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Intelligent Contact Lenses for Dynamic Ocular Drug Release

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Abstract:

Intelligent contact lenses represent a revolutionary advancement in ocular drug delivery, offering a precise, controlled, and patient-friendly alternative to conventional eye drops. These smart lenses integrate microelectronic sensors, stimuli-responsive polymers, and drug-loaded reservoirs to enable dynamic, on-demand drug release in response to physiological or external triggers such as pH, temperature, tear composition, or intraocular pressure. By maintaining sustained and localized drug concentration at the corneal surface, intelligent contact lenses enhance therapeutic efficacy while minimizing systemic side effects and dosing frequency. Recent developments in nanotechnology, biosensing, and wireless communication have further enabled real-time monitoring of ocular health parameters and personalized drug administration. Despite promising outcomes in preclinical studies, challenges such as biocompatibility, long-term stability, and large scale manufacturing remain. Future research aims to integrate these lenses into next-generation precision eye care systems that combine vision correction, disease monitoring, and adaptive drug delivery for conditions like glaucoma, dry eye syndrome, and diabetic retinopathy.

Keywords: Intelligent contact lenses, dynamic drug release, ocular drug delivery, stimuli-responsive polymers, Biosensors, personalized ophthalmic therapy.

Introduction

Timely and effective drug delivery to the eye is therefore crucial for preventing disease progression and preserving vision.

Ophthalmic drug delivery has always been a challenge for ophthalmologists and scientists from a variety of disciplines. It is estimated that the bioavailability of ophthalmic drugs is uncertain and is about 5% or less.

Conventional ophthalmic drug delivery systems have several limitations:

Low Bioavailability: Less than 5% of the drug reaches intraocular tissues due to tear

turnover, blinking, and nasolacrimal drainage.

Frequent Dosing: Short precorneal residence time necessitates multiple daily administrations, leading to poor patient compliance.

Systemic Side Effects: Significant drug loss through the nasolacrimal duct can cause systemic absorption and adverse effects.

Variable Drug Concentration: Peaks and troughs in drug levels can reduce therapeutic efficacy and may increase toxicity.

Poor Targeting: Conventional systems lack the ability to deliver drugs in a site-specific, sustained, or controlled manner. Stimuli-responsive (smart) systems represent the next generation because they can respond dynamically to physiological or external triggers—such as pH, temperature, light, or enzymes—to release the drug only when and where it is needed.

The idea of using contact lenses as a carrier of active ingredients is a relatively new strategy that is still being developed and improved.

Nevertheless, it is clear that the benefits associated with the use of these new ocular formulas are relevant for scientific advancement.

What are stimuli-responsive contact lenses?

These are “smart” contact lenses that change behavior (e.g. drug release, optical properties, sensing) in response to external or internal stimuli. Stimuli can be:

- Temperature
- Light (UV, visible)
- pH, ionic strength or chemical composition of tears
- Pressure (e.g. intraocular, pressure, IOP)
- Other biochemical cues

Uses include: on-demand drug delivery, sensing physiological parameters (temperature, IOP, glucose etc.), adaptive optics, protection from UV/light, etc.

Recent Examples / Research

IOP measurement + temperature-triggered drug release Stimulus(s):-Temperature & mechanical deformation (pressure)

Key results / notes:-In vivo rabbit glaucoma model: sustained drug release over 7 days, measurable IOP drop.[9]

Multifunctional UV-transition &

temperature-responsive lenses Stimulus(s):- UV light & physiological temperature (~33-38 °C)

Key results /notes: - Good optical properties, distinct changes; colorimetric variation sensitivity about 8% transmitted light per °C in relevant temp range.[10]

Materials used in stimuli- responsive lenses:-

Stimuli-responsive contact lenses use smart or functional materials that change their properties in response to external stimuli (pH, temperature, light, enzymes, electric/magnetic fields).

A. Base Hydrogels: Nowadays, conventional hydrogel-based soft contact lenses are the most proposed ones for therapeutic purposes [11] Hydrogels are generally defined as polymer networks extensively swollen with water.[11]

Due to the high porosity and surface area, hydrogels have the ability to incorporate active principles within their own network. Once the therapeutic hydrogel contact lenses are worn, the embedded drug is released to the post-lens tear fluid, thus, reaching the target tissue.

B. Oxygen Permeability, Transparency Requirement:

Low oxygen transfer through the contact lens can result in serious side effects. Since the human eye is insufficiently oxygenated by the system of blood vessels, and the oxygen supply is mainly carried out through exposure to air, oxygen delivery and effective carbon dioxide removal must be carried out through the contact lens, ensuring gas circulation. The gas permeability of soft contact lenses has been improved by silicone based polymer hydrogel lenses made of polydimethylsiloxane (PDMS). PDMS exhibits impressive permeability (Dk = 600

barrels) while maintaining comfort, wettability, and biofilm resistance compared to silicone-based hydrogel lenses. However, the long-worn contact lens must ensure oxygen permeability of not less than $Dk > 87$ barrels to avoid corneal hypoxia. Achieving Dk with conventional hydrophilic contact lenses on such a level is very difficult. [12]

Stimuli Responsive Polymers:

1. Stimulus:- pH responsive[13]

Material examples -Polyacrylic acid (PAA), chitosan, polymethacrylic acid.

Mechanism of Action:- Ionizable functional groups swell or shrink depending on pH → triggers drug release when tear pH changes (e.g., during injection/inflammation)

2. Stimulus:-

Temperature responsive [14]:- Poly(N isopropyl acrylamide) (PNIPAAm), PluronicF127

Mechanism of Action:- Exhibits LCST (lower critical solution temperature) behaviour → network collapses/swells around eye temperature (34- 35°C), releasing drug.

Base Material vs Stimuli-Responsive Polymer vs Advantages 1. Component:- Base material (lens matrix) [18,19]

Examples:- pHEMA (poly-2-hydroxyethyl methacrylate)

- -silicon hydrogel
- -PVA (polyvinyl alcohol)
- -PLGA films/nanoparticles (drug reservoir)

Role/Advantages:-

- Provides mechanical strength and transparency
- maintains oxygen permeability for corneal health (esp. silicone hydrogels)

excellent biocompatibility and lens comfort

Component:- Stimuli-responsive polymers [20,21,22]

Examples:- -polyacrylic acid (PAA)

- chitosan
- dextran matrices
- spiropyran
- polypyrrole

Role/Advantages:-

- enables smart drug release only when stimulus is present (precision delivery)
- achieves sustained and controlled release (hours to days)

Drugs delivered by stimuli-responsive contact lenses

Stimuli responsive contact lenses appear as an effective treatment option for a variety of eye dysfunctions. They provide the timely and effective release of drugs in corneal epithelial defects, help treat infections, and promote local healing [30].

Glaucoma — Timolol (β -blocker; sometimes combined with dorzolamide/latanoprost)

Stimulus: Temperature-responsive nanogels / thermoresponsive carriers (PNIPAAm, LCST type) or enzyme-responsive nanogels embedded in nanoporous/silicone-hydrogel lenses.

What it does: Thermo-sensitive nanogels/nanoparticles loaded with timolol are embedded into the lens matrix; the body/eye temperature or enzymatic environment triggers controlled swelling/deswelling and prolonged timolol release (hours → days/weeks in different designs), with demonstrated IOP lowering in animal/in vivo models in some studies. Many designs aim to avoid burst release and improve

bioavailability vs eye drops.

Status: Preclinical → some in vivo animal studies; active research toward clinical translation.[31]

Dry-eye disease — Cyclosporine A (CsA)

Stimulus: Various approaches (not always classic “on-demand” stimuli) — micelle/nanoparticle embedding, HA-micelles and sometimes tear-film triggered release; some systems exploit tear-film composition or hydration changes.

What it does: Cyclosporine (hydrophobic, potent anti-inflammatory) has been loaded into micelles/nanogels or embedded in silicone–hydrogel/pHEMA lenses to extend residence time and increase ocular bioavailability compared with eye drops. Improved wettability and sustained release have been reported.

Status: Several promising preclinical and ex vivo/in vivo studies; review/meta-analyses on CsA formulations support clinical efficacy of CsA for dry eye (eye-drop forms are approved; lens-based delivery is still mostly preclinical).[32]

Bacterial keratitis / ocular infection — Fluoroquinolones (e.g., moxifloxacin)

Stimulus: pH-sensitive nanovalves / coatings on mesoporous silica nanoparticles (MSNs) or pH-sensitive polymer coatings embedded in lenses.

What it does: MSNs loaded with moxifloxacin (or other antibiotics) are capped with pH-sensitive “gates” or polymers that remain closed during storage (neutral pH) but open under the slightly different pH environment or microenvironment (or on-demand stimuli) to release antibiotic at the ocular surface — improving local concentration and potentially reducing dosing frequency.

Status: Demonstrated in vitro and in animal

infection models for MSNs; translational work ongoing.[33]

Major Barriers & Risks

Material / Biocompatibility: ensuring that the embedded sensors, electronics, drug formulations don’t irritate, reduce corneal oxygen transmission, or degrade in tear fluids.

Power and Electronics Constraints: limited space, need for flexibility & transparency, avoiding heating or bulk.

Precision of Drug Release: avoiding burst releases, ensuring predictable release kinetics over lens wearing duration, variability among users (tear volume, blink rate, etc.).

Regulatory Pathways: device + drug + electronics = complex regulatory classification. Safety, long-term data, sterilization, stability are all critical.

Future Prospects

If key materials, manufacturing, safety and regulatory challenges are solved, SRCLs could markedly improve ocular bioavailability, personalize dosing, and reduce invasive procedures for many anterior-segment conditions with emerging routes (microfluidic/micropump designs, nanoparticle carriers and external triggers) also opening possibilities for controlled posterior segment dosing.[37]

Near-Term Realistic Developments (Next ~3-5 years)

Prototypes of smart contact lenses with drug reservoirs plus passive stimulus response (e.g. pH, temperature) in animal models.

Early human feasibility studies for sustained release contact lenses for anterior segment diseases (keratitis, post-surgical anti-inflammatories, and allergic conjunctivitis).

Development of lenses that integrate sensors and controlled drug release (not full closed

loop, but maybe triggered by external stimulus like light or heat).

Improvements in materials so that don't compromise comfort, oxygen permeability, clarity when embedding drug systems or electronics.

Conclusion

Stimuli-responsive contact lenses (SRCLs) are an innovative approach to ocular drug delivery that address the major drawbacks of conventional systems like eye drops and ointments. They can provide controlled, sustained, and stimulus-triggered drug release, ensuring that therapeutic levels are maintained on the corneal surface for longer periods.

There are current limitations that must be addressed before widespread clinical use. These include maintaining lens transparency, oxygen permeability, and comfort after drug loading; achieving precise and reproducible drug release kinetics; long-term biocompatibility and safety concerns; limited drug-loading capacity; complex manufacturing processes; and stringent regulatory requirements due to the device–drug combination nature of SRCLs.

Looking to the future, ongoing research is moving toward integrating biosensors, micro-reservoirs, and wireless control modules to develop closed-loop systems that release drugs on-demand based on real-time tear biomarkers or disease activity.

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