Introduction

The most dramatic complication of intraocular lenses (IOLs) implantation is endophthalmitis, an infection caused by bacteria that may occur in the post-surgical period [1]. It may cause severe inflammation, with risk of corneal opacification and even eye loss. The use of drug-loaded IOLs to prevent this problem has deserved special attention by the scientific community.

For their development, it is essential to ensure that specific microbiological safety requirements are satisfied. Although well-established terminal sterilization methods are available, concerns have raised regarding the undesirable effects that these techniques may have on the hydrogels. Another important issue is the effect of sterilization on the activity of the loaded drugs.

The main objective of this work is to contribute for the clarification of the effects of two different methods of sterilization, steam autoclaving and gamma irradiation, on several ophthalmic drugs and on a polymeric material currently used for the production of intraocular lenses (hydrophilic acrylate with 26% water uptake).

Experimental

Sterilization conditions

<table>
<thead>
<tr>
<th>Sterilization methods</th>
<th>Steam Pressure</th>
<th>Gamma radiation</th>
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</thead>
<tbody>
<tr>
<td>IOL MATERIAL:</td>
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<tr>
<td>Powder</td>
<td></td>
<td>kGy</td>
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<tr>
<td>Liquid</td>
<td></td>
<td>gjm</td>
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<td>DRUGS:</td>
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<tr>
<td>Moxifloxacin</td>
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<td>Ketorolac</td>
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<tr>
<td>Diclofenac</td>
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<td>Tetracycline</td>
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</table>

Material characterization

First step

- Effect of sterilization on drug
- Drug degradation
- Drug activity (antimicrobial and hydrophilic acrylate copolymer)

Second step

- Effect of sterilization on IOLs
- Swelling (30°C: transmittance, change in refractive index, opacity and bubble formation)

Third step

- Effect of sterilization on the drug release profile

Results

![Graph showing relative concentration of drugs before and after sterilization](image)

- The drugs sterilized with steam did not suffer degradation.
- The γ radiation led to different results depending on the form of presentation of the drugs:
  - powders were not degraded at any dose;
  - drugs in saline solutions suffered some degradation depending on the drug and radiation dose.
- Solutions with and without manniol did not present significant differences, which led to conclude that manniol at 5% does not prevent the degradation of the tested drugs, as was suggested by literature [2].
- Concerning the radiation doses, in the case of the solutions, generally 15 kGy and 25 kGy degraded all drugs. So, only 5 kGy was used in further studies. For this dose, diclofenac was the most affected.
- These results were confirmed by antimicrobial assays.

Conclusion

Steam and γ-radiation at 5 kGy do not lead to significant changes of the lenses properties, namely in their swelling behaviour, transmittance and hydrophilicity. However γ-radiation at 5 kGy origins some degradation of all the tested drugs.

Thus, steam seems to be the most promising method for terminal sterilization.

Next stage of this work is to study the drug release behaviour of drug load IOLs before and after sterilization.

References


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Figure 1. Relative concentration ([drug]_before sterilization/ [drug]_after sterilization) of the ophthalmic drugs before and after sterilization, determined by HPLC.

Figure 2. Swelling capacity at 30°C before and after sterilization.

Figure 3. Transmittance (UV-Vis spectroscopy) before and after sterilization.

Figure 4. Wettability (capric bubble method) before and after sterilization.