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Introduction

The treatment of endophthalmitis is based on eye drops instillations of fortified antibiotics and/or intraocular injections of ceftazidime and vancomycin. Hospital pharmacies have to make these ophthalmic preparations to mitigate the lack of patent medicines and store them to manage urgent requests. Numerous studies were carried out to determine the stability of these preparations.

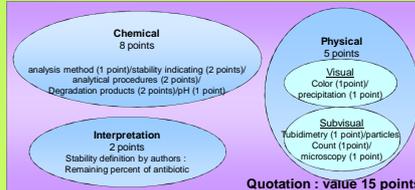
Objective



This work aims to analyze studies concerning the stability of eye drops and syringes for intraocular injection of ceftazidime and vancomycin.

Material and Method

Researches were based on references such as *Trissel's stability of compounded formulations*, *Handbook on injectable drugs*, or databases like Scopus. Keys words for research were : "stability, antibiotic, fortified antibiotic, intracameral, ceftazidime, vancomycin". Various criteria were listed depending on the study: the concentration of the solution, the solvent, the conditions of storage and the stability data. The studies were classified according to a [quotation](#). The highest value possible for the quotation is 15 points.



Results



Fortified vancomycin eye-drops

Concentration (mg/mL)	Dilution solvent	Container	Condition of storage	Stability	Quotation	References
25	5% G	G	-20°C	90 days	13	Int J Pharm, 2002;234:205-212
10	0.9% NaCl	G	-20°C	90 days	11	Hoppharm Vitel 2011
25	0.9% NaCl	G	-20°C	30 days	11	Cornea,2010;29:8 07-11
50	5% G	G	-20°C	75 days	11	Cornea,2010;29:8 07-11
50	0.9% NaCl	G	+4°C	28 days		
50	0.9% NaCl	G	+4°C	15 days	11	Personnal study not published
50	0.9% NaCl	G	+4°C	21 days	10	J Pharm Clin, 1999;18:183-189
50	0.9% NaCl	G	+25°C	15 days		
50	0.9% NaCl	G	+4°C	30 days	9	J Pharm Clin,1999;18:48-52
31	WFI or artificial tears	G	-10°C	45 days	8	Am J Health Syst Pharm, 1998;55:1386-8
5	5% G or 0.9% NaCl + buffer	G	+4°C	10 days	6	Am J Hosp Pharm, 1986;43:1729-1731
5	5% G or 0.9% NaCl + buffer	G	+24°C	63 days	6	Am J Hosp Pharm, 1986;43:1729-1731
5	WFI + buffer	G	+4°C	7 days	6	Yakugaku Zasshi, 2001;121:433-439
50	0.9% NaCl	G	+4°C	4 days	6	J Pharm Clin,1999;18:1,65-66
50	0.9% NaCl	G	-20°C	30 days	5	Pharm Hosp Fr, 2003;134:37-9
Vancomycin activity only						
50	5% G	G	+4°C	31 days	1	Kaohsiung J Med Sci, 1999;15:80-6
31	0.9% NaCl	G	-18°C	31 days		
31	0.9% NaCl	G	+4°C	28 days	2	Aust N Z J Ophth, 1999;27:426-430
50	BSS	G	+25°C	7 days	4	Acta Ophth, 2009;87:555-8
50	Artificial tears	G	+4°C	extemporaneous	2	Am J Health Syst Pharm, 1998; 55:463-6

Fortified ceftazidime eye-drops

Concentration (mg/mL)	Dilution solvent	Container	Condition of storage	Stability	Quotation	References
20	0.9 % NaCl	G	+4°C	10 days	11	Eur Hosp Pharm, 2003;6:17-23
50	citratebuffer + curator	G	+25°C	2 days		
50	0.9 % NaCl	G	+4°C	12 days	11	Acta Pol Pharm, 2011;68:99-107
50	0.9 % NaCl	G	+20°C	2 days		
50	0.9 % NaCl	G	-20°C	75 days	11	Cornea,2010;29:80 7-11
50	artificial tears	G	+4°C	7 days	9	J Pharm Clin Ther, 1999;24:299-302
50	0.9 % NaCl	G	+25°C	1 day		
20	0.9 % NaCl	G	+4°C	21 days	9	J Pharm Clin, 1999;18:48-52
50	0.9 % NaCl	G	+4°C	4 days	6	J Pharm Clin, 1999;18:1,65-66
-	WFI	G	+4°C	7 days	6	J Pharm Biomed Anal;1999;20:521-30
30-60	WFI	G	+4°C	10 days	4	Am J Hosp Pharm, 1992;49:2761-4
50	0.9 % NaCl	G	-20°C	30 days	NQ	Pharm Hosp Fr, 2003;134:37-9
Ceftazidime activity only						
10	WFI + buffer	G	+4°C	30 days	4	Acta Pol Pharm,2006;63:507-13
50	BSS	G	+20°C	14 days		
50	BSS	G	+4°C	7 days	4	Acta Ophth, 2009;87:555-8
50	BSS	G	+20°C	3 days		



Solutions are stored away from light to limit degradation of the antibiotic.
Freezing solutions used within 48 hours if preserved in the fridge.
Defrosting can be made at room temperature or in microwave for eye drops solutions.



Ceftazidime injectable solutions

Concentration (mg/mL)	Dilution solvent	Container	Condition of storage	Stability	Quotation	References
20	0.9% NaCl	PP	4°C	10 days	11	Eur Hosp Pharm, 2003;6:17-23
22,5	BSS	PP	-18°C	180 days	10	Poster HUG EAHP 2007 http://pharmaco.hug.ch/ehp/2007/
100	WFI	PP	-20°C	90 days	9	Am J Hosp Pharm, 1992;49:2954-6
40	5% G or 0.9% NaCl	PVC	+4°C	10 days		
40	5% G or 0.9% NaCl	PVC	+4°C	7 days	8	Can J Hosp Pharm, 1988;2:65,71
40	5% G or 0.9% NaCl	PVC	-10°C	90 days	6	J ClinPharmTher, 1988;13:199-205
60	WFI	PVC	+4°C	21 days		
60	WFI	PVC	-20°C	14 days	6	Am J Health-Syst Pharm, 1996;53:1302-5
30-60	WFI	PVC	+4°C	10 days	4	Am J Hosp Pharm, 1992;49:2761-4
30-60	WFI	PVC	-20°C	30 days		

0.9% NaCl : 0.9% sodium chloride_ 5% G : 5% glucose _ WFI : water for injections _ BSS : balanced salt solution
PP : polypropylene_PVC : polyvinyl chloride_PE : polyethylene_G : glass_EVA : ethylene vinyl acetate

Vancomycin injectable solutions

Concentration (mg/mL)	Dilution solvent	Container	Condition of storage	Stability	Quotation	References
10	5% G or 0.9% NaCl	PVC	+4°C	14 days	12	Am J Health Syst Pharm, 1998;52:2560-4
10	0.9% NaCl	EVA	+25°C	7 days	12	Hosp Pharm, 2001;36:1170-1173
10	0.9% NaCl	PP	+4°C	30 days		
10	0.9% NaCl	PP	+4°C	99 days	11	Personnal study not published
10	BSS	PP	-18°C	180 days	10	Poster HUG EAHP 2007 http://pharmaco.hug.ch/ehp/2007/
10	0.9% NaCl or 5% G or WFI	PP	+4°C	84 days	4	J Clin Pharm Ther, 1994;20:319-325
50	5% G	PP	+25°C	29 days		
50	5% G	PP	+4°C	1 day	3	Am J Hosp Pharm, 1987;44:802-804

Discussion

Arsene M et al. (J.Pharm.Clin,2002; 27:205-209) state that ceftazidime stability at 40 mg/mL at 20°C is **better in the glass container than PP container**, and this stability is better in **PP container than PVC container**. We base one's argument on that broaden researches on stability ceftazidime and vancomycin solutions in other containers. Solutions in **PE container** seem to have the same stability as PVC container.

Kwok AK et al. (Invest Ophthalmol Vis Sci, 2002;43:1182-8) demonstrate that **0.9% NaCl is preferred to BSS** as a dilution solvent for intravitreal injection, because precipitation in vitreous at body temperature occurs less and only free antibiotic molecules are efficient.

Antibiotic activity is preserved one month in the fridge and seems preserved longer in the freezer even if no study has proven that.

Conclusion

Freezing enables a **long-term storage** up to **4 months** of the standardized hospital preparations, which makes it possible to have an important stock and as a result to come up to the problem of urgent care. Thanks to this review the pharmacists can choose the best option, in collaboration with the medical teams (in particular for the choice of the solvent) and then optimize the therapeutic urgency.

Acknowledgements

Thanks to vichita OK who helped me to translate, Thanks to Dr. Jean Vigneron who managed me for this work

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