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Perspective materials for drug delivery in the ophthalmic dosage form: a short review of polymers for electrospinning

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Abstract

Background: The traditional ophthalmological dosage forms have a low bioavailability, a rapid precorneal clearance and a low corneal permeability. The gelling system or system with a prolonged action (prolonged eye-drops) may be overcome by the application of fibers. An innovative dosage form was described for ophthalmology and perspective drug development. The authors also conducted an overview of the polymers investigated in the production of films or tablets for oral dosage forms. The properties of fibers revealed fundamental differences from polymers. Combining different properties of pharmaceutical formulations appears to offer a synergy in bioavailability and sustained release with very comfortable conditions of use and prolonged action. Novel formulations, such as prolonged eye-drops and gels or thinnest films for the eye, will be developed and tested in vitro studies. This enhancement stipulates for perspective pharmaceutical development. **The aim of the study:** To describe the main types of fibers for the development of a potential ophthalmological dosage form. **Materials and methods:** The review of the articles with high CiteScore rating in Scopus and Web of Science. CiteScore is a simple way of measuring the citation impact of sources. Tasks: to describe suitable polymers for development of ocular dosage forms prepared by electrospinning. **Results:** The results of the review of the most useful polymers show that in most cases all polymers are used together. A huge number of ophthalmologic pathologies call for a correct approach to each nosology in each case. **Conclusion:** The electrospinning method will stipulate for the future development of customized tools for the treatment of ophthalmic pathologies. The development of an ophthalmic insert with the possible introduction of several medicinal substances depending on the condition of each patient is promising.

Keywords: nanofibers; electrospinning; ophthalmology; polymers; electrospun formulations; ocular formulation; PVP; PEO; PVA; CDs; PDS; Chitosan; Cellulose

Introduction. Most ocular drugs when given by topical administration are rapidly cleared by the aqueous humor flowing into the anterior chamber and flushing the drug out via the trabecular meshwork, should they permeate the cornea. The drug will often therefore fail to reach reproducible therapeutic levels near the retina. Unfortunately, drugs in solution can rapidly clear within hours from the posterior cavity upon IVT injection. This reduces efficacy and frequent injections are required, which can lead to undesirable side effects and reduce patient compliance [1]. Electrospinning is one of the technics for production of different fibers for medical and pharmaceutical needs. This technic is being used to enhance the solubility substances in ophthalmology. We have conducted an overview of the polymers investigated in the production of films or tablets for oral dosage forms. Previous studies [1, 2] of electrospun formulations of acyclovir, ciprofloxacin and cyanocobalamin for ocular drug delivery demonstrate that electrospun matrices, such as those prepared in this work, have potential for use as intravitreal implants and improve the solubility of such a water-insoluble substance like acyclovir.

The **aim** of this review is to describe the main types of fibers for the development of a potential ophthalmological dosage form.

Tasks: to describe suitable polymers for the development of ocular dosage forms prepared by electrospinning.

Results and discussion. The traditional ophthalmological dosage forms have a low bioavailability, a rapid precorneal clearance, and a low corneal permeability. The gelling system or system with a prolonged action (prolonged eye-drops) may be overcome by the application of fibers.

Anatomy of the eye is demonstrated in close connection with ophthalmic delivery and bioavailability of drugs. Combining different properties of pharmaceutical formulations appears to offer a synergy in bioavailability and sustained release with very comfortable conditions of use and prolonged action. Novel formulations, such as prolonged eye-drops and gels or thinnest films for the eye, will be developed and tested in vitro studies.

Table demonstrates the most useful types of polymers in ophthalmology.

Table

The most useful types of polymers in ophthalmology

Name of polymer	Short name of polymer	Properties	Use
poly(ε-caprolactone	PCL	Biodegradable thermoplastic polymer	Films, polymer for enhancing of the the mechanical properties for engineered nanotopology of structures [3]
poly(ethylene oxide)	PEO	Relatively high molecular weight, biocompatible material that effectively improves the mechanical and biological properties of composite hydrogels	In combination with chitosan is used for high antimicrobial effect [4]
polyvinyl alcohol	PVA	Presents biocompatibility, being prepared easily and having non-toxic solvent; water-soluble synthetic polymer; biodegradable	Used for incorporate molecules of biological origin, such as collagens, hyaluron and deoxyribonucleic acid[5]

Cyclodextrins	CDs	Most versatile substances produced by nature	Gels for drug delivery
Polydioxanone	PDS	Material for tissue regeneration [6]	Biological matrix
Chitosan	Chitosan	Biodegradability, biocompatibility, it has fungicidal, antimicrobial, and antitumor activity and also has strong healing properties, as it offers an excellent environment for cell adhesion and proliferation[7]	Producing of membranes for regeneration
Cellulose	Cellulose	High molecular weight polysaccharide in nature;	Using for medical applications[8]

PCL is one of the most useful polymers in the medicine, but in ophthalmology, fibers were described in papers [1] and [9]. Both studies report on fibers with antimicrobial agents. Karataş A. et all develop ofloxacin loaded electrospun fibers for ocular drug delivery. The microbiological study of properties of this fibers shows that freely released ofloxacin from fibers inhibited the growth of the tested bacteria. This study demonstrates that electrospinning had no adverse effects on the activity of the incorporated drug in fibers. That data is interesting for future development of dosage forms with antimicrobial agents for ophthalmology.

Simões S.M. [10] describes syringeable self-assembled cyclodextrin gels for drug delivery: CDs were obtained in two systems to form inclusion complexes. Both types of complexes show stability with variety of drugs via interactions between substances and polymers. Functional groups of polymers are not involved in the other complexes. Other authors, Hu QD et all [11], describe the host-guest interactions of αCD and βCD between polymer and substances. They also report about modification of CDs with polymers due to the potential benefits rendered by cationic protection and improved capability. This modifications help to improve the controlled release by application of responsive structures.

Another benefit of using CDs for nanomedicine includes electrospun fibers of cyclodextrins and poly(cyclodextrins) [12]. They include therapeutic agents. These complexes demonstrate a slowl release that is the most suitable for a perspective ocular dosage form.

Cellulose fibers (HPMC in this studies) with polyethylene oxide PEO [13] were produced by Aydogdu A et all. A uniform structure of these fibers was achieved by increasing a polymer concentration, and their structure was semicrystalline. For next studies and combining PEO with HPMC the developments of uniform and stability fibers for ocular films may be interesting.

In the other studies of Kuang G et al, there were developed polyblend nanofibers for local cancer treatment [14]. PEO was included in the mixture of polymers as a hydrophilic polymer. This study will be used in a new concept of local chemotherapy.

Cellulose derivatives were prepared by incorporating polyaniline (PAn) fibers into polyvinyl alcohol (PVA) by Bai Y. [15]. These fibers are interesting for ophthalmological drug development because they show excellent water-, thermal-, and near-infrared (NIR) light-properties. Of course, the concentration of polymers should be changed for drug development.

Karczewski A. et al have developed an antimicrobial drug delivery system [16] with PDS fibers. Chitosan, as a more adequate stimulus to facilitate the cell, was used in these fibers. This fiber shows an antimicrobial activity against all bacteria and is cell-friendly. The experience in the use of these fibers have a potential for ophtalmology drug development.

The results of the review of the most useful polymers show that in most cases all polymers are used together. A huge number of ophthalmologic pathologies call for a correct approach to each nosology in each case. The electrospinning method will stipulate for the future development of customized tools for the treatment of ophthalmic pathologies. The development of an ophthalmic insert with the possible introduction of several medicinal substances depending on the condition of each patient is promising.

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References

1. Baskakova A, Awwad S, Jiménez JQ, et al. Electrospun formulations of acyclovir, ciprofloxacin and cyanocobalamin for ocular drug delivery. Int J Pharm. 2016 Apr 11;502(1-2):208-18. DOI: https://doi.org/10.1016/j.ijpharm.2016.02.015

2. Meireles AB, Corrêa DK, da Silveira JV, et al. Trends in polymeric electrospun fibers and their use as oral biomaterials. J Exp Biol Med (Maywood). 2018 May;243(8):665-676. DOI: https://doi.org/10.1177/1535370218770404

3. Battistella E, Varoni E, Cochis A, et al. Degradable polymers may improve dental practice. J Appl Biomater Biomech. 2011;9:223-31. DOI: https://doi.org/10.5301/JABB.2011.8867

4. Xiao Y, Gong T, Jiang Y, et al. Fabrication and characterization of a glucose-sensitive antibacterial chitosan-polyethylene oxide hydrogel. J Polymer. 2016;82:1-10. DOI: https://doi.org/10.1016/j.polymer.2015.11.016

5. Kim GM, Asran AS, Michler GH, et al. Electrospun PVA/HAp nanocomposite nanofibers: biomimetics of mineralized hard tissues at a lower level of complexity. J Bioinspir Biomim. 2008;3:046003.

6. Bottino MC, Yassen GH, Platt JA, et al. A novel three dimensional scaffold for regenerative endodontics: materials and biological characterizations. J Tissue Eng Regen Med. 2015;9:116-23. DOI: https://doi.org/10.1002/term.1712

7. Furuya DC, Costa SA, Oliveira RC, et al. Fibers obtained from alginate, chitosan and hybrid used in the development of scaffolds. J Mat Res. 2017;20:377-86. DOI: http://dx.doi.org/10.1590/1980-5373-mr-2016-0509

8. Ao C, Niu Y, Zhang X, et al. Fabrication and characterization of electrospun cellulose/nano-hydroxyapatite nanofibers for bone tissue engineering. Int J Biol Macromol. 2017;97:568-73. DOI: https://doi.org/10.1016/j.ijbiomac.2016.12.091

9. Karataş A, Algan AH, Pekel-Bayramgil N, et al. Ofloxacin Loaded Electrospun Fibers for Ocular Drug Delivery: Effect of Formulation Variables on Fiber Morphology and Drug Release. J Curr Drug Deliv. 2016;13(3):433-43.

10. Simões SM, Veiga F, Torres-Labandeira JJ, et al. Syringeable self-assembled cyclodextrin gels for drug delivery. J Curr Top Med Chem. 2014;14(4):494-509.

11. Hu QD, Tang GP, Chu PK. Cyclodextrin-based host-guest supramolecular nanoparticles for delivery: from design to applications. Acc Chem Res. 2014 Jul 15;47(7):2017-25. DOI: 10.1021/ar500055s

12. Costoya A, Concheiro A, Alvarez-Lorenzo C. Electrospun Fibers of Cyclodextrins and Poly(cyclodextrins). Molecules. 2017 Feb 3;22(2).

13. Aydogdu A, Sumnu G, Sahin S. A novel electrospun hydroxypropyl methylcellulose/polyethylene oxide blend nanofibers: Morphology and physicochemical properties. J Carbohydr Polym. 2018 Feb 1;181:234-246. DOI: https://doi.org/10.1016/j.carbpol.2017.10.071

14. Kuang G, Zhang Z, Liu S, et al. Biomater Sci. Biphasic drug release from electrospun polyblend nanofibers for optimized local cancer treatment. 2018 Jan 30;6(2):324-331. DOI: 10.1039/C7BM01018D

15. Bai Y, Zhang J, Chen X. A Thermal-, Water-, and Near-Infrared Light-Induced Shape Memory Composite Based on Polyvinyl Alcohol and Polyaniline Fibers ACS Appl Mater Interfaces. 2018 Apr 25;10(16):14017-14025. DOI: 10.1021/acsami.8b01425

16. Karczewski A, Feitosa SA, Hamer EI, et al. Clindamycin-modified Triple Antibiotic Nanofibers: A Stain-free Antimicrobial Intracanal Drug Delivery System. J Endod. 2018 Jan;44(1):155-162. DOI: https://doi.org/10.1016/j.joen.2017.08.024

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