

Could we package atropine eye drops 0.1 and 0.5 mg/mL in Novelia® bottles ?

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Introduction

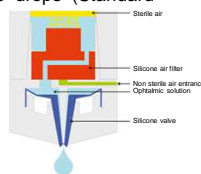
Our production unit aims to replace the current packaging of 0.1 and 0.5 mg/mL atropine eye drops (Standard multidose bottles in Low Density Polyethylene-LDPE) with Novelia® bottles (Nemera, France).



Novelia® is a multidose system in LDPE fitted with a tip including a silicone valve. This valve allows to preserve solution sterility for up to 30 days after opening.



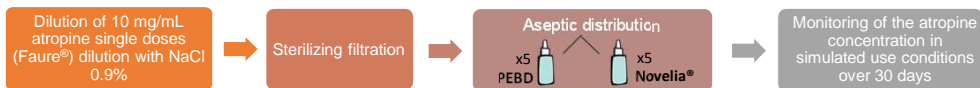
The objective is to determine whether Novelia® bottles are suitable for packaging atropine eye drops by assessing container-content interactions and validating sterility 30 days after opening in simulated use conditions.



Material & Method

To carry out the container-content interaction study, we compare the evolution of the atropine concentration of the drops extracted from the Novelia® bottles to those of the LDPE bottles according to Y. Le Basle and al. method¹.

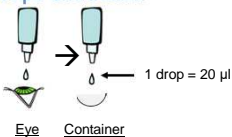
1. Preparation process of atropine eye drops



2. Initial concentration (Ci) measured at D0

3. Monitoring of atropine concentration by HPLC

a. Drops extraction



b. Concentration assay

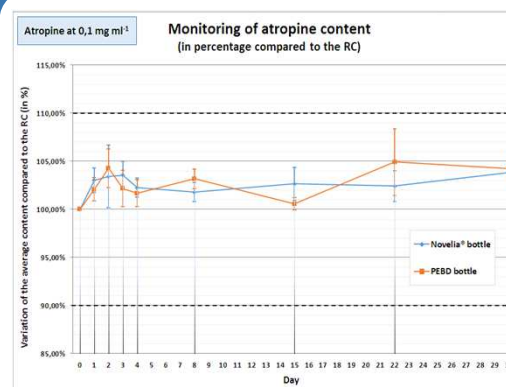


The dosage of atropine eye drops is one drop per day per eye. The administration is simulated by extracting 2 drops or 40 µl per day. These drops are then measured or eliminated according to the schedule defined in 3b.

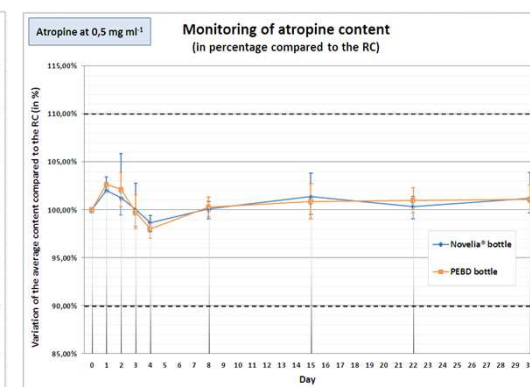
Reversed Phase UV HPLC	
Stationary phase : Hypersil BDS C18	Linearity [20 - 100 µg/mL] Y = 0,3768 X + 0,0065 R ² = 0,99955
Mobile phase : KH ₂ PO ₄ / C ₂ H ₅ N (80:20, v / v)	Average accuracy 99,72% IC [98,76% ; 100,68%]
Detection wavelength : 250 nm	Repeatability : CV < 0,5%
Flow rate : 0,85 ml.min ⁻¹	Reproducibility : CV < 3,17%
Temperature : 25 °C	Limit of detection 1,709 µg/mL
Pressure : 250 bar	

4. Sterility test by BactAlert® is performed on residual solution of Novelia® bottles on D30

Results



Ci 0,1 mg.mL⁻¹ = 97,06 µg/mL



Ci 0,5 mg.mL⁻¹ = 488,38 µg/mL

		Maximal variation of atropine concentration compared to Ci	Residual concentration (D30) Mean ± SD	
Atropine 0,1 mg/mL	Novelia® bottle	3,25 %	98,68 ± 1,71 µg/mL (101,67 ± 1,73%)	No difference between Novelia® bottles and PEBD bottles (p-value 0,1mg/mL = 0,74)
	PEBD bottle	3,47 %	99,69 ± 0,49 µg/mL (102,71 ± 0,49%)	
Atropine 0,5 mg/mL	Novelia® bottle	4,63 %	492,01 ± 22,78 µg/mL (100,74 ± 4,63%)	No difference between Novelia® bottles and PEBD bottles (p-value 0,5mg/mL = 0,64)
	PEBD bottle	1,86 %	488,21 ± 5,63 µg/mL (99,97 ± 1,15%)	

All of the BactAlert® performed on the residual solution of Novelia® bottles on D30 were negative

Conclusion

There is no interaction between atropine and the different materials of Novelia® device. The sterility of eye drops packaged in Novelia® bottles is maintained for up to 30 days after opening in simulated use conditions. Novelia® bottles are suitable for packaging 0.1 and 0.5 mg/mL atropine eye drops.

Reference

1. Yoan Le Basle et al. A sorption study between ophthalmics drugs and multi dose eyedroppers in simulated use conditions. Pharmaceutical Technology in Hospital Pharmacy. 2017