15èmes Rencontres Convergences
23èmes Journées européennes du GERPAC – 23 et 24 novembre 2020 - Congrès virtuel

Physicochemical and microbiological stability study of vancomycin 25 mg/ml eye drops stored at 2-8°C in low density polyethylene (LDPE) containers

Clement GIRARDET[a], Mai Huong LE NGUYEN[a], Lydie LETHIER[b], Samuel LIMAT[a,c], Christine FAGNONI-LEGAT[a], Yves GUILLAUME[a,b]

[a]Department of pharmacy, Besançon University Hospital, 3 Boulevard Alexandre Fleming, 25000 Besançon, France
[b]Department of analytical and physical chemistry, EA 481 "Integrative and Clinical Neuroscience", Faculty of medical sciences, Bourgogne Franche-Comté University, 25030 Besançon Cedex, France.
[c]Bourgogne Franche-Comté University, INSERM, EFS BFC, UMR 1098, 25000 Besançon, France

COM20-23133

Introduction

Vancomycin eye drops are frequently used for bacterial keratitis while this molecule is commercially unavailable in a suitable formulation for ophthalmic administration. Therefore, the hospital pharmacy was commissioned to produce preparations of fortified vancomycin eye drops available in case of urgent prescriptions. Stability of 20 days at 4 ° C and 15 days at room temperature has been demonstrated in the literature for vancomycin eye drops at 50 mg/ml. However, stability studies on this drug often lack some parameters and storage conditions of vancomycin 25 mg/ml solution.

Objectives

The aim of the study was to determine the physicochemical and microbiological stability of vancomycin 25mg/ml eye drops stored in low density polyethylene (LDPE) bottles under refrigeration conditions (2-8°C).

Material and Method

Multiple batches of vancomycin 25 mg/ml eye drops were aseptically prepared in a laminar-airflow cabinet by diluting an injectable commercialized product of vancomycin in powder with NaCl 0.9%. The solution was then injected through a 0.22 µm filter before bottling to minimize the risk of contamination. One of batches prepared was analyzed immediately and the rest were stored at 2-8°C for 31 days under two conditions: "open" and "close".

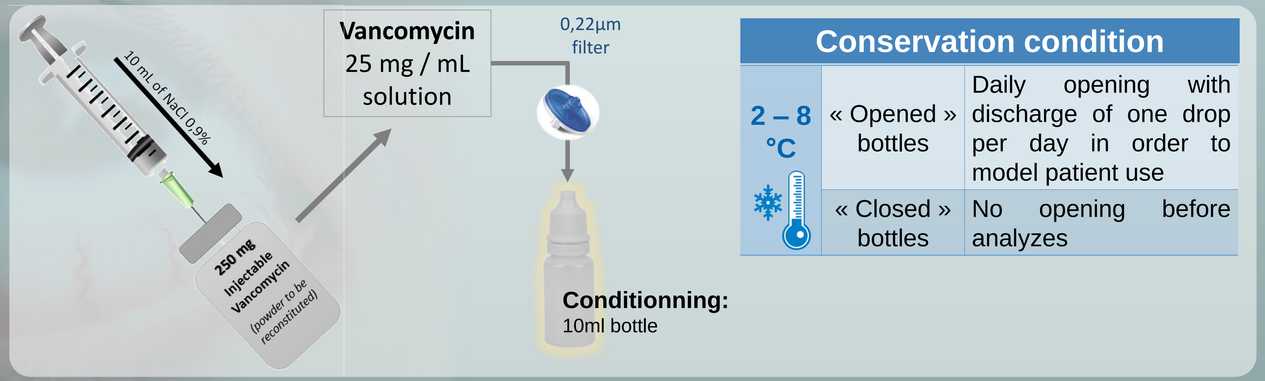
The physicochemical and microbiological characteristics tested for the stability study:

Macroscopic apperance | pH | Osmolarity | Sterility | Concentration (by HPLC*)

The test schedule :

Conservation condition	Test days
« Opened » bottles	**D0**, D3, D7, D10, D14, D17, **D21**, D24, D28 and **D31**
« Closed » bottles	**D0**, **D21** and **D31**

*High-performance liquid chromatography



Conservation condition		
2 – 8 °C	« Opened » bottles	Daily opening with discharge of one drop per day in order to model patient use
	« Closed » bottles	No opening before analyzes

Results

All samples remained clear, colorless and odorless with no precipitation or visible particles throughout the study. The pH and the osmolarity of all batches have insignificantly changed during storage in both "open" samples and "close" samples with a maximum deviation of 3% in pH (initial pH equal to 3,5) and 4% in osmolarity (initial osmolarity equal to 293 mosmol/l). All incubated samples found no sign of bacterial growth. The vancomycin concentration varied by no more than 3% of the initial concentration during the storage at 2-8°C whatever the opening state of the bottles, and no breakdown product was detected.

Table 1 – Results of physicochemical and bacteriological analyzes of Vancomycin eye drops at 25 mg / mL during the stability study

	Macroscopic apperance	pH	Osmolarity (mOsmol/L)	Sterility	Vancomycin (mg/mL)
Specifications	*Clear, colorless, no visible particles*	*3,0 – 4,0*	*293 ± 10%*	*Sterile*	*25,00 ± 10%*
D0	Yes	3,5	293	Sterile	24,95
D21 « open »	Yes	3,6	305	Sterile	25,50
D21 « close »	Yes	3,6	305	Sterile	24,16
D31 « open »	Yes	3,5	305	Sterile	25,10
D31 « close »	Yes	3,5	304	Sterile	24,79

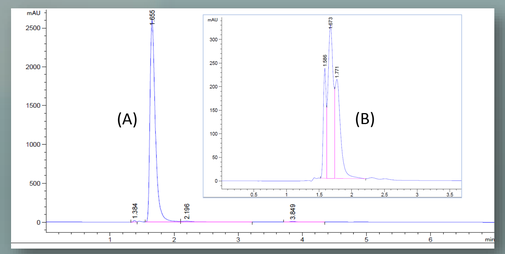


Figure 1 – Vancomycin chromatography

The typical curve (A) of the dosages of vancomycin showing the absence of degradation; in comparison with curve (B) of vancomycin eye drops stressed by temperature and pH. Two peaks of degraded products were observed in the stressed sample.

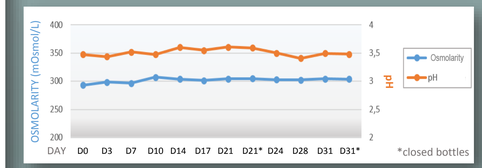


Figure 2 – Evolution of osmolarity and pH during the study

Conclusion

A range of studies has described a worse stability of vancomycin solution at room temperature[1], this is the reason why we did not design our study at this storage condition. To conclude, vancomycin 25mg/ml eye drops were stable for a month under refrigeration storage and could be used within 31 days after opening without exceeding the BBD.

[1]Curti C, Lamy E, Primas N, Fersing C, Jean C, Bertault-Peres P, et al. Stability studies of five anti-infectious eye drops under exhaustive storage conditions. Pharm. 1 déc 2017;72(12):741-6.