



MICROBIOLOGICAL CONTAMINATION FOLLOWING THE USE OF TWO COMPOUNDED FORMULATIONS OF TACROLIMUS EYE DROPS

M. Puente-Iglesias^{1,2*}, A. Castro-Balado^{1,2}, E. Torres-Sangiao³, A. Cuartero-Martínez^{1,2}, M. González-Barcia^{1,2}, I. Zarra-Ferro^{1,2} and A. Fernández-Ferreiro^{1,2}

¹ Pharmacy Department, University Clinical Hospital of Santiago de Compostela, Spain

² FarmaCHUSLab Group, Health Research Institute of Santiago de Compostela (IDIS), Spain

³ Microbiology Department, University Clinical Hospital of Santiago de Compostela, Spain

BACKGROUND AND IMPORTANCE



Tacrolimus eye drops are sterile formulations prepared in hospital pharmacy departments. The conventional formulation (F1) is composed of Prograf® (contains ethanol as a solubiliser, which may potentially cause irritation to the ocular surface) diluted in Liquifilm® (polyvinyl alcohol 1.4% w/v, benzalkonium chloride 0.050% w/v). A novel ethanol-free formulation (F2) has been developed using hydroxypropyl-beta-cyclodextrin (HPβCD) to dilute tacrolimus raw material in Liquifilm®.



Tacrolimus 0.03%

Prograf® ampoules (ethanol)
Liquifilm®



Tacrolimus 0.015%

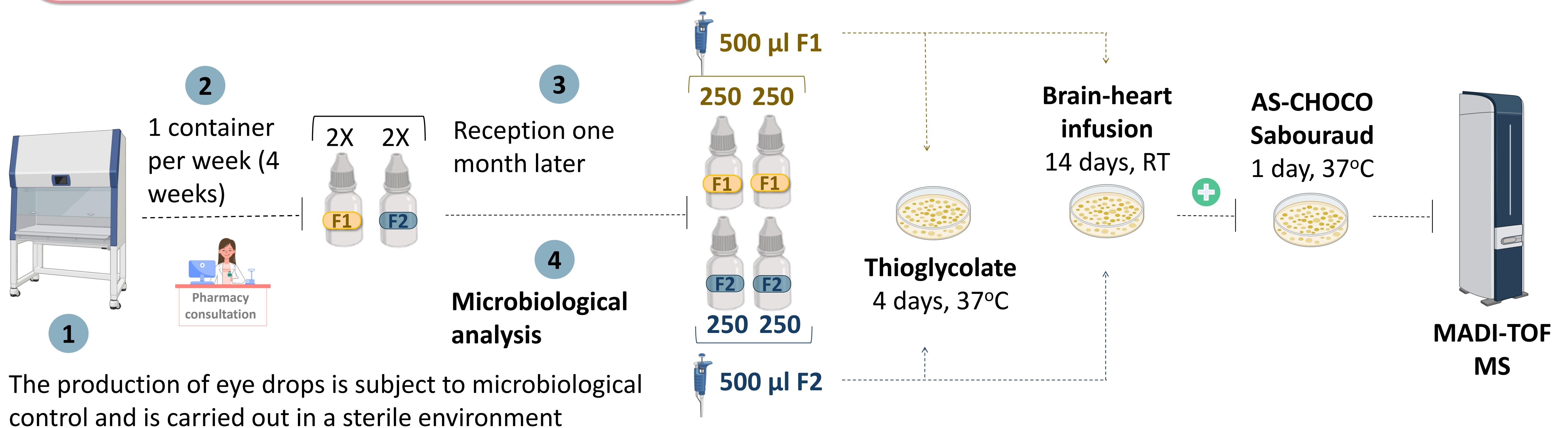
Tacrolimus raw material
HPβCD
Liquifilm®

AIM AND OBJECTIVE



To determine microbial contamination derived from the use of both formulations

MATERIAL AND METHODS



RESULTS

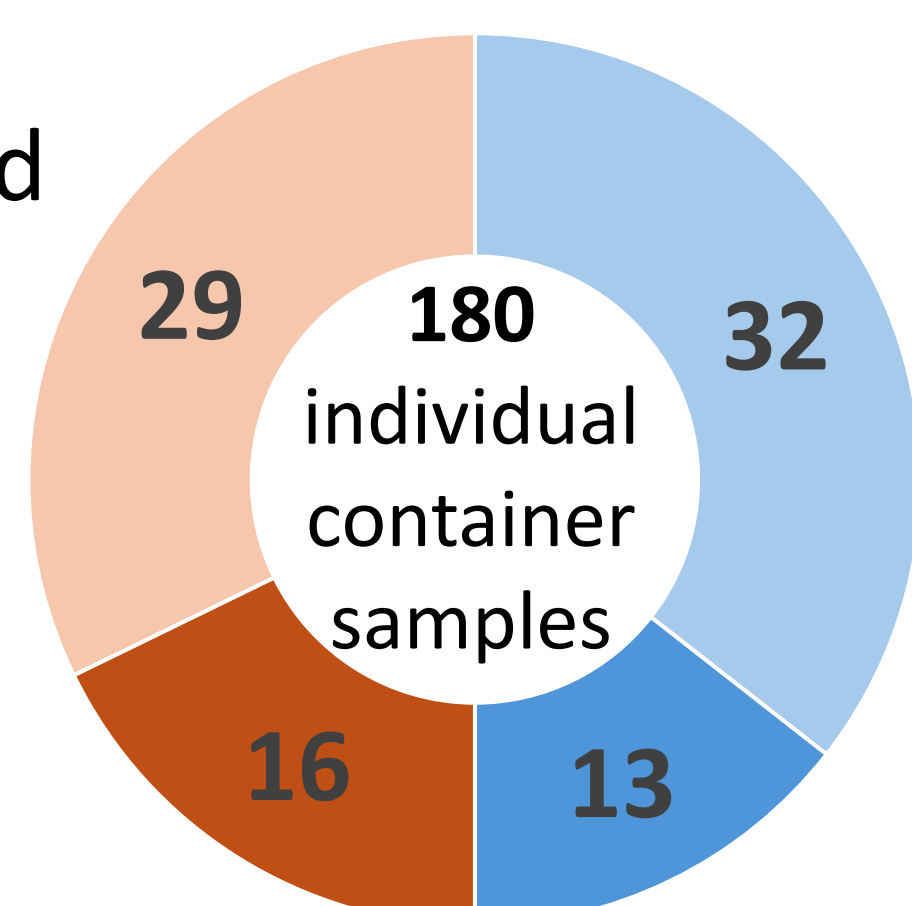


A total of 45 patients returned their used containers

- 16 + samples of F1
- 13 + samples of F2



Microbiology controls during processing were negative



- Positive F1
- Negative F1
- Negative F2
- Positive F2

Acinetobacter sp. (n=1)
Bacillus sp. (n=3)
Chryseobacterium indologenes (n=1)
Elizabethkingia miricola (n=2)
Enterococcus faecalis (n=1)
Pantoea agglomerans (n=2)
Pseudomonas sp. (n=5)
Raoultella ornithinolytica (n=1)
Serratia sp. (n=9)
Stenotrophomonas maltophilia (n=5)
Rahnella aquatilis (n=2)



None of the patients showed signs of infection at annual follow-up

CONCLUSION AND RELEVANCE



Both tacrolimus formulations were similarly contaminated due to **improper manipulation** by the patient. The incorporation of cyclodextrins is expected to mitigate ocular irritation while maintaining an equivalent risk of microbial contamination. Furthermore, patients should be instructed in adequate manipulation of eye drops