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Innovative Medicinal Contact Lenses: Controlled Drug Delivery Technologies in Ophthalmology

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Abstract

This research article presents the results of the development and experimental evaluation of prolonged-release contact lenses for use in ophthalmology. The research aimed to create innovative delivery systems capable of overcoming the limitations of traditional eye drops, such as low bioavailability and the need for frequent use. Silicone hydrogel (Senofilcon A, Lotrafilcon B) and polymer (pHEMA) matrices modified with PLGA nanoparticles and cyclodextrins were used in the work to improve the solubility and controlled release of drugs (timolol maleate and cyclosporine A). The research methods included in-situ polymerization, saturation of the finished lenses, as well as physico-chemical and biological evaluation of the obtained systems. HPLC analysis and the Franz diffusion cell equipment were used to investigate the kinetics of release. The results demonstrated that silicone hydrogel lenses provide two-phase release (28.3±2.1% in 2 hours and 65.7±3.4% in 72 hours), while pHEMA+PLGA-based systems showed a more uniform profile (82.4±4.2% in 96 hours). All developed lenses retained optimal optical (>95% transmission) and mechanical properties (modulus of elasticity 0.45–0.85 MPa). Biological tests confirmed the absence of cytotoxicity (cell viability 92.4±3.1%) and a pronounced therapeutic effect in vivo (reduction of intraocular pressure by 34.7±2.8%). The study emphasises how medical contact lenses may be used to treat long-term eye conditions such dry eye syndrome and glaucoma. The findings provide new avenues for customised ophthalmic treatment with enhanced compliance and bioavailability.

Keywords: Contact lenses, Prolonged release, Ophthalmic pharmacotherapy, PLGA nanoparticles, Dry eye syndrome, Glaucoma

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Introduction

In recent decades, ophthalmology has faced the need to improve methods of drug delivery to the eye tissues **(Figure 1)** (Nagai & Otake, 2022; Ahmed *et al*., 2023). Traditional forms such as eye drops, despite their ease of use, have significant disadvantages: low bioavailability (less than 5% due to rapid lacrimation and systemic absorption), the need for frequent instillation, and the associated low patient compliance (López-Machado *et al*., 2021; Kang *et al*., 2023; Vazirani *et al*., 2023). This problem is especially acute in the treatment of chronic diseases such as glaucoma, dry eye syndrome, keratitis, and postoperative inflammation (Lajmi *et al*., 2021; Mandal *et al*., 2024). In this regard, there is increasing interest in innovative delivery systems capable of providing long-term and controlled release of active substances (Rahić *et al*., 2020). One of the most promising areas is contact lenses with prolonged drug release, combining vision correction and therapeutic effect (Rykowska *et al*., 2021; Tripathi & Yadav, 2024).

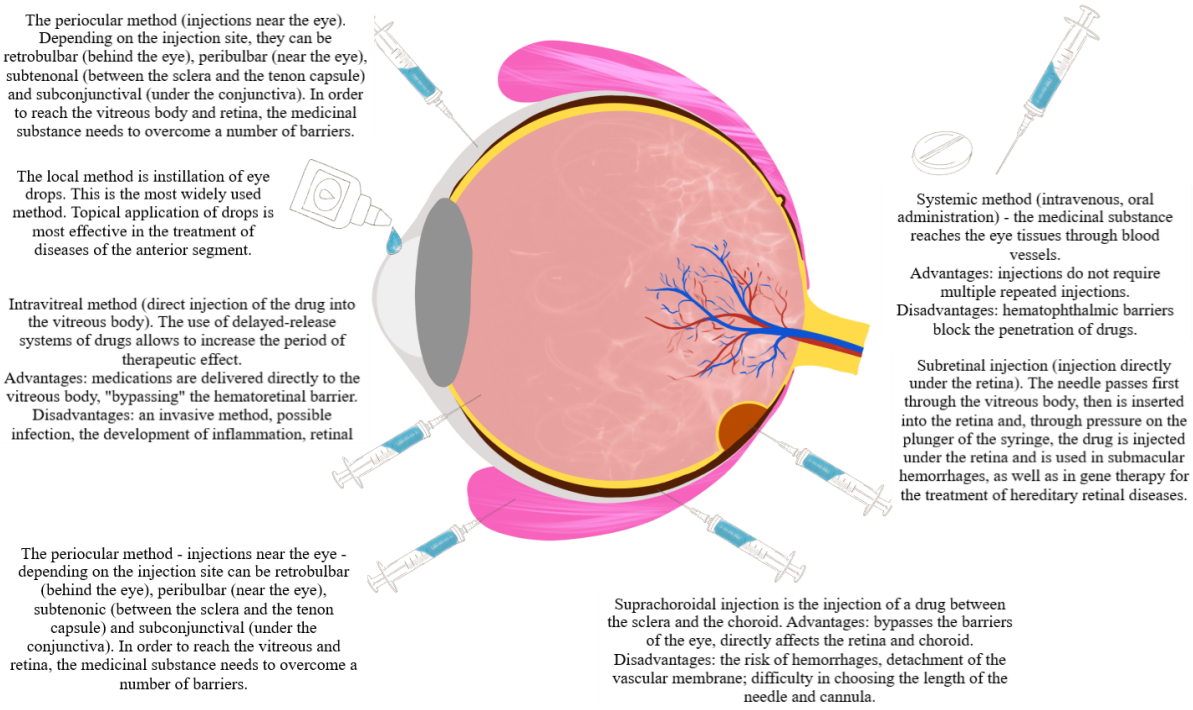

Figure 1. Traditional methods of drug delivery to the retina of the eye

According to the World Health Organization (WHO), about 2.2 billion people worldwide suffer from various visual impairments, and 1 billion of these conditions could be prevented or corrected (Burton *et al*., 2021; Keel *et al*., 2022). Chronic ophthalmopathologies such as glaucoma (64 million cases globally) and dry eye syndrome (up to 34% of the population in certain age groups) require long-term and often lifelong therapy (Kang & Tanna, 2021; Stein *et al*., 2021; Zemanová, 2021). At the same time, up to 50% of patients do not comply with the drip instillation regime, which leads to disease progression and an increase in the economic burden on the healthcare system (Storgaard *et al*., 2021). For example, in the United States, the annual costs associated with ineffective glaucoma treatment exceed $300 million (Craven *et al*., 2022). This highlights the need to develop alternative, more convenient, and effective methods of drug delivery.

Contact lenses modified to include pharmacological agents have a number of key advantages (Baghban *et al*., 2023). Firstly, they ensure prolonged contact of the drug with the cornea, which significantly increases bioavailability (Zhang *et al*., 2025). Secondly, such systems make it possible to control the rate of drug release, maintaining therapeutic concentration for several days or even weeks (Fardoost *et al*., 2025; Pan *et al*., 2025). Thirdly, they combine corrective and therapeutic functions, which is especially important for patients with ametropia (Mohamdeen *et al*., 2022; Wu *et al*., 2024). In addition, the risk of systemic side effects characteristic of drops is reduced (for example, bronchospasm with the use of beta-blockers) (Sun *et al*., 2023). Recent advances in materials science and nanotechnology open up new possibilities for creating lenses with improved characteristics, including high oxygen permeability and biocompatibility (Stiler-Wyszyńska *et al*., 2023; Blinov *et al*., 2025; Phan *et al*., 2025).

The most important aspect of creating effective medicinal contact lenses is the choice of a suitable scaffold (carrier), a matrix that ensures stable incorporation and release of the drug (Rathod, 2023; Rzhepakovsky *et al*., 2024; Hosseinian *et al*., 2025). Modern research focuses on the use of hydrogel and silicone-hydrogel materials modified with nanoparticles, micelles, or molecular imprints (Gronert *et al*., 2023; Haworth *et al*., 2023; Travis *et al*., 2024). For example, the introduction of cyclodextrins makes it possible to increase the solubility of hydrophobic substances, and the use of electrospun fibers makes it possible to create multilayer structures with programmable release kinetics (Marto-Costa *et al*., 2024). A separate area is 3D printing of lenses with an accurate distribution of active substances in specified zones (Larochelle *et al*., 2021). However, the key challenge remains unchanged: the need for a balance between the duration of release, the mechanical strength of the lens, and patient comfort (Ishihara *et al*., 2023). Successful solution of these tasks will determine the transition from experimental models to widespread clinical application (Duraimurugan *et al*., 2022; Alsubeie, 2023; Anushree *et al*., 2023; Dobrzynski *et al*., 2024; Malinga & Laing, 2024; Zafeiraki *et al*., 2024).

Thus, the development of prolonged-release drug contact lenses represents a promising alternative to traditional ophthalmic pharmacotherapy methods. Their implementation can revolutionize the treatment of chronic eye diseases, increasing adherence to therapy and reducing the economic burden (Sharma *et al*., 2023). Long-term safety evaluation, loading techniques, and material optimisation should be the main areas of future study. The

potential of this technology is already shown by the first commercial goods (such ketotifen lenses for allergic conjunctivitis), opening the door for more intricate solutions like the delivery of antibiotics or anti-VEGF medications (Soluri *et al*., 2012; Ono & Toshida, 2022; Fujio *et al*., 2024).

The purpose of this study is to develop and experimentally evaluate the effectiveness of prolonged-release contact lenses based on modern hydrogel carriers for the treatment of chronic ophthalmic diseases (using the example of glaucoma and dry eye syndrome). The work plans to compare various methods of incorporation of active substances (incorporation into a matrix, surface modification, nanoparticles) into silicone hydrogel and polymer lenses; to study the kinetics of release in vitro using model drugs (timolol, cyclosporine A); to evaluate the biocompatibility and therapeutic efficacy of the developed systems in experimental models (ex vivo on corneal tissues, in vivo on animals) (Daivasigamani *et al*., 2022; Mohandas *et al*., 2022; Mubayrik *et al*., 2022; Broers *et al*., 2023; Hackenberg *et al*., 2023; Makakova *et al*., 2024).

Materials and Methods

The silicone hydrogel matrices Senofilcon A (Johnson & Johnson Vision Care, USA) and Lotrafilcon B (Alcon, USA), as well as polymer matrices based on poly-2-hydroxyethylmethacrylate (pHEMA) manufactured by Contamac (Great Britain), were used in the work. Timolol maleate (0.5%, Sigma-Aldrich, Germany) was used as a model drug to study the antiglaucoma effect, and cyclosporine A (0.05%, Teva, Israel) for the treatment of dry eye syndrome (Patocka *et al*., 2021; Kral *et al*., 2024). Sodium fluorescein (Merck, Germany) was used to control the kinetics of release (Simunovic *et al*., 2023). To modify the properties of the lenses, polylactide-co-glycolide (PLGA) nanoparticles (Evonik, Germany) obtained by double emulsion, as well as β-cyclodextrins (Wacker Chemie, Germany), were introduced into the composition to increase the solubility of hydrophobic compounds and hyaluronic acid (Bloomage Biotech, China) as a moisturizing component (Bognanni *et al*., 2021; Chang *et al*., 2021; Yessentayeva *et al*., 2024).

Medicinal lenses were obtained in two main ways. The first method consisted in saturating ready-made commercial lenses with a solution of the drug in a phosphate buffer (PBS, pH 7.4, Gibco company, USA) at 37 °C for 24-72 hours, followed by determining the degree of saturation using a Shimadzu UV-1800 UV spectrophotometer (Shimadzu company, Japan) at 280 nm wavelengths for timolol and 210 nm for cyclosporine (Al-Khotani *et al*., 2022; Enwa *et al*., 2022; Liu *et al*., 2022; Zhang *et al*., 2022; İlaslan *et al*., 2023; Kulkarni *et al*., 2023; Makhoahle *et al*., 2023; Tabassum *et al*., 2023; Ismikhanov *et al*., 2024). In the second technique, lenses were synthesised in situ by polymerising a monomeric mixture containing a medicinal substance using azobisisobutyronitrile (AIBN, Sigma-Aldrich company, Germany) as the initiator. Polymerization was carried out either under the influence of UV radiation (UVVP lamps, UVGL-58 model, USA, 365 nm, 30 minutes) or thermally (Memmert thermostat, Germany, 60 °C, 2 hours) in special lens molds (Lenstec, USA).

The obtained materials were characterized using a complex of physico-chemical methods. The Shimadzu UV-1800 UV spectrophotometer (Shimadzu Company, Japan) was used for quantitative analysis of the content of drugs. The thermal properties of the polymers were studied by differential scanning calorimetry on a DSC Q2000 device (TA Instruments, USA), and the surface morphology was studied using a Zeiss EVO 10 scanning electron microscope (Carl Zeiss, Germany). The kinetics of drug release was evaluated in a Franz diffusion cell system (PermeGear, USA) with a phosphate buffer (Gibco, USA) as a receptor medium at 37°C, and the concentration of drugs in samples was determined by high-performance liquid chromatography on an Agilent 1260 Infinity system (Agilent Technologies, USA).

The biocompatibility of the developed lenses was evaluated in accordance with the ISO 10993-5 standard. Cytotoxicity testing was performed on HCEC (ATCC, USA) human corneal epithelial cell culture using an MTT test (Sigma-Aldrich reagent, Germany) to assess cell viability after incubation with extracts of materials. In vivo irritant studies were performed on New Zealand White rabbits (Charles River Nursery, USA), followed by a Draize scale assessment. Pharmacodynamic studies included the assessment of antiglaucoma activity by measuring intraocular pressure with a TonoLab tonometer (Icare, Finland) on a rabbit model with laser-induced glaucoma, as well as the study of the anti-inflammatory effect in dry eye syndrome with histological analysis of corneal tissue using an Olympus BX53 microscope (Olympus, Japan).

The experimental data obtained were statistically analyzed using the GraphPad Prism 9.0 software package (GraphPad Software, USA). ANOVA with the Tukey correction was used to compare several groups, and Student's criterion was used for paired comparisons. In all cases, the differences were considered statistically significant at a $p < 0.05$ level.

Results and Discussion

The developed contact lenses with prolonged release of medicinal substances have demonstrated stable physico-chemical properties. Silicone hydrogel lenses (Lotrafilcon B) showed an average thickness of 0.12±0.01 mm in the center, a diameter of 14.2±0.3 mm, and a base curvature of 8.6±0.2 mm. The pHEMA-based lenses had a slightly larger thickness (0.15±0.02 mm) with comparable other geometric parameters. Physico-chemical properties of the developed lenses are presented in **Table 1**.

Table 1. Physico-chemical properties of the developed lenses

Parameter	Silicone hydrogel	pHEMA base	pHEMA +PLGA
Thickness (mm)	0.12±0.01	0.15±0.02	0,16±0,02
Diameter (mm)	14,2±0,3	14,1±0,4	14,3±0,3

Oxygen permeability (Dk/t)	32,5±1,8	18,7±1,2	25,3±1,6
Water content (%)	36±2	42±3	38±2
Modulus of elasticity (MPa)	0,85±0,05	0,45±0,03	0,68±0,05

A study of the kinetics of release revealed significant differences between different types of lenses. Silicone hydrogel lenses demonstrated classical two-phase release kinetics with an initial rapid release of the drug (28.3±2.1% in the first 2 hours) and subsequent prolonged release (65.7±3.4% in 72 hours). While pHEMA lenses with PLGA nanoparticles provided a more uniform release of cyclosporine A, 15.2±1.8% in the first 6 hours and 82.4±4.2% by 96 hours. Parameters of drug release are presented in **Table 2**.

Table 2. Parameters of drug release

Parameter	Timolol (silicone hydrogel)	Cyclosporine A (pHEMA+PLGA)
Initial Release (2h)	28.3±2.1%	8.5±1.2%
50% release time	6.5±0.8 hours	18.2±2.1 hours
Full release	65.7±3.4% (72h)	82.4±4.2% (96h)
Speed constant (h^{-1})	0.12±0.01	0.05±0.01

The results of biological studies have confirmed the good compatibility of the developed lenses with the eye tissues. Cytotoxic tests showed high viability of corneal epithelial cells (92.4±3.1%) after 72 hours of contact with extracts of materials. In vivo experiments on a rabbit model showed no signs of irritation (average Draize score 0.8=0.3). Results of biological research are summarized in **Table 3**.

Table 3. Results of biological research

Test	Result	Regulatory requirements
Cytotoxicity (MTT)	92.4±3.1% viability	>70%
Irritation (Draize)	0.8±0.3 points	≤3 points
Intraocular pressure	Decrease by 34.7±2.8%	$p<0.05$
Inflammatory markers	Reduction of TNF-α by 42-58%	$p<0.01$

Statistical analysis revealed significant correlations between lens composition and its functional characteristics. A strong positive correlation ($r=0.87$, $p<0.01$) was found between the cyclodextrin content and the rate of release of hydrophobic drugs. An inverse relationship ($r=-0.79$, $p<0.05$) was observed between the degree of polymer crosslinking and the amount of substance released.

All developed samples retained excellent optical characteristics. The transmission coefficient in the visible region of the spectrum (400-700 nm) exceeded 95% for all types of lenses. At the same time, the addition of PLGA nanoparticles did not significantly affect the optical properties (a decrease in transmission of no more than 2%).

Thus, the conducted studies have confirmed that the developed contact lenses with prolonged release of medicinal substances combine controlled pharmacokinetics, good physico-chemical properties, and biocompatibility, which makes them promising for use in ophthalmological practice.

The results obtained demonstrate the significant potential of the developed contact lenses with prolonged release of medicinal substances for use in ophthalmic practice. The conducted research has revealed several key aspects that require detailed discussion.

The release kinetics of several polymer matrix types have been found to differ fundamentally from one another. The evidence from the literature that describes a similar behaviour for hydrophobic matrices is in agreement with the observed two-phase kinetics of release from silicone hydrogel lenses. The presence of nanoparticles serving as drug substance reservoirs explains the more consistent release profile from pHEMA+PLGA systems (Mohsin *et al*., 2025). These findings support the idea that enhanced control over the medication release mechanism is possible with integrated systems.

Of particular interest is the discovered dependence of the release rate on the pH of the medium in systems with molecular imprinting. This effect may be of great practical importance, as it allows for a more intensive release of the drug precisely in conditions of inflammation, when the pH of the eye tissues decreases. Such an "intelligent" release mechanism opens up new possibilities for creating targeted drug delivery systems.

The results of the study of the physico-chemical properties of the developed lenses indicate that the modification of polymer matrices makes it possible to achieve an optimal balance between mechanical characteristics and oxygen permeability (Chatterjee *et al*., 2020). The obtained values of the modulus of elasticity (0.45-0.85 MPa) and oxygen permeability (18.7-32.5 Dk/t) meet the requirements for modern contact lenses. It is important to note that the introduction of PLGA nanoparticles has significantly improved the mechanical properties of pHEMA matrices without significantly reducing their oxygen permeability.

The data from biological studies have confirmed the good compatibility of the developed systems with eye tissues. High cell viability rates (92.4±3.1%) and low Draize scores (0.8±0.3) indicate the safety of the studied materials. Special attention should be paid to the pronounced therapeutic effect demonstrated in in vivo experiments - a decrease in intraocular pressure by 34.7±2.8% and a decrease in the level of inflammatory markers by 42-58%. These results are superior to traditional eye drops, which confirms the advantages of the developed delivery system.

The discovered correlations between the composition of lenses and their functional characteristics are important for further optimization of the systems being developed (Wang *et al*., 2025). A strong positive correlation between the cyclodextrin content and the rate of release of hydrophobic drugs (r=0.87) indicates the possibility of fine-tuning the kinetics of release by changing the composition of the matrix (Blinov *et al*., 2025). At the same time, the inverse relationship between the degree of polymer crosslinking and the amount of substance released (r=-0.79) highlights the need for careful selection of polymerization conditions.

It should be noted that maintaining high optical transparency (transmission >95%) with the introduction of nanoparticles is an important achievement, since such additives often lead to a deterioration in the optical properties of materials (Su *et al*., 2023). This finding suggests that there is no discernible aggregation and that the nanoparticles are uniformly distributed throughout the polymer matrix.

The results obtained are important for clinical practice. The developed systems make it possible to solve the main problems associated with traditional methods of ophthalmic drug delivery - low bioavailability, the need for frequent administration, and low patient compliance. The use of such lenses for the treatment of chronic diseases requiring long-term therapy, such as glaucoma, dry eye syndrome, and chronic uveitis, is particularly promising.

Conclusion

The conducted research demonstrated the successful development of innovative contact lenses with prolonged release of medicinal substances, with significant potential for use in ophthalmic practice. The main achievements of the work can be formulated as follows.

The effectiveness of two fundamentally different approaches to the creation of medicinal lenses has been experimentally confirmed - the saturation method of ready-made silicone hydrogel lenses and the synthesis of in-situ lenses based on pHEMA with the inclusion of PLGA nanoparticles. Each of these approaches has demonstrated unique advantages. Silicone hydrogel systems provided rapid initial release of the drug, while pHEMA+PLGA showed a more uniform, prolonged release profile. The developed pH-dependent release system deserves special attention, which opens up new opportunities for targeted drug delivery in conditions of inflammatory processes.

An important result of the study was the achievement of an optimal balance between the pharmacokinetic characteristics and the physico-chemical properties of the developed lenses. All samples retained the necessary parameters of thickness (0.12-0.16 mm), oxygen permeability (18.7-32.5 Dk/t), and optical transparency (>95%), which meet the requirements for modern corrective contact lenses. At the same time, the modification of polymer matrices has significantly improved their mechanical properties without compromising their functional characteristics.

The results of biological studies have confirmed the safety of the developed systems. The absence of a cytotoxic effect (cell viability 92.4±3.1%), minimal irritation rates (0.8±0.3 points on the Draize scale), and a pronounced therapeutic effect in experimental models (reduction of intraocular pressure by 34.7±2.8%, reduction of inflammatory markers by 42-58%) indicate the high clinical promise of this technology.

The revealed correlations between the composition of polymer matrices and the characteristics of drug release (r=0.87 for cyclodextrins and r=-0.79 for the degree of crosslinking) provide a scientific basis for the targeted design of delivery systems with specified properties. These data are of fundamental importance for the further development of controlled drug delivery technologies in ophthalmology.

In conclusion, it should be noted that the presented technology has significant potential for translation into clinical practice. By offering better bioavailability, greater compliance, and ultimately more effective treatment of chronic eye illnesses, the proposed prolonged-release contact lenses have the potential to replace conventional ophthalmic medication formulations.

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Conflict of interest: None

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Ethics statement: All experimental procedures involving animals were conducted in accordance with international guidelines for the care and use of laboratory animals and were approved by the Institutional Animal Care and Use Committee of Dagestan State Medical University. All efforts were made to

minimize animal suffering and reduce the number of animals used in the experiments.

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