262]. By delivering ozone within a lipid bilayer, these systems achieve potent microbicidal activity while limiting direct oxidative damage to the ocular surface. In vitro work consistently demonstrates significant reductions in biofilm biomass and viable counts following exposure to ozonated liposomal formulations, supporting their potential use in both acute therapy and prophylactic regimens for high-risk wearers [263,264].

For lens-care applications, liposome-based disinfecting solutions have been proposed to enhance biofilm removal and improve comfort by incorporating phospholipids that mimic the tear film; these systems can be engineered to release antimicrobial agents, such as biguanides, quaternary ammonium compounds, or low-dose ozone, over time, maintaining microbicidal activity in storage cases while reducing ocular surface toxicity upon lens insertion. Complementary nanotechnologies reinforce this rationale: Hendiger et al. and Heine et al. demonstrated that silver-based antimicrobial nanoparticles exhibit strong anti-biofilm activity against *Acanthamoeba* and *Staphylococcus aureus*, respectively [265,266], supporting the broader concept of nanocarrier-based disinfection. For *Acanthamoeba* keratitis specifically, Siddiqui, Lloyd, and Khan have highlighted the potential of drug-eluting contact lenses to deliver biguanides or diamidines with improved corneal penetration and reduced epithelial toxicity, addressing one of the major limitations of current therapy [267].

8. Liposomes Versus Other Nanocarriers for Ocular Drug Delivery

Despite the significant progress achieved with liposomal formulations, no single nanocarrier platform is universally optimal for all ocular therapeutic applications. The selection of an appropriate delivery system depends on multiple factors, including the physicochemical properties of the drug, target ocular tissue, desired release profile, formulation stability, manufacturing feasibility, and clinical objectives [268]. While liposomes are widely recognized for their biomimetic characteristics and formulation flexibility, alternative nanosystems may offer advantages under specific conditions, such as enhanced structural robustness, prolonged drug retention, or simplified production processes. Consequently, direct comparison of the major nanocarrier platforms is important for identifying

their respective strengths and limitations and for guiding the rational design of ocular drug delivery strategies. Table 4 provides a comparative overview of the principal nanocarrier systems investigated for ophthalmic applications, highlighting key distinctions that influence their therapeutic performance and translational potential.

Table 4. Comparative Analysis of Nanocarrier Platforms for Ocular Antimicrobial Delivery: Therapeutic Advantages, Limitations, and Translational Considerations.

Nanocarrier System	Structure	Key Advantages	Main Limitations	Translational Considerations	Representative Ocular Applications	Ref.
Liposomes	Phospholipid bilayer vesicles containing an aqueous core	High biocompatibility; ability to encapsulate hydrophilic and lipophilic drugs; surface modification; co-delivery of multiple agents	Drug leakage; phospholipid oxidation and hydrolysis; storage instability; formulation variability	Encapsulation efficiency and drug loading depend on lipid composition and preparation method; moderate-to-high manufacturing complexity; sterilization and batch reproducibility remain major challenges	Delivery of antibiotics, antifungals, antivirals, and anti-inflammatory agents; promising activity against AMR and biofilm-associated ocular infections	[180,218,223]
Solid lipid nanoparticles (SLNs)	Solid lipid matrix stabilized by surfactants	Improved physical stability; sustained drug release; suitable for lipophilic drugs; scalable production	Limited loading of hydrophilic drugs; possible drug expulsion during lipid crystallization	Relatively simpler manufacturing compared with liposomes; moderate production cost; scalability is feasible	Sustained ocular delivery of antimicrobial and anti-inflammatory drugs; mainly preclinical applications	[269,270]
Lipid nanoparticles (LNPs)	Ionizable lipids combined with helper lipids and stabilizing components	Efficient intracellular delivery; high encapsulation efficiency for nucleic acids and complex molecules; established manufacturing platforms	Limited evidence in ocular antimicrobial therapy; formulation complexity; possible lipid-related toxicity concerns	Large-scale production is increasingly feasible; manufacturing expertise exists from nucleic acid delivery platforms; clinical translation in ocular infection remains limited	Emerging platform for gene delivery and future antimicrobial applications	[172]
Polymeric nanoparticles (PNPs)	Biodegradable polymer matrices such as PLGA and chitosan	High structural stability; controlled release; tunable degradation; potential mucoadhesion and targeting	Burst release; polymer degradation concerns; possible long-term tissue accumulation	Moderate manufacturing complexity; scalable production possible; cost depends on polymer and fabrication method	Delivery of antimicrobial agents for keratitis and other ocular infections; anti-biofilm potential in preclinical studies	[271,272]
Nanoemulsions	Surfactant-stabilized oil/water nanodroplets	Excellent solubilization of poorly water-soluble drugs; good ocular spreading; relatively simple production	Limited intracellular delivery; surfactant-related tolerability concerns; limited multi-drug loading capability	Low manufacturing complexity; relatively low production cost; favourable scalability	Delivery of antimicrobial, antifungal, and antiviral compounds; improved ocular bioavailability in experimental models	[273,274]
Micelles	Self-assembled amphiphilic structures with hydrophobic cores	Enhanced solubilization of poorly water-soluble drugs; small size; simple preparation	Low structural stability after dilution; limited drug loading; potential leakage	Low-to-moderate manufacturing complexity; cost-effective production; limited clinical evidence	Experimental ocular delivery of hydrophobic drugs and antimicrobial compounds	[275]
Dendrimers	Highly branched polymeric nanostructures with functional surface groups	Precise size control; multifunctional surface modification; potential targeting capability	Complex synthesis; possible cytotoxicity depending on surface charge; limited clinical experience	High manufacturing complexity and production cost; regulatory experience remains limited	Experimental ocular drug delivery and potential antimicrobial applications	[276]

Although liposomes remain among the most extensively investigated nanocarriers for ocular antimicrobial delivery, their therapeutic advantages should be considered alongside important translational limitations [218]. Liposomes provide unique benefits, including biomimetic interactions with biological membranes, flexibility for loading diverse therapeutic molecules, and opportunities for surface functionalization. However, challenges related to formulation stability, sterilization, large-scale manufacturing, and batch-to-batch reproducibility continue to limit their clinical translation.

Compared with other nanocarrier platforms, polymeric nanoparticles and solid lipid nanoparticles generally provide higher structural stability and more straightforward man-

ufacturing processes [270], whereas nanoemulsions offer advantages in scalability and cost-effectiveness [275]. However, these systems may present limitations related to drug loading flexibility, intracellular delivery, or ocular tolerability. Emerging platforms such as lipid nanoparticles, dendrimers, and micelles provide promising opportunities for targeted and intracellular delivery but remain at earlier stages of development for ocular antimicrobial applications.

Therefore, the selection of an optimal nanocarrier should not rely solely on antimicrobial efficacy but should also consider encapsulation efficiency, drug loading capacity, manufacturing feasibility, scalability, production cost, stability, and regulatory acceptance. Future clinical translation of ocular nanomedicines will likely depend on balancing therapeutic performance with reproducible and economically feasible manufacturing strategies.

9. Clinical Translation and Regulatory Challenges

9.1. Are There Any Clinical Trials?

To date, no liposomal ophthalmic formulation specifically developed for the treatment of antimicrobial-resistant (AMR) ocular infections or biofilm-associated ocular infections has received regulatory approval. Although several liposomal systems have demonstrated promising antimicrobial activity in preclinical models and some have progressed to early clinical evaluation for ocular diseases, translation into approved therapies remains limited [157,223]. Current clinical investigations of liposomal ophthalmic products have primarily focused on improving drug delivery, ocular retention, and tolerability of existing therapeutics rather than directly targeting AMR mechanisms or biofilm-associated infections. Examples include liposomal formulations of antifungal, antiviral, anti-inflammatory, and glaucoma therapies, which have provided valuable information regarding ocular safety, pharmacokinetics, and formulation feasibility [221]. However, the transition from experimental models to clinically approved antimicrobial liposomal products continues to be restricted by challenges including insufficient late-stage clinical evidence, lack of standardized evaluation protocols, manufacturing complexity, sterilization requirements, and regulatory uncertainty associated with nanomedicine-based ophthalmic products.

Clinical translation of liposomal formulations for ocular drug delivery remains a complex and multifactorial challenge, despite decades of compelling preclinical evidence demonstrating improved bioavailability, enhanced corneal penetration, and the ability to overcome antimicrobial resistance. Only a limited number of liposomal ophthalmic formulations have progressed beyond preclinical evaluation, and most remain at early clinical or investigational stages rather than achieving regulatory approval for ocular indications. A summary of clinically investigated and translationally relevant liposomal ophthalmic formulations is provided in Table 5. Importantly, despite extensive preclinical evidence supporting improved ocular retention, penetration, and therapeutic efficacy, no liposomal formulation specifically approved for the treatment of antimicrobial-resistant ocular infections is currently available. Existing clinical investigations have primarily focused on improving ocular bioavailability, reducing toxicity, or enabling sustained delivery of established therapeutic agents rather than directly addressing AMR-associated ocular infections.

Table 5. Clinical and Investigational Status of Liposomal Ophthalmic Formulations.

Formulation/Drug	Therapeutic Application	Development Stage	Main Outcome	Current Translational Status	Ref.
Liposomal amphotericin B	Fungal keratitis	Clinical investigation/experimental use	Improved ocular tolerability and reduced free-drug toxicity compared with conventional amphotericin B	No approved liposomal ophthalmic product; further clinical validation required	[277]
Liposomal acyclovir	HSV keratitis	Investigational	Improved ocular retention and potential enhancement of antiviral delivery	Limited clinical development	[278]
Liposomal cyclosporine A	Dry eye disease	Clinical investigation	Improved ocular surface delivery and anti-inflammatory effects	No specific AMR-related application	[279]
Liposomal dexamethasone	Uveitis/inflammatory disorders	Preclinical–clinical translational studies	Sustained corticosteroid delivery and immunomodulatory activity	Regulatory translation remains limited	[280]
Liposomal timolol	Glaucoma	Preclinical/early translational studies	Prolonged ocular retention and hypotensive effects	Not clinically approved	[281]
Antimicrobial-loaded engineered liposomes	AMR-associated ocular infections	Mainly preclinical	Enhanced antimicrobial exposure, biofilm targeting, and improved penetration in experimental models	No clinically approved AMR-targeted liposomal therapy	[150,216]

Over the past decade, several first-in-human and Phase I/II trials have evaluated liposomes, lipid nanoparticles, and select polymeric systems for anterior and posterior segment diseases, consistently reporting favorable safety, tolerability, and pharmacokinetic profiles, but with few pivotal Phase III trials to support regulatory approval [282]. For example, small-scale clinical investigations of liposomal amphotericin B for fungal keratitis and liposomal acyclovir for recurrent HSV keratitis have shown acceptable safety and improved ocular retention, yet large multicenter randomized trials remain absent. Similarly, liposomal cyclosporine formulations have been explored in dry eye disease, with systematic reviews by Gao et al. and Bian and colleagues highlighting the heterogeneity of available formulations and the lack of standardized clinical endpoints across trials [283,284].

Regulatory bottlenecks arise from stringent sterility requirements for ophthalmic products, the difficulty of standardizing nanocarrier manufacturing processes, and the high cost of ophthalmic clinical trials. Variability in formulation parameters, such as lipid composition, vesicle size, encapsulation efficiency, and surface modifications, further complicates reproducibility and regulatory assessment. Reviews such as Nsairat et al. emphasize that current regulatory frameworks lack nanocarrier-specific pathways, forcing developers to rely on bridging data from conventional formulations supplemented by targeted ocular toxicity studies [285]. Even formulations with intrinsic antimicrobial activity, such as ozonated-oil liposomes explored by Rizzo et al. and Pastore et al., face challenges in demonstrating consistent efficacy and long-term safety across diverse patient populations [286,287].

In inflammatory disease, Aksenova et al. demonstrated that a liposomal dexamethasone formulation produced meaningful immunomodulatory effects in experimental autoimmune uveitis, supporting its translational potential [288]. Although not liposomal, clinically approved sustained-release ocular nanomedicine platforms such as the dexamethasone intravitreal implant Ozurdex® (AbbVie Inc., North Chicago, IL, USA) provide valuable translational insights into regulatory approval pathways and long-term intraocular drug delivery. Across the recent literature, the intravitreal dexamethasone implant (Ozurdex®) has consistently demonstrated substantial therapeutic value in non-infectious uveitis. In a large multicenter investigation, Mathis et al. reported rapid suppression of

intraocular inflammation, with marked reductions in vitritis and macular edema accompanied by meaningful visual improvement; importantly, intraocular pressure elevations remained largely controllable with topical medication [289]. These findings align with the real-world evidence presented by Butt and Devonport, who observed significant decreases in retinal thickness and inflammatory activity in patients with posterior uveitis, noting that many individuals achieved prolonged remission after a single implant—an outcome that underscores the advantages of sustained corticosteroid release [290]. Complementing these results, Gupta et al. documented robust anatomical and functional gains when the implant was used as monotherapy for uveitic macular edema, together with a low incidence of adverse events, thereby supporting its suitability as a standalone therapeutic option in appropriately selected cases [291]. Early-phase studies in glaucoma and ocular hypertension, such as the liposomal gel delivery system for timolol developed by Bose et al. and the ethosomal timolol formulation tested by Uner and co-workers, demonstrate promising pharmacodynamic effects but remain far from late-phase evaluation [292,293]. Additional translational work, including the pharmacokinetic case study by Valkama et al. on intravitreal liposomes delivering a cyclic GMP derivative, highlights the need for standardized release and distribution models to support regulatory submissions [294].

9.2. Scale-Up Difficulties

Scaling ophthalmic nanomedicines from bench to GMP-compliant manufacture presents substantial challenges in reproducibility, batch-to-batch consistency, and process control, largely due to the sensitivity of lipid-based systems to subtle variations in formulation and processing conditions. Critical quality attributes, including particle-size distribution, surface charge, encapsulation efficiency, sterility, and ocular tolerability, depend heavily on precise control of mixing dynamics, solvent-removal rates, lipid purity, and excipient quality [295,296]. Studies from 2020–2025 consistently show that laboratory-scale methods such as thin-film hydration, manual extrusion, microfluidics, or small-scale solvent evaporation do not directly translate to industrial equipment such as high-pressure homogenizers or large-volume microfluidic reactors without significant reformulation and implementation of process-analytical technologies (PAT). For example, Pittiu and colleagues demonstrated that post-manufacturing dilution in microfluidic liposome production can dramatically alter encapsulation efficiency and lipid retention, underscoring the fragility of scale-dependent parameters [297]. Similarly, Gkionis et al. showed that microfluidic-assisted fabrication of phosphatidylcholine liposomes requires tight control of flow rates and solvent ratios to maintain vesicle uniformity, conditions that become increasingly difficult to reproduce at industrial scale [298]. Continuous-flow systems, such as the millireactor approach evaluated by Yanar et al., offer improved scalability but still exhibit sensitivity to fluidic instabilities and shear-dependent vesicle formation [299].

Multilamellar and deformable liposomes are particularly prone to aggregation, fusion, and variable drug loading when process conditions shift even slightly, complicating scale-up and regulatory validation. The structural instability of cationic formulations, highlighted by Dominguez-Arca et al., further illustrates how small deviations in surfactant concentration or mixing energy can alter vesicle morphology and charge, impacting both safety and efficacy [300]. Additional constraints arise from the need to maintain sterility and prevent oxidation or drug leakage during manufacturing, as high temperatures, shear forces, or prolonged processing can destabilize vesicles. Economic and supply-chain factors, including sourcing GMP-grade lipids, securing sterile single-use systems, and maintaining cold-chain logistics, further increase the cost and complexity of industrial production, particularly for small companies advancing early-stage candidates. Reviews by Basak and Das emphasize that industrial liposome production requires specialized

equipment, rigorous validation, and continuous monitoring to ensure consistency across large batches [301], while Kruglov and Borshchevsky highlight the importance of Quality-by-Design (QbD) frameworks for defining critical process parameters and establishing robust control strategies [302].

9.3. Sterilization Issues

Sterility is a non-negotiable regulatory requirement for ophthalmic nanocarriers, yet achieving it without compromising nanoparticle integrity remains one of the most significant barriers to clinical translation. Conventional sterilization methods, such as autoclaving, high-temperature steam, ethylene oxide, or dry heat, are generally incompatible with lipid-based systems, as they disrupt phospholipid bilayers, induce vesicle aggregation, accelerate drug leakage, and may generate toxic degradation products [303]. Sterile filtration through 0.22 µm membranes is the preferred approach when feasible, but it is limited to small unilamellar vesicles and cannot be applied to multilamellar liposomes, larger nanoparticles, or viscous formulations; moreover, filtration does not remove endotoxins, necessitating additional controls. As highlighted by Tremouille and Charcosset, purification and sterilization steps must be integrated into the manufacturing workflow because post-processing sterilization often destabilizes nanocarriers [304].

Recent experimental work has therefore shifted toward aseptic manufacturing, low-temperature sterilization, and terminal sterilization supported by protective excipients or cryoprotectants. Gamma irradiation has emerged as a promising strategy: several studies report minimal oxidative damage when antioxidant systems are incorporated, though irradiation parameters must be carefully optimized to avoid vesicle fusion or destabilization. Penoy and colleagues demonstrated that supercritical CO₂ can be used to simultaneously produce and sterilize liposomes in a one-step process, offering a scalable alternative that avoids thermal degradation [305]. Continuous-manufacturing approaches, such as those described by AlTerawi et al., further illustrate how controlled processing environments can support sterile production without exposing liposomes to damaging conditions [306].

Some lipid systems offer intrinsic antimicrobial advantages. Ozonated-oil liposomes, for example, reduce contamination risk during storage and use due to their inherent microbicidal activity, an effect supported by clinical and translational studies showing reduced ocular microbial load and improved prophylactic performance. However, antimicrobial excipients must be balanced carefully to avoid ocular irritation or inflammatory responses. Regulatory guidance emphasizes the need for orthogonal sterility-assurance data, including endotoxin testing, container-closure integrity, and stability under intended sterilization conditions, because sterilization can alter particle-size distribution, surface charge, and drug-release kinetics. Novel concepts such as enzyme-triggered sterilization, exemplified by the pectinase-responsive liposomes developed by Li et al., highlight the growing interest in on-demand antimicrobial activation, though these approaches remain far from ophthalmic translation [307].

9.4. Regulatory Hurdles for Ophthalmic Nanomedicine

Regulatory pathways for ophthalmic nanomedicines, including liposomes, lipid nanoparticles, and polymeric systems, remain complex and highly scrutinized because neither European nor U.S. regulatory agencies have established harmonized nanomedicine-specific frameworks for ocular products [239]. Consequently, these formulations are generally evaluated on a case-by-case basis using conventional pharmaceutical guidelines supplemented by additional nanocarrier-specific characterization and safety data. Regulators require comprehensive physicochemical characterization, including particle size

distribution, surface charge, encapsulation efficiency, release kinetics, and long-term stability, together with ocular-specific toxicological assessments addressing corneal irritation, intraocular inflammation, biodistribution, and tissue retention [240]. Additional concerns unique to nanocarriers, such as immunogenicity, complement activation, degradation products, and interactions with ocular tissues, further increase regulatory complexity. Other studies emphasize that the structural complexity of liposomal systems complicates the prediction of in vivo behavior and batch-to-batch reproducibility, thereby increasing the evidentiary requirements for regulatory approval [308]. Endotoxin testing, sterility assurance, container-closure integrity, and validated analytical methods remain mandatory, particularly for multifunctional formulations such as liposomes co-delivering antimicrobial and anti-inflammatory agents, which may also be regulated as combination products [250].

Beyond regulatory documentation, formulation-specific safety issues represent another important determinant of regulatory acceptance. Cationic lipids such as DOTAP and stearylamine exhibit strong electrostatic interactions with the negatively charged ocular surface, improving mucoadhesion but also producing dose-dependent cytotoxicity through disruption of corneal epithelial membranes at elevated concentrations [211]. Similarly, sterilization strategies can directly influence product quality and regulatory approval. Terminal sterilization methods, including autoclaving, sterile filtration, and gamma irradiation, may alter vesicle integrity, phospholipid stability, or drug-release characteristics, highlighting the need for carefully validated sterilization approaches that preserve nanoparticle functionality [242]. These challenges are particularly relevant for complex lipid-based formulations, where even minor changes in manufacturing conditions may significantly affect product quality and clinical performance.

Recent regulatory analyses increasingly advocate early scientific advice from the EMA, FDA, and national regulatory agencies to reduce development risks and facilitate regulatory alignment. As highlighted by Shahrer and Fouda, developers are progressively incorporating GLP-validated ocular models, robust comparability strategies, GMP-compliant manufacturing, and Quality by Design (QbD) principles throughout product development to satisfy evolving regulatory expectations [309]. Similar conclusions were reached by Mangla et al., who emphasized the continuing need for harmonized standards governing nanocarrier characterization, safety evaluation, and long-term surveillance [310]. For ophthalmic nanomedicines specifically, Shastri further noted that regulatory expectations are increasingly converging with those applied to ocular biologics, requiring comprehensive assessment of tissue penetration, immune activation, and off-target distribution [311].

Successful clinical translation of ophthalmic nanomedicines will depend on integrating robust formulation design with reproducible manufacturing, standardized characterization protocols, and well-designed multicenter clinical studies demonstrating long-term safety, efficacy, and product consistency. Although many regulatory challenges are shared across nanocarrier platforms, important differences remain. Liposomes provide excellent biocompatibility and formulation flexibility but require stringent control of membrane stability and manufacturing reproducibility. Polymeric nanoparticles generally offer greater structural stability and sustained drug release, whereas lipid nanoparticles benefit from rapidly advancing industrial manufacturing platforms established for nucleic acid therapeutics [251]. Nanoemulsions are comparatively easier to manufacture and scale up but may provide less flexibility for complex multidrug formulations. Consequently, future regulatory approval of ocular antimicrobial nanomedicines will depend not only on therapeutic efficacy but also on manufacturability, quality assurance, regulatory feasibility, and long-term clinical applicability [312] (Figure 6).

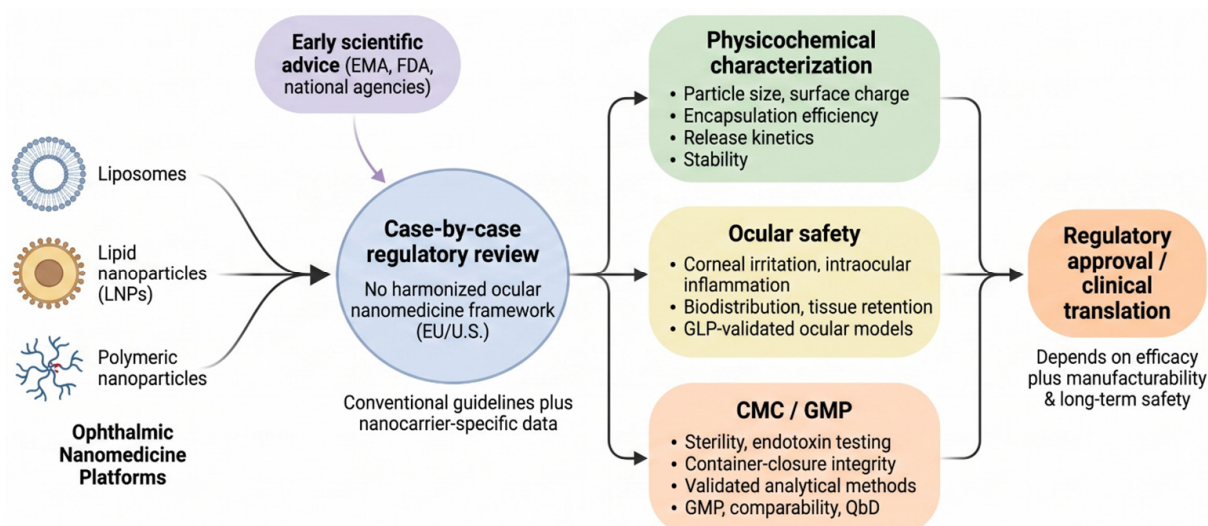


Figure 6. Translational roadmap for liposomal ocular nanomedicines from laboratory development to clinical implementation. Created in BioRender. Hajareh Haghighi, F. (2026) <https://BioRender.com/ik6lg1k> (accessed on 7 June 2026).

10. Future Perspectives

The future of liposomal ocular drug delivery lies in integrating advanced formulation strategies, targeting mechanisms, and precision medicine approaches to overcome current limitations and address complex ocular pathologies. Recent advances in nanotechnology, bioengineering, and computational modeling offer multiple avenues to enhance the therapeutic potential of liposomes while ensuring safety, efficacy, and patient-specific optimization.

10.1. pH-Responsive Liposomes

Stimulus-responsive liposomes represent one of the most promising directions in next-generation ocular nanotherapy, offering the ability to release drugs selectively in response to pathological microenvironments characteristic of infection, inflammation, and chronic ocular disease. Among these, pH-responsive liposomes have gained particular traction because infected or inflamed ocular tissues often exhibit localized acidification (pH 6.0–6.8), enabling protonation-induced destabilization of liposomal membranes, enhanced fusion, or triggered leakage precisely at the disease site. Recent advances in ocular nanocarrier design highlight increasingly sophisticated lipid compositions and polymer–lipid hybrids engineered to undergo phase transitions, membrane destabilization, or charge-switching under mildly acidic conditions typical of bacterial keratitis, conjunctivitis, postoperative inflammation, and even posterior-segment disorders. Reviews such as those by Tsirogianni, Chountoulesi, and Pippa emphasize how pH-labile linkers, ionizable lipids, and acid-sensitive polymer coatings can be tuned to maintain stability in tear fluid and vitreous humor while enabling controlled release upon encountering acidic or enzyme-rich microenvironments [313].

Beyond infections, stimulus-responsive liposomes are emerging in glaucoma therapy, where oxidative stress, altered enzymatic activity, and microenvironmental pH shifts can be leveraged for controlled release. For example, Badran et al. demonstrated that chitosan-coated deformable liposomes incorporated into thermosensitive gels improved intraocular pressure control while enhancing corneal penetration and prolonging drug residence time—features that could be further optimized through pH-responsive design [314]. In antiviral therapy, Markowicz-Piasecka and colleagues highlight the potential of pH-triggered systems to improve intracellular delivery of acyclovir and ganciclovir, particularly in recurrent

HSV keratitis where epithelial acidity and inflammation can be exploited for targeted release [315]. More broadly, Guo et al. outline emerging strategies integrating pH responsiveness with additional stimuli modalities, such as redox-responsive, enzyme-responsive, or light-triggered mechanisms, to achieve multi-level control over drug-release kinetics and tissue targeting [316]. Enzyme-responsive liposomes, for instance, degrade in the presence of bacterial or host-derived enzymes, enhancing penetration into biofilms and infected tissues, while redox-responsive systems exploit oxidative stress in glaucoma or uveitis.

Outside ophthalmology, pH-responsive liposomes have demonstrated potent site-specific release in oncology, as shown by Lin et al. with cytotoxin-loaded liposomes triggered by acidic tumor microenvironments [317], and by Wang and co-workers, who developed polyunsaturated-fatty-acid-conjugated liposomes that undergo ion-pairing and self-assembly at acidic pH to enhance antitumor efficacy [318]. These mechanistic insights directly inform ocular applications, where similar microenvironmental cues can be harnessed to overcome barriers such as the corneal epithelium, conjunctival clearance, and the blood–retinal barrier.

Future research is expected to focus on hybrid liposomes incorporating pH-labile linkers, ionizable lipids, and responsive polymer coatings capable of adapting dynamically to the ocular environment. Collectively, these smart liposomal systems offer a pathway toward precision therapy for infectious keratitis, uveitis, glaucoma, and postoperative inflammation, with the potential to reduce dosing frequency, overcome resistance mechanisms linked to insufficient drug exposure, and ultimately improve patient outcomes. As ocular nanomedicine moves toward personalized, pathology-specific delivery, stimulus-responsive liposomes, particularly pH-sensitive variants, are poised to become foundational components of next-generation therapeutic platforms.

10.2. Targeted Liposomes

Ligand-modified liposomes are emerging as a transformative strategy in ocular nanotherapy, enabling selective interaction with specific cell types, receptors, and extracellular-matrix components to overcome the unique anatomical and physiological barriers of the eye. The ocular surface and posterior segment present numerous molecular targets, including integrins, transferrin receptors, folate receptors, CD44/hyaluronic-acid receptors, mucin-associated glycans, and inflammation-associated adhesion molecules, that can be exploited to enhance liposomal adhesion, penetration, and intracellular uptake [319]. Recent advances in biomimetic surface engineering demonstrate that ligand-decorated liposomes exhibit superior retention on the ocular surface, improved mucin interaction, and enhanced bioavailability compared with non-targeted formulations, effectively countering tear turnover, blinking, and mucosal clearance. For example, Wong et al. developed mucin-targeting aptamer-functionalized liposomes for cyclosporine A, achieving markedly improved ocular-surface residence and therapeutic performance in dry-eye models [320]. Similarly, hyaluronic-acid-modified liposomes, such as those described by Ni and colleagues, demonstrate enhanced interaction with mucin and epithelial CD44 receptors, improving penetration and retention on mucosal surfaces [321].

In posterior-segment diseases such as diabetic retinopathy and age-related macular degeneration, ligand-targeted liposomes have shown potential to facilitate receptor-mediated transcytosis across the blood–retinal barrier, reducing reliance on invasive intravitreal injections. Mitochondrion-targeted liposomes, such as the ROS-responsive quercetin system developed by Zhao et al., illustrate how organelle-level targeting can attenuate retinal ischemia–reperfusion injury by modulating SIRT1/FOXO3A and MAPK signaling pathways [322]. In glaucoma therapy, targeted nanoparticles—including ligand-modified liposomes—have demonstrated improved accumulation in the trabecular mesh-

work and retinal ganglion cells, supporting enhanced neuroprotection and intraocular-pressure regulation.

Targeted liposomes are also being explored for selective delivery of antimicrobial and anti-inflammatory agents in ocular infections, where receptor-mediated endocytosis and cell-specific uptake can increase drug concentrations in infected or inflamed tissues while minimizing off-target exposure. This approach is particularly relevant for intracellular pathogens and biofilm-associated infections. Singla and co-workers demonstrated the power of hetero-multivalent targeting in liposomal systems designed to bind multiple *Pseudomonas aeruginosa* surface receptors simultaneously, significantly enhancing antimicrobial efficacy in vitro and in vivo [9]. In corneal injury, Wang et al. showed that ferrostatin-1-loaded targeted liposomes can modulate ferroptosis pathways to treat alkali-burn injury, highlighting the therapeutic potential of receptor-directed delivery in acute inflammation [323].

Combining targeting ligands with deformable liposomes, PEGylated liposomes, or stimulus-responsive architectures further improves penetration through ocular barriers and prolongs residence time. Looking ahead, future research is expected to focus on multi-ligand liposomes capable of dual or sequential targeting, such as inflammation markers plus cell-specific receptors, as well as adaptive systems that respond dynamically to disease progression. Integration with imaging agents may enable theranostic liposomes for real-time monitoring of drug distribution and therapeutic response.

10.3. AI-Assisted Liposome Design

Artificial intelligence (AI) is poised to transform the design and optimization of ocular liposomes by enabling predictive modeling of lipid composition, vesicle stability, drug-encapsulation efficiency, and ocular pharmacokinetics, parameters that traditionally require labor-intensive, iterative experimentation. Although AI-specific studies in ocular liposomal systems are still emerging, advances in nanocarrier modeling and ocular drug-delivery science provide a strong foundation for integrating machine learning into formulation development [324]. The complexity of lipid–drug interactions, membrane fluidity, release kinetics, and surface chemistry, highlighted across recent reviews of liposome-based ocular therapeutics, makes these systems ideal candidates for AI-driven multi-objective optimization. Recent models utilize deep artificial neural networks (ANNs) integrated with molecular dynamics (MD) simulations to evaluate how precise structural shifts, such as phospholipid acyl chain length, degrees of unsaturation, and cholesterol packing concentrations, influence thermodynamic parameters. These AI algorithms successfully predict compound encapsulation yields and bilayer phase-transition values prior to wet-lab synthesis, cutting out empirical trial-and-error. The relevance of such computational tools becomes clear when examining targeted liposomal systems designed to counter oxidative stress. It is important to distinguish between experimentally validated applications of artificial intelligence in nanomedicine and its proposed future role in ocular liposomal development. To date, the direct application of AI for designing and optimizing liposomal formulations specifically for ocular antimicrobial therapy remains limited. However, machine learning approaches have been experimentally validated in broader nanomedicine contexts for predicting nanoparticle characteristics, including size distribution, encapsulation efficiency, stability, and biological interactions [325]. These validated computational strategies provide a methodological framework that could be adapted to ocular liposome development, but their predictive accuracy, generalizability, and clinical relevance still require validation using standardized ocular formulation datasets and experimentally confirmed outcomes. Zhang et al. developed foam-cell-targeted liposomes co-encapsulating SOD and catalase, using a lipid composition optimized for enzyme protection and controlled

release. Their formulation significantly reduced oxidative stress markers and foam-cell formation, illustrating how lipid composition dictates vesicle performance under redox-active conditions [326]. Likewise, Zhang, Sun, et al. created curcumin-loaded liposomes embedded in a thermoresponsive gel to mitigate UV-induced oxidative photodamage in mice. The antioxidant-enriched bilayer improved curcumin retention and stability, leading to marked reductions in ROS, inflammatory cytokines, and tissue injury. These systems highlight how lipid structure, unsaturation, and oxidative environment shape vesicle behavior, precisely the relationships ANN–MD hybrid models aim to predict [327]. Posterior-segment delivery research further emphasizes the importance of computational modeling to predict permeability across ocular barriers and optimize nanoparticle size, charge, and ligand density for retinal targeting.

In glaucoma therapy, where stimulus-responsive liposomes are being developed to exploit oxidative stress and pH shifts, AI could accelerate the design of responsive lipids and polymer–lipid hybrids by predicting protonation behavior, degradation rates, and drug-release profiles under pathological conditions. Broader analyses of AI-enabled ocular nanotechnology, such as those by Kanugo and Teli, highlight the potential of machine learning to integrate imaging, pharmacokinetics, and nanocarrier design into unified predictive platforms for ocular disease management [328]. Similarly, Devaraj and Guruswamy emphasize the role of AI in forecasting antimicrobial efficacy, ocular irritation, and immunogenicity, reducing reliance on animal testing and enabling safer early-stage screening of nanocarriers [329].

AI-assisted formulation platforms could manage the vast design space of lipid types, cholesterol ratios, PEGylation densities, and ligand modifications, simultaneously maximizing stability, minimizing toxicity, and tailoring release kinetics for specific ocular tissues. Future applications may include integration of patient-specific ocular parameters, automated formulation platforms, and predictive toxicology models; however, these concepts remain prospective and require substantial experimental validation before clinical implementation. Integration with automated microfluidic manufacturing could enable rapid prototyping of AI-optimized formulations, while predictive toxicology models may help anticipate long-term safety and inflammatory responses.

10.4. Personalized Ocular Nanotherapy

Personalized ocular nanotherapy represents a paradigm shift in liposomal drug delivery, aiming to tailor formulations to individual patient characteristics, disease phenotypes, and microenvironmental conditions that profoundly influence therapeutic outcomes. Recent advances in liposome-based ocular therapeutics highlight the substantial heterogeneity across ocular diseases, including variations in tear-film composition, corneal permeability, inflammatory cytokine profiles, ocular microbiome diversity, and retinal pathology, all of which shape nanoparticle transport, drug clearance, and tissue penetration. Posterior-segment disorders such as diabetic retinopathy and age-related macular degeneration exemplify the need for individualized approaches, as patients exhibit distinct blood–retinal barrier integrity, metabolic states, and inflammatory signatures that affect liposomal biodistribution. Reviews such as those by Su, Fan, and Pang emphasize that inter-patient variability in retinal physiology and disease progression significantly alters the pharmacokinetics of nanoformulations, reinforcing the need for precision-tailored delivery systems [330].

Stimulus-responsive systems for glaucoma further demonstrate how disease-specific cues, such as oxidative stress, altered enzymatic activity, or localized acidification, can be leveraged to design personalized liposomes that release drugs selectively under pathological conditions, minimizing systemic exposure and reducing side effects. Variability in patient response to existing liposomal glaucoma therapies suggests that future formulations

may be customized based on genetic markers, intraocular-pressure dynamics, trabecular-meshwork physiology, or aqueous-humor metabolomics. Advances in biodistribution imaging, such as the *in vivo* X-ray fluorescence mapping developed by Saladino et al., provide powerful tools for quantifying patient-specific liposome distribution and optimizing dosing strategies [331].

Beyond synthetic nanocarriers, hybrid biogenic systems are emerging as a frontier in personalized therapy. Piffoux and colleagues demonstrated that extracellular vesicles fused with liposomes can generate personalized, patient-derived nanocarriers with enhanced biocompatibility and tailored targeting profiles, an approach with strong translational potential for ocular diseases characterized by immune dysregulation or chronic inflammation [332]. Personalized liposomes may incorporate patient-specific ligand profiles, tailored drug combinations, or adaptive release mechanisms that respond to real-time changes in ocular physiology or pathogen resistance patterns.

Future directions include modular liposome libraries that can be rapidly assembled based on patient data, integration with AI-driven predictive models to optimize formulation parameters, and minimally invasive sampling techniques, such as tear proteomics, conjunctival cytology, or aqueous-humor metabolomics, to guide individualized design.

10.5. Combination with Gene Therapy

Combining liposomal drug delivery with gene therapy represents a powerful future direction for treating complex ocular diseases that require both molecular correction and pharmacological support. Liposomes provide a biocompatible and versatile platform capable of encapsulating nucleic acids, including plasmids, siRNA, mRNA, microRNA, and CRISPR–Cas components, while simultaneously carrying small-molecule drugs that modulate inflammation, angiogenesis, fibrosis, or neurodegeneration. Their ability to protect genetic cargo from enzymatic degradation in the tear film, aqueous humor, and vitreous makes them particularly attractive for ocular applications [333,334]. Posterior-segment delivery research underscores the potential of liposomal gene therapy for retinal diseases such as age-related macular degeneration, retinitis pigmentosa, and diabetic retinopathy, where crossing the blood–retinal barrier remains a major challenge. Ligand-modified or receptor-targeted liposomes may facilitate transcytosis and cell-specific uptake, a strategy supported by brain-targeted liposomal gene delivery studies such as those by dos Santos Rodrigues et al., who demonstrated transferrin- and penetratin-tagged liposomes for ApoE-2 gene delivery [335].

Stimulus-responsive systems for glaucoma further suggest that integrating gene-silencing agents with pH- or redox-responsive liposomes could enable selective modulation of pathological pathways, such as TGF- β signaling, extracellular-matrix remodeling, or trabecular-meshwork fibrosis, while minimizing off-target effects. Existing liposomal glaucoma treatments already demonstrate improved corneal penetration and sustained release, indicating that co-delivery of neuroprotective genes and intraocular-pressure-lowering drugs may enhance long-term outcomes and reduce the need for repeated invasive procedures [336]. Broader reviews of innovative ocular nanoformulations highlight the feasibility of hybrid systems that combine lipid vesicles with viral or non-viral vectors, enabling synergistic therapeutic effects and improved safety profiles. For example, Cheng and colleagues developed hybrid nanovesicles combining gene-engineered exosomes with thermosensitive liposomes to enhance immunotherapy and photothermal therapy, illustrating the potential of multi-component systems [337]. Similarly, Yu et al. introduced a glutathione-sensitive “nanoglue” platform that anchors nucleic acids onto liposomes for combined photo-gene therapy, demonstrating how responsive chemistries can enhance genetic payload delivery [338].

Non-viral liposomal gene delivery continues to advance rapidly. Belhadj et al. compare liposomes with extracellular vesicles as next-generation non-viral vectors, highlighting liposomes tunability and scalability for clinical translation [339]. Cationic and surface-engineered liposomes, such as the polyethyleneimine-modified systems described by Mendes et al., enable efficient siRNA delivery while co-encapsulating chemotherapeutics or anti-inflammatory agents, offering a blueprint for future ocular combination therapies [340]. Lipid-nanoparticle research, including the landscape analysis by Tenchov et al., further demonstrates how lessons from mRNA vaccine development can accelerate ocular gene-liposome hybrid design, particularly in optimizing ionizable lipids and endosomal-escape mechanisms [341].

Future research will likely focus on multifunctional liposomes capable of sequential or simultaneous release of genetic and pharmacological agents, as well as ligand-modified systems that target specific retinal or corneal cell populations. Integration with CRISPR-based editing tools may enable precise correction of mutations underlying inherited retinal diseases, while advances in microfluidic manufacturing will support scalable production of gene-liposome hybrids (Figure 7).

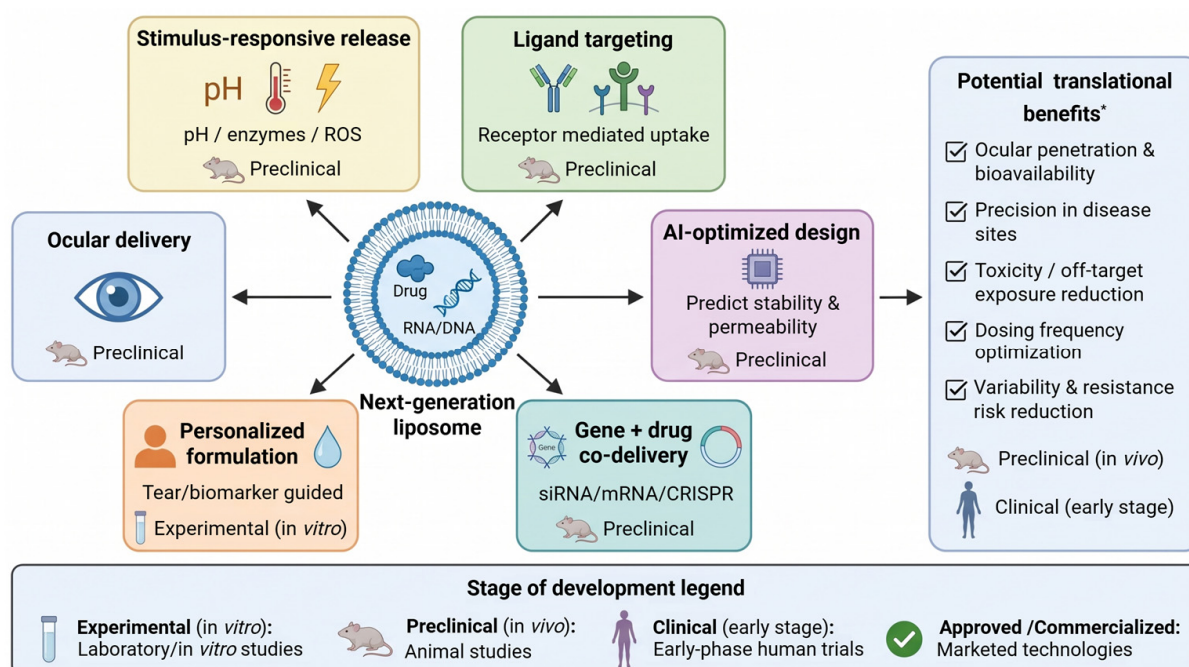


Figure 7. Overview of next-generation liposomal strategies for ocular drug delivery. Emerging approaches, including stimulus-responsive release, ligand-mediated targeting, AI-assisted design, gene and drug co-delivery, and personalized formulations, are presented together with their current stage of development (experimental, preclinical, clinical, or approved). These technologies offer potential translational benefits, including improved ocular penetration, targeting precision, bioavailability, dosing optimization, and reduced off-target effects and variability, although many remain under preclinical investigation. Created in BioRender. Hajareh Haghighi, F. (2026) <https://BioRender.com/ik6lg1k> (accessed on 7 June 2026).

11. Conclusions

The escalating antimicrobial resistance (AMR) crisis represents a significant challenge in the management of ocular infections. Bacterial, fungal, and viral pathogens increasingly exhibit multidrug resistance, biofilm formation, and intracellular persistence, which reduce the efficacy of conventional topical or systemic therapies. In particular, biofilm-associated infections, whether on the corneal surface, contact lenses, or intraocular implants, demonstrate markedly enhanced tolerance to standard antimicrobial agents, contribut-

ing to treatment failure, recurrent infections, and vision-threatening complications. The growing prevalence of multidrug-resistant pathogens underscores the urgent need for innovative strategies that not only deliver therapeutics effectively but also overcome resistance mechanisms at the site of infection.

Liposomal drug delivery emerges as a multifunctional solution capable of addressing many of these challenges. Their unique bilayer architecture allows simultaneous encapsulation of hydrophilic and lipophilic drugs, while surface modifications, such as cationic charge or PEGylation, facilitate enhanced corneal penetration, prolonged ocular residence, and intracellular delivery. Liposomes can disrupt bacterial membranes, penetrate biofilms, and sustain local drug concentrations, leading to reduced minimum inhibitory concentrations (MICs) and improved therapeutic outcomes. Furthermore, co-delivery strategies combining antibiotics with anti-inflammatory agents or antimicrobial peptides highlight the versatility of liposomes in tackling complex ocular pathologies. Preclinical studies and early clinical investigations demonstrate their potential in treating bacterial, fungal, and viral keratitis, endophthalmitis, and contact lens-associated infections, with improved efficacy, reduced toxicity, and enhanced tolerability compared to conventional formulations.

Despite their promise, several gaps remain that limit full clinical translation. Stability issues, including vesicle aggregation, drug leakage, and susceptibility to oxidation, pose significant formulation challenges. Sterility and scale-up difficulties further complicate industrial production and regulatory approval. While stimulus-responsive, targeted, and personalized liposomal strategies are emerging, these approaches require rigorous preclinical validation and extensive clinical trials to demonstrate safety, efficacy, and reproducibility. Moreover, standardized guidelines for quality control, characterization, and regulatory assessment of ocular nanomedicines are still evolving, adding complexity to their translation.

In conclusion, liposomal ocular drug delivery represents a highly versatile and biologically relevant platform with the potential to transform the management of resistant and biofilm-associated eye infections. Their multifunctional properties, ranging from enhanced penetration and sustained release to co-delivery and biofilm disruption, position them as a promising solution to the AMR crisis in ophthalmology. Addressing remaining formulation, manufacturing, and regulatory challenges will be critical for realizing their full clinical potential. Future research integrating targeted, stimulus-responsive, and AI-assisted liposome design, along with personalized therapeutic strategies, is likely to establish liposomal nanomedicine as a cornerstone in the treatment of complex ocular infections.

Author Contributions: Writing—original draft preparation, P.S.P. and R.B.; writing—review and editing, C.P. and L.C.; visualization, R.B. and F.H.H.; permission acquisition, F.H.H.; supervision, C.P. and L.C. All authors have read and agreed to the published version of the manuscript.

Funding: This research and the APC were funded by Indo-Italian Executive Programme Of Cooperation In Scientific and Technological Cooperation Significant Bilateral Project 2025-27 Cup N. B83c24008870001. Title of the Project: “Peptide hydrogel/Ag-nanoparticle composites as sustainable approach for treatment of fungal ocular infections”.

Data Availability Statement: The original contributions presented in this study are included in the article. Further inquiries can be directed to the corresponding author.

Acknowledgments: All figures included in this review article were created using the AI-assisted features of BioRender. The graphical abstract was created in BioRender. Created in BioRender. Hajareh Haghighi, F. (2026) <https://BioRender.com/ik6lg1k> (accessed on 7 June 2026). The authors reviewed and, where necessary, refined all figures and take full responsibility for their final content. Appropriate BioRender licenses were obtained for all figures included in the manuscript.

Conflicts of Interest: The authors declare no conflicts of interest.

References

- Chronopoulou, L.; Binaymotlagh, R.; Bozzi, M.; Colone, M.; Stringaro, A.R.; Sciandra, F.; Palocci, C. Microfluidic synthesis of phosphatidylcholine liposomes for verbascoside delivery into C2C12 cells. *J. Nanopart. Res.* **2025**, *27*, 171. [\[CrossRef\]](#)
- Kiuchi, M.; Takeoka, S.; Sou, K. Microfluidic Preparation of Size- and Lamellarity- Controlled Liposomes Using a Static Mixer and the Advantage of a Multilamellar Structure in Biosensing Applications. *Front. Bioeng. Biotechnol.* **2026**, *13*, 1715496. [\[CrossRef\]](#) [\[PubMed\]](#)
- Cheng, Y.; Hay, C.D.; Mahuttanatan, S.M.; Hindley, J.W.; Ces, O.; Elani, Y. Microfluidic Technologies for Lipid Vesicle Generation. *Lab Chip* **2024**, *24*, 4679–4716. [\[CrossRef\]](#) [\[PubMed\]](#)
- Afrin, S.; Debele, T.A.; Park, Y.C. Enhanced Biofilm Inhibition via Extracellular Polymeric Substances (EPS)-Binding Liposomes. *Korean J. Chem. Eng.* **2026**, *43*, 311–320. [\[CrossRef\]](#)
- Lu, H.; Zhang, S.; Wang, J.; Chen, Q. A Review on Polymer and Lipid-Based Nanocarriers and Its Application to Nano-Pharmaceutical and Food-Based Systems. *Front. Nutr.* **2021**, *8*, 783831. [\[CrossRef\]](#) [\[PubMed\]](#)
- Ahsan, A.; Thomas, N.; Barnes, T.J.; Subramaniam, S.; Loh, T.C.; Joyce, P.; Prestidge, C.A. Lipid Nanocarriers-Enabled Delivery of Antibiotics and Antimicrobial Adjuvants to Overcome Bacterial Biofilms. *Pharmaceutics* **2024**, *16*, 396. [\[CrossRef\]](#) [\[PubMed\]](#)
- Wroblewska, K.B.; Jadach, B.; Muszalska-Lokos, I. Progress in Drug Formulation Design and Delivery of Medicinal Substances Used in Ophthalmology. *Int. J. Pharm.* **2021**, *607*, 121021. [\[CrossRef\]](#) [\[PubMed\]](#)
- Puglia, C.; Santonocito, D.; Romeo, G.; Intagliata, S.; Romano, G.L.; Stretto, E.; Novelli, E.; Ostacolo, C.; Campiglia, P.; Sommella, E.M.; et al. Lipid Nanoparticles Traverse Non-Corneal Path to Reach the Posterior Eye Segment: In Vivo Evidence. *Molecules* **2021**, *26*, 4673. [\[CrossRef\]](#) [\[PubMed\]](#)
- Koehler, J.K.; Gedda, L.; Wurster, L.; Schnur, J.; Edwards, K.; Heerklotz, H.; Massing, U. Tailoring the Lamellarity of Liposomes Prepared by Dual Centrifugation. *Pharmaceutics* **2023**, *15*, 706. [\[CrossRef\]](#) [\[PubMed\]](#)
- Nair, K.S.; Bajaj, H. Advances in Giant Unilamellar Vesicle Preparation Techniques and Applications. *Adv. Colloid Interface Sci.* **2023**, *318*, 102935. [\[CrossRef\]](#) [\[PubMed\]](#)
- Valentine, M.L.; Waterland, M.K.; Fathizadeh, A.; Elber, R.; Baiz, C.R. Interfacial Dynamics in Lipid Membranes: The Effects of Headgroup Structures. *J. Phys. Chem. B* **2021**, *125*, 1343–1350. [\[CrossRef\]](#) [\[PubMed\]](#)
- Song, F.; Yang, G.; Wang, Y.; Tian, S. Effect of Phospholipids on Membrane Characteristics and Storage Stability of Liposomes. *Innov. Food Sci. Emerg. Technol.* **2022**, *81*, 103155. [\[CrossRef\]](#)
- Guo, L.; Zhang, J.; Li, Y.; Cheng, M.; Liu, Y.; Lu, G.; Shen, Y.; Shen, H.; Yu, Z. Hyperbranched Macromonomer-Based Gelation of Hyaluronic Acid for Efficient Liposome Encapsulated and Improved Transdermal Delivery. *Macromol. Rapid Commun.* **2025**, *46*, 2500310. [\[CrossRef\]](#) [\[PubMed\]](#)
- Neunert, G.; Tomaszewska-Gras, J.; Baj, A.; Gauza-Włodarczyk, M.; Witkowski, S.; Polewski, K. Phase Transitions and Structural Changes in DPPC Liposomes Induced by a 1-Carba-Alpha-Tocopherol Analogue. *Molecules* **2021**, *26*, 2851. [\[CrossRef\]](#) [\[PubMed\]](#)
- Neunert, G.; Tomaszewska-Gras, J.; Baj, A.; Gauza-Włodarczyk, M.; Witkowski, S.; Polewski, K. Changes in DPPC Liposomes Structure Induced by a 1-Carba-Alpha-Tocopherol Analogue. *Curr. Top. Chem. Biochem* **2022**, *2*, 69–90. [\[CrossRef\]](#)
- Pavlovic, N.; Mijalković, J.; Balanč, B.; Luković, N.; Knežević-Jugović, Z. Role of Cholesterol in Modifying the Physical and Stability Properties of Liposomes and In Vitro Release of Vitamin B12. *Eng. Proc.* **2025**, *99*, 10. [\[CrossRef\]](#)
- Pruchnik, H.; Gliszczynska, A.; Włoch, A. Evaluation of the Physico-Chemical Properties of Liposomes Assembled from Bioconjugates of Anisic Acid with Phosphatidylcholine. *Int. J. Mol. Sci.* **2021**, *22*, 13146. [\[CrossRef\]](#) [\[PubMed\]](#)
- Šturm, L.; Poklar Ulrih, N. Basic Methods for Preparation of Liposomes and Studying Their Interactions with Different Compounds, with the Emphasis on Polyphenols. *Int. J. Mol. Sci.* **2021**, *22*, 6547. [\[CrossRef\]](#) [\[PubMed\]](#)
- Dou, T.; Zens, C.; Schroder, K.; Jiang, Y.; Makarov, A.A.; Kupfer, S.; Kuroski, D. Solid-to-Liposome Conformational Transition of Phosphatidylcholine and Phosphatidylserine Probed by Atomic Force Microscopy, Infrared Spectroscopy, and Density Functional Theory Calculations. *Anal. Chem.* **2022**, *94*, 13243–13249. [\[CrossRef\]](#) [\[PubMed\]](#)
- Hashemzadeh, H.; Javadi, H.; Darvishi, M.H. Study of Structural Stability and Formation Mechanisms in DSPC and DPSM Liposomes: A Coarse-Grained Molecular Dynamics Simulation. *Sci. Rep.* **2020**, *10*, 1837. [\[CrossRef\]](#) [\[PubMed\]](#)
- Vivas, C.V.; da Cunha, A.R.; Lamy, M.T.; Duarte, E.L.; Muniz, G.S.V. DODAB-ODN Lipoplex Structure is Highly Dependent on ODN Concentration: A Multitechnique Experimental Study. *Biochem Biophys. Rep.* **2025**, *43*, 102128. [\[CrossRef\]](#) [\[PubMed\]](#)
- Zhao, J.; Sun, J.; Zhang, K.; Wang, S.; Ding, W.; Li, Z. Effect of Positively Charged Lipids (DOTAP) on the Insertion of Carbon Nanotubes into Liposomes and the Separation Performance of Thin-Film Nanocomposite Membranes. *Separations* **2024**, *11*, 75. [\[CrossRef\]](#)
- Zadeh, B.S.M.; Feghhi, M. Cationic Liposomes as Promising Vehicles for Timolol/Brimonidine Combination Ocular Delivery in Glaucoma: Formulation Development and In Vitro/In vivo Evaluation. *Res. Sq.* **2022**, preprint. [\[CrossRef\]](#) [\[PubMed\]](#)
- Bogdanov, A.; Janovák, L.; Vraneš, J.; Meštrović, T.; Ljubin-Sternak, S.; Cseh, Z.; Endrész, V.; Burián, K.; Vanić, Ž.; Virok, D.P. Liposomal Encapsulation Increases the Efficacy of Azithromycin against *Chlamydia trachomatis*. *Pharmaceutics* **2022**, *14*, 36. [\[CrossRef\]](#) [\[PubMed\]](#)

25. Martins, L.S.; Duarte, E.L.; Lamy, M.T.; Rozenfeld, J.H.K. DODAB Vesicle Containing Lysophosphatidylcholines: The Relevance of Acyl Chain Saturation on the Membrane Structure and Thermal Properties. *Biophys. Chem.* **2023**, *300*, 107075. [[CrossRef](#)] [[PubMed](#)]
26. Rapaka, H.; Manturthi, S.; Gosangi, M.; Lochania, B.; Marepally, S.; Patri, S.V. Effect of Methylation of the Hydrophilic Domain of Tocopheryl Ammonium-Based Lipids on their Nucleic Acid Delivery Properties. *ACS Omega* **2022**, *7*, 15396–15403. [[CrossRef](#)] [[PubMed](#)]
27. Li, K.-M.; Song, P.; He, X.-P.; Li, N. Probing Membrane Structure of Lipid Nanomedicines Using Solution Small-Angle X-Ray Scattering: Applications and Prospects. *Membranes* **2025**, *15*, 382. [[CrossRef](#)] [[PubMed](#)]
28. Voutyritsa, E.; Oikonomou, A.; Bolis, G.; Papageorgiou, V.; Vougiatzi, A.S.; Hatzakis, N.S. Polymer Functionalized Liposomes as Universal Nanocarriers for Drug Delivery: Single Particle Insights on Size-Dependent Performance and Intracellular Behaviour. *ACS Appl. Mater. Interfaces* **2025**, *17*, 70442–70453. [[CrossRef](#)] [[PubMed](#)]
29. Arunachalam, B.; Jaganathan, M.; Palanisamy, T.; Dhathatheryan, A. Physico-Chemical Studies of Elastic Compliance and Adsorption of DOPC Vesicle and its Mixture with Charged Lipids at Fluid/Solid Interface. *Colloids Surf. B Bionterfaces* **2021**, *199*, 111544. [[CrossRef](#)] [[PubMed](#)]
30. Choi, S.Y.; Cho, C.S.; Kim, S.; Kim, J.K.; Kim, H.; Kim, K.H.; Jo, D.H.; Lee, H. Vitreous Humor-Mimetic Liposomes Enable Effective Gene Delivery to the Eye Via Intravitreal Injection. *Biomaterials* **2026**, *334*, 124226. [[CrossRef](#)] [[PubMed](#)]
31. Patel, P.; Bhimajiyani, G.; Rathod, A.; Chauhan, M.; Dave, M.; Trada, A.; Prajapati, B.G. Recent Advances in Liposome-Based Nanocarriers for Ocular Therapeutics. *BioMed Mater. Devices* **2025**. [[CrossRef](#)]
32. Allam, A.; Elsabahy, M.; El Badry, M.; Elaraky, N.E. Betaxolol-Loaded Niosomes Integrated Within pH-Sensitive In situ Forming Gel for Management of Glaucoma. *Int. J. Pharm.* **2021**, *598*, 120380. [[CrossRef](#)] [[PubMed](#)]
33. Amin, M.; Lammers, T.; Hagen, T.L.M. Temperature-Sensitive Polymers to Promote Heat-Triggered Drug Release from Liposomes: Towards Bypassing EPR. *Adv. Drug Deliv. Rev.* **2022**, *189*, 114503. [[CrossRef](#)] [[PubMed](#)]
34. Mondal, A.; Kayal, A.; De, M. Development of Photo-ROS Responsive Liposome for the Delivery of an Antibacterial Agent by Targeting the Bacterial Membrane. *Chem. Commun.* **2026**, *62*, 5744–5748. [[CrossRef](#)] [[PubMed](#)]
35. Yuan, Z.; Das, S.; Do, C.; Park, Y.C. Effect of Cholesterol on Nano-Structural Alteration of Light-Activable Liposomes Via Laser Irradiation: Small Angle Neutron Scattering Study. *Colloids Surf. A Physicochem Eng. Asp.* **2022**, *641*, 128548. [[CrossRef](#)] [[PubMed](#)]
36. Zhang, C.; Zhao, Y.; Wang, Y.; Wang, K.; Li, S.; Wang, Y. Stimuli-Responsive Systems: A Focus on Controlled Drug Delivery for Posterior Segment Ocular Diseases. *Responsive Mater.* **2025**, *3*, e70029. [[CrossRef](#)]
37. Xu, S.; Zhang, Y.; Li, J.; Zhang, X.; Wang, W. External Stimuli-Responsive Drug Delivery to the Posterior Segment of the Eye. *Drug Deliv.* **2025**, *32*, 2476140. [[CrossRef](#)] [[PubMed](#)]
38. Mishra, G.P.; Bagui, M.; Tamboli, V.; Mitra, A.K. Recent applications of liposomes in ophthalmic drug delivery. *J. Drug Deliv.* **2011**, *2011*, 863734. [[CrossRef](#)] [[PubMed](#)]
39. Gross, N.; Ranjbar, M.; Evers, C.; Hua, J.; Martin, G.; Schulze, B.; Michaelis, U.; Hansen, L.L.; Agostini, H.T. Choroidal Neovascularization Reduced by Targeted Drug Delivery with Cationic Liposome-Encapsulated Paclitaxel or Targeted Photodynamic Therapy with Verteporfin Encapsulated in Cationic Liposomes. *Mol. Vis.* **2013**, *19*, 54–61. [[PubMed](#)]
40. Geng, S.; Yang, B.; Wang, G.; Qin, G.; Wada, S.; Wang, J.-Y. Two Cholesterol Derivative-Based PEGylated Liposomes as Drug Delivery System, Study on Pharmacokinetics and Drug Delivery to Retina. *Nanotechnology* **2014**, *25*, 275103. [[CrossRef](#)] [[PubMed](#)]
41. Dave, J.; Jani, H.; Patel, Y.; Mohite, P.; Puri, A.; Chidrawar, V.R.; Datta, D.; Bandi, S.P.; Ranch, K.; Singh, S. Polyol-Modified Deformable Liposomes Fortified Contact Lenses for Improved Ocular Permeability. *Nanomedicine* **2025**, *20*, 649–662. [[CrossRef](#)] [[PubMed](#)]
42. Mahlumba, P.; Choonara, Y.E.; Kumar, P.; Du Toit, L.C.; Pillay, V. Stimuli-Responsive Polymeric Systems for Controlled Protein and Peptide Delivery: Future Implications for Ocular Delivery. *Molecules* **2016**, *21*, 1002. [[CrossRef](#)] [[PubMed](#)]
43. Lopez-Cano, J.J.; Gonzales-Cela-Casamayor, M.A.; Andres-Guerrero, V.; Herrero-Vanrell, R.; Molina-Martinez, I.T. Liposomes as Vehicles for Topical Ophthalmic Drug Delivery and Ocular Surface Protection. *Expert Opin. Drug Deliv.* **2021**, *18*, 819–847. [[CrossRef](#)] [[PubMed](#)]
44. Karaz, S.; Senses, E. Liposomes Under Shear: Structure, Dynamics, and Drug Delivery Applications. *Adv. NanoBiomed Res.* **2023**, *3*, 2200101. [[CrossRef](#)]
45. Brugnara, M.; Vicario-de-la-Torre, M.; Casamayor, M.A.G.-C.; Lopez-Cano, J.-J.; Bravo-Osuna, I.; Huete-Toral, F.; Rubio, M.L.G.; Carracedo, G.; Molina-Martinez, I.T.; Andres-Guerrero, V.; et al. Enhancing the Hypotensive Effect of Latanoprost by Combining Synthetic Phosphatidylcholine Liposomes with Hyaluronic Acid and Osmoprotective Agents. *Drug Deliv. Transl. Res.* **2024**, *14*, 2804–2822. [[CrossRef](#)] [[PubMed](#)]
46. Sun, C.; Zhang, S.; Xu, N.; Liu, K.; Wie, F.; Zhang, X.; Zhang, J.; Gao, S.; Yu, Y.; Ding, X. Topical Ophthalmic Liposomes Dual-Modified with Penetration and Hyaluronic Acid for the Noninvasive Treatment of Neovascular Age-Related Macular Degeneration. *Int. J. Nanomed.* **2024**, *19*, 1887–1908. [[CrossRef](#)] [[PubMed](#)]

47. Zhang, Y.; Zhou, T.; Wang, K.; Luo, C.; Lv, Z.; Han, H.; Yao, K. Corneal Mucin-Targeting Liposome Nanoplatfroms Enable Treatment of Dry Eye Disease by Integrated Regulation of Ferroptosis and Inflammation. *Adv. Sci.* **2024**, *12*, 2411172. [[CrossRef](#)] [[PubMed](#)]
48. Huang, K.; Guo, R.; Luo, H.; Liu, H.; Chen, D.; Deng, T.; Li, J.; He, J.; Xu, Z.; Li, M.; et al. Mucoadhesive Liposomal Delivery System Synergizing Anti-Inflammation and Anti-Oxidant for Enhanced Treatment Against Dry Eye Disease. *J. Control Release* **2024**, *368*, 318–328. [[CrossRef](#)] [[PubMed](#)]
49. Brugnera, M.; Vicario-de-la-Torre, M.; Gonzalez-Cela-Casamayor, M.A.; Gonzalez-Fernandez, F.M.; Ferraboschi, I.; Andres-Guerrero, V.; Nicoli, S.; Sissa, C.; Pescina, S.; Herrero-Vanrell, R.; et al. Disclosing Long-Term Tolerance, Efficacy and Penetration Properties of Hyaluronic Acid-Coated Latanoprost-Loaded Liposomes as Chronic Glaucoma Therapy. *J. Control Release* **2025**, *379*, 730–742. [[CrossRef](#)] [[PubMed](#)]
50. Bonechi, C.; Mahdizadeh, F.F.; Talarico, L.; Pepi, S.; Tamasi, G.; Leone, G.; Consumi, M.; Donati, A.; Magnani, A. Liposomal Encapsulation of Citicoline for Ocular Drug Delivery. *Int. J. Mol. Sci.* **2023**, *24*, 16864. [[CrossRef](#)] [[PubMed](#)]
51. Yang, D.; Han, Y.; Wang, Y.; Pan, Y.; Zheng, L.; Liu, Z.; Li, C.; Wu, Y.; Li, H. Highly Effective Corneal Permeability of Reactive Oxygen Species-Responsive Nano-Formulation Encapsulated Cyclosporine A for Dry Eye Management. *Chem. Eng. J.* **2023**, *469*, 143968. [[CrossRef](#)]
52. Wong, K.-Y.; Liu, Y.; Wong, M.-S.; Liu, J. Cornea-SELEX for Aptamer Targeting the Surface of Eyes and Liposomal Drug Delivery. *Exploration* **2024**, *4*, 20230008. [[CrossRef](#)] [[PubMed](#)]
53. Battista, S.; Marsicano, V.; Arcadi, A.; Galantini, L.; Aschi, M.; Allegritti, E.; Del Giudice, A.; Giansanti, L. UV Properties and Loading into Liposomes of Quinoline Derivatives. *Colloids Interfaces* **2021**, *5*, 28. [[CrossRef](#)]
54. Moiseev, R.V.; Kaldybekov, D.B.; Filippov, S.K.; Radulescu, A.; Khutoryanskiy, V.V. Maleimide-Decorated PEGylated Mucoadhesive Liposomes for Ocular Drug Delivery. *Langmuir* **2022**, *45*, 13870–13879. [[CrossRef](#)] [[PubMed](#)]
55. Tierney, K.J.; Block, D.E.; Longo, M.L. Elasticity and Phase Behavior of DPPC Membrane Modulated by Cholesterol, Ergosterol, and Ethanol. *Biophys. J.* **2005**, *89*, 2481–2493. [[CrossRef](#)] [[PubMed](#)]
56. Natsaridis, E.; Gkartziou, F.; Mourtas, S.; Stuart, M.C.A.; Kolonitsiou, F.; Klepetsanis, P.; Spiliopoulou, I.; Antimisariis, S.G. Moxifloxacin Liposomes: Effect of Liposome Preparation Method on Physicochemical Properties and Antimicrobial Activity against *Staphylococcus epidermidis*. *Pharmaceutics* **2022**, *14*, 370. [[CrossRef](#)] [[PubMed](#)]
57. Huang, H.; Yang, X.R.; Li, H.L.; Lu, H.S.; Oswald, J.; Liu, Y.M.; Zeng, J.; Jin, C.; Peng, X.; Liu, J.; et al. IRGD Decorated Liposomes: A Novel Actively Penetrating Topical Ocular Drug Delivery Strategy. *Nano Res.* **2020**, *13*, 3105–3109. [[CrossRef](#)]
58. Csorba, A.; Katona, G.; Budai-Szűcs, M.; Balogh-Weiser, D.; Fadda, A.M.; Caddeo, C.; Takács, A.I.; Matyus, P.; Balogh, G.T.; Nagy, Z.Z. Effect of Liposomal Formulation of Ascorbic Acid on Corneal Permeability. *Sci. Rep.* **2023**, *13*, 3448. [[CrossRef](#)] [[PubMed](#)]
59. Zhan, C.; Santamaria, C.M.; Wang, W.; McAlvin, J.B.; Kohane, D.S. Long-Acting Liposomal Corneal Anesthetics. *Biomaterials* **2018**, *181*, 372–377. [[CrossRef](#)] [[PubMed](#)]
60. Thanuja, M.Y.; Suraksha, S.T.; Samarth, V.S.; Keerthana, G.S.; Chandan Vasudev, S.; Sudhir, H.R. Fusogenic Liposome-Coated Nanoparticles for Rapid Internalization into Donor Corneal Endothelial Tissue to Enable Prophylaxis Before Transplantation. *Nanoscale Adv.* **2023**, *5*, 6410–6422. [[CrossRef](#)] [[PubMed](#)]
61. Liao, Y.; Jiang, H.; Du, Y.; Xiong, X.; Zhang, Y.; Du, Z. Using Convolutional Neural Network as a Statistical Algorithm to Explore the Therapeutic Effect of Insulin Liposomes on Corneal Inflammation. *Comput. Intell. Neurosci.* **2022**, *1*, 1169438. [[CrossRef](#)] [[PubMed](#)]
62. Moghimipour, E.; Farrokhi, S.; Salimi, A. Enhanced Corneal Permeation of Pilocarpine Using Liposome Technology. *J. Kerman Univ. Med. Sci.* **2021**, *28*, 462–470. [[CrossRef](#)]
63. Shimokawa, T.; Fukuta, T.; Inagi, T.; Kogure, K. Protective Effect of High-Affinity Liposomes Encapsulating Astaxanthin Against Corneal Disorder in the In vivo Rat Dry Disease Model. *J. Clin. Biochem Nutr.* **2020**, *66*, 224–232. [[CrossRef](#)] [[PubMed](#)]
64. Lin, X.; Yu, X.; Chen, X.; Sheng, S.; Wang, J.; Wang, B.; Xu, W. Inhibition of Neovascularization and Inflammation in a Mouse Model of Corneal Alkali Burns Using Cationic Liposomal Tacrolimus. *Front. Bioeng. Biotechnol.* **2021**, *9*, 791954. [[CrossRef](#)] [[PubMed](#)]
65. Na, K.-S.; Kim, D.; Kim, H.; Koh, W.-G.; Lee, H.J. The Combined Effect of Epidermal Growth Factor and Keratocyte Growth Factor Delivered by Hyaluronic Acid Hydrogel on Corneal Wound Healing. *Int. J. Biol. Macromol.* **2024**, *270*, 132365. [[CrossRef](#)] [[PubMed](#)]
66. Tang, Q.; Lu, B.; Jian, H.; Chen, X.; Fu, Q.; Han, H.; Luo, C.; Yin, H.; Qin, Z.; Lyu, D.; et al. Exosomes-Loaded Thermosensitive Hydrogels for Corneal Epithelium and Stroma Regeneration. *Biomaterials* **2022**, *280*, 121320. [[CrossRef](#)] [[PubMed](#)]
67. Tawfik, E.A.; Alshamsan, A.; Kalam, M.A.; Raish, M.; Alkholief, M.; Stapleton, P.; Harvey, K.; Craig, D.Q.M.; Barker, S.A. In Vitro and In Vivo Biological Assessment of Dual Drug-Loaded Coaxial Nanofibers for the Treatment of Corneal Abrasion. *Int. J. Pharm.* **2021**, *604*, 120732. [[CrossRef](#)] [[PubMed](#)]

68. Sun, L.; Fan, M.; Huang, D.; Li, B.; Xu, R.; Gao, F.; Chen, Y. Clodronate-Loaded Liposomal and Fibroblast-Derived Exosomal Hybrid System for Enhanced Drug Delivery to Pulmonary Fibrosis. *Biomaterials* **2021**, *271*, 120761. [\[CrossRef\]](#) [\[PubMed\]](#)
69. Binaymotlagh, R.; Hajareh Haghighi, F.; Chronopoulou, L.; Palocci, C. Liposome–Hydrogel Composites for Controlled Drug Delivery Applications. *Gels* **2024**, *10*, 284. [\[CrossRef\]](#) [\[PubMed\]](#)
70. Shukr, M.H.; Ismail, S.; El-Hossary, G.G.; El-Shazly, A.H. Design and Evaluation of Mucoadhesive in Situ Liposomal Gel for Sustained Ocular Delivery of Travoprost Using Two Steps Factorial Design. *J. Drug Deliv. Sci. Technol.* **2021**, *61*, 102333. [\[CrossRef\]](#)
71. Pande, S. Liposomes for Drug Delivery: Review of Vesicular Composition, Factors Affecting Drug Release and Drug Loading in Liposomes. *Artif. Cells Nanomed. Biotechnol.* **2023**, *51*, 428–440. [\[CrossRef\]](#) [\[PubMed\]](#)
72. Londhe, V.Y.; Sharma, S. Formulation, Characterization, Optimization and In-vivo Evaluation of Methazolamide Liposomal In-situ Gel for Treating Glaucoma. *J. Drug Deliv. Sci. Technol.* **2022**, *67*, 102951. [\[CrossRef\]](#)
73. Blazaki, S.; Pachis, K.; Tzatzarakis, M.; Tsilimbaris, M.; Antimisariis, S.G. Novel Liposome Aggregate Platform (LAP) System for Sustained Retention of Drugs in the Posterior Ocular Segment Following Intravitreal Injection. *Int. J. Pharm.* **2020**, *576*, 118987. [\[CrossRef\]](#) [\[PubMed\]](#)
74. Fathalla, D.; Fouad, E.A.; Soliman, G.M. Latanoprost niosomes as a sustained release ocular delivery system for the management of glaucoma. *Drug Dev. Ind. Pharm.* **2020**, *46*, 806–813. [\[CrossRef\]](#) [\[PubMed\]](#)
75. Sung, M.S.; Moon, M.J.; Thomas, R.G.; Kim, S.Y.; Lee, J.S.; Jeong, Y.Y.; Park, I.-K.; Park, S.W. Intravitreal Injection of Liposomes Loaded with a Histone Deacetylase Inhibitor Promotes Retinal Ganglion Cell Survival in a Mouse Model of Optic Nerve Crush. *Int. J. Mol. Sci.* **2020**, *21*, 9297. [\[CrossRef\]](#) [\[PubMed\]](#)
76. Mu, H.; Wang, Y.; Chu, Y.; Jiang, Y.; Hua, H.; Chu, L.; Wang, K.; Wang, A.; Liu, W.; Li, Y.; et al. Multivesicular Liposomes for Sustained Release of Bevacizumab in Treating Laser-Induced Choroidal Neovascularization. *Drug Deliv.* **2018**, *25*, 1372–1383. [\[CrossRef\]](#) [\[PubMed\]](#)
77. Belamkar, A.; Harris, A.; Zukerman, R.; Siesky, B.; Oddone, F.; Verticchio Vercellin, A.; Ciulla, T.A. Sustained Release Glaucoma Therapies: Novel Modalities for Overcoming Key Treatment Barriers Associated with Topical Medications. *Ann. Med.* **2022**, *54*, 343–358. [\[CrossRef\]](#) [\[PubMed\]](#)
78. Al-Amin, M.D.; Mastrotto, F.; Subrizi, A.; Sen, M.; Turunen, T.; Arango-Gonzalez, B.; Ueffing, M.; Malfanti, A.; Urtti, A.; Salmaso, S.; et al. Tailoring Surface Properties of fLiposomes for Doxamethasone Intraocular Administration. *J. Control Release* **2023**, *354*, 323–336. [\[CrossRef\]](#) [\[PubMed\]](#)
79. Fan, Y.; Marioli, M.; Zhang, K. Analytical Characterization of Liposomes and Other Lipid Nanoparticles for Drug Delivery. *J. Pharm. BioMed Anal.* **2021**, *192*, 113642. [\[CrossRef\]](#) [\[PubMed\]](#)
80. Navarro-Partida, J.; Altamirano-Vallejo, J.C.; Gonzalez-De la Rosa, A.; Armendariz-Borunda, J.; Castro-Castaneda, C.R.; Santos, A. Safety and Tolerability of Topical Ophthalmic Triamcinolone Acetonide-Loaded Liposomes Formulation and Evaluation of Its Biologic Activity in Patients with Diabetic Macular Edema. *Pharmaceutics* **2021**, *13*, 322. [\[CrossRef\]](#) [\[PubMed\]](#)
81. Tang, H.; Xie, Y.; Zhu, M.; Jia, J.; Liu, R.; Shen, Y.; Zheng, Y.; Guo, X.; Miao, D.; Pei, J. Estrone-Conjugated PEGylated Liposome Co-Loaded Paclitaxel and Carboplatin Improve Anti-Tumor Efficacy in Ovarian Cancer and Reduce Acute Toxicity of Chemo-Drugs. *Int. J. Nanomed.* **2022**, *17*, 3013–3041. [\[CrossRef\]](#) [\[PubMed\]](#)
82. Syama, K.; Jokubek, Z.J.; Zaifman, J.; Tam, Y.Y.C.; Zou, S. Development of Lipid Nanoparticles and Liposomes Reference Materials (II): Cytotoxic Profiles. *Sci. Rep.* **2022**, *12*, 18071. [\[CrossRef\]](#) [\[PubMed\]](#)
83. Dymek, M.; Sikora, E. Liposomes as Biocompatible and Smart Delivery Systems—The Current State. *Adv. Colloid Interface Sci.* **2022**, *309*, 102757. [\[CrossRef\]](#) [\[PubMed\]](#)
84. Amalia, H.; Ridwan, R.; Estuningtyas, A.; Sitompul, R.; Adawiyah, R.; Freisleben, H.-J. Efficacy of Liposomal Amphotericin B Eye Drops at Two Concentrations in Experimental Aspergillus Keratomycosis in Rabbits. *Acta Biochim. Indones.* **2026**, *9*, 240. [\[CrossRef\]](#)
85. Bulboacă, A.E.; Porfire, A.; Bolboacă, S.D.; Nicula, C.A.; Feștilă, D.G.; Roman, A.; Râmnoveanu, R.M.; Râmnoveanu, A.; Dogaru, G.; Boarescu, P.-M.; et al. Protective Effects of Liposomal Curcumin on Oxidative Stress/Antioxidant Imbalance, Metalloproteinases 2 and -9, Histological Changes and Renal Function in Experimental Nephrotoxicity Induced by Gentamicin. *Antioxidants* **2021**, *10*, 325. [\[CrossRef\]](#) [\[PubMed\]](#)
86. Sampath, S.; Saravanan, M.K.T.; Basumatary, N.; Kumari, M.; Shellaiah, M.; Bhushan, M. Chapter 17—Liposome-Derived Nanotherapeutics Against Drug-Resistant Microbes. In *Nanotherapeutics Combating Microbial Infections and Antimicrobial Resistance*; Elsevier: Amsterdam, The Netherlands, 2026; Volume 2, pp. 375–390. [\[CrossRef\]](#)
87. Kapoor, D.U.; Khanday, M.A.; Pareek, A.; Prajapati, B.G. Reengineering Infection Treatment: Liposome-Based Innovations in Antibacterial Delivery. *Res. Chem.* **2025**, *16*, 102417. [\[CrossRef\]](#)
88. Ezzat, H.; Rady, M.; Hathout, R.M.; Abdel-Halim, M.; Mansour, S. Enhanced Anti-Bacterial Effect of Kojic Acid Using Gelatinized Core Liposomes: A Potential Approach to Combat Antibiotic Resistance. *J. Drug Deliv. Sci. Technol.* **2021**, *64*, 102625. [\[CrossRef\]](#)
89. Osei Duah Junior, I.; Ampong, J.; Danquah, C.A. Mechanisms and Evolution of Antimicrobial Resistance in Ophthalmology: Surveillance, Clinical Implications, and Future Therapies. *Antibiotics* **2025**, *14*, 1167. [\[CrossRef\]](#) [\[PubMed\]](#)

90. Ahmed, E.T.M.; Hassan, M.; Shamma, R.N.; Makky, A.; Hassan, D.H. Controlling the Evolution of Selective Vancomycin Resistance through Successful Ophthalmic Eye-Drop Preparation of Vancomycin-Loaded Nanoliposomes Using the Active-Loading Method. *Pharmaceutics* **2023**, *15*, 1636. [\[CrossRef\]](#) [\[PubMed\]](#)
91. dos Santos, G.A.; Ferreira-Nunes, R.; Dalmolin, L.F. Besifloxacin liposomes with positively charged additives for an improved topical ocular delivery. *Sci. Rep.* **2020**, *10*, 19285. [\[CrossRef\]](#) [\[PubMed\]](#)
92. Abraham, K.S.; Ravi, S.S.S.; Vajravelu, L.K. Comparative Analysis of Biofilm in Bacterial and Fungal Isolates from Contact Lens and Non-Contact Lens Associated Keratitis. *medRxiv* **2024**, preprint. [\[CrossRef\]](#)
93. Kluz, M.; Oppenheimer-Shaanan, Y.; Dadosh, T.; Morandi, M.I.; Avinoam, O.; Raanan, C.; Goldsmith, M.; Goldberg, R.; Klein, J. Designer Liposomal Nanocarriers are Effective Biofilm Eradicators. *ACS Nano* **2022**, *16*, 15792–15804. [\[CrossRef\]](#) [\[PubMed\]](#)
94. Wang, Y.; Hu, Y.; An, J.; Zhang, H.; Liu, X.; Li, X.; Zhang, Z.; Zhang, X. Liposome-Based Permeable Eyedrops for Effective Posterior Segment Drug Delivery. *Adv. Funct. Mater.* **2024**, *34*, 2403142. [\[CrossRef\]](#)
95. Bigdeli, A.; Makhmalzadeh, B.S.; Feghhi, M.; Soleimani Biatiani, E. Cationic Liposomes as Promising Vehicles for Timolol/Brimonidine Combination Ocular Delivery in Glaucoma: Formulation Development and in Vitro/in Vivo Evaluation. *Drug Deliv. Transl. Res.* **2023**, *13*, 1035–1047. [\[CrossRef\]](#) [\[PubMed\]](#)
96. Santana, J.E.G.; Oliveira-Tintino, C.D.D.M.; Gonçalves Alencar, G.; Siqueira, G.M.; Sampaio Alves, D.; Moura, T.F.; Tintino, S.R.; de Menezes, I.R.A.; Rodrigues, J.P.V.; Gonçalves, V.B.P.; et al. Comparative Antibacterial and Efflux Pump Inhibitory Activity of Isolated Nerolidol, Farnesol, and α -Bisabolol Sesquiterpenes and Their Liposomal Nanoformulations. *Molecules* **2023**, *28*, 7649. [\[CrossRef\]](#) [\[PubMed\]](#)
97. Alluhaim, W.; Alkhulaifi, M.M.; Alzahrani, R.R.; Alrfaei, B.M.; Yassin, A.E.B.; Alghoribi, M.F.; Alsaadi, A.M.; Al-Asmari, A.I.; Al-Fahad, A.J.; Ali, R.; et al. Effectiveness of a Novel Liposomal Methylglyoxal–Tobramycin Formulation in Reducing Biofilm Formation and Bacterial Adhesion. *Antibiotics* **2025**, *14*, 3. [\[CrossRef\]](#) [\[PubMed\]](#)
98. Wu, B.; Li, M.; Hong, W.; Lv, Q.; Li, Y.; Xie, S.; Han, J.; Tian, B. Cell Penetrating Peptide TAT-Functionalized Liposomes for Efficient Ophthalmic Delivery of Flurbiprofen: Penetration and its Underlying Mechanism, Retention, Anti-Inflammation and Biocompatibility. *Int. J. Pharm.* **2021**, *598*, 120405. [\[CrossRef\]](#) [\[PubMed\]](#)
99. Meagher, R.B.; Lewis, Z.A.; Ambati, S.; Lin, X. Aiming for a Bull's-Eye: Targeting Antifungals to Fungi with Dectin-Decorated Liposomes. *PLoS Pathog.* **2021**, *17*, e1009699. [\[CrossRef\]](#) [\[PubMed\]](#)
100. Dey, S.; Patel, J.; Anand, B.S.; Jain-Vakkalagadda, B.; Kalil, P.; Pal, D.; Ganapathy, V.; Mitra, A.K. Molecular Evidence and Functional Expression of P-Glycoprotein (MDR1) in Human and Rabbit Cornea and Corneal Epithelial Cell Lines. *Investig. Ophthalmol. Vis. Sci.* **2003**, *44*, 2909–2918. [\[CrossRef\]](#) [\[PubMed\]](#)
101. Lee, J.; Pelis, R.M. Drug Transport by the Blood-Aqueous Humor Barrier of the Eye. *Drug Metab. Dispos.* **2016**, *44*, 1675–1681. [\[CrossRef\]](#) [\[PubMed\]](#)
102. Faraag, A.H.I.; Shafaa, M.W.; Elkholy, N.S.; Abdel-Hafez, L.J.M. Stress Impact of Liposomes Loaded with Ciprofloxacin on the Expression Level of *MepA* and *NorB* Efflux Pumps of Methicillin-Resistant *Staphylococcus aureus*. *Int. Microbiol.* **2022**, *25*, 427–446. [\[CrossRef\]](#) [\[PubMed\]](#)
103. Li, W.-R.; Zhang, Z.-Q.; Liao, K.; Shi, Q.-S.; Huang, X.-B.; Xie, X.-B. Efflux Pumps of *Pseudomonas aeruginosa* and their Regulatory Mechanisms Underlying Multidrug Resistance. *Int. Biodeterior. Biodegrad* **2025**, *202*, 106096. [\[CrossRef\]](#)
104. Wang, Y. Liposome as a Delivery System for the Treatment of Biofilm-Mediated Infections. *J. Appl. Microbiol.* **2021**, *131*, 2626–2639. [\[CrossRef\]](#) [\[PubMed\]](#)
105. Mazzantini, D.; Massimino, M.; Calvigioni, M.; Rossi, V.; Celandroni, F.; Lupetti, A.; Batoni, G.; Ghelardi, E. Anti-Staphylococcal Biofilm Effects of a Liposome-Based Formulation Containing Citrus Polyphenols. *Antibiotics* **2024**, *13*, 318. [\[CrossRef\]](#) [\[PubMed\]](#)
106. Man, Y.; Tang, H.; Wang, Y.; Yang, R.; Yan, D.; Yu, Q.; Zhang, L.; Mei, L.; Qi, J.; Shao, L. Casin-Liposome Complex Loading Basil Essential Oil: Preparation, Antibacterial Effect, and Preservative Effect on Brainsed Beef. *Food Chem.* **2026**, *511*, 148807. [\[CrossRef\]](#) [\[PubMed\]](#)
107. Burks, S.R.; Legenzov, E.A.; Martin, E.W.; Li, C.; Lu, W.; Kao, J.P.Y. Co-Encapsulating the Fusogenic Peptide INF7 and Molecular Imaging Probes in Liposomes Increases Intracellular Signal and Probe Retention. *PLoS ONE* **2015**, *10*, e0120982. [\[CrossRef\]](#) [\[PubMed\]](#)
108. Pinho, J.O.; Ferreira, M.; Coelho, M.; Pinto, S.N.; Aguiar, S.I.; Gaspar, M.M. Liposomal Rifabutin—A Promising Antibiotic Repurposing Strategy against Methicillin-Resistant *Staphylococcus aureus* Infections. *Pharmaceutics* **2024**, *17*, 470. [\[CrossRef\]](#) [\[PubMed\]](#)
109. Majlesi, S.; Divsar, F.; Moshiri Langroudi, M.; Ize, N.; Malek, M.A.; Yousefipour, S.; Zendehtrokh, S.J.; Mirdamadi, A.; Jafarim, Z.; Zahmatkesh, H.; et al. Synthesis of Stable Micelle/Liposome Nanocarriers to Deliver Silibinin into Ciprofloxacin Resistant Isolates of *Escherichia coli* with Effects on Biofilm Formation and Efflux Pumps. *3 Biotech.* **2026**, *16*, 107. [\[CrossRef\]](#) [\[PubMed\]](#)
110. Guo, Q.; Wu, Z.; Tao, B.; Wang, Q.; Huang, C.; Gao, Y.; Wang, Y.-E.; Wu, X.; Chen, Y.; Guo, T.; et al. Essential Oil-Antibiotics Synergistic Delivery Strategy via Phenylboronic-Acid-Functionalized Liposomes for Targeted Treatment of MRSA Pneumonia. *ACS Infect. Dis.* **2025**, *11*, 2553–2567. [\[CrossRef\]](#) [\[PubMed\]](#)

111. Sackey, T.; Kannan, U.; Majumder, S.; John, J.; Viau, C.; Feng, Z.; Benoit-Biancamano, M.O.; Ronholm, J.; George, S. Nanoliposome Mediated Co-Delivery of Amoxicillin and Tazobactam Remediate Intracellular Infection by a Multidrug-Resistant *Salmonella enterica* serovar Typhimurium. *J. Antibiot.* **2026**, *79*, 337–350. [[CrossRef](#)] [[PubMed](#)]
112. Ramzan, M.; Khan, T.; Siddique, M.U.M.; Shahid, M. Biocompatible Cationic 5-Fluorouracil Loaded Elastic Liposomes for Ocular Delivery: In vitro, Ex vivo, and In vivo Evaluation. *J. Drug Deliv. Sci. Technol.* **2024**, *101*, 106278. [[CrossRef](#)]
113. Ren, T.; Lin, X.; Zhang, Q.; You, D.; Liu, X.; Tao, X.; Gou, J.; Zhang, Y.; Yin, T.; He, H.; et al. Encapsulation of Azithromycin Ion Pair in Liposome for Enhancing Ocular Delivery and Therapeutic Efficacy on Dry Eye. *Mol. Pharm.* **2018**, *15*, 4862–4871. [[CrossRef](#)] [[PubMed](#)]
114. Albash, R.; Abdellatif, M.M.; Hassan, M.; Badawi, M.N. Tailoring Terpesomes and Leciplex for the Effective Ocular Conveyance of Moxifloxacin Hydrochloride (Comparative Assessment): In-vitro, Ex-vivo, and In-vivo Evaluation. *Int. J. Nanomed.* **2021**, *16*, 5247–5263. [[CrossRef](#)] [[PubMed](#)]
115. Wong, C.W.; Wong, E.; Metselaar, J.M.; Storm, G.; Wong, T.T. Liposomal Drug Delivery System for Anti-Inflammatory Treatment After Cataract Surgery: A Phase I/II Clinical Trial. *Drug Deliv. Transl. Res.* **2022**, *12*, 7–14. [[CrossRef](#)] [[PubMed](#)]
116. Elhabal, S.F.; Faheem, A.M.; Hababeh, S.; Nelson, J.; Elzohairy, N.A.; AbdelGhany Morsy, S.A.; Ewedah, T.M.; Mousa, I.S.; Fouad, M.A.; Hamdan, A.M.E. Dissolving Microneedles Containing Lactoferrin Nanosuspension for Enhancement of Antimicrobial and Anti-Inflammatory Effects in the Treatment of Dry Eye Disease. *Pharmaceutics* **2025**, *17*, 653. [[CrossRef](#)] [[PubMed](#)]
117. Terreni, E.; Burgalassi, S.; Chetoni, P.; Tampucci, S.; Zucchetti, E.; Fais, R.; Ghelardi, E.; Lupetti, A.; Monti, D. Development and Characterization of a Novel Peptide-Loaded Antimicrobial Ocular Insert. *Biomolecules* **2020**, *10*, 664. [[CrossRef](#)] [[PubMed](#)]
118. Huang, H.; Xie, Y.; Zhong, J.; Fu, Z.; Wu, P.; Chen, X.; Xiao, Z.; Yuan, J.; Shi, X.; Liang, D. Antimicrobial Peptides Loaded Collagen Nanosheets with Enhanced Antibacterial Activity, Corneal Wound Healing and M1 Macrophage Polarization in Bacterial Keratitis. *Compos. Part B Eng.* **2024**, *275*, 111283. [[CrossRef](#)]
119. Youssef, A.A.A.; Dudhipala, N.; Majumdar, S. Dual Drug Loaded Lipid Nanocarrier Formulations for Topical Ocular Applications. *Int. J. Nanomed.* **2022**, *17*, 2283–2299. [[CrossRef](#)] [[PubMed](#)]
120. Qiu, L.; Zhang, J.; Liu, S.; Li, B.; Wang, J.; Tang, J.; Pu, X.; Huang, Z.; Liao, X.; Yin, G. Dendritic Oligoethylenimine Decorated Liposome with Augmented Corneal Retention and Permeation for Efficient Topical Delivery of Antiglaucoma Drugs. *Nano Lett.* **2023**, *23*, 11193–11202. [[CrossRef](#)] [[PubMed](#)]
121. Koca, D.S.; Dietrich-Ntoukas, T. Frequency of Topical Immunomodulatory and Immunosuppressive Therapies for Ocular Chronic Graft-versus-Host Disease. *J. Clin. Med.* **2024**, *13*, 4728. [[CrossRef](#)] [[PubMed](#)]
122. Omar, W.M.; Shalaby, R.A.; Saher, O.; Nemr, A.A.; Fatouh, A.M. Engineered Brimonidine Tartrate Aminosomes as a Mucoadhesive Platform for Sustained Glaucoma Management: Optimization, In Vitro Characterization, and In Vivo Evaluation. *Pharmaceutics* **2026**, *18*, 422. [[CrossRef](#)] [[PubMed](#)]
123. Chang, M.-C.; Kuo, Y.-J.; Hung, K.-H.; Peng, C.-L.; Chen, K.-Y.; Yeh, L.-K. Liposomal Dexamethasone-Moxifloxacin Nanoparticle Combination with Collagen/Gelatin/Alginate Hydrogel for Corneal Infection Treatment and Wound Healing. *BioMed Mater.* **2020**, *15*, 055022. [[CrossRef](#)] [[PubMed](#)]
124. Caballo-González, M.Á.; Gómez-Ballesteros, M.; Brugnera, M.; Benitez-del-Castillo, J.M.; Gonzalez-Alonso-Alegre, E.M.; Rodriguez-Alvaro, A.; De-las-Heras, B.; Gil-Alegre, E.; Vicario-de-la-Torre, M.; Herrero-Vanrell, R.; et al. A Liposomal Formulation of Cyclosporine a Shows Promising Results in Treating Symptoms of Moderate to Severe Dry Eye Disease in Dogs. *Drug Deliv. Transl. Res.* **2026**, *16*, 1035–1051. [[CrossRef](#)] [[PubMed](#)]
125. Sharma, V.K.; Srinivasan, H.; Sakai, V.G.; Mitra, S. Dioctadecyldimethylammonium Bromide, a Surfactant Model for the Cell Membrane: Importance of Microscopic Dynamics. *Struct. Dyn.* **2020**, *7*, 051301. [[CrossRef](#)] [[PubMed](#)]
126. da Silva, C.N.; Silva, F.R.D.; Dourado, L.F.N.; Reis, P.V.M.D.; Silva, R.O.; da Costa, B.L.; Nunes, P.S.; Amaral, F.A.; Santos, V.L.D.; de Lima, M.E.; et al. A New Topical Eye Drop Containing LyeTxI-b, A Synthetic Peptide Designed from A *Lycosa erithrognata* Venom Toxin, Was Effective to Treat Resistant Bacterial Keratitis. *Toxins* **2019**, *11*, 203. [[CrossRef](#)] [[PubMed](#)]
127. van Gent, M.E.; Ali, M.; Nibbering, P.H.; Kłodzińska, S.N. Current Advances in Lipid and Polymeric Antimicrobial Peptide Delivery Systems and Coatings for the Prevention and Treatment of Bacterial Infections. *Pharmaceutics* **2021**, *13*, 1840. [[CrossRef](#)] [[PubMed](#)]
128. Shannon, A.H.; Adelman, S.A.; Hisey, E.A.; Potnis, S.S.; Roza, V.; Yung, M.W.; Li, J.Y.; Murphy, C.J.; Thomasy, S.M.; Leonard, B.C. Antimicrobial Peptide Expression at the Ocular Surface and Their Therapeutic Use in the Treatment of Microbial Keratitis. *Front. Microbiol.* **2022**, *13*, 857735. [[CrossRef](#)] [[PubMed](#)]
129. Bhat, U.M.; Khan, N.A.; Raza, S.N.; Ali, M.; Mehdi, S.; Mohiuddin, I.; Shakeel, F.; Bhat, Z.A.; Bader, G.N.; Chashoo, I.A.; et al. Ciprofloxacin Hydrochloride-Loaded Ocular Silk Fibroin Liposomes: Formulation, Characterization, In vitro Cytotoxicity, and Antimicrobial Activity. *Heliyon* **2024**, *10*, e38777. [[CrossRef](#)] [[PubMed](#)]
130. Campardelli, R.; Trucillo, P.; Reverchon, E. Supercritical Assisted Process for the Efficient Production of Liposomes Containing Antibiotics for Ocular Delivery. *J. CO2 Util.* **2018**, *25*, 235–241. [[CrossRef](#)]

131. Moorcroft, S.C.T.; Roach, L.; Jayne, D.G.; Ong, Z.Y.; Evans, S.D. Nanoparticle-Loaded Hydrogel for the Light-Activated Release and Photothermal Enhancement of Antimicrobial Properties. *ACS Appl. Mater. Interfaces* **2020**, *12*, 24544–24554. [[CrossRef](#)] [[PubMed](#)]
132. Nirbhavane, P.; Sharma, G.; Singh, B.; Begun, G.; Gones, M.-C.; Rauz, S.; Vincent, R.; Denniston, A.K.; Hill, L.J.; Katare, O.P. Triamcinolone Acetonide Loaded-Cationic Nano-Lipoidal Formulation for Uveitis: Evidences of Improved Biopharmaceutical Performance and Anti-Inflammatory Activity. *Colloids Surf. B Bionterfaces* **2020**, *190*, 110902. [[CrossRef](#)] [[PubMed](#)]
133. Sarfraz, M.; Afzal, A.; Yang, T.; Gai, Y.; Raza, S.M.; Khan, M.W.; Cheng, Y.; Ma, X.; Xiang, G. Development of Dual Drug Loaded Nanosized Liposomal Formulation by A Reengineered Ethanolic Injection Method and Its Pre-Clinical Pharmacokinetic Studies. *Pharmaceutics* **2018**, *10*, 151. [[CrossRef](#)] [[PubMed](#)]
134. Singh, N.; Romero, M.; Travanut, A.; Monteiro, P.F.; Jordan-Lluch, E.; Hardie, K.R.; Williams, P.; Alexander, M.R.; Alexander, C. Dual Bioresponsive Antibiotic and Quorum Sensing Inhibitor Combination Nanoparticles for Treatment of *Pseudomonas aeruginosa* Biofilm In vitro and Ex vivo. *Biomater. Sci.* **2019**, *7*, 4099–4111. [[CrossRef](#)] [[PubMed](#)]
135. Gelen-Gungor, D.; Nigiz, S.; Ozkul, C.; Eroglu, H.; Nemutlu, E.; Ulubayram, K.; Mao, Y.; Michniak-Kohn, B.; Eroglu, I. Co-Delivery of Azithromycin and Nisin Through Liposomes for Skin Infection to Reduce Antimicrobial Drug Resistance. *Int. J. Pharm.* **2025**, *679*, 125764. [[CrossRef](#)] [[PubMed](#)]
136. Bai, J.; Hao, J.; Wei, C.; Gao, Q.; Yu, B.; Guo, P.; Yang, Y. Brazilin and Streptomycin Co-Loaded Liposomes: Preparation, Characterization, Antimicrobial Properties and Preservation Effects on Blueberry. *SSRN* **2024**, *83*, 109433. [[CrossRef](#)]
137. Liu, B.; Zhang, J.; Liu, Z.; Wang, P.; Zhang, Y.; He, H.; Yin, T.; Gou, J.; Tang, X. Research on the Preparation Process of the Cytarabine/Daunorubicin Dual-Encapsulation Liposome and its Physicochemical Properties and Performances In vitro/vivo. *Int. J. Pharm.* **2023**, *646*, 123500. [[CrossRef](#)] [[PubMed](#)]
138. Nordström, R.; Zhu, L.; Härmark, J.; Levi-Kalishman, Y.; Koren, E.; Barenholz, Y.; Levinton, G.; Shamrakov, D. Quantitative Cryo-TEM Reveals New Structural Details of Doxil-Like PEGylated Liposomal Doxorubicin Formulation. *Pharmaceutics* **2021**, *13*, 123. [[CrossRef](#)] [[PubMed](#)]
139. Molugu, T.R.; Thurmond, R.L.; Alam, T.M.; Trouad, T.P.; Brown, M.F. Phospholipid Headgroups Govern Area per Lipid and Emergent Elastic Properties of Bilayers. *Biophys. J.* **2022**, *121*, 4205–4220. [[CrossRef](#)] [[PubMed](#)]
140. Belay, W.Y.; Getachew, M.; Tegegne, B.A.; Teffera, Z.H.; Dagne, A.; Zeleke, T.K.; Abebe, R.B.; Gedif, A.A.; Fenta, A.; Yirdaw, G.; et al. Mechanism of Antibacterial Resistance, Strategies and Next-Generation Antimicrobials to Contain Antimicrobial Resistance: A Review. *Front. Pharmacol.* **2024**, *15*, 1444781. [[CrossRef](#)] [[PubMed](#)]
141. Murugaiyan, J.; Kumar, P.A.; Rao, G.S.; Iskandar, K.; Hawser, S.; Hays, J.P.; Mohsen, Y.; Adukkadukkam, S.; Awuah, W.A.; Jose, R.A.M.; et al. Progress in Alternative Strategies to Combat Antimicrobial Resistance: Focus on Antibiotics. *Antibiotics* **2022**, *11*, 200. [[CrossRef](#)] [[PubMed](#)]
142. Deborah, P.M.; Padmaja, N. Bacterial Isolates and Their Biofilm Formation on Contact Lenses. *IP Int. J. Med. Microbiol. Trop. Dis.* **2022**, *8*, 10–14. [[CrossRef](#)]
143. Makhlof, Z.; Ali, A.A.; Al-Sayah, M.H. Liposomes-Based Drug Delivery Systems of Anti-Biofilm Agents to Combat Bacterial Biofilm Formation. *Antibiotics* **2023**, *12*, 875. [[CrossRef](#)] [[PubMed](#)]
144. Ghosh, R.; De, M. Liposome-Based Antibacterial Delivery: An Emergent Approach to Combat Bacterial Infections. *ACS Omega* **2023**, *8*, 35442–35451. [[CrossRef](#)] [[PubMed](#)]
145. Mozafari, M.R.; Torkaman, S.; Karamouzian, F.M.; Rasti, B.; Baral, B. Antimicrobial Applications of Nanoliposome Encapsulated Silver Nanoparticles: A Potential Strategy to Overcome Bacterial Resistance. *Curr. Nanosci.* **2021**, *17*, 26–40. [[CrossRef](#)]
146. Prabakaran, A.; Amit, A. Biophysical Analysis on Molecular Interactions Between Chitosan-Coated Sinapic Acid Loaded Liposomes and Mucin. *Biochim Biophys. Acta Gen. Subj.* **2024**, *1868*, 130517. [[CrossRef](#)] [[PubMed](#)]
147. Sebaaly, C.; Trifan, A.; Sieniawska, E.; Greige-Gerges, H. Chitosan-Coating Effect on the Characteristics of Liposomes: A Focus on Bioactive Compounds and Essential Oils: A Review. *Processes* **2021**, *9*, 445. [[CrossRef](#)]
148. Zhang, J.; Qin, J.; Fu, Z.; Tang, W.; Pu, C.; Sun, Q. Synergistic Bactericidal and Antibiofilm Effects of Curcumin and Nisin Dual-Loaded Liposomes Combined with Photodynamic Treatment on *Listeria monocytogenes*. *Food Chem.* **2025**, *429*, 145557. [[CrossRef](#)] [[PubMed](#)]
149. Fabiano, M.G.; Maurizi, L.; Forte, J.; D'Intino, E.; Ammendolia, M.G.; Corinti, D.; Tagueha, A.D.; Relucenti, M.; Donfrancesco, O.; Rinaldi, F.; et al. A Green Strategy for Resveratrol Nanodelivery: A Multidisciplinary Approach for the Physicochemical Characterization of Thymus-Base Liposomes with Anti-Biofilm Activity Against *Listeria monocytogenes*. *J. Drug Deliv. Sci. Technol.* **2026**, *117*, 108027. [[CrossRef](#)]
150. Borro, B.C.; Toussaint, M.S.; Bucciarelli, S.; Malmsten, M. Effects of Charge Contrast and Composition on Microgel Formation and Interactions with Bacteria-Mimicking Liposomes. *Biochim. Biophys. Acta Gen. Subj.* **2021**, *1865*, 129485. [[CrossRef](#)] [[PubMed](#)]
151. Miatmoto, A.; Asmoro, F.H.; Azhari, A.A.; Rosita, N.; Huang, C.-S. The Effect of 1,2-Dioleoyl-3-Trimethylammonium Propane (DOTAP) Addition on the Physical Characteristics of β -Ionone Liposomes. *Sci. Rep.* **2023**, *13*, 4324. [[CrossRef](#)] [[PubMed](#)]

152. Németh, Z.; Csóka, I.; Semnani Jazani, R.; Sipos, B.; Haspel, H.; Kozma, G.; Kónya, Z.; Dobó, D.G. Quality by Design-Driven Zeta Potential Optimisation Study of Liposomes with Charge Imparting Membrane Additives. *Pharmaceutics* **2022**, *14*, 1798. [[CrossRef](#)] [[PubMed](#)]
153. Mihailescu, M.; Worchester, D.L.; Carroll, C.L.; Chamberlin, A.R.; White, S.H. DOTAP: Structure, Hydration, and the Counterion Effect. *Biophys. J.* **2023**, *122*, 1086–1093. [[CrossRef](#)] [[PubMed](#)]
154. Coronel, M.B.M.; Fraenza, C.C.; Anardo, E. On the Deformability of Additivated Phosphatidylcoline Liposomes: Molecular Dynamic Regimes and Membrane Elasticity. *Chem. Phys. Lipids* **2023**, *252*, 105290. [[CrossRef](#)] [[PubMed](#)]
155. Tang, H.; Li, X.; Jin, L.; Dong, J.; Yang, L.; Li, C.; Zhang, L.; Cheng, F. Applications and Latest Research Progress of Liposomes in the Treatment of Ocular Disease. *Biointerphases* **2025**, *20*, 010801. [[CrossRef](#)] [[PubMed](#)]
156. Huang, X.; Li, L.; Chen, Z.; Yu, H.; You, X.; Kong, N.; Tao, W.; Zhou, X.; Huang, J. Nanomedicine for the Detection and Treatment of Ocular Bacterial Infections. *Adv. Mater.* **2023**, *35*, e2302431. [[CrossRef](#)] [[PubMed](#)]
157. Vicario-de-la-Torre, M.; Caballo-González, M.; Vico, E.; Morales-Fernández, L.; Arriola-Villalobos, P.; De Las Heras, B.; Benítez-del-Castillo, J.M.; Guzmán, M.; Millar, T.; Herrero-Vanrell, R.; et al. Novel Nano-Liposome Formulation for Dry Eyes with Components Similar to the Preocular Tear Film. *Polymers* **2018**, *10*, 425. [[CrossRef](#)] [[PubMed](#)]
158. Lu, J.; Zhu, X.; Zhang, M.; Jiang, X.; Guo, W.; Jiang, F.; Cao, F. In vitro and In vivo Assessment of Structural Integrity of HPCD Complex@Liposome Nanocomposites from Ocular Surface to the Posterior Segment of the Eye. *Carbohydr. Polym.* **2023**, *315*, 120960. [[CrossRef](#)] [[PubMed](#)]
159. Gu, H.; Chen, P.; Liu, X.; Lian, Y.; Xi, J.; Song, J.; Li, X. Trimethylated Chitosan-Coated Flexible Liposomes with Resveratrol for Topical Drug Delivery to Reduce Blue-Light-Induced Retinal Damage. *Int. J. Biol. Macromol.* **2023**, *252*, 126480. [[CrossRef](#)] [[PubMed](#)]
160. Gentili, V.; Strazzabosco, G.; Salgari, N.; Mancini, A.; Rizzo, S.; Beltrami, S.; Schiuma, G.; Casciano, F.; Alogna, A.; Passarella, D.; et al. Ozonated Oil in Liposome Eyedrops Reduces the Formation of Biofilm, Selection of Antibiotic-Resistant Bacteria, and Adhesion of Bacteria to Human Corneal Cells. *Int. J. Mol. Sci.* **2023**, *24*, 14078. [[CrossRef](#)] [[PubMed](#)]
161. Obuobi, S.; Mauandi, V.; Nor, N.A.M.; Lee, B.J.; Lakshminarayanan, R.; Ee, P.L.R. Nucleic Acid Peptide Nanogels for the Treatment of Bacterial Keratitis. *Nanoscale* **2020**, *12*, 17411–17425. [[CrossRef](#)] [[PubMed](#)]
162. Qiao, H.; Xu, Z.; Sun, M.; Fu, S.; Zhao, F.; Wang, D.; He, Z.; Zhai, Y.; Sun, J. Rebamipide Liposome as an Effective Ocular Delivery System for the Management of Dry Eye Disease. *J. Drug Deliv. Sci. Technol.* **2022**, *75*, 103654. [[CrossRef](#)]
163. Ullmann, K.; Facht, L.; Nirschl, H.; Leneweit, G. Monolayer/Bilayer Equilibrium of Phospholipids in Gel or Liquid States: Interfacial Adsorption via Monomer or Liposome Diffusion? *Gels* **2023**, *9*, 803. [[CrossRef](#)] [[PubMed](#)]
164. Tavakoli, S.; Kari, O.K.; Turunen, T.; Lajunen, T.; Schmitt, M.; Lehitnen, J.; Tasaka, F.; Parkkila, P.; Ndika, J.; Viitala, T.; et al. Diffusion and Protein Corona Formation of Lipid-Based Nanoparticles in the Vitreous Humor: Profiling and Pharmacokinetic Consideration. *Mol. Pharm.* **2021**, *18*, 699–713. [[CrossRef](#)] [[PubMed](#)]
165. Dai, J.; Bai, M.; Aziz, T.; Alshehri, F.; Alharbi, N.K.; Shami, A.; Al-Joufi, F.A.; Cui, H.; Lin, L. Charge-Governed Ionic Essential Oil-Loaded Liposomes for Enhanced Penetration and Removal of *Listeria monocytogenes* Biofilms. *Food Res. Int.* **2026**, *229*, 118488. [[CrossRef](#)] [[PubMed](#)]
166. Martinez Espinoza, M.I.; Gül, S.; Mugnaini, L.; Cellesi, F. Oligo(Ethylene Glycol) Methacrylate Copolymer-Modified Liposomes for Temperature-Responsive Drug Delivery System. *Molecules* **2024**, *29*, 5511. [[CrossRef](#)] [[PubMed](#)]
167. Gladkikh, D.V.; Shmendel, E.V.; Maslov, M.A.; Zenkova, M.A.; Chernolovskaya, E.L. Impact of Cationic:Helper Lipid Ratios and PEG-Lipid Architecture on siRNA Delivery Performance of 2X3-Based Liposomal Formulations. *J. Liposome Res.* **2026**, *1*–13. [[CrossRef](#)] [[PubMed](#)]
168. Chen, X.; Wu, J.; Lin, X.; Wu, X.; Yu, X.; Wang, B.; Xu, W. Tacrolimus Loaded Cationic Liposomes for Dry Eye Treatment. *Front. Pharmacol.* **2022**, *13*, 838168. [[CrossRef](#)] [[PubMed](#)]
169. Soni, P.K.; Saini, T.R. Formulation Design and Optimization of Cationic-Charged Liposomes of Brimonidine Tartrate for Effective Ocular Drug Delivery by Design of Experiment (DoE) Approach. *Drug Dev. Ind. Pharm.* **2021**, *47*, 1847–1866. [[CrossRef](#)] [[PubMed](#)]
170. Arta, A.; Eriksen, A.Z.; Melander, F.; Kempen, P.; Larsen, M.; Andersen, T.L.; Urquhart, A.J. Endothelial Protein C–Targeting Liposomes Show Enhanced Uptake and Improved Therapeutic Efficacy in Human Retinal Endothelial Cells. *Investig. Ophthalmol. Vis. Sci.* **2018**, *59*, 2119–2132. [[CrossRef](#)] [[PubMed](#)]
171. Liu, Y.; Castro Bravo, K.M.; Liu, J. Targeted Liposomal Drug Delivery: A Nanoscience and Biophysical Perspective. *Nanoscale Horiz.* **2021**, *6*, 78–94. [[CrossRef](#)] [[PubMed](#)]
172. Yuba, E. Development of Functional Liposomes by Modification of Stimuli-Responsive Materials and their Biomedical Applications. *J. Mater. Chem. B* **2020**, *8*, 1093–1107. [[CrossRef](#)] [[PubMed](#)]
173. Ogawa, K.; Nishi, A.; Umezawa, N.; Higuchi, T.; Ozeki, T. *Staphylococcus aureus*–Directed Liposome for Targeted Chemotherapy Against Infection—Evaluation of Affinity and Antibacterial Activity. *J. Nanopart. Res.* **2025**, *27*, 237. [[CrossRef](#)]

174. Xia, M.; Cao, S.; Liu, Z.; Zhao, J.; Yuan, Y.; Ni, J.; Guo, Z.; Wang, W.; Yin, H.; Zou, Z. Multifunctional Nano-Delivery System Based on DNase I and Photodynamic Therapy for Combatting *Enterococcus faecalis* Biofilm Infections. *Sci. Rep.* **2025**, *15*, 23343. [\[CrossRef\]](#) [\[PubMed\]](#)
175. Li, R.; Liu, B.; Wang, C.; Sun, Z.; Lv, S.; Tian, L.; Xiao, M.; Zheng, Q.; Shi, L.; Zhu, C. A pH-Responsive Charge-Reversal Liposome with Enhanced Biofilm Penetration for Multimodal Synergistic Therapy of Bacterial Infections. *BMEMat* **2026**, *4*, e70014. [\[CrossRef\]](#)
176. Liu, X.; Huang, Z.; Hu, C.; Zhao, Y.; Pan, H.; Wu, Y.; Fang, X.; Chen, J.; Liu, Y.; Wang, G.; et al. Ultrasound-Activated and P-Selection-Targeted Liposomes Overcome Biofilm Barriers for Surgical Site Infections Therapy. *J. Nanobiotechnol.* **2025**, *23*, 741. [\[CrossRef\]](#) [\[PubMed\]](#)
177. Sharaf, M.; Al-Laith, Z.N.; Khan, T.U.; Elkelish, A.; Abdel-Maksoud, M.S.; Elrefaei, N.G.; Alawam, A.S.; Liu, C.-G. Mucoadhesive Lignin-Liposome Nanocarriers of Coptisine: A Multifunctional Strategy Against Antibiotic-Resistant *Helicobacter pylori* Biofilms. *Bioorg. Chem.* **2026**, *170*, 109399. [\[CrossRef\]](#) [\[PubMed\]](#)
178. Ma, J.; Teng, Z.; Ding, L.; Peng, X.; Xie, Y.; Long, Q.; Jiang, L.; Huo, S.; Liang, X.; Liu, G. Ultrasound-Triggered Nano-Bomb: Bacteria-Targeted Oxygen-Supplying Liposomes as Seed Bubbles for Enhanced Mechano-Sonodynamic Therapy of *Pseudomonas aeruginosa* Biofilms. *Adv. Func. Mater.* **2025**, *35*, 2501347. [\[CrossRef\]](#)
179. Urquhart, A.J.; Eriksen, A.Z. Recent Developments in Liposomal Drug Delivery Systems for the Treatment of Retinal Disease. *Drug Discov. Today* **2019**, *24*, 1660–1668. [\[CrossRef\]](#) [\[PubMed\]](#)
180. Tasharrofi, N.; Nourozi, M.; Marzban, A. How Liposomes Pave the Way for Ocular Drug Delivery After Topical Administration. *J. Drug Deliv. Sci. Technol.* **2022**, *67*, 103045. [\[CrossRef\]](#)
181. Ferreira, M.; Ogren, M.; Dias, J.N.R.; Silva, M.; Gil, S.; Tavares, L.; Aires-da-Silva, F.; Gaspar, M.M.; Aguiar, S.I. Liposomes as Antibiotic Delivery Systems: A Promising Nanotechnological Strategy against Antimicrobial Resistance. *Molecules* **2021**, *26*, 2047. [\[CrossRef\]](#) [\[PubMed\]](#)
182. Dias-Souza, M.V.; Ul Haq, I.; Pagnin, S.; Veiga, A.A.; dos Santos, V.L. Liposome-Encapsulated Antibiotics and Biosurfactants: An Effective Strategy to Boost Biofilm Eradication in Cooling Towers. *Microb. Cell Fact.* **2025**, *24*, 135. [\[CrossRef\]](#) [\[PubMed\]](#)
183. Okafor, N.I.; Omoteso, O.A.; Choonara, Y.E. The Modification of Conventional Liposomes for Targeted Antimicrobial Delivery to Treat Infectious Diseases. *Discov. Nano* **2025**, *20*, 19. [\[CrossRef\]](#) [\[PubMed\]](#)
184. Nagai, K.; Nagai, S. Two Cases Report of Successful Treatment of Refractory Mac Pulmonary Disease in Two Different Elderly Patients Using a Regimen Using a Drug with an Innovative Drug Delivery System, Liposomal Amikacin (ALIS), at Half the Standard Dose. *Preprints* **2025**, 2025121285. [\[CrossRef\]](#)
185. Dalabehera, M.; Rathore, C.; Mehta, J.; Subudhi, R.N.; Chaudhari, S.; Poonia, N.; Lal, U.R.; Kumari, A. Fabrication and Optimization of Chebulinic Acid-Loaded Liposomes Based on Carbopol-gel Employing Box-Behnken Design for Vulvovaginal Candidiasis. *J. Pharm. Innov.* **2025**, *20*, 260. [\[CrossRef\]](#)
186. Tufail, S.; Pisani, S.; Trespidi, G.; Dorati, R.; Genta, I.; Buroni, S.; Conti, B. Liposomal Tobramycin and Ceftazidime as Advanced Nanocarriers Against *Pseudomonas aeruginosa* Infections. *Int. J. Pharm.* **2026**, *689*, 126472. [\[CrossRef\]](#) [\[PubMed\]](#)
187. Ireland, R.E.; Nunez, A.; Butcher, W.; Davies, C.; Blanchard, J.D.; Dayton, F.; Gonda, I.; Harding, S.V.; Nelson, M. Inhaled Liposomal Ciprofloxacin Protects Against Lethal Tularemia in the Common Marmoset. *Antimicrob. Agents Chemother.* **2025**, *70*, e01232-25. [\[CrossRef\]](#) [\[PubMed\]](#)
188. Huo, Z.; Li, Y.; Zhong, C.; Xie, Z.; Wang, F.; He, Y.; Shi, Y.; Zhang, Y. Cationic Liposome-Fused Endolysin Lys40 Overcomes Outer Membrane Barriers and Enhances Survival in *Salmonella*-Infected Chicks. *Animals* **2026**, *16*, 1193. [\[CrossRef\]](#) [\[PubMed\]](#)
189. Ribeiro, L.M.; Bonatto, C.C.; Silva, L.P. Engineering Stability: Cholesterol-Modulated Liposome Response to Physical and Chemical Stressors for Enhanced Antimicrobial Activity. *Pharmaceuticals* **2026**, *19*, 366. [\[CrossRef\]](#) [\[PubMed\]](#)
190. Maxwell, A.; Pahal, S.; Chaudhari, P.; Chaudhari, B.B.; Peri, S.; Moorkoth, S.; Ghate, V.; Vemula, P.K.; Lewis, S. Microneedle-Mediated Delivery of Amikacin-Liposomes: A Minimally Invasive Strategy against Bacterial Septicemia. *J. Pharm. Innov.* **2025**, *20*, 160. [\[CrossRef\]](#)
191. Abbasi, A.; McCall, A.; Jiang, Z.; LeBlanc, B.W.; Shukla, A. Bacterial Enzyme-Responsive Hydrogels for Triggered Delivery of Antibiotics to Infected Wounds. *Sci. Adv.* **2026**, *12*, eadz0786. [\[CrossRef\]](#) [\[PubMed\]](#)
192. Platon, V.-M.; Craciun, A.M.; Rosca, I.; Simionescu, N.; Marin, L. Multifunctional Erythromycin-Loaded Liposomes: A Methodological Optimization for Enhanced Mucoadhesive, Antioxidant Activity, and Biocompatibility. *Biomater. Sci.* **2026**, *14*, 140–160. [\[CrossRef\]](#) [\[PubMed\]](#)
193. Song, P.; Zhang, Z.; Zhang, R.; Hu, W.; Rao, S.; Yang, Y.; Chang, C. Liposome-Encapsulated Egg Yolk Immunoglobulin (IgY) Enhances Anti-*Helicobacter Pylori* Efficacy by Alleviating Gastric Inflammation, Oxidative Stress, and Regulating Gut Microbiota. *Food Biosci.* **2026**, *79*, 108768. [\[CrossRef\]](#)
194. Yan, D.; Wang, Y.; Yang, R.; Man, Y.; Tang, H.; Yu, Q.; Shao, L. Liposome-Delivered Natural Antimicrobials in Food: Antibacterial Efficacy and Mechanism. *Food Sci.* **2025**, *73*, 107525. [\[CrossRef\]](#)

195. Shalaby, T.I.; Eldeen, M.A.; Akl, M.A.; Ibrahim, H.A.H.; Fekry, N.M.; Alshaya, D.S.; Fayad, E.; Khodear, G.A.M. Synergistic Cytotoxicity of Paclitaxel-Loaded Liposomes and Epigallocatechin-3-Gallate in MCF-7 Breast Cancer Cells: An In vitro Nanotechnology-Enhanced Approach. *J. Drug Deliv. Sci. Technol.* **2026**, *117*, 108007. [\[CrossRef\]](#)
196. Zubareva, A.; Svirshchevskaya, E.; Vodennikova, A.; Dolya, D.; Nedoluzhko, A.; Skorik, Y. Hybrid DEAE-Chitosan/Liposome System for Efficient DNA Vaccine Delivery. *Fish. Shellfish Immunol.* **2025**, *167*, 110846. [\[CrossRef\]](#)
197. Zhou, H.; Dong, S.; Si, Z.; Niu, H.; Mao, J.; Chen, Y.; Li, Y.; Wu, W. Aptamer-Based Nanoparticle Drug Delivery System Designed for Targeting GPC3-Positive Liver Cancer. *J. Pharm. Anal.* **2026**, *16*, 101614. [\[CrossRef\]](#)
198. Kolarikova, M.; Hasikova, B.; Langova, K.; Benda, A.; Panek, D.; Cockova, Z.; Dilenki, H.; Malina, L.; Valkova, L.; Kolarova, H. Hyaluronic Acid-Functionalized Liposomes for CD44-Targeted Anticancer Therapy: In vitro Induced Cytotoxicity in HeLa Cells. *BioMed Pharmacother.* **2025**, *193*, 118783. [\[CrossRef\]](#) [\[PubMed\]](#)
199. Negari, I.P.; Khoerunnisa, A.N.; Tarwadi; Sari, A.N.; Pambudi, S.; Faizal, I.; Septani, C.M. Effect of PEI25k/DOTAP/Cholesterol Liposomal Formulation on the Immunogenicity of SARS-CoV-2 Spike Protein-Encoding DNA Vaccine. *BioTechnologia* **2026**, *107*, 3–22. [\[CrossRef\]](#) [\[PubMed\]](#)
200. Gardea-Gutierrez, D.; Roman-Aguirre, M.; Koera-Valencia, R.; Sanchez-Ramirez, B.; Perfecto-Avalos, Y.; Montes-Fonseca, S.L. Flexible Asymmetric Liposomes as a Platform for Improved Plasmid DNA Delivery: An In vitro Study. *OpenNano* **2026**, *28*, 100283. [\[CrossRef\]](#)
201. Yin, X.; Harmancey, R.; McPherson, D.D.; Kim, H.; Huang, S.-L. Liposome-Based Carriers for CRISPR Genome Editing. *Int. J. Mol. Sci.* **2023**, *24*, 12844. [\[CrossRef\]](#) [\[PubMed\]](#)
202. Mirkani, A.; Nabid, M.R.; Pakian, S. Mucoadhesive Cationic Liposome Nanoparticles Coated with Methacrylamide Hyaluronic Acid for Ocular Drug Delivery. *ACS Appl. Nano Mater.* **2025**, *8*, 23370–23387. [\[CrossRef\]](#)
203. Tan, G.; Yu, S.; Pan, H.; Li, J.; Liu, D.; Yuan, K.; Yang, X.; Pan, W. Bioadhesive Chitosan-Loaded Liposomes: A More Efficient and Higher Permeable Ocular Delivery Platform for Timolol Maleate. *Int. J. Biol. Macromol.* **2017**, *94*, 355–363. [\[CrossRef\]](#) [\[PubMed\]](#)
204. Hallan, S.S.; Marchetti, P.; Bortolotti, D.; Sguizzato, M.; Esposito, E.; Mariani, P.; Trapella, C.; Rizzo, R.; Cortesi, R. Design of Nanosystems for the Delivery of Quorum Sensing Inhibitors: A Preliminary Study. *Molecules* **2020**, *25*, 5655. [\[CrossRef\]](#) [\[PubMed\]](#)
205. Bandara, H.M.H.; Hewavitharana, A.K.; Shaw, P.N.; Smyth, H.D.C.; Samaranyake, L.P. A Novel, Quorum Sensor-Infused Liposomal Drug Delivery System Suppresses *Candida albicans* Biofilms. *Int. J. Pharm.* **2020**, *578*, 119096. [\[CrossRef\]](#) [\[PubMed\]](#)
206. Lu, H.D.; Pearson, E.; Ristroph, K.D.; Duncan, G.A.; Ensign, L.M.; Suk, J.S.; Hanes, J.; Prud'homme, R.K. *Pseudomonas aeruginosa* Pyocyanin Production Reduced by Quorum-Sensing Inhibiting Nanocarriers. *Int. J. Pharm.* **2018**, *544*, 75–82. [\[CrossRef\]](#) [\[PubMed\]](#)
207. Tiwari, S.; Gidwani, B.; Vyas, A. Quorum Sensing in Gram-Negative Bacteria: Strategies to Overcome Antibiotic Resistance in Ocular Infections. *Curr. Mol. Med.* **2024**, *24*, 876–888. [\[CrossRef\]](#) [\[PubMed\]](#)
208. Hamdy, S.A.; Hatem, S.; Elosaily, H.; Hassan, A.G.A.-E.; Elshimy, R.; Osman, A.H.; El-Shiekh, R.A. Therapeutic Targeting of Ocular Diseases with Emphasis on PI3K/Akt, and OPRL Pathways by *Hedera helix* L. saponins: A New Approach for the Treatment of *Pseudomonas aeruginosa*-Induced Bacterial Keratitis. *Nat. Prod. Bioprospect.* **2025**, *15*, 30. [\[CrossRef\]](#) [\[PubMed\]](#)
209. Vetrivel, A.; Vetrivel, P.; Dhandapani, K.; Natchimuthu, S.; Ramasamy, M.; Madheswaran, S.; Murugesan, R. Inhibition of Biofilm Formation, Quorum Sensing and Virulence Factor Production in *Pseudomonas aeruginosa* PAO1 by Selected LasR Inhibitors. *Int. Microbiol.* **2023**, *26*, 851–868. [\[CrossRef\]](#) [\[PubMed\]](#)
210. Chakraborty, S.; Baidara, P.; Das, S.; Mondal, S.K.; Sharma, P.; Jose, T.A.; Kumaravel, V.; Manoharan, R.; Mandal, S.M. Dual Antibiotic-Infused Liposomes to Control Methicillin-Resistant *Staphylococcus aureus*. *Medicines* **2025**, *12*, 14. [\[CrossRef\]](#) [\[PubMed\]](#)
211. Zhang, J.; Liu, Z.; Tao, C.; Lin, X.; Zhang, M.; Zeng, L.; Chen, X.; Song, H. Cationic Nanoemulsions with Prolonged Retention Time as Promising Carriers for Ophthalmic Delivery of Tacrolimus. *Eur. J. Pharm. Sci.* **2020**, *144*, 105229. [\[CrossRef\]](#) [\[PubMed\]](#)
212. Alzahrani, R.R.; Alkhulaifi, M.M.; Albekairy, A.M.; Alrfaei, B.M.; Ali, R.; Ehaideb, S.N.; Assiri, M.A.; Yassin, A.E.B.; Halwani, M.A. Enhancement of Tobramycin and Amikacin Activities by Co-Encapsulation in Liposomal-Thymoquinone Formulation: Antibacterial, Antibiofilm, and Cytocompatibility Study. *Ther. Deliv.* **2026**, *17*, 217–231. [\[CrossRef\]](#) [\[PubMed\]](#)
213. de Paiva, C.S.; Schwartz, C.E.; Gjørstrup, P.; Pflugfelder, S.C. Resolvin E1 (RX-10001) Reduces Corneal Epithelial Barrier Disruption and Protects Against Goblet Cell Loss in a Murine Model of Dry Eye. *Cornea* **2012**, *31*, 1299–1303. [\[CrossRef\]](#) [\[PubMed\]](#)
214. Bhattacharjee, A.; Das, P.J.; Adhikari, P.; Marbaniang, D.; Pal, P.; Ray, S.; Mazumder, B. Novel Drug Delivery Systems for Ocular Therapy: With Special Reference to Liposomal Ocular Delivery. *Eur. J. Ophthalmol.* **2019**, *29*, 113–126. [\[CrossRef\]](#) [\[PubMed\]](#)
215. Geng, T.; Huo, G.; Liu, Y.; Xue, H.; Zuo, X.; Gu, Z.; Lin, H. Preparation of AAptamine-Loaded Fusogenic Liposomes and Evaluation of Its Enhanced Antibacterial Activity Against MRSA. *Drug Dev. Res.* **2026**, *87*, e70279. [\[CrossRef\]](#) [\[PubMed\]](#)
216. Grandi, G.; Cavallo, R.; Zanotto, E.; Cipriani, R.; Panico, C.; Protti, R.; Scapagnini, G.; Davinelli, S.; Costagliola, C. In vitro Antimicrobial Activity of Ozonated Oil in Liposome Eye-Drop Against Multidrug-Resistant Bacteria. *Open Med.* **2022**, *17*, 1057–1063. [\[CrossRef\]](#) [\[PubMed\]](#)
217. Sanap, S.N.; Bisen, A.C.; Mishra, A.; Biswas, A.; Agrowal, S.; Yadav, K.S.; Krishna, A.; Chopra, S.; Mugale, M.N.; Bhatta, R.S. QbD Based Antifungal Drug-Loaded Ophthalmic Liposomal Formulation for the Management of Fungal Keratitis: In vitro, Ex vivo and In vivo Pharmacokinetic Studies. *J. Drug Deliv. Sci. Technol.* **2022**, *74*, 103517. [\[CrossRef\]](#)

218. L'Exact, M.; Comeau, C.; Bourhis, A.; Boisvert, O.; Frohlich, U.; Letourneau, D.; Marsault, E.; Lavigne, P.; Grandbois, M.; Boudreau, P.-L. Beyond Rule-of-five: Permeability Assessment of Semipeptidic Macrocylces. *Biochim. Biophys. Acta Biomembr.* **2023**, *1865*, 184196. [[CrossRef](#)] [[PubMed](#)]
219. Sufian, M.A.; Abbas, G.; Rasul, A.; Irfan, M.; Khan, H.U. Moxifloxacin-loaded Nanoparticles of Thiolated Xyloglucan for Ocular Drug Delivery: Permeation, Mucoadhesion and Pharmacokinetic Evaluation. *Int. J. Biol. Macromol.* **2024**, *270*, 132522. [[CrossRef](#)] [[PubMed](#)]
220. Su, J.; Lu, W.; Guo, Y.; Liu, Z.; Wang, X.; Yan, H.; Zhang, R.X. Depot Unilamellar Liposomes to Sustain Transscleral Drug Co-Delivery for Ophthalmic Infection Therapy. *J. Drug Deliv. Sci. Technol.* **2023**, *86*, 104629. [[CrossRef](#)]
221. Kuang, L.; Rossa, A.E.; Chen, L.; Kanu, L.N.; Boychev, N.; Ghaffar, A.; Peng, C.; Bispo, P.J.M.; Romanowski, E.G.; Kohane, D.S.; et al. Overcoming Antimicrobial Resistance in Bacterial Keratitis with an Antibiotic-Eluting Contact Lens. *Investig. Ophthalmol. Vis. Sci.* **2025**, *66*, 38. [[CrossRef](#)] [[PubMed](#)]
222. Duman, G.; Yildir, I.; Macit, M.; Genc, E.; Sumer, E.; Kale, S.; Deniz, I. Development and Evaluation of 3D-Printed Ocular Insert Containing Liposomal Moxifloxacin. *J. Drug Deliv. Sci. Technol.* **2024**, *92*, 105353. [[CrossRef](#)]
223. Panthi, V.K.; Fairfull-Smith, K.E.; Islam, N. Liposomal Drug Delivery Strategies to Eradicate Bacterial Biofilms: Challenges, Recent Advances, and Future Perspective. *Int. J. Pharm.* **2024**, *655*, 124046. [[CrossRef](#)] [[PubMed](#)]
224. Kanaan, H.T.; Duncan, R.M.; Al-Jamal, W.T.; Jones, D.S.; Andrews, G.P.; Gilmore, B.; Yardley, V.; Farrington, N.; Stott, K.E.; Lawrance, D.; et al. Liposomal Antimicrobials in the Fight Against Bacterial and Fungal Pathogens: Clinical Successes and Development Challenges. *Int. J. Pharm. X* **2026**, *11*, 100478. [[CrossRef](#)] [[PubMed](#)]
225. Fegghi, M.; Makhmalzadeh, B.S.; Farrahi, F.; Akmal, M.; Hasanvand, N. Anti-Microbial Effect and in Vivo Ocular Delivery of Ciprofloxacin-Loaded Liposomes Through Rabbit's Eye. *Curr. Eye Res.* **2020**, *45*, 1245–1251. [[CrossRef](#)] [[PubMed](#)]
226. Al-Joufi, F.A.; Salem-Bekhit, M.M.; Taha, E.I.; Ibrahim, M.A.; Muharram, M.M.; Alshehri, S.; Ghoneim, M.M.; Shakeel, F. Enhancing Ocular Bioavailability of Ciprofloxacin Using Colloidal Lipid-Based Carrier for the Management of Post-Surgical Infection. *Molecules* **2022**, *27*, 733. [[CrossRef](#)] [[PubMed](#)]
227. Aleksieva, O.; Sakovych, V. Efficacy of a New Comprehensive Method of Treatment for Bacterial Keratitis. *Ukr. J. Ophthalmol.* **2025**, *1*, 22–29. [[CrossRef](#)]
228. Sakovych, V.M.; Aleksieva, O.V. Using a Liposomal Ozone-Based Solution in Comprehensive Treatment of Bacterial Keratitis. *J. Ophthalmol.* **2022**, *5*, 19–22. [[CrossRef](#)]
229. Chen, Q.; Han, X.; Liu, L.; Duan, Y.; Chen, Y.; Shi, L.; Lin, Q.; Shen, L. Multifunctional Polymer Vesicles for Synergistic Antibiotic-Antioxidant Treatment of Bacterial Keratitis. *Biomacromolecules* **2023**, *24*, 5230–5244. [[CrossRef](#)] [[PubMed](#)]
230. Roy, G.; Galigama, R.D.; Thorat, V.S.; Maallela, L.S.; Roy, S.; Garg, P.; Venuganti, V.V.K. Amphotericin B Containing Microneedle Ocular Patch for Effective Treatment of Fungal Keratitis. *Int. J. Pharm.* **2019**, *572*, 118808. [[CrossRef](#)] [[PubMed](#)]
231. Villanueva-Martinez, A.; Molina-Alejandre, O.; Flores-Perez, A.; Nava-Arzaluz, M.G.; Lopez-Mera, G.H.; Cruz-Morales, R.D.; Sanchez-Garcia, D.; Becerril-Osnaya, A.; Perez-Carranza, A.; Pinon-Segundo, E.; et al. Methylene Blue-Loaded Flexible Liposomes Improve the Efficacy of Photodynamic Therapy for the Treatment of Bacterial Keratitis. *J. Drug Sci. Technol.* **2025**, *108*, 106906. [[CrossRef](#)]
232. Badran, M.M.; Alsubaie, A.; Bekhit, M.M.S.; Alomrani, A.H.; Almomen, A. Layer-by-Layer Biopolymer-Coated Deformable Liposomes-In Situ Gel: A Hybrid Strategy for Enhanced Ocular Delivery of Itraconazole: In Vitro and In Vivo Appraisal. *Gels* **2025**, *11*, 19. [[CrossRef](#)] [[PubMed](#)]
233. Sathe, P.; Kailasam, V.; Nagarjuna, V.; Sharma, H.; Velpandian, T.; Garg, P.; Nirmal, J. Nanomicelles Empower Natamycin in Treating Fungal Keratitis: An In vitro, Ex vivo, and In vivo Study. *Int. J. Pharm.* **2024**, *656*, 124118. [[CrossRef](#)] [[PubMed](#)]
234. Cai, C.; Youssef, A.A.A.; Joshi, P.H.; Varner, C.; Dudhipala, N.; Majumdar, S. Improved Topical Ophthalmic Natamycin Suspension for the Treatment of Fungal Keratitis. *J. Ocul. Pharmacol. Ther.* **2024**, *40*, 67–77. [[CrossRef](#)] [[PubMed](#)]
235. Velpandian, T.; Nirmal, J.; Sharma, H.P.; Sharma, S.; Sharma, N.; Halder, N. Novel Water Soluble Sterile Natamycin Formulation (Natsol) for Fungal Keratitis. *Eur. J. Pharm. Sci.* **2021**, *163*, 105857. [[CrossRef](#)] [[PubMed](#)]
236. Reddy, D.C.; Asif, M.I.; Bari, A.; Velpandian, T.; Agarwal, T.; Maharana, P.K.; Sinha, R.; Satpahty, G.; Dada, T.; Titiyal, J.S.; et al. Comparative Evaluation of Topical Monotherapy (Natamycin or Natasol) and Combination Therapy (Natamycin and Voriconazole) in Mild-Moderate Fungal Keratitis. *Cornea* **2024**, *44*, 970–975. [[CrossRef](#)] [[PubMed](#)]
237. Rohita, H.; Shankar, S.; Yadav, S.; Shah, S.G.; Chugh, A. Enhanced In vivo Antifungal Activity of Novel Cell Penetrating Peptide Natamycin Conjugate for Efficient Fungal Keratitis Management. *Int. J. Pharm.* **2021**, *600*, 120484. [[CrossRef](#)] [[PubMed](#)]
238. Ahmed, S.; Amin, M.M.; El-Korany, S.M.; Sayed, S. Corneal Targeted Fenticonazole Nitrate-Loaded Novasomes for the Management of Ocular Candidiasis: Preparation, In vitro Characterization, Ex vivo and In vivo Assessments. *Drug Deliv.* **2022**, *29*, 2428–2441. [[CrossRef](#)] [[PubMed](#)]
239. Suriyaamporn, P.; Opanasopit, P.; Rangsimawong, W.; Ngawhirunpat, T. Optimal Design of Novel Microemulsions-Based Two-Layered Dissolving Microneedles for Delivering Fluconazole in Treatment of Fungal Eye Infection. *Pharmaceutics* **2022**, *14*, 472. [[CrossRef](#)] [[PubMed](#)]

240. Abd-Elmonem, E.M.; Makky, A.M.; Khalil, I.A.; Abd-Elsalam, W.H. Nanoformulations of Antifungal Agents for the Management of Ocular Fungal Infections. *BioNanoScience* **2025**, *15*, 418. [\[CrossRef\]](#)
241. Zhang, Z.H.; Teng, F.; Sun, Q.X.; Wang, S.Z.; Liu, C.; Zhao, G.Q. Rapamycin Liposome Gutta Inhibiting Fungal Keratitis of Rats. *Int. J. Ophthalmol.* **2019**, *12*, 536–541. [\[CrossRef\]](#) [\[PubMed\]](#)
242. Zhong, Y.; Wang, K.; Zhang, Y.; Yin, Q.; Li, S.; Wang, J.; Zhang, X.; Han, H.; Yao, K. Ocular Wnt/ β -Catenin Pathway Inhibitor XAV939-Loaded Liposomes for Treating Alkali-Burned Corneal Wound and Neovascularization. *Front. Bioeng. Biotechnol.* **2021**, *9*, 753879. [\[CrossRef\]](#) [\[PubMed\]](#)
243. Boucher, R.; Boutolleau, D.; Burrel, S.; Haigh, O.; Barreau, E.; Benali, M.; Meziou, S.; Labetoulle, M.; Rousseau, A. Pathophysiology and Treatment of Acyclovir-Resistant Herpes Simplex Virus Keratitis. *J. Fr. Ophthalmol.* **2025**, *48*, 104433. [\[CrossRef\]](#) [\[PubMed\]](#)
244. De Clerck, I.; Walgrave, V.; Snoeck, R.; Andrei, G.; Blanckaert, J.; Mulliez, E.; Delbeke, H. Putting Drug Resistant Epithelial Herpes Keratitis in the Spotlight: A Case Series. *Am. J. Ophthalmol. Case Rep.* **2022**, *25*, 101268. [\[CrossRef\]](#) [\[PubMed\]](#)
245. Pandey, M.; Choudhury, H.; Abdul-Aziz, A.; Bhattamisra, S.K.; Gorain, B.; Su, J.S.T.; Tan, C.L.; Chin, W.Y.; Yip, K.Y. Advancement on Sustained Antiviral Ocular Drug Delivery for Herpes Simplex Virus Keratitis: Recent Update on Potential Investigation. *Pharmaceutics* **2021**, *13*, 1. [\[CrossRef\]](#) [\[PubMed\]](#)
246. Shen, W.; Wang, C.; Jiang, C.; He, Y.; Liang, Q.; Hu, K. Targeted Delivery of Herpes Simplex Virus Glycoprotein D to CD169⁺ Macrophages Using Ganglioside Liposomes Alleviates Herpes Simplex Keratitis in Mice. *J. Control Release* **2024**, *365*, 208–218. [\[CrossRef\]](#) [\[PubMed\]](#)
247. Ribeiro, M.C.S.; de Miranda, M.C.; Cunha, P.D.S.; Andrade, G.F.; Fulgêncio, G.O.; Gomes, D.A.; Fialho, S.L.; Pittella, F.; Charrueau, C.; Escriou, V.; et al. Neuroprotective Effect of siRNA Entrapped in Hyaluronic Acid-Coated Lipoplexes by Intravitreal Administration. *Pharmaceutics* **2021**, *13*, 845. [\[CrossRef\]](#) [\[PubMed\]](#)
248. Gonzalez-De la Rosa, A.; Navarro-Partida, J.; Altamirano-Vallejo, J.C.; Hernandez-Gamez, A.G.; Garcia-Bañuelos, J.J.; Armendariz-Borunda, J.; Santos, A. Novel Triamcinolone Acetonide-Loaded Liposomes Topical Formulation for the Treatment of Cystoid Macular Edema After Cataract Surgery: A Pilot Study. *J. Ocul. Pharmacol. Ther.* **2019**, *35*, 106–115. [\[CrossRef\]](#) [\[PubMed\]](#)
249. Grzybowski, A.; Bajoriūnaitė, A.; Žemaitienė, R. The Rising Importance of Antiseptics in Ophthalmology: From Endophthalmitis Prevention to Treatment of Ocular Infections. *Ophthalmol. Ther.* **2025**, *14*, 2735–2752. [\[CrossRef\]](#) [\[PubMed\]](#)
250. Fan, W.; Han, H.; Chen, Y.; Zhang, X.; Gao, Y.; Li, S.; Jin, Q.; Ji, J.; Yao, K. Antimicrobial Nanomedicine for Ocular Bacterial and Fungal Infection. *Drug Deliv. Transl. Res.* **2021**, *11*, 1352–1375. [\[CrossRef\]](#) [\[PubMed\]](#)
251. Tsoka, P.; Scoulica, E.; Magkafouraki, E.; Natsaridis, E.; Antimisariis, S.; Tsilimbaris, M.K. Novel Liposomal Formulation for Sustained Release of Moxifloxacin; Efficacy in Experimental Bacterial Endophthalmitis. *Investig. Ophthalmol. Vis. Sci.* **2022**, *63*, 2127-F0143.
252. Youssef, A.; Dudhipala, N.; Majumdar, S. Ciprofloxacin Loaded Nanostructured Lipid Carriers Incorporated into In-Situ Gels to Improve Management of Bacterial Endophthalmitis. *Pharmaceutics* **2020**, *12*, 572. [\[CrossRef\]](#) [\[PubMed\]](#)
253. Luaces-Rodríguez, A.; González-Barcia, M.; Blanco-Teijeiro, M.J.; Gil-Martínez, M.; Gonzalez, F.; Gómez-Ulla, F.; Lamas, M.-J.; Otero-Espinar, F.-J.; Fernández-Ferreiro, A. Review of Intraocular Pharmacokinetics of Anti-Infectives Commonly Used in the Treatment of Infectious Endophthalmitis. *Pharmaceutics* **2018**, *10*, 66. [\[CrossRef\]](#) [\[PubMed\]](#)
254. Sakai, D.; Imai, H.; Nakamura, M. Multiple Intravitreal Liposomal Amphotericin B for a Case of *Candida glabrata* Endophthalmitis. *Case Rep. Ophthalmol.* **2021**, *12*, 485–491. [\[CrossRef\]](#) [\[PubMed\]](#)
255. Hammer, M.; Skrzpczyk, L.; Wohlfart, S.; Ackermann, B.C.; Geisweid, L.; Pohl, S.W.; Karaivanova, M.; Herth, J.; Augustin, V.A.; Studier-Fischer, A.; et al. Methotrexate-Loaded Liposomal Formulation Enables 6-Week Sustained Intraocular Therapeutic Drug Release in a Porcine Model. *Adv. Healthc. Mater.* **2025**, *15*, e03230. [\[CrossRef\]](#) [\[PubMed\]](#)
256. Yu, A.; Hu, Y.; Ma, X.; Mo, L.; Pan, M.; Bi, X.; Wu, Y.; Wang, J.; Li, X. Sequential Drug Release of Co-Assembled Supramolecular Hydrogel as Synergistic Therapy Against *Staphylococcus Aureus* Endophthalmitis. *Chem. Eng. J.* **2022**, *427*, 130979. [\[CrossRef\]](#)
257. Anchala, M.; Gadam Setty, R.P.; Maram, S.; Penugonda, S.; Pappur, A. Causes and Awareness on Contact Lens to Prevent Opportunistic Infections. *Asian J. Med. Pharm. Sci.* **2025**, *13*, 78–86. [\[CrossRef\]](#)
258. Quan, J.H.; Gao, F.F.; Ismail, H.A.H.A.; Yuk, J.M.; Cha, G.H.; Chu, J.Q.; Lee, Y.H. Silver Nanoparticle-Induced Apoptosis in ARPE-19 Cells Is Inhibited by *Toxoplasma gondii* Pre-Infection Through Suppression of NOX4-Dependent ROS Generation. *Int. J. Nanomed.* **2020**, *15*, 3695–3716. [\[CrossRef\]](#) [\[PubMed\]](#)
259. Oraibi, A.I.; Ai-Saedi, M.; Jabbar, M.; Jabbar, R.; Adnan, A. Isolation and Molecular Diagnosis of Bacteria from the Contact Lenses of Women. *J. Biosci. Appl. Res.* **2025**, *11*, 1157–1171. [\[CrossRef\]](#)
260. Rathee, A.; Yadav, P.; Naina, S.; Bareja, R. Prospective Study on Bacterial Growth in Contact Lens Users Before and After Hygiene Education. *Int. J. Med. Public Health* **2026**, *16*, 139–144.
261. Maulvi, F.A.; Kanani, P.A.; Jadav, H.J.; Desai, B.V.; Desai, D.T.; Patel, H.P.; Shetty, K.H.; Shah, D.O.; Willcox, M.D.P. Timolol-Eluting Graphene Oxide Laden Silicone Contact Lens: Control Release Profile with Improved Critical Lens Properties. *J. Drug Deliv. Sci. Technol.* **2022**, *69*, 103134. [\[CrossRef\]](#)

262. Teixeira, J.; do Monte, Z.L.; Tenreiro, S.; Salema-Oom, M.; Silva, D.C.; Saramago, B.; Serro, A.P. Citicoline Eluting Hydrogels for Therapeutic Contact Lenses Intended to Treat Neurodegenerative Diabetic Ocular Disease. *Int. J. Pharm.* **2024**, *667*, 124908. [[CrossRef](#)] [[PubMed](#)]
263. Li, Y.; Huang, C.; Yang, X.; Zhang, X. Ofloxacin Laden Microemulsion Contact Lens to Treat Conjunctivitis. *J. Biomater. Sci. Polym. Ed.* **2020**, *31*, 1566–1579. [[CrossRef](#)] [[PubMed](#)]
264. Srinivasarao, D.A.; Reddy, S.S.; Reddy, G.B.; Katti, D.S. Simultaneous Amelioration of Diabetic Ocular Complications in Lens and Retinal Tissue Using a Non-Invasive Drug Delivery System. *Int. J. Pharm.* **2021**, *608*, 121045. [[CrossRef](#)] [[PubMed](#)]
265. Hendiger, E.B.; Padzik, M.; Sifaoui, I.; Reyes-Batlle, M.; López-Arencibia, A.; Rizo-Liendo, A.; Bethencourt-Estrella, C.J.; San Nicolás-Hernández, D.; Chiboub, O.; Rodríguez-Expósito, R.L.; et al. Silver Nanoparticles as a Novel Potential Preventive Agent against *Acanthamoeba* Keratitis. *Pathogens* **2020**, *9*, 350. [[CrossRef](#)] [[PubMed](#)]
266. Heine, N.; Doll-Nikutta, K.; Stein, F.; Jakobi, J.; Ingendoh-Tsakmakidis, A.; Rehbock, C.; Winkel, A.; Barcikowski, S.; Stiesch, M. Anti-Biofilm Properties of Leser-Synthesized Ultrapure Silver-Gold-Alloy Nanoparticles Against *Staphylococcus Aureus*. *Sci. Rep.* **2024**, *14*, 3405. [[CrossRef](#)] [[PubMed](#)]
267. Siddiqui, R.; Lloyd, D.; Khan, N.A. Drug-Eluting Contact Lenses in the Treatment of *Acanthamoeba* Keratitis. *Clin. Exp. Optom.* **2025**, *109*, 1085–1088. [[CrossRef](#)] [[PubMed](#)]
268. Onugwu, A.L.; Nwagwu, C.S.; Onugwu, O.S.; Echezona, A.C.; Agbo, C.P.; Ihm, S.A.; Ehem, P.; Nnamani, P.O.; Attama, A.A.; Khutoryanskiy, V.V. Nanotechnology Based Drug Delivery Systems for the Treatment of Anterior Segment Eye Diseases. *J. Control Release* **2023**, *354*, 465–488. [[CrossRef](#)] [[PubMed](#)]
269. Viegas, C.; Patrício, A.B.; Prata, J.M.; Nadtman, A.; Chintamaneni, P.K.; Fonte, P. Solid Lipid Nanoparticles vs. Nanostructured Lipid Carriers: A Comparative Review. *Pharmaceutics* **2023**, *15*, 1593. [[CrossRef](#)] [[PubMed](#)]
270. Nicoleti, L.R.; Di Filippo, L.D.; Duarte, J.L.; Luiz, M.T.; Sábio, R.M.; Chorilli, M. Development, Characterization and In vitro Cytotoxicity of Kaempferol-Loaded Nanostructured Lipid Carriers in Glioblastoma Multiforme Cells. *Colloids Surf. B Biointerfaces* **2023**, *226*, 113309. [[CrossRef](#)] [[PubMed](#)]
271. Gebreel, R.M.; Edris, N.A.; Elmofly, H.M.; Tadros, M.I.; El-Nabarawi, M.A.; Hassan, D.H. Development and Characterization of PLGA Nanoparticle-Laden Hydrogels for Sustained Ocular Delivery of Norfloxacin in the Treatment of *Pseudomonas* Keratitis: An Experimental Study. *Drug Des. Dev. Ther.* **2021**, *15*, 399–418. [[CrossRef](#)] [[PubMed](#)]
272. Alanazi, J.S.; Alqahtani, F.Y.; Aleanizy, F.S.; Radwan, A.A.; Bari, A.; Alqahtani, Q.H.; Abdelhady, H.G.; Alsarra, I. MicroRNA-539-5p-Loaded PLGA Nanoparticles Grafted with iRGD as a Targeting Treatment for Choroidal Neovascularization. *Pharmaceutics* **2022**, *14*, 243. [[CrossRef](#)] [[PubMed](#)]
273. Kassaei, S.N.; Mahboobian, M.M. Besifloxacin-Loaded Ocular Nanoemulsions: Design, Formulation and Efficacy Evaluation. *Drug Deliv. Transl. Res.* **2022**, *12*, 229–239. [[CrossRef](#)] [[PubMed](#)]
274. Youssef, A.A.A.; Thakkar, R.; Senapati, S.; Joshi, P.H.; Dudhipala, N.; Majumdar, S. Design of Topical Moxifloxacin Mucoadhesive Nanoemulsion for the Management of Ocular Bacterial Infections. *Pharmaceutics* **2022**, *14*, 1246. [[CrossRef](#)] [[PubMed](#)]
275. Lu, P.; Liang, Z.; Zhang, Z.; Yang, J.; Song, F.; Zhou, T.; Li, J.; Zhang, J. Novel Nanomicelle Butenafine Formulation for Ocular Drug Delivery Against Fungal Keratitis: In Vitro and In Vivo Study. *Eur. J. Pharm. Sci.* **2024**, *192*, 106629. [[CrossRef](#)] [[PubMed](#)]
276. Liu, P.; Chen, G.; Zhang, J. A Review of Liposomes as a Drug Delivery System: Current Status of Approved Products, Regulatory Environments, and Future Perspectives. *Molecules* **2022**, *27*, 1372. [[CrossRef](#)] [[PubMed](#)]
277. Mishra, A.; Bano, M.; Bisen, A.C.; Verma, S.; Sanap, S.N.; Kishor, R.; Shukla, P.K.; Bhatta, R.S. Topical Corneal Targeted Sustained Release Amphotericin B Liposomal Formulation for the Treatment of Fungal Keratitis and its PK-PD Evaluation. *J. Drug Deliv. Sci. Technol.* **2020**, *60*, 101944. [[CrossRef](#)]
278. Mahboobian, M.M.; Mohammadi, M.; Mansouri, Z. Development of Thermoresponsive In situ Gel Nanoemulsions for Ocular Delivery of Acyclovir. *J. Drug Deliv. Sci. Technol.* **2020**, *55*, 101400. [[CrossRef](#)]
279. Gehlsen, U.; Siebelmann, S.; Steven, P. Tolerance and Adherence to Cationic 0,1% Cyclosporine in Ocular Graft-versus-Host Disease. *Ophthalmic Res.* **2021**, *64*, 77–84. [[CrossRef](#)] [[PubMed](#)]
280. Sorfraz, M.; Behl, G.; Rani, S.; O'Reilly, N.; McLoughlin, P.; O'Donovan, O.; Reynolds, A.L.; Lynch, J.; Fitzhenry, L. Development and In vitro and Ex vivo Characterization of a Twin Nanoparticulate System to Enhance Ocular Absorption and Prolong Retention of Dexamethasone in the Eye: From Lab to Pilot Scale Optimization. *Nanoscale Adv.* **2025**, *7*, 3125–3142. [[CrossRef](#)] [[PubMed](#)]
281. Paul, S.; Bose, A.; Ray, K.; Majumdar, S.; Karati, D.; Mukherjee, S.; Prajapati, B. Statistically Optimized Liposomal Formulation of Dorzolamide Hydrochloride for Sustained Ocular Delivery: In vitro and Allergic Evaluation in Rabbit. *Drug Dev. Ind. Pharm.* **2026**, *52*, 584–601. [[CrossRef](#)] [[PubMed](#)]
282. Pavlovic, N.; Mijalkovic, J.; Dordevic, V.; Pecarski, D.; Bugarski, B.; Knezevic-Jugovic, Z. Ultrasonication for Production of Nanoliposomes with Encapsulated Soy Protein Concentrate Hydrolysate: Process Optimization, Vesicle Characterization and In vitro Digestion. *Food Chem. X* **2022**, *15*, 100370. [[CrossRef](#)] [[PubMed](#)]
283. Gao, D.; Da, Z.; Yang, K.; Shi, Y. Comparison of Seven Cyclosporine A Formulations for Dry Eye Disease: A Systematic Review and Network Meta-Analysis. *Front. Pharmacol.* **2022**, *13*, 882803. [[CrossRef](#)] [[PubMed](#)]

284. Bian, X.; Ma, J.; Liu, Y.; Feng, Y.; Liu, Z.; Zhang, B.; Huang, B. Cyclosporine A in the Treatment of Dry Eye Disease: A Narrative Review. *Front. Ophthalmol.* **2025**, *5*, 1700163. [[CrossRef](#)] [[PubMed](#)]
285. Nsairat, J.; Khater, D.; Sayed, U.; Odeh, F.; Bawab, A.A.; Alshaer, W. Liposomes: Structures, Composition, Types, and Clinical Application. *Heliyon* **2022**, *8*, e09394. [[CrossRef](#)] [[PubMed](#)]
286. Rizzo, S.; Savastano, M.C.; Bortolotti, D.; Savastano, A.; Gambini, G.; Caccuri, F.; Gentili, V.; Rizzo, R. COVID-19 Ocular Prophylaxis: The Potential Role of Ozonated-Oils in Liposome Eyedrop Gel. *Transl. Vis. Sci. Technol.* **2021**, *10*, 7. [[CrossRef](#)] [[PubMed](#)]
287. Pastore, M.R.; Verdimonti, E.; El Majdoubi El Idrissi, K.; Presotto, M.; Borelli, M.; Miere, A.; Tognetto, D.; Souied, E.H. Tolerability of 0.5% Liposomal Ozonated Oil Versus 0.6% Povidone-Iodine in Antiseptic Prophylaxis for Intravitreal Injections. *Ophthalmol. Ther.* **2026**, *15*, 415–426. [[CrossRef](#)] [[PubMed](#)]
288. Aksenova, S.V.; Malkina, M.V.; Zaborovskii, A.V.; Yunina, D.V.; Tararina, L.A.; Khozina, E.A.; Shlyapkina, V.I.; Kulikov, O.A.; Pyataev, N.A. Liposomal Form of Dexamethasone in Experimental Autoimmune Uveitis: Clinical and Immunological Effects. *Pharm. Chem. J.* **2023**, *57*, 1153–1158. [[CrossRef](#)]
289. Mathis, T.; Cerquaglia, A.; Weber, M.; Guillaume-Sallit, R.; Malcles, A.; Voirin, N.; Servant, M.; Sudhalkar, A.; Bilgic, A.; Denis, P.; et al. Uveitis Treated with Dexamethasone Implant. *Retina* **2021**, *41*, 620–629. [[CrossRef](#)] [[PubMed](#)]
290. Butt, F.; Devonport, H. Treatment of Non-Infectious Posterior Uveitis with Dexamethasone Intravitreal Implants in a Real-World Setting. *Clin. Ophthalmol.* **2023**, *17*, 601–611. [[CrossRef](#)] [[PubMed](#)]
291. Gupta, R.B.; Ilin, J.; Gottlieb, C.C. Efficacy of Intravitreal Dexamethasone Implant Used as Monotherapy for the Treatment of Macular Edema in Non-Infectious Uveitis: A Retrospective Analysis. *J. Ophthalmic Inflamm. Infect.* **2023**, *13*, 42. [[CrossRef](#)] [[PubMed](#)]
292. Bose, A.; Majumdar, S.; Halder, A. Preparation, In-Vitro and Ex-Vivo of Liposomal Gel Delivery System for Timolol Maleate. *Res. J. Technol.* **2024**, *17*, 5761–5767. [[CrossRef](#)]
293. Uner, B.; Ozdemir, S.; Pilevne, S.N.; Celebi, A.R.C. Timolol-Loaded Ethosomes for Ophthalmic Delivery: Reduction of High Intraocular Pressure In vivo. *Int. J. Pharm.* **2023**, *640*, 123021. [[CrossRef](#)] [[PubMed](#)]
294. Valkama, E.; Sadeghi, A.; Toropainen, E.; Perez, O.; Schipper, N.; Ruponen, M.; Urtti, A.; Lajunen, T. Drug Release and Pharmacokinetics of Intravitreal Liposomes Injections: A Case Study with Cyclic Guanosine Monophosphate Derivative. *Eur. J. Pharm. Sci.* **2025**, *214*, 107291. [[CrossRef](#)] [[PubMed](#)]
295. van den Broek, M.R.P.; Versluis, M.; van der Berg, A.; Segers, T. Functionalized Monodisperse Microbubble Production: Microfluidic Method for Fast, Controlled, and Automated Removal of Excess Coating Material. *Microsyst. Nanoeng.* **2024**, *10*, 120. [[CrossRef](#)] [[PubMed](#)]
296. Hajimirzaei, S.F.; Pakian, S.; Mirkani, A.; Nabid, M.R. Extraction of Phospholipid-rich Fraction from Egg Yolk and Soybean for the Development of Vitamin C-Encapsulated Liposomes via a Microfluidic Device. *Food Chem.* **2025**, *494*, 146260. [[CrossRef](#)] [[PubMed](#)]
297. Pittiu, A.; Pannuzzo, M.; Casula, L.; Pireddu, R.; Valenti, D.; Cardia, M.C.; Lai, F.; Rosa, A.; Sinico, C.; Schlich, M. Production of Liposomes by Microfluidics: The Impact of Post-Manufacturing Dilution on Drug Encapsulation and Lipid Loss. *Int. J. Pharm.* **2024**, *664*, 124641. [[CrossRef](#)] [[PubMed](#)]
298. Gkionis, L.; Aojula, H.; Harris, L.K.; Tirella, A. Microfluidic-Assisted Fabrication of Phosphatidylcholine-Based Liposomes for Controlled Drug Delivery of Chemotherapeutics. *Int. J. Pharm.* **2021**, *604*, 120711. [[CrossRef](#)] [[PubMed](#)]
299. Yanar, F.; Mosayyebi, A.; Nastruzzi, C.; Carugo, D.; Zhang, X. Continuous-Flow Production of Liposomes with a Millireactor under Varying Fluidic Conditions. *Pharmaceutics* **2020**, *12*, 1001. [[CrossRef](#)] [[PubMed](#)]
300. Dominguez-Arca, V.; Sabin, J.; Garcia-Rio, L.; Bastos, M.; Taboada, P.; Barbosa, S.; Prieto, G. On the Structure and Stability of Novel Cationic DPPC liposomes Doped with Gemini Surfactants. *J. Mol. Liq.* **2022**, *366*, 120230. [[CrossRef](#)]
301. Basak, S.; Das, T.K. Liposome-Based Drug Delivery Systems: From Laboratory Research to Industrial Production—Instruments and Challenges. *ChemEngineering* **2025**, *9*, 56. [[CrossRef](#)]
302. Kruglov, E.; Borshchevsky, G. The Use of Modern QbD Approaches in the Pharmaceutical Development of Technology of Liposomal Eye Drops. *Ann. Machnikov's Inst.* **2022**, *1*, 28–32. [[CrossRef](#)]
303. Peng, Y.; Pang, S.; Zeng, Y.; Wei, J.; Lu, J.; Ruan, Y.; Hong, X.; He, X.; Chu, X.; Guo, Y.; et al. Antibiotic-Free Ocular Sterilization While Suppressing Immune Response to Protect Corneal Transparency in Infectious Keratitis Treatment. *J. Control Release* **2024**, *374*, 563–576. [[CrossRef](#)] [[PubMed](#)]
304. Tremouille, L.; Charcosset, C. Preparation of Liposomes, Lipid Nanoparticles, or Polymer Nanoparticles by Nanoprecipitation and Their Purification: Where are Membrane Processes. *Curr. Opin. Colloid Interface Sci.* **2026**, *82*, 101989. [[CrossRef](#)]
305. Penoy, N.; Delma, K.C.; Homkar, N.; Sakira, A.K.; Egrek, S.; Sacheli, R.; Sacre, P.-Y.; Grignard, B.; Hayette, M.-P.; Some, T.I.; et al. Development and Optimization of a One Step Process for the Production and Sterilization of Liposomes Using Supercritical CO₂. *Int. J. Pharm.* **2024**, *651*, 123769. [[CrossRef](#)] [[PubMed](#)]

306. AlTerawi, A.M.; Aldaqqa, R.R.; Sunbul, F.S.; Edwards, D.; da Rocha, S.R. Abstract 1796: Development of a CSF-1Ri Liposomal Formulation Using a Continuous Manufacturing Approach and Design of Experiments (DOE). *Cancer Res.* **2025**, *85*, 1796. [\[CrossRef\]](#)
307. Li, Z.; Dong, Y.; Wu, T.; Zhu, W.; Jing, H.; Jiang, T.; Liu, Y.; Xiao, Y.; Zhong, T. Pectin-Coated Liposomes for Pectinase-Triggered Thymol Release: A Novel On-Demand Sterilization Approach for Orange Preservation. *Food Hydrocol* **2026**, *171*, 111792. [\[CrossRef\]](#)
308. Hoffman, J.J.; Arunga, S.; Mohamed Ahmed, A.H.A.; Hu, V.H.; Burton, M.J. Management of Filamentous Fungal Keratitis: A Pragmatic Approach. *J. Fungi* **2022**, *8*, 1067. [\[CrossRef\]](#) [\[PubMed\]](#)
309. Shahror, R.A.; Fouda, A.Y. Recent Advances and Future Challenges in Nanosystems for Ocular Drug Delivery. *J. Pharmacol. Exp. Ther.* **2025**, *392*, 103738. [\[CrossRef\]](#) [\[PubMed\]](#)
310. Mangla, B.; Kumar, P.; Javed, S.; Pathan, T.; Ahsan, W.; Aggarwal, G. Regulating Nanomedicines: Challenges, Opportunities, and the Path Forward. *Nanomedicine* **2025**, *20*, 1911–1927. [\[CrossRef\]](#) [\[PubMed\]](#)
311. Shastri, D.H. Chapter Eight, Delivery of Therapeutic Proteins to Ocular Tissues: Barriers, Approaches, Regulatory Considerations and Future Perspectives. In *Progress in Molecular Biology and Translational Science*; Elsevier: Amsterdam, The Netherlands, 2025; Volume 212, pp. 261–277. [\[CrossRef\]](#) [\[PubMed\]](#)
312. Rajan, P.; Koilpillai, J.; Narayanasamy, D. Advancing Ocular Medication Delivery with Nano-Engineered Solutions: A Comprehensive Review of Innovations, Obstacles, and Clinical Impact. *Cureus* **2024**, *16*, e66476. [\[CrossRef\]](#) [\[PubMed\]](#)
313. Tsirogianni, A.G.; Chountoules, M.; Pippa, N. Recent Advances in pH-Responsive Liposomes: Lessons Learnt and New Directions in Nanomedicine Development. *Materials* **2025**, *18*, 4295. [\[CrossRef\]](#) [\[PubMed\]](#)
314. Badran, M.M.; Alomrani, A.H.; Almomen, A.; Bin Jardan, Y.A.; Abou El Ela, A.E.S. Novel Metoprolol-Loaded Chitosan-Coated Deformable Liposomes in Thermosensitive in Situ Gels for the Management of Glaucoma: A Repurposing Approach. *Gels* **2022**, *8*, 635. [\[CrossRef\]](#) [\[PubMed\]](#)
315. Markowicz-Piasecka, M.; Kaczmarek, A.; Bialek, K.; Świnoga, P.; Zawadzka, E.; Piechota-Urbańska, M. Innovative Approaches to Antiviral Eye Drop Development: Acyclovir and Ganciclovir in Focus. *Acta Pol. Pharm.* **2025**, *82*, 425–442. [\[CrossRef\]](#) [\[PubMed\]](#)
316. Guo, Y.; Li, N.; Zhang, D.; Gu, J.; Liao, Z.; Teng, Z.; Du, X.; Timashev, P.S.; Chen, S.; Huo, S. Advancing Design Strategies in Smart Stimulus-Responsive Liposomes for Drug Release and Nanomedicine. *BMEMat* **2025**, *4*, e70045. [\[CrossRef\]](#)
317. Lin, Q.; Jing, Y.; Yan, C.; Chen, X.; Zhang, Q.; Lin, X.; Xu, Y.; Chen, B. Design and Application of pH-Responsive Liposomes for Site-Specific Delivery of Cytotoxin from *Cobra Venom*. *Int. J. Nanomed.* **2024**, *19*, 5381–5395. [\[CrossRef\]](#) [\[PubMed\]](#)
318. Wang, Y.; Fan, P.; Zhu, L.; Zhuang, W.; Jiang, L.; Zhang, H.; Huang, H. Enhanced In vitro Antitumor Efficacy of a Polyunsaturated Fatty Acid-Conjugated pH-Responsive Self-Assembled Ion-Pairing Liposome-Encapsulated Prodrug. *Nanotechnology* **2020**, *31*, 155101. [\[CrossRef\]](#) [\[PubMed\]](#)
319. Olsman, M.; Sereti, V.; Muhlenpfordt, M.; Johnsen, K.B.; Andersen, T.L.; Urquhart, A.J.; de Lange Davies, C. Focused Ultrasound and Microbubble Treatment Increases Delivery of Transferrin Receptor-Targeting Liposomes to the Brain. *Ultrasound Med. Biol.* **2021**, *47*, 1343–1355. [\[CrossRef\]](#) [\[PubMed\]](#)
320. Wong, K.-Y.; Lui, Y.; Zhou, L.; Wong, M.-S.; Liu, J. Mucin-Targeting-Aptamer Functionalized Liposomes for Delivery of Cyclosporin A for Dry Eye Disease. *J. Mater. Chem. B* **2023**, *11*, 4684–4694. [\[CrossRef\]](#) [\[PubMed\]](#)
321. Ni, C.; Zhang, Z.; Wang, Y.; Zhang, Z.; Guo, X.; Lv, H. Hyaluronic Acid and HA-Modified Cationic Liposomes for Promoting Skin Penetration and Retention. *J. Control Release* **2023**, *357*, 432–443. [\[CrossRef\]](#) [\[PubMed\]](#)
322. Zhao, L.; Ling, L.; Lu, J.; Jiang, F.; Sun, J.; Zhang, Z.; Huang, Y.; Liu, X.; Zhu, Y.; Fu, X.; et al. Reactive Oxygen Species-Responsive Mitochondria-Targeted Liposomal Quercetin Attenuates Retinal Ischemia-Reperfusion Injury Via Regulating SIRT1/FOXO3A and p38 MAPK Signaling Pathways. *Bioeng. Transl. Med.* **2022**, *8*, e10460. [\[CrossRef\]](#) [\[PubMed\]](#)
323. Wang, K.; Jian, L.; Zhong, Y.; Zhang, Y.; Yin, Q.; Li, S.; Zhang, X.; Han, H.; Yao, K. Ferrostatin-1 Loaded Liposome for Treatment of Corneal Alkali Burn Via Targeting Ferroptosis. *Bioeng. Transl. Med.* **2021**, *7*, e10276. [\[CrossRef\]](#) [\[PubMed\]](#)
324. Rusciano, D. A Personal Scientific Journey in Ophthalmology: Twenty-Five Years of Translating Research into Novel Therapies. *Pharmaceuticals* **2025**, *18*, 883. [\[CrossRef\]](#) [\[PubMed\]](#)
325. Khalil, A.; Barras, A.; Boukherroub, R.; Tseng, C.L.; Devos, D.; Burnouf, T.; Neuhaus, W.; Szunerits, S. Enhancing Paracellular and Transcellular Permeability Using Nanotechnological Approaches for the Treatment of Brain and Retinal Diseases. *Nanoscale Horiz.* **2023**, *9*, 14–43. [\[CrossRef\]](#) [\[PubMed\]](#)
326. Zhang, S.; Liu, D.; Zhang, J.; Liu, S.; Sun, R.; Huo, R.; Cui, C. Foam Cell Targeted Liposomes Co-Encapsulating Superoxide Dismutase and Catalase to Attenuate Atherosclerosis by Inhibiting Oxidative Stress. *Discov. Med.* **2024**, *36*, 343–354. [\[CrossRef\]](#) [\[PubMed\]](#)
327. Zhang, Y.; Sun, B.; Wang, L.; Shen, W.; Shen, S.; Cheng, X.; Liu, X.; Xia, H. Curcumin-Loaded Liposomes in Gel Protect the Skin of Mice against Oxidative Stress from Photodamage Induced by UV Irradiation. *Gels* **2024**, *10*, 596. [\[CrossRef\]](#) [\[PubMed\]](#)
328. Kanugo, A.; Teli, N. Recent Advances in Artificial Intelligence and Nanotechnology-Driven Strategies for Diagnosis and Therapy of Ocular Disease. *Curr. Drug Deliv.* **2025**, *22*, e15672018383855. [\[CrossRef\]](#) [\[PubMed\]](#)

329. Devaraj, S.; Guruswamy, N. AI-Enabled Ocular Drug Delivery Systems for the Management of Eye Infections. *Biotech. Res. Asia* **2026**, *23*, 628–647. [[CrossRef](#)]
330. Su, Y.; Fan, X.; Pang, Y. Nano-Based Ocular Drug Delivery System: An Insight Into the Preclinical/Clinical Studies and their Potential in the Treatment of Posterior Ocular Disease. *Biomater. Sci.* **2023**, *11*, 4490–4507. [[CrossRef](#)] [[PubMed](#)]
331. Saladino, G.M.; Chao, P.-H.; Brodin, B.; Li, S.-D.; Hertz, H.M. Liposome Biodistribution Mapping with In vivo X-Ray Fluorescence Imaging. *Nanoscale* **2024**, *16*, 17404–17411. [[CrossRef](#)] [[PubMed](#)]
332. Piffoux, M.; Silva, A.K.A.; Gazeau, F.; Taresté, D. Modification of Extracellular Vesicles by Fusion with Liposomes for the Design of Personalized Biogenic Drug Delivery Systems. *ACS Nano* **2018**, *12*, 6830–6842. [[CrossRef](#)] [[PubMed](#)]
333. Nazeri, S.A.; Rezayat, S.M.; Amani, A.; Hadjati, J.; Partoazar, A.; Zamani, P.; Mashreghi, M.; Jaafari, M.R. A Novel Formulation of Cyclosporine A/Phosphatidylserine-Containing Liposomes Using Remote Loading Method: Potential Product for Immunosuppressive Effects. *J. Drug Deliv. Sci. Technol.* **2022**, *77*, 103902. [[CrossRef](#)]
334. Liu, C.; Zhang, L.; Zhu, W.; Guo, R.; Sun, H.; Chen, X.; Deng, N. Barriers and Strategies of Cationic Liposomes for Cancer Gene Therapy. *Mol. Ther. Methods Clin. Dev.* **2020**, *18*, 751–764. [[CrossRef](#)] [[PubMed](#)]
335. Dos Santos Rodrigues, B.; Kanekiyo, T.; Singh, J. ApoE-2 Brain-Targeted Gene Therapy Through Transferrin and Penetratin Tagged Liposomal Nanoparticles. *Pharm. Res.* **2019**, *36*, 161. [[CrossRef](#)] [[PubMed](#)]
336. Yan, Y.; Li, X.Q.; Duan, J.L.; Bao, C.J.; Cui, Y.N.; Su, Z.B.; Xu, J.R.; Luo, Q.; Chen, M.; Xie, Y.; et al. Nanosized Functional miRNA Liposomes and Application in the Treatment of TNBC by Silencing Slug Gene. *Int. J. Nanomed.* **2019**, *14*, 3645–3667. [[CrossRef](#)] [[PubMed](#)]
337. Cheng, L.; Zhang, X.; Tang, J.; Lv, Q.; Liu, J. Gene-Engineered Exosomes-Thermosensitive Liposomes Hybrid Nanovesicles by the Blockade of CD47 Signal for Combined Photothermal Therapy and Cancer Immunotherapy. *Biomaterials* **2021**, *275*, 120964. [[CrossRef](#)] [[PubMed](#)]
338. Yu, Y.; Wang, Z.; Wu, S.; Zhu, C.; Meng, X.; Li, C.; Cheng, S.; Tao, W.; Wang, F. Glutathione-Sensitive Nanoglue Platform with Effective Nucleic Acids Gluing onto Liposomes for Photo-Genes Therapy. *ACS Appl. Mater. Interfaces* **2022**, *14*, 25126–25134. [[CrossRef](#)] [[PubMed](#)]
339. Belhadj, Z.; Qie, Y.; Carney, R.P.; Li, Y.; Nie, G. Current Advances in Non-Viral Gene Delivery Systems: Liposomes Versus Extracellular Vesicles. *BMEMat* **2023**, *1*, e12018. [[CrossRef](#)]
340. Mendes, L.P.; Sarisozen, C.; Luther, E.; Pan, J.; Torchilin, V.P. Surface-Engineered Polyethyleneimine-Modified Liposomes as Novel Carrier of siRNA and Chemotherapeutics for Combination Treatment of Drug-Resistant Cancers. *Drug Deliv.* **2019**, *26*, 443–458. [[CrossRef](#)] [[PubMed](#)]
341. Tenchov, R.; Bird, R.; Curtze, A.E.; Zhou, Q. Lipid Nanoparticles-From Liposomes to mRNA Vaccine Delivery, a Landscape of Research Diversity and Advancement. *ACS Nano* **2021**, *15*, 16982–17015. [[CrossRef](#)] [[PubMed](#)]

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.