Sterilization of ophthalmic drugs and intraocular lenses

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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

Sterilization methods		Steam Pressure (60 min, 121ºC and 1 bar)	Gamma radiation (3 doses: 5, 15 and 25 kGy)
IOL MATERIAL:	Hydrophilic acrylate with 26% water uptake	• Sample in aqueous solution in NaCl 130 mM	• Sample in aqueous solution in NaCl 130 mM
DRUGS:	Moxifloxacin	• Aqueous solution in NaCl 130 mM	• Powder • Aqueous solutions in NaCl 130 mM • Aqueous solutions in NaCl 130 mM with 5% mannitol
	Diclofenac		
	Ketorolac		

Material characterization

First step – Effect of sterilization on the drugs
- Drug degradation (HPLC)
- Drug activity (Antimicrobial tests: *Staphylococcus aureus* and *Staphylococcus epidermidis)*

Second step – Effect of sterilization on IOLs
- Swelling (36ºC)
- Transparency (UV-Vis spectroscopy)
- Wettability (captive bubble method)

Third step – Effect of sterilization on the drug release profile
- Next stage of this work

Results

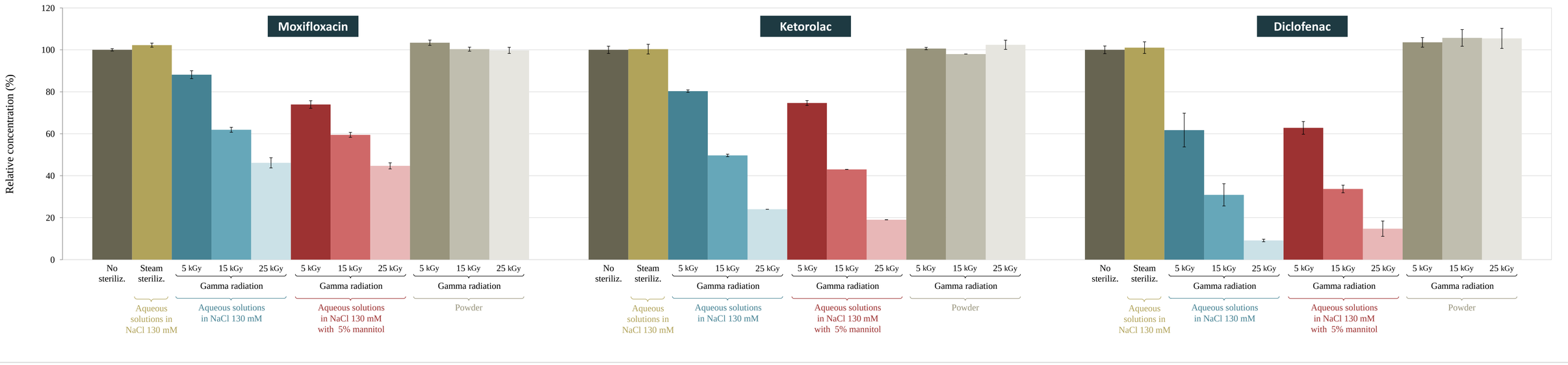

Figure 1. Relative concentration ($[drug]_{after\ sterilization}$/ $[drug]_{before\ sterilization}$x100) of the ophthalmic drugs before and after sterilization, determined by HPLC.

- 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 mannitol did not present significant differences, which led to conclude that mannitol 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.

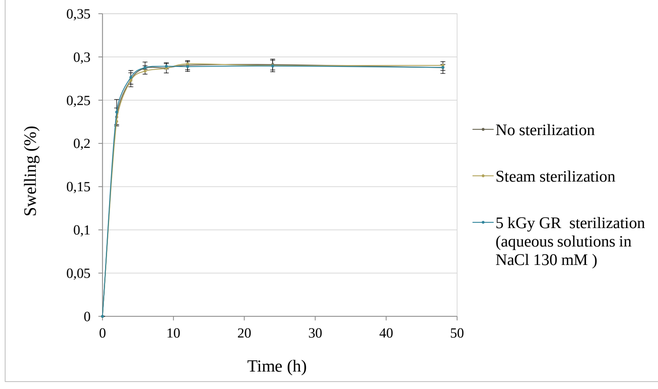

Figure 2. Swelling capacity at 36ºC before and after sterilization.

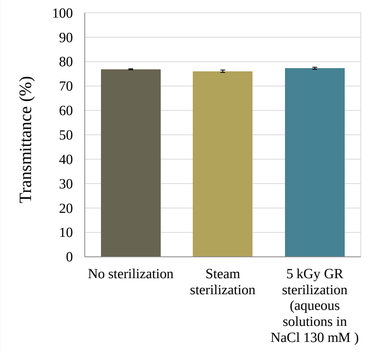

Figure 3. Transmittance (UV-Vis spectroscopy) before and after sterilization.

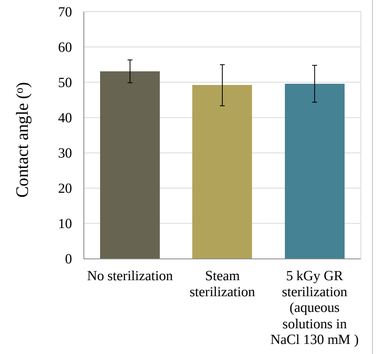

Figure 4. Wettability (captive bubble method) before and after sterilization.

Steam sterilization and γ-radiation sterilization with a dose of 5 kGy did not affect the transmittance and swelling behaviour of the lenses, but their hydrophilicity slightly increased.

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

[1] Taban M., *et al*. (2005) *Arch Ophthalmol*. **123(5):**613.

[2] Terryn H., *et al*. (2007) *Int. J. Pharm*. **343(1-2):**4.

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