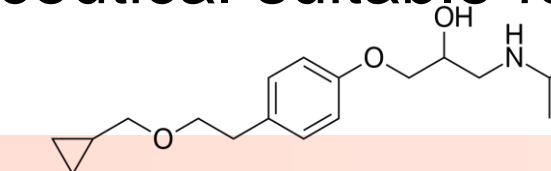


Introduction : Betaxolol (BTX) is a cardioselective β -blocker used in pediatrics, off-label, in the dynamic exploration of somatotrophic function. Due to the lack of a pharmaceutical suitable for children, we developed a hospital preparation of a 1 mg/mL BTX oral suspension (OS).

Objective : to study the physicochemical and microbiological stability of BTX oral suspensions over time, to establish their expiration dates based on their storage conditions.



Materials and methods

FORMULATION for a batch of 20 bottles of 25 mL dosed at 1mg/mL

- 25 Kerlone® 20 mg tablets from the Cheplapharm laboratory (peeled off)
- 500 mL SyrSpend® SF PH4 Liquid Unflavored from the Fagron laboratory

ÉTUDE DE STABILITÉ on 3 independent batches of 20 bottles, 3 storage conditions:

- 4-8°C sealed bottles (T_0 , T_7 , T_{15} , T_{30} , T_{45} , T_{60} et T_{90})
 - 4-8°C opened bottles (T_0 , T_7 , T_{15} , T_{30})
 - 20-25°C sealed bottles (T_0 , T_7 , T_{15})
- Analysis of various parameters over time and comparison with the reference value measured at T_0

MICROBIOLOGICAL PARAMETERS

- Aerobic microbial enumeration (TAMC) + yeast and molds (TYMC)** (Eur. Ph. 2.6.12)
- Antimicrobial preservation test** (Eur. Ph. 5.1.3) tested with 4 microbial strains (*Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Candida albicans* et *Aspergillus brasiliensis*)

Stability criteria :

- TAMC < 200 UFC/mL and TYMC < 20 UFC/mL (Eur. Ph. 2.6.12)
- Intentionally contaminated bottles for antimicrobial preservation test: 3-log reduction for TAMC and 1-log reduction for TYMC (Eur. Ph. 5.1.3)

PHYSICOCHEMICAL PARAMETERS

- Active ingredient content + monitoring of degradation products** (Eur. Ph. 2.2.29)
- pH** (Eur. Ph. 2.2.3)
- Viscosity** (Eur. Ph. 2.2.)

Stability criteria :

- Parameter variation < 10% from the reference value measured at T_0 (USP)
- Increase of any impurity < 0,2% (USP)

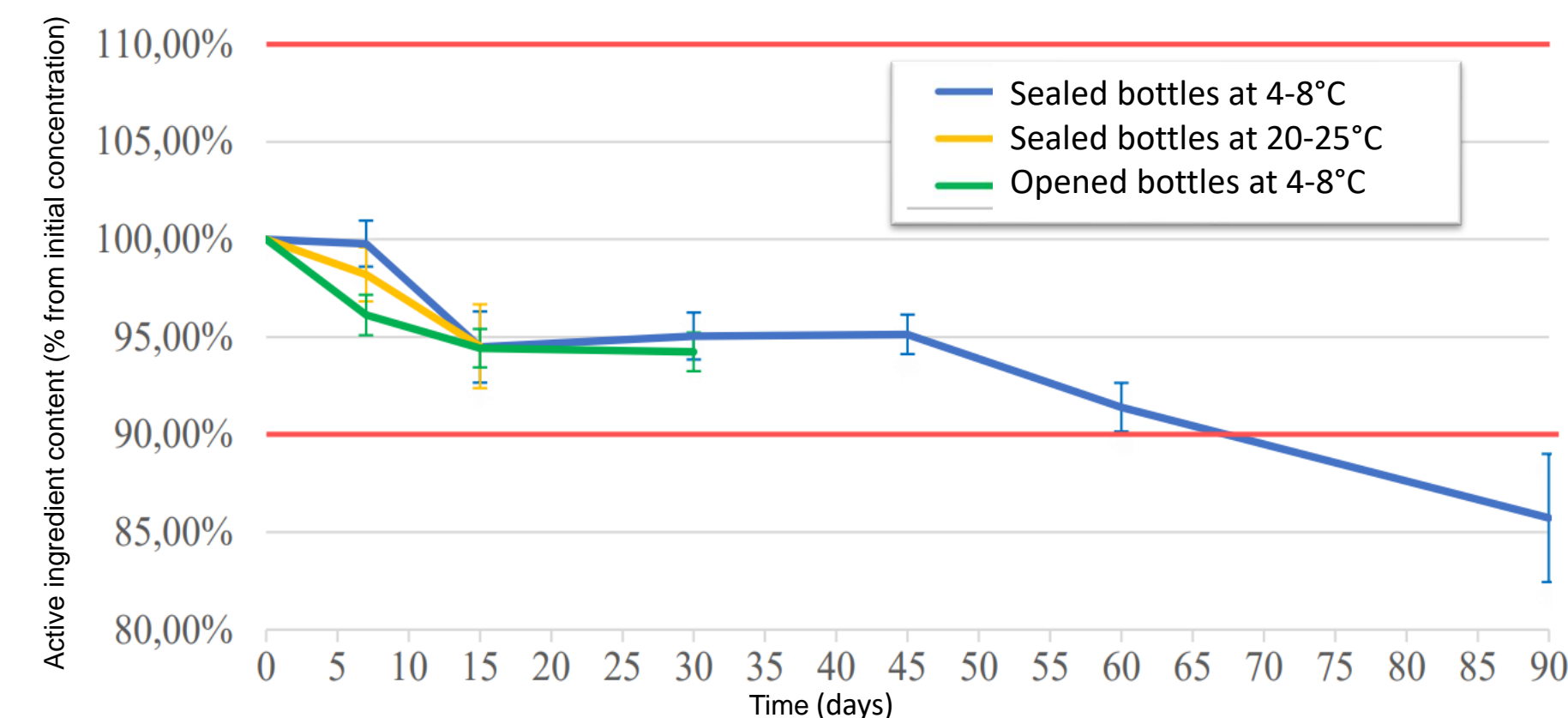
Results

MICROBIOLOGICAL STABILITY

- Microbiological enumeration** ✓ Complies with Eur. Ph. over time in the 3 storage conditions
- Antimicrobial preservation** ✓ Complies at all sampling times (T_0 , T_{30} , T_{60} and T_{90}) for each of the strains tested, in the 3 storage conditions

PHYSICOCHEMICAL STABILITY

- Viscosity** ✓ Stable (424 – 546 Cp) over time in the 3 storage conditions
- pH** ✓ Stable (4,02 – 4,92) over time in the 3 storage conditions
- Content** ✓ Until T_{60} all deviations are < 10%
✗ At T_{90} for storage at 4-8°C sealed bottles, the deviation is > 10%
- Degradation products** ✓ Formation of a degradation product remaining < 0,2% (identified during forced oxidative degradation, probably due to dissolved oxygen present in the OS)



Expression of betaxolol suspensions content in percent deviation from initial concentration with representation of the 95% confidence interval

Non-compliant on the 90th day, the betaxolol content of OS was the study's limiting factor.

The solution is stable:

- 60 days** for sealed bottles stored at 4-8°C.
- 30 days** after opening for bottles stored at 4-8°C
- 15 days** for sealed bottles stored at 20-25°C

Conclusion : BTX oral suspensions made with Syrspond® SF PH4 liquid are stable at **4-8°C for 60 days when sealed and 30 days after opening**.

We have also shown that the **sealed** preparations are stable for **14 days at room temperature**, which is an important information in case of a cold chain break.