

# Stability of cyclosporine eye drops.

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Some hospital pharmacies prepare cyclosporine 0.1, 1 and 2% eye drops for the treatment of ophthalmologic inflammatory pathologies. The stability of cyclosporine eye-drop is not widely known. We have studied this stability 3 months in the refrigerator followed by one week after opening and adaptation of a dropper.

## Main Outcome Measures

For each concentration → 3 series of 25 eye drops

Physical chemical study

pH  
Osmolality  
Particle evaluation  
Chromatographic analysis

Microbiological study on R2A media

Daytime of control: 0-1-2-3-7-10-14-21-30-60-90

Preparation: evaporation of the ethanol contained in Sandimmun® (26 in 28 %) with a nitrogen flow (0.2 bar, 10 h)  
+ dilution in artificial tears (Dulcilarmes®)

Study with the dropper (some put in slept position to estimate interaction between cyclosporine and PVC of the dropper)

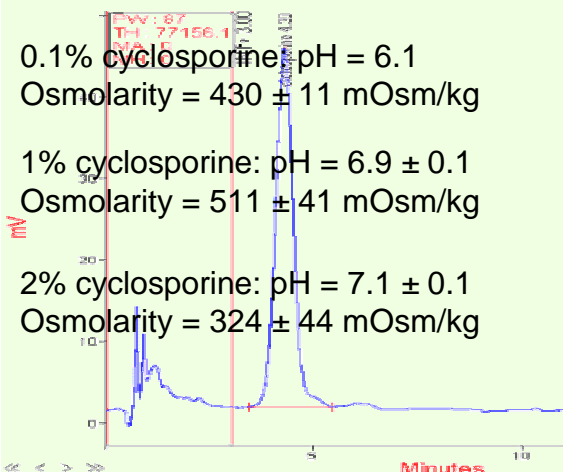
## Results

### Physical chemical study

0.1% cyclosporine pH = 6.1  
Osmolality = 430 ± 11 mOsm/kg

1% cyclosporine: pH = 6.9 ± 0.1  
Osmolality = 511 ± 41 mOsm/kg

2% cyclosporine: pH = 7.1 ± 0.1  
Osmolality = 324 ± 44 mOsm/kg



	0,1% Cyclosporine		1% Cyclosporine		2% Cyclosporine	
	C (mg/ml)	Variation from D0	C (mg/ml)	Variation from D0	C (mg/ml)	Variation from D0
<b>D0</b>	1,015		10,438		20,076	
<b>D1</b>	0,979	-4%	10,247	-2%	19,978	0%
<b>D2</b>	0,972	-4%	10,783	3%	19,457	-3%
<b>D3</b>	0,982	-3%	10,248	-2%	20,191	1%
<b>D7</b>	0,964	1%	10,144	-3%	20,760	3%
<b>D10</b>	1,036	2%	10,800	3%	19,473	-3%
<b>D14</b>	1,067	5%	10,127	-3%	19,730	-2%
<b>D21</b>	1,069	5%	10,590	1%	20,732	3%
<b>D30</b>	1,036	2%	10,663	2%	20,133	0%
<b>D60</b>	1,059	4%	10,823	4%	20,456	2%
<b>D90</b>	1,062	5%	10,933	5%	20,923	4%

Concentration of cyclosporine varied by no more than 5% of the initial concentration and no breakdown product was evidenced

Study with the dropper: ex with 1% cyclosporine

	eye drops in up position		eye drops in slept position	
	C (mg/ml)	Variation from first day	C (mg/ml)	Variation from first day
<b>D0</b>	10,69 ± 0,40		10,52 ± 0,27	
<b>D1</b>	10,45 ± 0,50	-2%	10,19 ± 0,70	-3%
<b>D2</b>	10,75 ± 0,43	1%	10,55 ± 0,66	0%
<b>D3</b>	10,37 ± 0,18	-3%	10,66 ± 0,41	1%
<b>D7</b>	10,64 ± 0,44	0%	10,51 ± 0,34	0%

No significant interaction between cyclosporine and PVC of the droppers

### Microbiological study

No contamination after 3 months of storage in the refrigerator and one week after opening and fitting the dropper

## CONCLUSION

Cyclosporine 0.1, 1 and 2 % eye drops can be kept during 3 months in the refrigerator. After their opening and adaptation of the dropper, they can be maintained one week in the refrigerator.