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P-60

Therapeutic Relevance of Drug-loaded Electrospun Nanofiber-based Ophthalmic Inserts

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1. Introduction

The unique anatomy and physiology of the eye, makes the targeting of ocular diseases a very difficult and challenging process. Conventional administration of eye drops and ointments has limited bioavailability, while systemic administration is associated with severe toxicity. Direct administration of the drug to the site of action can be done invasively based on intraocular routes. There are many alternative approaches have been investigated to increase the bioavailability by increasing the permeation and residence time. Of which nanofiber-based ophthalmic inserts as novel drug delivery systems have received a potential interest. Nanofiber-based formulations are produced mainly by electrospinning process with unique properties making them a suitable candidate for delivery of various drugs and pharmaceuticals along with biomedical applications such as tissue reconstitution. Therefore, nanofiber-based ocular inserts are considered as a promising, non-invasive method for anterior and posterior ocular diseases targeting.

2. Methods

A systematic search was performed in PubMed, Ovid Medline, Web of Science, ScienceDirect, Scopus, Reaxys, Google Scholar, and Google Patents/ Espacenet taking "drug-loaded", "nanofibers", and "ophthalmic inserts" and their equivalent terms as keywords. The search was limited to original and peer-reviewed studies published in 2011–2021 in English language.

3. Results

Only 13 out of 795 articles and 15 out of 197 patents were included in this study. According to the extracted relevant information, the results revealed no or lower eye toxicity; the formulations were compatible with the eye and the particle size showed no signs of ocular irritation.

Studies focus was mainly on increased residence time and bioavailability. It is demonstrated that the drug release can be modulated from a few minutes up to a month based on the polymer base used and the properties of nanofibers, and the majority of studies showed controlled drug release.

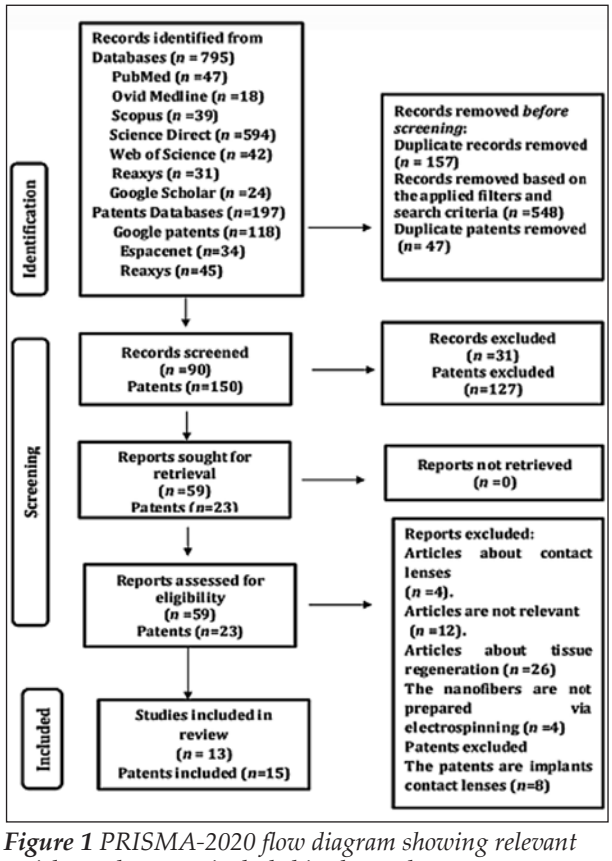

Figure 1 *PRISMA-2020 flow diagram showing relevant articles and patents included in the study*

Table 1 *Nanofibrous ophthalmic inserts included in the study*

No	Loaded Drug/Concentration	Indication	Diameter of nanofibers	Drug Release
1	Besiloxacin HCl (40 μg/1 cm^2)	Bacterial keratitis	Less than 1057 nm	for 7 days
2	Moxifloxacin HCl (1% *w/v*) pirfenidone (2% *w/v*)	Corneal abrasion	630 ± 300 nm	over 24 h
3	Dexamethasone (1, 5, and 10% *w/w*)	Anti-inflammatory	Within nanometer size	36 h for 10%
4	Gentamicin (10% *w/w*) and methylprednisolone (6% *w/w*)	Antibacterial/Anti-inflammatory	70–650 nm	For 9-day period.
5	Ferulic acid (FA, 5.7 % *w/w*) and ε -polylysine (ε-PL) (17.6% *w/w*)	antioxidant and antimicrobial	Approx. 100 nm to 1 mm	ε -PL within 30 min and FA- within 20 min
6	Triamcinolone acetonide (TA) (2 mg/cm^2)	Anti-inflammatory	1–3 μm	up to 30 days
7	Azithromycin (10% *w/w*)	Antimicrobial	119.01–171.61 nm	6-8 days
8	Fluocinolone acetonide (1–5% *w/w*)	Anti-inflammatory	350–400 nm	up to 11 days
9	Azithromycin (10mg/1cm^2)	Antibacterial	200–550 nm	over 10 days
10	Timolol maleate (0.5% *w/v*), and dorzolamide hydrochloride (0.2% *w/v*)	Glaucoma treament	200–400 nm	up to 24 h
11	Ofloxacin (OFX) (0.6% *w/v*)	Antimicrobial	123 –159 nm	up to 95 h
12	Triamcinolone acetonide (1% *w/v*)	Anti-inflammatory	1201–72 nm	up to 4 days

4. Conclusions

Eye problems are increasing daily; therefore, a smart approach is needed in order to overcome the barriers present in the eye which interfere with drug delivery particularly when using conventional eye formulations. Different unconventional approaches are available, but every approach comes with some limitations. Nanofibers have gained attention recently, since they have superior advantages compared to other available systems; they are less irritating to the eye, they can be used to provide sustained release, and successful posterior eye targeting. Ocular inserts provide increased bioavailability through the prolonged residence time of the drug on the conjunctival surface; they can also be formulated using different preservative-free polymeric materials. A synergistic effect could be obtained by formulating ocular inserts with nanofibrous architecture. Many published studies confirm the possibility of using such systems as an alternative to conventional topical formulations with better results.

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